**Supplementary Table 1. LDSC Estimates of Genetic Correlations**

| | Insomnia_complaints | Insomnia_symptoms | Sleep_duration | Total MTAG |
|---|---|---|---|---|
| Insomnia_complaints | 1.000 | 0.9717 (0.0214) | -0.4722 (0.058) | 0.3621 (0.0785) |
| Insomnia_symptoms | 0.9717 (0.0214) | 1.000 | -0.5087 (0.0555) | 0.2161 (0.0888) |
| Sleep_duration | -0.4722 (0.058) | -0.5087 (0.0555) | 1.000 | 0.5282 (0.0553) |

Standard errors are in parentheses

**Supplementary Table 2. LDSC Estimates of heritability**

| | Insomnia_complaints | Insomnia_symptoms | Sleep_duration | Total MTAG |
|---|---|---|---|---|
| Heritability (*h2*) | 0.0473 (0.0048) | 0.1324 (0.012) | 0.0575 (0.0059) | 0.0988 (0.0082) |

Standard errors are in parentheses

**Supplementary Table 3. LDSC Estimates of Intercepts**

| | Insomnia_complaints | Insomnia_symptoms | Sleep_duration | Total MTAG |
|---|---|---|---|---|
| Intercepts | 1.0028 (0.007) | 1.0021 (0.008) | 1.013 (0.0077) | 1.4869 (0.0091) |

Standard errors are in parentheses

**Supplementary Table 4. Summary of GWAS and MTAG Results**

| | N | *SNPs* | GWAS mean $\chi 2$ | MTAG mean $\chi 2$ | GWAS equiv. N |
|---|---|---|---|---|---|
| Insomnia_complaints | 113006 | 8,270,035 | 1.082 | 1.119 | 163188 |
| Insomnia_symptoms | 59128 | 8,270,035 | 1.118 | 1.127 | 63055 |
| Sleep_duration | 111975 | 8,270,035 | 1.108 | 1.119 | 122792 |

GWAS equiv. *N:* GWAS-equivalent sample size.

**Supplementary Table 5. Summary of gene-based for GWAS and MTAG Results**

| CHR | START | STOP | ZSTAT | P | Gene | Phenotype |
|---|---|---|---|---|---|---|
| 2 | 66650584 | 66811001 | 5.0352 | 2.39E-07 | MEIS1 | GWAS (insomnia complaints) |
| 7 | 113716382 | 114343827 | 4.6247 | 1.88E-06 | FOXP2 | GWAS (insomnia complaints) |
| 2 | 66650584 | 66811001 | 6.0123 | 9.14E-10 | MEIS1 | GWAS (insomnia symptoms) |
| 18 | 52879562 | 53342018 | 4.9847 | 3.1E-07 | TCF4 | GWAS (insomnia symptoms) |
| 2 | 215265789 | 215453683 | 4.8941 | 4.94E-07 | VWC2L | GWAS (insomnia symptoms) |
| 8 | 8630864 | 8761155 | 4.8816 | 5.26E-07 | MFHAS1 | GWAS (insomnia symptoms) |
| 9 | 96328689 | 96451869 | 4.8595 | 5.89E-07 | PHF2 | GWAS (insomnia symptoms) |
| 17 | 43118978 | 43196384 | 4.8504 | 6.16E-07 | NMT1 | GWAS (insomnia symptoms) |
| 1 | 201788269 | 201863422 | 4.7338 | 1.1E-06 | IPO9 | GWAS (insomnia symptoms) |
| 1 | 17856330 | 18034369 | 4.5841 | 2.28E-06 | ARHGEF10L | GWAS (insomnia symptoms) |
| 17 | 36876488 | 36901297 | 4.5637 | 2.51E-06 | CISD3 | GWAS (insomnia symptoms) |
| 8 | 9901778 | 10296401 | 5.9232 | 1.58E-09 | MSRA | GWAS (sleep duration) |
| 7 | 113716382 | 114343827 | 5.7134 | 5.54E-09 | FOXP2 | GWAS (sleep duration) |
| 22 | 39120730 | 39200148 | 5.4345 | 2.75E-08 | SUN2 | GWAS (sleep duration) |
| 22 | 39164513 | 39200203 | 4.683 | 1.41E-06 | DNAL4 | GWAS (sleep duration) |
| 8 | 9911778 | 10286401 | 6.6278 | 1.7E-11 | MSRA | MTAG (sleep duration) |
| 7 | 113726382 | 114333827 | 6.3221 | 1.29E-10 | FOXP2 | MTAG (sleep duration) |
| 8 | 8640864 | 8751155 | 4.9964 | 2.92E-07 | MFHAS1 | MTAG (sleep duration) |
| 22 | 39130730 | 39190148 | 4.9692 | 3.36E-07 | SUN2 | MTAG (sleep duration) |
| 8 | 10753555 | 11058875 | 4.7961 | 8.09E-07 | XKR6 | MTAG (sleep duration) |
| 22 | 22108789 | 22221970 | 4.6685 | 1.52E-06 | MAPK1 | MTAG (sleep duration) |
| 2 | 66660584 | 66801001 | 5.7648 | 4.09E-09 | MEIS1 | MTAG (insomnia complaints) |
| 7 | 113726382 | 114333827 | 5.6069 | 1.03E-08 | FOXP2 | MTAG (insomnia complaints) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 201798269 | 201853422 | 4.8774 | 5.37E-07 | IPO9 | MTAG (insomnia complaints) |
| 3 | 49158547 | 49170551 | 4.7712 | 9.16E-07 | LAMB2 | MTAG(insomnia complaints) |
| 8 | 8640864 | 8751155 | 4.7044 | 1.27E-06 | MFHAS1 | MTAG(insomnia complaints) |
| 12 | 57482677 | 57489259 | 4.6871 | 1.39E-06 | NAB2 | MTAG(insomnia complaints) |
| 2 | 215275789 | 215443683 | 4.6867 | 1.39E-06 | VWC2L | MTAG(insomnia complaints) |
| 8 | 9911778 | 10286401 | 4.6574 | 1.60E-06 | MSRA | MTAG(insomnia complaints) |
| 15 | 74275547 | 74286963 | 4.6082 | 2.03E-06 | STOML1 | MTAG(insomnia complaints) |
| 18 | 52889562 | 53332018 | 4.6048 | 2.06E-06 | TCF4 | MTAG(insomnia complaints) |
| 2 | 66660584 | 66801001 | 5.7192 | 5.35E-09 | MEIS1 | MTAG(insomnia symptoms) |
| 7 | 113726382 | 114333827 | 5.4951 | 1.95E-08 | FOXP2 | MTAG(insomnia symptoms) |
| 8 | 8640864 | 8751155 | 5.1199 | 1.53E-07 | MFHAS1 | MTAG(insomnia symptoms) |
| 8 | 9911778 | 10286401 | 5.0284 | 2.47E-07 | MSRA | MTAG(insomnia symptoms) |
| 18 | 52889562 | 53332018 | 4.944 | 3.83E-07 | TCF4 | MTAG(insomnia symptoms) |
| 12 | 57482677 | 57489259 | 4.9345 | 4.02E-07 | NAB2 | MTAG(insomnia symptoms) |
| 1 | 201798269 | 201853422 | 4.9201 | 4.32E-07 | IPO9 | MTAG(insomnia symptoms) |
| 3 | 49158547 | 49170551 | 4.7899 | 8.34E-07 | LAMB2 | MTAG(insomnia symptoms) |
| 5 | 88013975 | 88199922 | 4.7146 | 1.21E-06 | MEF2C | MTAG(insomnia symptoms) |
| 2 | 215275789 | 215443683 | 4.6613 | 1.57E-06 | VWC2L | MTAG(insomnia symptoms) |
| 15 | 74275547 | 74286963 | 4.6505 | 1.66E-06 | STOML1 | MTAG(insomnia symptoms) |
| 8 | 11141925 | 11185646 | 4.5996 | 2.12E-06 | MTMR9 | MTAG(insomnia symptoms) |
| 17 | 43128978 | 43186384 | 4.577 | 2.36E-06 | NMT1 | MTAG(insomnia symptoms) |
| 15 | 66839517 | 66858317 | 4.5575 | 2.59E-06 | LCTL | MTAG(insomnia symptoms) |

## Supplementary Table 6. Genes in each cluster

| Module | Nodes in Module | Node List |
|---|---|---|
| 0 | 132 | ACSS2,ADH1A,ADH1B,ADH1C,ADH4,ADH5,ADH6,ADH7,AIFM2,ALDH1A1,ALDH2,ALDH3A1,APAF1,APP,AQP1,AQP2,AQP3,AQP5,AQP6,AQP7,ATF1,ATF2,BAX,BBC3,BCL6,BNIP3L,CASP6,CCL22,CDC25B,CIRH1A,CREB1,CREBBP,CYP11A1,CYP11B1,CYP11B2,CYP19A1,CYP1A1,CYP1A2,CYP1B1,CYP24A1,CYP26C1,CYP27A1,CYP27B1,CYP2C18,CYP2C19,CYP2C8,CYP2C9,CYP2E1,CYP2F1,CYP2S1,CYP3A4,CYP3A5,CYP3A7,CYP4A11,CYP4F11,CYP4F22,CYP7A1,CYP7B1,CYP8B1,DDX47,DKC1,DUSP3,DUSP4,DUSP6,DUSP7,ELK1,EPHX1,FBL,FDX1,FDX1L,FDXR,FOS,FOXO1,FOXO3,FOXO4,JUN,MAPK10,MAPK11,MAPK14,MAPK7,MAPK8,MAPK9,MAPKAPK2,MDM2,MEF2A,MEF2C,MYO5B,NCOA1,NCOA2,NDRG1,NFATC1,NFATC2,NFATC3,NHP2,NOC4L,NOP10,NOP2,NOP56,NOP58,NR1H4,NR4A1,PARP2,PERP,PIAS1,PMAIP1,PPP3CA,PPP3CB,PPP3R1,PRELID1,PTGIS,PTGS1,RAB11FIP2,RPS14,RPS2,RPS6KA5,RPS7,RPS9,RXRA,SMOX,SNU13,STEAP3,TBXAS1,TP53,TP53AIP1,TP53I3,TP63,TP73,TRIAP1,UBC,UTP11L,UTP14A,ZNF420 |
| 1 | 100 | AKT1,AKT1S1,AKT2,AKT3,BTC,CASP9,CD19,CD28,CD80,CD86,CLEC7A,CYP4F2,DNM1,DNM2,EGF,EGFR,ERBB2,ERBB3,ERBB4,EREG,FGF1,FGF10,FGF16,FGF17,FGF18,FGF19,FGF2,FGF20,FGF22,FGF23,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,FGFR1,FGFR2,FGFR3,FGFR4,FRS2,FYN,GAB1,GRB2,HBEGF,INS,INSR,IRS1,IRS2,ITGAM,ITGB2,KIT,KITLG,KL,KLB,LCK,MAP2K1,MAPK1,MAPK3,MAPKAP1,MLST8,MTOR,NRG1,NRG2,NRG3,NRG4,PDGFA,PDGFB,PDGFRA,PDGFRB,PDPK1,PIK3CA,PIK3CB,PIK3CD,PIK3R1,PIK3R2,PIK3R3,PLCG2,PPP2CA,PPP2CB,PPP2R1A,PPP2R1B,PPP2R5D,PRKCD,PRR5,PTK6,PTPN11,RICTOR,RPS6,RPS6KA1,RPS6KA2,RPS6KA3,RPS6KB2,SRC,SYK,TP53BP2,TRAT1,TSC2,VAV1 |

| | | |
|---|---|---|
| 2 | 90 | BIRC2,BIRC3,BTRC,CCND1,CCNE1,CCNE2,CDC25A,CDC34,CDC6,CDK2,CDKN1A,CDKN1B,CHM,CKS1B,CUL1,FBXW11,FZR1,GMNN,GSK3B,IGFBP3,IKBKE,MAP3K14,MAX,MYC,NFKB2,NFKBIA,NFKBIB,NOL11,ORC1,PPP1R13B,PSMA1,PSMA2,PSMA3,PSMA4,PSMA5,PSMA6,PSMA7,PSMA8,PSMB1,PSMB10,PSMB11,PSMB2,PSMB3,PSMB4,PSMB5,PSMB6,PSMB7,PSMB8,PSMB9,PSMC1,PSMC2,PSMC3,PSMC4,PSMC5,PSMC6,PSMD1,PSMD10,PSMD11,PSMD12,PSMD13,PSMD14,PSMD2,PSMD3,PSMD4,PSMD5,PSMD6,PSMD7,PSMD8,PSMD9,PSME1,PSME2,PSME3,PSME4,PSMF1,RABGGTA,RABGGTB,RBX1,RELB,RPS27A,SKP1,SKP2,TNIP2,TRAF3,UBA3,UBA52,UBE2D1,UBE2D2,UBE2D3,UBE2M,WEE1 |
| 3 | 83 | AGER,BCL10,BID,BPI,BTK,CARD11,CARD9,CASP1,CASP10,CASP2,CASP8,CD14,CD180,CD36,CHUK,CRADD,DHX9,ECSIT,FADD,FAS,HMGB1,IKBKB,IKBKG,IL1B,IRAK1,IRAK2,IRAK3,IRAK4,IRF3,IRF7,LBP,LY86,LY96,MALT1,MAP2K3,MAP2K4,MAP2K6,MAP2K7,MAP3K1,MAP3K7,MAP3K8,MAPKAPK3,MYD88,NFKB1,NLRC4,NOD1,NOD2,PELI1,PELI2,PELI3,PIDD1,PYCARD,RELA,RIPK1,RIPK2,RIPK3,S100A12,S100B,SAA1,SARM1,SIGIRR,SOCS1,TAB1,TAB2,TAB3,TANK,TBK1,TICAM1,TICAM2,TIRAP,TLR1,TLR10,TLR2,TLR3,TLR4,TLR5,TLR6,TNFRSF10A,TNFRSF10B,TNFRSF10C,TNFRSF10D,TRAF6,UBE2V1 |
| 4 | 72 | ATM,BIRC5,CCNA1,CCNA2,CCNH,CDC45,CDC7,CDK4,CDK7,CDT1,CETN2,CHD1L,CUL4A,CUL4B,DBF4,DDB1,DDB2,E2F1,E2F2,E2F3,ERCC1,ERCC2,ERCC3,ERCC4,ERCC5,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,MAOA,MAOB,MCM10,MCM2,MCM3,MCM4,MCM5,MCM6,MCM7,MCM8,MNAT1,ORC2,ORC3,ORC4,ORC5,ORC6,PARP1,PIAS3,POLA1,POLA2,POLE,POLE2,PRIM1,PRIM2,RAD23A,RAD23B,RB1,RNF111,RPA1,RPA2,RPA3,RPA4,SUMO1,SUMO2,SUMO3,UBB,UBE2I,UBE2N,UBE2V2,USP45,XPA,XPC |
| 5 | 46 | ADCY1,ADCY2,ADCY3,ADCY4,ADCY5,ADCY6,ADCY7,ADCY8,ADCY9,AHCYL1,AVP,AVPR2,BAD,CALM1,CYP17A1,GNAS,GNB1,GNB2,GNB3,GNB4,GNB5,GNG10,GNG11,GNG12,GNG13,GNG2,GNG3,GNG4,GNG5,GNG7,GNG8,GNGT1,GNGT2,GSK3A,ITPR1,ITPR2,ITPR3,POMC,PRKACA,PRKACB,PRKACG,PRKAR1A,PRKAR1B,PRKAR2A,PRKAR2B,RAB11A |

| | | |
|---|---|---|
| 6 | 24 | ATP6AP1,ATP6V0A1,ATP6V0A2,ATP6V0A4,ATP6V0B,ATP6V0C,ATP6V0D1,ATP6V0D2,ATP6V0E1,ATP6V0E2,ATP6V1A,ATP6V1B1,ATP6V1B2,ATP6V1C1,ATP6V1C2,ATP6V1D,ATP6V1E1,ATP6V1E2,ATP6V1F,ATP6V1G1,ATP6V1G2,ATP6V1G3,ATP6V1H,TCIRG1 |
| 7 | 4 | DCAF13,PWP2,TBL3,WDR3 |
| 8 | 3 | IMP3,IMP4,MPHOSPH10 |
| 9 | 2 | RRP9,WDR36 |
| 10 | 2 | CYP2A13,CYP2B6 |

## Supplementary Table 7: GO enrichment analysis for each cluster.

| Module | Gene Set | Number OfProteinInGene Set | ProteinFromModule | P | FDR | Nodes |
|---|---|---|---|---|---|---|
| 0 | MyD88-independent toll-like receptor signa | 60 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ling path way | | | | | |
| 0 | xeno biotic meta bolic proce ss | 139 | 45 | 1.11E -16 | 5.33 E-15 | FDXR,CYP1B1,CYP27A1,ALDH3A1,FDX1,CYP2E1,ADH7,CYP2C19,CYP4F22,CYP2C18,CYP19A1,ADH5,ADH4,CYP27B1,CYP11A1,EPHX1,CYP4F11,CYP2C9,CYP2C8,CYP11B2,CYP2S1,CYP11B1,CYP1A2,TBXAS1,CYP1A1,ALDH2,PTGIS,CYP4A11,CYP7B1,CYP26C1,ALDH1A1,ACSS2,ADH1C,ADH1B,ADH1A,CYP3A4,CYP3A5,CYP7A1,PTGS1,CYP3A7,CYP2F1,SMOX,CYP8B1,FDX1L,CYP24A1 |
| 0 | toll-li ke recep tor 4 signa ling path way | 76 | 18 | 1.11E -16 | 5.33 E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | steroid metabolic process | 56 | 15 | 1.11E-16 | 5.33E-15 | FDXR,CYP1B1,FDX1,CYP2E1,CYP2C19,CYP19A1,CYP27B1,CYP11A1,CYP2C9,CYP11B2,CYP11B1,CYP3A4,CYP3A5,FDX1L,CYP24A1 |
| 0 | toll-like receptor TLR1:TLR2 signaling pathway | 55 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | stress-activated MAPK cascade | 46 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | toll-like receptor 3 signaling pathway | 63 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | toll-like receptor 2 signaling pathway | 57 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | sterol metabolic process | 16 | 12 | 1.11E-16 | 5.33E-15 | FDXR,CYP1B1,CYP27A1,FDX1,CYP19A1,CYP11A1,CYP11B2,CYP11B1,CYP7B1,CYP7A1,CYP8B1,FDX1L |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | oxidation-reduction process | 386 | 39 | 1.11E-16 | 5.33E-15 | STEAP3,FDXR,CYP1B1,CYP27A1,ALDH3A1,FDX1,CYP2E1,ADH7,CYP2C19,CYP4F22,CYP2C18,CYP19A1,ADH6,CYP27B1,CYP11A1,CYP4F11,CYP2C9,CYP2C8,TP53I3,CYP11B2,CYP2S1,CYP11B1,CYP1A2,TBXAS1,CYP1A1,AIFM2,PTGIS,CYP4A11,CYP7B1,CYP26C1,CYP3A4,CYP7A1,PTGS1,CYP3A7,CYP2F1,SMOX,CYP8B1,FDX1L,CYP24A1 |
| 0 | toll-like receptor TLR6:TLR2 signaling pathway | 55 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | epoxygenase P450 | 16 | 11 | 1.11E-16 | 5.33E-15 | CYP1B1,CYP2E1,CYP2C19,CYP2C18,CYP2C9,CYP2C8,CYP2S1,CYP1A2,CYP1A1,CYP4A11,CYP2F1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | path way | | | | | |
| 0 | TRIF -dependent toll-like receptor signaling pathway | 58 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | small molecule metabolic process | 1229 | 50 | 1.11E-16 | 5.33E-15 | AQP1,FDXR,CYP1B1,CYP27A1,ALDH3A1,FDX1,MAPKAPK2,CYP2E1,ADH7,CYP2C19,CYP4F22,CYP2C18,CYP19A1,ADH5,ADH4,CYP27B1,CYP11A1,UBC,CREBBP,EPHX1,CYP4F11,CYP2C9,CYP2C8,CYP11B2,CYP2S1,CYP11B1,CYP1A2,TBXAS1,CYP1A1,ALDH2,PTGIS,CYP4A11,CYP7B1,CYP26C1,ALDH1A1,ACSS2,ADH1C,ADH1B,ADH1A,CYP3A4,CYP3A5,CYP7A1,PTGS1,CYP3A7,RXRA,CYP2F1,SMOX,CYP8B1,FDX1L,CYP24A1 |
| 0 | toll-like receptor 10 signaling pathway | 49 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | toll-like receptor 5 signa | 49 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ling path way | | | | | |
| 0 | MyD88-dependent toll-like receptor signaling pathway | 64 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | toll-like receptor 9 signaling pathway | 55 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | toll-like receptor signaling pathway | 84 | 18 | 1.11E-16 | 5.33E-15 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,UBC,JUN,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | ethanol oxidation | 11 | 9 | 1.04E-14 | 4.80E-13 | ADH7,ADH5,ADH4,ALDH2,ALDH1A1,ACSS2,ADH1C,ADH1B,ADH1A |
| 0 | exogenous drug catabolic process | 14 | 9 | 8.94E-14 | 3.93E-12 | CYP2E1,CYP2C19,CYP2C18,CYP2C9,CYP2C8,CYP2S1,CYP1A2,CYP3A4,CYP2F1 |
| 0 | arachidonic acid metabolic process | 42 | 11 | 2.27E-12 | 9.53E-11 | CYP1B1,MAPKAPK2,CYP2C19,CYP2C9,CYP2C8,CYP1A2,TBXAS1,CYP1A1,PTGIS,CYP4A11,PTGS1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | omega-hydroxylase P450 pathway | 8 | 7 | 6.42E-12 | 2.57E-10 | CYP1B1,CYP2C19,CYP2C9,CYP2C8,CYP1A2,CYP1A1,CYP4A11 |
| 0 | drug metabolic process | 24 | 8 | 3.78E-10 | 1.44E-08 | CYP2E1,CYP2C19,CYP2C9,CYP2C8,CYP1A2,CYP1A1,ADH1A,CYP3A4 |
| 0 | glycerol transport | 8 | 6 | 5.35E-10 | 1.93E-08 | AQP6,AQP7,AQP5,AQP2,AQP3,AQP1 |
| 0 | cellular water homeostasis | 9 | 6 | 1.08E-09 | 3.66E-08 | AQP6,AQP7,AQP5,AQP2,AQP3,AQP1 |
| 0 | C21-steroid horm | 9 | 6 | 1.08E-09 | 3.66E-08 | FDXR,FDX1,CYP11A1,CYP11B2,CYP11B1,FDX1L |

| | | | | | | |
|---|---|---|---|---|---|---|
| | one biosynthetic process | | | | | |
| 0 | nerve growth factor receptor signaling pathway | 312 | 19 | 1.89E-09 | 6.25E-08 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,FOXO4,FOXO3,FOXO1,UBC,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | monoterpenoid metabolic process | 5 | 5 | 3.72E-09 | 1.15E-07 | CYP2E1,CYP2C19,CYP2C9,CYP1A2,CYP3A4 |
| 0 | oxidative deme | 6 | 5 | 9.17E-09 | 2.75E-07 | CYP2C9,CYP2C8,CYP1A2,CYP3A4,CYP3A5 |

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|---|---|---|---|---|---|---|
| 0 | thylation positive regulation of apoptotic process | 249 | 16 | 1.91E-08 | 5.50E-07 | STEAP3,CYP1B1,BNIP3L,UTP11L,FOXO3,FOXO1,UBC,PMAIP1,NR4A1,BCL6,AIFM2,APAF1,DUSP6,MAPK8,RXRA,BAX |
| 0 | calcineurin-NFAT signaling cascade | 7 | 5 | 1.97E-08 | 5.50E-07 | PPP3R1,NFATC3,NFATC2,NFATC1,PPP3CA |
| 0 | water transport | 27 | 7 | 2.69E-08 | 7.54E-07 | AQP6,AQP7,AQP5,AQP2,AQP3,AQP1,RAB11FIP2 |
| 0 | rRNA processing | 60 | 9 | 2.85E-08 | 7.70E-07 | FBL,UTP11L,DKC1,NOP2,NOP10,UTP14A,NOC4L,NOP56,NOP58 |

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|---|---|---|---|---|---|---|
| 0 | cellular response to UV vitamin D | 28 | 7 | 3.44E-08 | 8.95E-07 | AQP1,TP63,TP53,CREBBP,TP73,TRIAP1,MAPK9 |
| 0 | metabolic process cholesterol | 9 | 5 | 6.78E-08 | 1.70E-06 | CYP27B1,CYP11A1,CYP1A1,CYP3A4,CYP24A1 |
| 0 | metabolic process drug | 50 | 8 | 1.06E-07 | 2.54E-06 | FDXR,CYP27A1,FDX1,CYP11A1,CYP11B2,CYP11B1,CYP7B1,RXRA |
| 0 | catabolic process | 4 | 4 | 1.44E-07 | 3.46E-06 | CYP2C9,CYP1A2,CYP3A4,CYP3A5 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 0 | innate immune response | 800 | 27 | 1.62E-07 | 3.74E-06 | ATF1,ELK1,RPS6KA5,MEF2A,MEF2C,MAPKAPK2,FOXO4,FOXO3,FOXO1,PPP3R1,UBC,CREBBP,JUN,NFATC3,NFATC2,NFATC1,PPP3CA,DUSP4,DUSP3,DUSP6,DUSP7,CREB1,MAPK9,MAPK8,MAPK7,MAPK14,MAPK11 |
| 0 | renal water homeostasis | 24 | 6 | 3.38E-07 | 7.68E-06 | AQP2,AQP3,AQP1,RAB11FIP2,CYP11B2,CYP4A11 |
| 0 | heterocycle metabolic process | 5 | 4 | 3.49E-07 | 7.68E-06 | CYP2E1,CYP2C19,CYP1A2,CYP3A4 |
| 0 | regulation of sequence-specific | 14 | 5 | 5.91E-07 | 1.30E-05 | JUN,MAPK9,MAPK8,MAPK14,MAPK11 |

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|---|---|---|---|---|---|---|
| 0 | DNA binding transcription factor activity stimulatory C-type lectin receptor signaling pathway | 86 | 8 | 5.83E-06 | 1.22E-04 | RPS6KA5,PPP3R1,UBC,CREBBP,NFATC3,NFATC2,NFATC1,PPP3CA |
| 0 | secondary metabolite biosyntheti | 4 | 3 | 1.34E-05 | 2.82E-04 | CYP11A1,CYP11B2,CYP11B1 |

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|---|---|---|---|---|---|---|
| | c process | | | | | |
| 0 | Fc-epsilon receptor signaling pathway | 369 | 15 | 1.50E-05 | 3.00E-04 | FOXO4,FOXO3,FOXO1,PPP3R1,UBC,JUN,NFATC3,NFATC2,NFATC1,PPP3CA,DUSP6,DUSP7,CREB1,MAPK9,MAPK8 |
| 0 | bile acid metabolic process | 28 | 5 | 1.67E-05 | 3.35E-04 | CYP27A1,CYP7B1,CYP7A1,RXRA,CYP8B1 |
| 0 | bile acid biosynthetic process | 15 | 4 | 2.60E-05 | 4.69E-04 | CYP27A1,CYP7B1,CYP7A1,CYP8B1 |
| 0 | retinol | 15 | 4 | 2.60E-05 | 4.69E-04 | CYP1B1,ADH7,ADH4,ALDH1A1 |

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|---|---|---|---|---|---|---|
| | metabolic process alcohol | | | | | |
| 0 | metabolic process icosanoid | 5 | 3 | 2.60E-05 | 4.69E-04 | ADH4,ALDH2,ADH1A |
| 0 | metabolic process | 5 | 3 | 2.60E-05 | 4.69E-04 | CYP4F22,TBXAS1,PTGIS |
| 0 | excretion | 32 | 5 | 3.15E-05 | 5.35E-04 | AQP6,AQP7,AQP5,AQP2,AQP3 |
| 0 | positive regulation of neuron apopt | 32 | 5 | 3.15E-05 | 5.35E-04 | TP53,FOXO3,PMAIP1,JUN,BBC3 |

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|---|---|---|---|---|---|---|
| | otic process | | | | | |
| 0 | response to vitamin D | 16 | 4 | 3.33E-05 | 5.67E-04 | AQP3,CYP27B1,RXRA,CYP24A1 |
| 0 | release of cytochrome c from mitochondria | 17 | 4 | 4.21E-05 | 7.16E-04 | PMAIP1,JUN,BBC3,MAPK9 |
| 0 | response to X-ray | 18 | 4 | 5.25E-05 | 8.40E-04 | TP63,TP53,PMAIP1,TP73 |
| 0 | positive regulation of transcripti | 799 | 22 | 6.25E-05 | 1.00E-03 | ATF1,ELK1,RPS6KA5,TP63,MEF2A,MEF2C,FOXO3,FOXO1,PPP3R1,UBC,CREBBP,JUN,NFATC3,NFATC2,NFATC1,NR4A1,TP73,TRIAP1,PPP3CA,CREB1,RXRA,MAPK7 |

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|---|---|---|---|---|---|---|
| | on from RNA polymerase II promoter activation of | | | | | |
| 0 | MAPK activity | 90 | 7 | 6.95E-05 | 1.05E-03 | MAPKAPK2,UBC,TP73,DUSP6,DUSP7,MAPK14,MAPK11 |
| 0 | cellular aldehyde metabolic process | 7 | 3 | 7.03E-05 | 1.05E-03 | ALDH3A1,ADH4,ALDH1A1 |
| 0 | cellular respo | 93 | 7 | 8.51E-05 | 1.28E-03 | AQP1,NDRG1,UBC,PMAIP1,CREBBP,BBC3,PTGIS |

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|---|---|---|---|---|---|---|
| | nse to hypoxia | | | | | |
| 0 | apoptotic process | 483 | 16 | 8.85E-05 | 1.33E-03 | STEAP3,TP53AIP1,TP63,MEF2A,MEF2C,TP53,FOXO1,PPP3R1,UBC,PMAIP1,PRELID1,BBC3,CASP6,APAF1,MAPK8,MAPK14 |
| | intrinsic apoptotic signaling pathway | | | | | |
| 0 | positive regulation of | 43 | 5 | 1.25E-04 | 1.88E-03 | PPP3R1,PMAIP1,BBC3,APAF1,MAPK8 |
| | protein insertion into mitoc | | | | | |
| 0 | | 23 | 4 | 1.34E-04 | 1.88E-03 | PPP3R1,PMAIP1,BBC3,MAPK8 |

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|---|---|---|---|---|---|---|
| | hondrial membrane involved in apoptotic signaling pathway inactivation of | | | | | |
| 0 | MAPK activity positive regulation of musc | 24 | 4 | 1.58E-04 | 2.21E-03 | DUSP4,DUSP3,DUSP6,DUSP7 |
| 0 | | 24 | 4 | 1.58E-04 | 2.21E-03 | MEF2A,MEF2C,MAPK14,MAPK11 |

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|---|---|---|---|---|---|---|
| | le cell differentiation positive regulation of | | | | | |
| 0 | transcription, DNA-dependent | 406 | 14 | 1.66E-04 | 2.33E-03 | ELK1,TP63,MEF2C,PIAS1,FOXO4,FOXO3,FOXO1,CREBBP,JUN,NFATC2,NFATC1,TP73,CREB1,MAPK9 |
| 0 | odontogenesis | 25 | 4 | 1.84E-04 | 2.58E-03 | AQP6,AQP5,AQP3,AQP1 |
| 0 | telomere maintenance via telomerase | 10 | 3 | 2.00E-04 | 2.60E-03 | DKC1,NHP2,NOP10 |

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|---|---|---|---|---|---|---|
| 0 | positive regulation of cyclase activity | 2 | 2 | 2.37E-04 | 2.84E-03 | MAPK8,MAPK14 |
| 0 | rRNA pseudouridine synthesis | 2 | 2 | 2.37E-04 | 2.84E-03 | DKC1,NHP2 |
| 0 | regulation of membrane lipid distribution | 2 | 2 | 2.37E-04 | 2.84E-03 | PRELID1,TRIAP1 |

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|---|---|---|---|---|---|---|
| 0 | alkaloid catabolic process | 2 | 2 | 2.37E-04 | 2.84E-03 | CYP3A4,CYP3A5 |
| 0 | urea transmembrane transport | 2 | 2 | 2.37E-04 | 2.84E-03 | AQP7,AQP3 |
| 0 | rRNA modification | 2 | 2 | 2.37E-04 | 2.84E-03 | NOP56,NOP58 |
| 0 | renal water transport | 2 | 2 | 2.37E-04 | 2.84E-03 | AQP2,AQP1 |
| 0 | cardiac muscle hyper | 11 | 3 | 2.64E-04 | 3.17E-03 | MEF2C,NFATC3,PPP3CA |

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|---|---|---|---|---|---|---|
| | trophy in response to stress muscle | | | | | |
| 0 | cell differentiation response to | 28 | 4 | 2.82E-04 | 3.39E-03 | MEF2A,MEF2C,MAPK14,MAPK11 |
| 0 | organic nitrogen | 12 | 3 | 3.40E-04 | 4.08E-03 | CYP2E1,TP73,PTGS1 |
| 0 | programmed cell death | 120 | 7 | 3.97E-04 | 4.37E-03 | PPP3R1,UBC,PMAIP1,BBC3,CASP6,APAF1,MAPK8 |
| 0 | DNA damage respo | 13 | 3 | 4.29E-04 | 4.72E-03 | FOXO3,NDRG1,TRIAP1 |

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|---|---|---|---|---|---|---|
| | nse, signal transduction by p53 class mediator | | | | | |
| 0 | cyclooxygenase pathway | 13 | 3 | 4.29E-04 | 4.72E-03 | TBXAS1,PTGIS,PTGS1 |
| 0 | cellular response to transforming growth factor beta | 33 | 4 | 5.22E-04 | 4.76E-03 | MEF2C,CYP11A1,APAF1,MAPK7 |

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|---|---|---|---|---|---|---|
| | stimulus | | | | | |
| 0 | cellular response to calcium ion positive regulation | 33 | 4 | 5.22E-04 | 4.76E-03 | MEF2A,MEF2C,JUN,NFATC3 |
| 0 | of interleukin-12 secretion | 3 | 2 | 5.29E-04 | 4.76E-03 | MAPK14,MAPK11 |
| 0 | response to nitrosative stress | 3 | 2 | 5.29E-04 | 4.76E-03 | ADH5,DUSP6 |

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|---|---|---|---|---|---|---|
| 0 | positive regulation of phospholipid transport | 3 | 2 | 5.29E-04 | 4.76E-03 | PRELID1,TRIAP1 |
| 0 | aldosterone biosynthetic process | 3 | 2 | 5.29E-04 | 4.76E-03 | CYP11B2,CYP11B1 |
| 0 | cellular response to mercury ion | 3 | 2 | 5.29E-04 | 4.76E-03 | AQP2,AQP1 |

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|---|---|---|---|---|---|---|
| 0 | vitamin D catabolic process | 3 | 2 | 5.29E-04 | 4.76E-03 | CYP27B1,CYP24A1 |
| 0 | cortisol biosynthetic process | 3 | 2 | 5.29E-04 | 4.76E-03 | CYP11B2,CYP11B1 |
| 0 | monocarboxylic acid metabolic process | 3 | 2 | 5.29E-04 | 4.76E-03 | CYP2C9,CYP1A2 |
| 0 | carbon dioxide trans | 3 | 2 | 5.29E-04 | 4.76E-03 | AQP5,AQP1 |

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|---|---|---|---|---|---|---|
| | port | | | | | |
| 0 | negative regulation of mitochondrial membrane potential | 3 | 2 | 5.29E-04 | 4.76E-03 | PMAIP1,PRELID1 |
| 0 | JUN phosphorylation | 3 | 2 | 5.29E-04 | 4.76E-03 | MAPK9,MAPK8 |
| 0 | response to drug | 256 | 10 | 5.74E-04 | 5.17E-03 | AQP1,ALDH3A1,CYP11A1,JUN,NFATC2,CYP1A1,TP73,DUSP6,CREB1,MAPK9 |
| 0 | regulation of reactive | 17 | 3 | 9.30E-04 | 8.37E-03 | CYP1B1,FOXO3,FOXO1 |

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|---|---|---|---|---|---|---|
| 0 | oxygen species metabolic process | 4 | 2 | 9.34E-04 | 8.40E-03 | |
| 0 | p38 MAPK cascade | 4 | 2 | 9.34E-04 | 8.40E-03 | MAPKAPK2,MAPK14 |
| 0 | steroid catabolic process | 4 | 2 | 9.34E-04 | 8.40E-03 | CYP1A2,CYP3A4 |
| 0 | cerebrospinal fluid secretion | 4 | 2 | 9.34E-04 | 8.40E-03 | AQP1,TP73 |

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|---|---|---|---|---|---|---|
| 0 | cellular response to copper ion | 5 | 2 | 1.45E-03 | 0.0116 | AQP2,AQP1 |
| 0 | snoRNA localization | 5 | 2 | 1.45E-03 | 0.0116 | FBL,NOP58 |
| 0 | ethanol catabolic process | 5 | 2 | 1.45E-03 | 0.0116 | ADH7,ALDH2 |
| 0 | dibenzo-p-dioxin metabolic process | 5 | 2 | 1.45E-03 | 0.0116 | CYP11A1,CYP1A2 |

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|---|---|---|---|---|---|---|
| 0 | cellular response to potassium ion regulation | 5 | 2 | 1.45E-03 | 0.0116 | CYP11B2,CYP11B1 |
| 0 | of germinal center formation positive regulation | 5 | 2 | 1.45E-03 | 0.0116 | MEF2C,BCL6 |
| 0 | of erythrocyte differentiat | 20 | 3 | 1.48E-03 | 0.0118 | FOXO3,MAPK14,MAPK11 |

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|---|---|---|---|---|---|---|
| | ion | | | | | |
| 0 | cellular response to peptide hormone stimulus | 20 | 3 | 1.48E-03 | 0.0118 | CYP11A1,CYP11B2,CYP11B1 |
| 0 | vitamin metabolic process | 75 | 5 | 1.53E-03 | 0.0122 | CYP27B1,PTGIS,CYP26C1,RXRA,CYP24A1 |
| 0 | response to DNA damage stimu | 153 | 7 | 1.62E-03 | 0.0129 | TP63,MAPKAPK2,FOXO1,NFATC2,BCL6,TP73,BBC3 |

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|---|---|---|---|---|---|---|
| | lus | | | | | |
| 0 | response to stress | 45 | 4 | 1.63E-03 | 0.0131 | MAPKAPK2,MAPK9,MAPK8,MAPK11 |
| 0 | DNA damage response, signal transduction by p53 class mediator resulting in induction of apoptosis | 22 | 3 | 1.94E-03 | 0.0151 | TP63,PMAIP1,TP73 |

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|---|---|---|---|---|---|---|
| 0 | positive regulation of protein metabolic process | 6 | 2 | 2.07E-03 | 0.0151 | MAPK8,MAPK7 |
| 0 | positive regulation of NFAT protein import into nucleus | 6 | 2 | 2.07E-03 | 0.0151 | PPP3R1,PPP3CA |

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|---|---|---|---|---|---|---|
| 0 | ventricular cardiac muscle cell differentiation | 6 | 2 | 2.07E-03 | 0.0151 | MEF2C,RXRA |
| 0 | germinal center formation | 6 | 2 | 2.07E-03 | 0.0151 | MEF2C,BCL6 |
| 0 | transcription from RNA polymerase II promoter | 469 | 13 | 2.09E-03 | 0.0151 | ATF1,ELK1,MEF2A,MEF2C,FOXO4,FOXO3,JUN,NFATC3,NFATC2,NFATC1,NR4A1,TP73,CREB1 |

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|---|---|---|---|---|---|---|
| 0 | aging | 119 | 6 | 2.15E-03 | 0.0151 | ALDH3A1,JUN,CYP1A1,APAF1,PTGS1,RXRA |
| 0 | peptidyl-tyrosine dephosphorylation | 82 | 5 | 2.25E-03 | 0.0157 | CDC25B,DUSP4,DUSP3,DUSP6,DUSP7 |
| 0 | MAPK cascade positive regulation | 209 | 8 | 2.31E-03 | 0.0162 | MEF2A,MEF2C,MAPKAPK2,UBC,DUSP4,DUSP6,DUSP7,MAPK10 |
| 0 | of apoptotic signaling pathway | 24 | 3 | 2.47E-03 | 0.0173 | TP63,APAF1,MAPK9 |

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|---|---|---|---|---|---|---|
| 0 | pancreatic juice secretion | 7 | 2 | 2.80E-03 | 0.0196 | AQP5,AQP1 |
| 0 | cellular response to lipopolysaccharide | 88 | 5 | 3.04E-03 | 0.0213 | MEF2C,CYP11A1,MAPK9,MAPK8,MAPK14 |
| 0 | response to gamma radiation | 26 | 3 | 3.09E-03 | 0.0217 | TP63,CYP11A1,TP73 |
| 0 | negative regulation of cardiac | 8 | 2 | 3.63E-03 | 0.0254 | TP73,MAPK11 |

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|---|---|---|---|---|---|---|
| 0 | muscle cell proliferation protein acetylation positive regulation of histone deacetylation estrogen biosynthetic proce | 8 | 2 | 3.63E-03 | 0.0254 | FOXO1,CREBBP |
| 0 | | 8 | 2 | 3.63E-03 | 0.0254 | TP53,BCL6 |
| 0 | | 8 | 2 | 3.63E-03 | 0.0254 | CYP19A1,CYP11A1 |

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|---|---|---|---|---|---|---|
| | ss | | | | | |
| 0 | intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress | 28 | 3 | 3.80E-03 | 0.0266 | PMAIP1,BBC3,APAF1 |
| 0 | response to toxin | 59 | 4 | 4.29E-03 | 0.0274 | CYP1B1,EPHX1,MAPK9,CYP2F1 |
| 0 | cellular response to | 60 | 4 | 4.55E-03 | 0.0274 | CYP11A1,PTGIS,MAPK9,CCL22 |

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|---|---|---|---|---|---|---|
| 0 | interleukin-1 androgen metabolic process | 9 | 2 | 4.56E-03 | 0.0274 | CYP19A1,CYP3A4 |
| 0 | 3'-UTR-mediated mRNA stabilization | 9 | 2 | 4.56E-03 | 0.0274 | MAPKAPK2,MAPK14 |
| 0 | hydrogen peroxide biosynthetic proce | 9 | 2 | 4.56E-03 | 0.0274 | CYP1A2,CYP1A1 |

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|---|---|---|---|---|---|---|
| | ss | | | | | |
| 0 | regulation of neural precursor cell proliferation negative regulation | 9 | 2 | 4.56E-03 | 0.0274 | FOXO3,FOXO1 |
| 0 | of cellular senescence | 9 | 2 | 4.56E-03 | 0.0274 | TP63,BCL6 |
| 0 | mitotic cell | 9 | 2 | 4.56E-03 | 0.0274 | TP63,TP73 |

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|---|---|---|---|---|---|---|
| | cycle G1/S transition DNA damage checkpoint | | | | | |
| 0 | glucocorticoid biosynthetic process response to | 9 | 2 | 4.56E-03 | 0.0274 | CYP11A1,CYP11B1 |
| 0 | lipopolysaccharide regulation of | 144 | 6 | 5.42E-03 | 0.0325 | MAPKAPK2,ADH5,CYP27B1,JUN,CYP1A2,CYP1A1 |
| 0 | | 32 | 3 | 5.50E-03 | 0.033 | CREB1,MAPK9,MAPK8 |

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|---|---|---|---|---|---|---|
| 0 | circadian rhythm axon regeneration | 10 | 2 | 5.59E-03 | 0.0335 | JUN,RXRA |
| 0 | phospholipid transport | 10 | 2 | 5.59E-03 | 0.0335 | PRELID1,TRIAP1 |
| 0 | DNA damage response, signal transduction by p53 class medi | 10 | 2 | 5.59E-03 | 0.0335 | TP63,TP73 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ator resulting in transcription of p21 class mediator positive regulation of B cell proliferation | | | | | |
| 0 | epidermal growth factor receptor | 33 | 3 | 5.99E-03 | 0.0359 | MEF2C,NFATC2,BCL6 |
| 0 | | 250 | 8 | 6.69E-03 | 0.0401 | RPS6KA5,FOXO4,FOXO3,FOXO1,UBC,DUSP6,DUSP7,CREB1 |

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|---|---|---|---|---|---|---|
| | signaling pathway | | | | | |
| 0 | cellular respiration | 11 | 2 | 6.71E-03 | 0.0403 | NFATC3,CYP1A2 |
| 0 | cellular response to nitric oxide | 11 | 2 | 6.71E-03 | 0.0403 | AQP1,FOXO1 |
| 0 | inflammatory response | 310 | 9 | 7.57E-03 | 0.0438 | RPS6KA5,MAPKAPK2,NFATC3,CYP4F11,BCL6,TP73,PTGS1,RXRA,CCL22 |
| 0 | sodium ion homeostasis | 12 | 2 | 7.93E-03 | 0.0438 | CYP11B2,CYP4A11 |

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|---|---|---|---|---|---|---|
| 0 | prostaglandin biosynthetic process | 13 | 2 | 9.24E-03 | 0.0438 | PTGIS,PTGS1 |
| 0 | leukotriene metabolic process | 13 | 2 | 9.24E-03 | 0.0438 | MAPKAPK2,CYP4A11 |
| 0 | activation of cysteine-type endopeptidase activity invol | 74 | 4 | 9.36E-03 | 0.0438 | PMAIP1,BBC3,APAF1,MAPK9 |

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|---|---|---|---|---|---|---|
| 0 | ved in apoptotic process regulation of mRNA stability | 75 | 4 | 9.80E-03 | 0.0438 | MAPKAPK2,UBC,MAPK14,MAPK11 |
| 1 | axon guidance | 439 | 41 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,FRS2,EREG,BTC,PDGFB,PDGFA,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,NRG1,DNM1,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,PTPN11,KITLG |

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|---|---|---|---|---|---|---|
| 1 | insulin receptor signaling pathway | 239 | 50 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT2,AKT1,PDGFRB,PDGFRA,RPS6,FRS2,EREG,BTC,PDGFB,PDGFA,PIK3R3,PIK3R2,FGF20,FGF23,KL,INSR,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,MLST8,PDPK1,GAB1,NRG1,PIK3CA,NRG4,KIT,HBEGF,INS,ERBB4,MAPK1,EGF,PTPN11,KITLG |
| 1 | MAPK cascade | 209 | 40 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,FRS2,EREG,BTC,PDGFB,PDGFA,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,NRG1,NRG4,KIT,HBEGF,INS,ERBB4,MAPK1,MAPK3,EGF,KITLG |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | nerve growth factor receptor signaling pathway | 312 | 55 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CD19,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR2,FGF10,FGFR1,MLST8,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,AKT1S1,HBEGF,SRC,ERBB4,MAPK1,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |
| 1 | innate immune response | 800 | 59 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CLEC7A,CD19,FGF20,FGF23,KL,PTK6,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR2,FGF10,FGFR1,ITGAM,MLST8,SYK,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,FYN,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |

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|---|---|---|---|---|---|---|
| 1 | Fc-epsilon receptor signaling pathway | 369 | 54 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CD19,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR2,FGF10,FGFR1,MLST8,SYK,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,HBEGF,ERBB4,MAPK1,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |
| 1 | positive regulation of cell proliferation | 354 | 33 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,EREG,BTC,PDGFB,PDGFA,FGF20,INSR,FGF17,FGF19,FGF18,FGFR4,FGFR3,FGFR2,FGFR1,KIT,HBEGF,INS,ERBB4,MAPK1,EGF |

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|---|---|---|---|---|---|---|
| 1 | fibroblast growth factor receptor signaling pathway | 234 | 58 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF2,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CD19,FGF20,FGF23,FGF22,KL,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR3,FGFR2,FGF10,FGFR1,MLST8,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,HBEGF,SRC,PPP2CA,ERBB4,MAPK1,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |
| 1 | Ras protein signal transduction | 192 | 39 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,FRS2,EREG,BTC,PDGFB,PDGFA,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,NRG1,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,KITLG |

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|---|---|---|---|---|---|---|
| 1 | small GTPase mediated signal transduction | 522 | 42 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,FRS2,EREG,BTC,PDGFB,PDGFA,PIK3R2,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,PDPK1,NRG1,VAV1,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,KITLG |
| 1 | activation of MAPKK activity | 181 | 39 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF2,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,PDGFRB,PDGFRA,FRS2,EREG,BTC,PDGFB,PDGFA,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,NRG1,NRG4,KIT,HBEGF,ERBB4,MAPK1,EGF,KITLG |

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|---|---|---|---|---|---|---|
| 1 | phosphatidylinositol-mediated signaling | 101 | 54 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CD19,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR2,FGF10,FGFR1,PIK3CD,PIK3CB,MLST8,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,HBEGF,ERBB4,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |
| 1 | vascular endothelial growth factor receptor signaling pathway | 220 | 45 | 1.11E-16 | 8.55E-15 | KLB,IRS1,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,GRB2,FGFR4,FGFR2,FGF10,FGFR1,MLST8,PDPK1,NRG1,PIK3CA,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,KITLG |

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|---|---|---|---|---|---|---|
| 1 | epidermal growth factor receptor signaling pathway | 250 | 54 | 1.11E-16 | 8.55E-15 | CD86,KLB,IRS1,CD80,IRS2,FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF8,FGF9,AKT1,PDGFRB,PDGFRA,FRS2,EREG,BTC,MAPKAP1,PDGFB,PDGFA,PIK3R2,CD19,FGF20,FGF23,KL,FGF17,FGF16,FGF19,FGF18,CD28,GRB2,FGFR4,FGFR2,FGF10,FGFR1,MLST8,PDPK1,GAB1,NRG1,PIK3CA,LCK,NRG4,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,TRAT1,PTPN11,KITLG,RPS6KB2 |
| 1 | positive regulation of ERK 1 and ERK 2 cascade | 132 | 17 | 1.44E-15 | 1.02E-13 | FGF1,FGF2,FGF4,PDGFRB,PDGFRA,PDGFB,PDGFA,FGF20,FGF23,FGF19,FGF18,FGFR4,FGFR2,FGF10,SRC,ERBB4,PTPN11 |
| 1 | peptidyl-tyrosi | 97 | 15 | 5.44E-15 | 3.64E-13 | PDGFRB,PDGFRA,PDGFB,INSR,FGFR4,FGFR3,FGFR2,FGFR1,KIT,SRC,EGFR,ERBB3,ERBB4,ERBB2,EGF |

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|---|---|---|---|---|---|---|
| | ne phos phory lation T cell costi mulat ion positi ve regul ation of | | | | | |
| 1 | phos phati dylin ositol 3-kin ase casca de positi ve regul ation of | 61 | 12 | 2.07E -13 | 1.30 E-11 | CD86,CD80,AKT1,MAPKAP1,CD28,GRB2,MLST8,PDPK1,PIK3CA,LCK,SRC,PTPN11 |
| 1 | | 46 | 11 | 2.72E -13 | 1.61 E-11 | PDGFRB,PDGFRA,PDGFB,PDGFA,CD28,FGFR1,PRR5,NRG1,KIT,INS,ERBB4 |
| 1 | | 27 | 9 | 2.34E -12 | 1.31 E-10 | FGF8,PDGFRB,EREG,BTC,PDGFB,INSR,CD28,INS,EGF |

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|---|---|---|---|---|---|---|
| 1 | mitosis positive regulation of cell division | 34 | 9 | 1.78E-11 | 9.41E-10 | FGF1,FGF3,FGF4,FGF5,FGF6,FGF7,FGF9,PDGFA,FGFR2 |
| 1 | organ induction | 13 | 7 | 2.57E-11 | 1.31E-09 | FGF1,FGF2,FGF3,FGF8,FRS2,FGF10,FGFR1 |
| 1 | signal transduction | 858 | 29 | 4.66E-11 | 2.28E-09 | IRS1,IRS2,FGF1,FGF3,FGF4,FGF6,FGF7,FGF9,AKT2,AKT3,AKT1,PDGFRB,PIK3R1,TP53BP2,FGF20,FGF17,FGF16,FGF18,PPP2R5D,DNM2,KIT,HBEGF,SRC,ERBB4,MAPK1,EGF,TRAT1,KITLG,RPS6KB2 |
| 1 | cell-cell signaling | 220 | 16 | 5.11E-11 | 2.35E-09 | CD86,CD80,FGF3,FGF4,FGF5,FGF6,FGF9,EREG,PDGFA,FGF20,FGF17,FGF16,FGF18,GRB2,FGFR2,INS |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of cell migration | 133 | 13 | 1.10E-10 | 4.86E-09 | IRS1,IRS2,FGF1,AKT2,PDGFRB,PDGFRA,PDGFB,PDGFA,INSR,KIT,HBEGF,INS,MAPK1 |
| 1 | positive regulation of DNA replication | 32 | 8 | 3.83E-10 | 1.65E-08 | PDGFRA,EREG,PDGFB,PDGFA,INSR,FGF10,INS,KITLG |
| 1 | positive regulation of peptidyl-tyrosine phos | 69 | 10 | 4.27E-10 | 1.75E-08 | CD80,FGF7,PDGFB,FGF10,MLST8,SYK,NRG1,SRC,INS,KITLG |

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|---|---|---|---|---|---|---|
| | phorylation | | | | | |
| 1 | protein autophosphorylation positive regulation | 122 | 12 | 5.60E-10 | 2.19E-08 | AKT1,PDGFRB,PDGFRA,INSR,PTK6,FGFR4,FGFR2,FGFR1,PDPK1,KIT,SRC,ERBB4 |
| 1 | of glucose import positive regulation | 22 | 7 | 9.61E-10 | 3.65E-08 | IRS1,IRS2,AKT2,AKT1,INSR,FGF19,INS |
| 1 | of glycogen | 12 | 6 | 1.10E-09 | 4.07E-08 | IRS1,IRS2,AKT2,AKT1,INSR,INS |

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|---|---|---|---|---|---|---|
| 1 | biosynthetic process wound healing positive regulation of | 58 | 9 | 1.84E-09 | 6.46E-08 | FGF2,FGF7,PDGFRB,PDGFRA,EREG,PDGFA,FGF10,NRG1,INS |
| 1 | MAP kinase activity positive regulation | 43 | 8 | 3.78E-09 | 1.28E-07 | FGF1,PDGFRB,PDGFB,PDGFA,FGF18,FGFR1,EGF,KITLG |
| 1 | of glucose | 7 | 5 | 4.86E-09 | 1.60E-07 | IRS1,AKT2,PIK3R3,PIK3R2,PTPN11 |

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|---|---|---|---|---|---|---|
| 1 | import in response to insulin stimulus positive regulation of cardiac muscle cell proliferation | 18 | 6 | 1.20E-08 | 3.85E-07 | FGF2,FGF9,FGFR2,FGFR1,NRG1,ERBB4 |
| 1 | positive regulation of | 20 | 6 | 2.24E-08 | 6.93E-07 | IRS1,PDGFRB,PDGFRA,PDGFB,KIT,ERBB4 |

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|---|---|---|---|---|---|---|
| 1 | phosphatidylinositol 3-kinase activity platelet-derived growth factor receptor signaling pathway | 22 | 6 | 3.91E-08 | 1.17E-06 | PDGFRB,PDGFRA,PDGFB,PDGFA,GAB1,PTPN11 |
| 1 | transmembrane receptor protei | 84 | 9 | 4.33E-08 | 1.26E-06 | PTK6,SYK,NRG1,LCK,EGFR,ERBB3,ERBB4,ERBB2,FYN |

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|---|---|---|---|---|---|---|
| | n tyrosine kinase signaling pathway positive regulation of protein | | | | | |
| 1 | kinase B signaling cascade protein | 60 | 8 | 4.83E-08 | 1.37E-06 | FGF2,PDGFA,INSR,CD28,NRG1,HBEGF,SRC,INS |
| 1 | phosphory | 358 | 16 | 4.90E-08 | 1.37E-06 | RPS6KA3,AKT2,RPS6KA2,AKT3,RPS6KA1,AKT1,MAP2K1,PDGFB,PTK6,FGFR1,SYK,PDPK1,PIK3CA,LCK,MAPK1,RPS6KB2 |

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|---|---|---|---|---|---|---|
| | lation | | | | | |
| 1 | positive regulation of mesenchymal cell proliferation | 23 | 6 | 5.07E-08 | 1.37E-06 | IRS1,IRS2,FGF9,PDGFA,FGFR2,FGFR1 |
| 1 | angiogenesis positive regulation | 188 | 12 | 6.41E-08 | 1.67E-06 | FGF1,FGF6,FGF9,EREG,PDGFA,FGF18,FGFR2,FGF10,FGFR1,SYK,PIK3CA,EGF |
| 1 | of MAPKKK | 5 | 4 | 1.15E-07 | 2.98E-06 | KLB,FGF23,KL,FGFR1 |

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|---|---|---|---|---|---|---|
| 1 | cascade by fibroblast growth factor receptor signaling pathway platelet activation positive regulation | 164 | 11 | 1.44E-07 | 3.60E-06 | AKT1,PDGFB,PDGFA,GRB2,SYK,PDPK1,PIK3CA,LCK,SRC,MAPK1,EGF |
| 1 | of MAPK cascade | 70 | 8 | 1.55E-07 | 3.87E-06 | PDGFB,PDGFA,INSR,FGFR2,FGF10,FGFR1,KIT,INS |

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|---|---|---|---|---|---|---|
| 1 | intracellular signal transduction positive regulation of | 300 | 14 | 2.18E-07 | 5.24E-06 | CD80,RPS6KA3,RPS6KA2,RPS6KA1,AKT1,PRKCD,PLCG2,PDPK1,NRG1,NRG2,NRG3,NRG4,SRC,RPS6KB2 |
| 1 | phosphoinositide phospholipase C activity positive regulation of | 6 | 4 | 2.36E-07 | 5.43E-06 | PDGFRB,PDGFRA,FGFR1,KIT |
| 1 | glucose | 7 | 4 | 4.34E-07 | 9.55E-06 | IRS1,IRS2,AKT2,AKT1 |

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|---|---|---|---|---|---|---|
| 1 | metabolic process | 7 | 4 | 4.34E-07 | 9.55E-06 | FGF3,FGF8,FGFR2,FGF10 |
| 1 | otic vesicle formation | 377 | 15 | 5.81E-07 | 1.28E-05 | AKT1,PDGFB,PDGFA,PIK3R2,CYP4F2,GRB2,ITGAM,SYK,PDPK1,PIK3CA,LCK,SRC,MAPK1,EGF,PTPN11 |
| 1 | blood coagulation | 61 | 7 | 9.29E-07 | 2.04E-05 | IRS1,IRS2,AKT2,AKT1,PIK3R2,INSR,PDPK1 |
| 1 | cellular response to insulin stimulus | 39 | 6 | 1.08E-06 | 2.27E-05 | INSR,PTK6,SYK,LCK,SRC,FYN |
| | peptidyl-tyrosine autop | | | | | |

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|---|---|---|---|---|---|---|
| 1 | hosphorylation positive regulation of smooth muscle cell proliferation | 45 | 6 | 2.45E-06 | 4.90E-05 | FGF2,PDGFRB,EREG,PDGFB,FGFR2,HBEGF |
| 1 | ERBB signaling pathway | 3 | 3 | 2.48E-06 | 4.90E-05 | NRG1,MAPK1,PTPN11 |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of metanephric mesenchymal cell migration by platelet-derived growth factor receptor-beta signaling | 3 | 3 | 2.48E-06 | 4.90E-05 | PDGFRB,PDGFB,PDGFA |

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|---|---|---|---|---|---|---|
| | path way | | | | | |
| 1 | mam mary gland epith elial cell differ entiat ion branc hing invol ved in saliva ry | 11 | 4 | 2.58E -06 | 4.90 E-05 | FGF2,AKT2,AKT1,ERBB4 |
| 1 | | 11 | 4 | 2.58E -06 | 4.90 E-05 | FGF7,FGF8,FGFR2,FGFR1 |

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|---|---|---|---|---|---|---|
| 1 | gland morphogenesis positive regulation of fibroblast proliferation positive regulation of epithelial cell proliferation | 47 | 6 | 3.14E-06 | 5.97E-05 | PDGFRA,EREG,BTC,PDGFB,PDGFA,FGF10 |
| 1 | | 52 | 6 | 5.57E-06 | 1.00E-04 | FGF1,FGF2,FGF7,FGF9,FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| 1 | negative regulation of plasma membrane long-chain fatty acid transport | 4 | 3 | 5.85E-06 | 1.05E-04 | IRS2,AKT2,AKT1 |
| 1 | regulation of branching involved in salivary gland | 4 | 3 | 5.85E-06 | 1.05E-04 | FGF7,FGF10,FGFR1 |

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| 1 | morphogenesis by mesenchymal-epithelial signaling protein kinase B signaling cascade | 31 | 5 | 7.07E-06 | 1.20E-04 | IRS1,AKT2,AKT1,PIK3CA,RPS6KB2 |
| 1 | phosphatidylinositol phosphorylation | 31 | 5 | 7.07E-06 | 1.20E-04 | PIK3R3,PIK3R2,PIK3CD,PIK3CB,PIK3CA |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of nitric oxide biosynthetic process | 32 | 5 | 8.23E-06 | 1.40E-04 | AKT2,AKT1,INSR,DNM2,INS |
| 1 | activation of protein kinase B activity | 15 | 4 | 8.70E-06 | 1.48E-04 | PDGFB,INSR,PDPK1,INS |
| 1 | glucose homeostasis | 88 | 7 | 1.01E-05 | 1.61E-04 | IRS1,AKT1,RPS6,INSR,FGFR4,INS,PTPN11 |

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|---|---|---|---|---|---|---|
| 1 | activation of MAPK activity | 90 | 7 | 1.16E-05 | 1.86E-04 | FRS2,EREG,INSR,FGF10,KIT,MAPK1,PTPN11 |
| 1 | leukocyte migration | 95 | 7 | 1.64E-05 | 2.63E-04 | PIK3R2,GRB2,ITGAM,PIK3CA,LCK,SRC,PTPN11 |
| 1 | cell chemotaxis | 37 | 5 | 1.65E-05 | 2.63E-04 | PDGFRB,PDGFRA,PDGFB,KIT,HBEGF |
| 1 | positive regulation of keratinocyte migration | 6 | 3 | 1.95E-05 | 2.92E-04 | FGF7,FGF10,HBEGF |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of phospholipase activity negative regulation of | 6 | 3 | 1.95E-05 | 2.92E-04 | FGFR2,FGFR1,PDPK1 |
| 1 | platelet activation negative regulation of | 8 | 3 | 4.57E-05 | 6.85E-04 | PDGFRA,PDGFB,PDGFA |
| 1 | neuron | 8 | 3 | 4.57E-05 | 6.85E-04 | NRG1,NRG3,ERBB4 |

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|---|---|---|---|---|---|---|
| | migration | | | | | |
| 1 | T cell receptor signaling pathway | 116 | 7 | 5.76E-05 | 8.07E-04 | PIK3R2,CD28,PDPK1,PIK3CA,LCK,MAPK1,TRAT1 |
| 1 | positive regulation of DNA biosynthetic process | 9 | 3 | 6.46E-05 | 8.40E-04 | PDGFRB,PDGFB,FGFR4 |
| 1 | positive regulation of | 9 | 3 | 6.46E-05 | 8.40E-04 | CD80,CD28,SYK |

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| 1 | alpha-beta T cell proliferation positive regulation of fatty acid beta-oxidation lung-associated mesenchyme development | 9 | 3 | 6.46E-05 | 8.40E-04 | IRS1,IRS2,AKT2 |
| 1 | | 9 | 3 | 6.46E-05 | 8.40E-04 | FGF9,FGFR2,FGFR1 |

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|---|---|---|---|---|---|---|
| 1 | activation of transmembrane receptor protein tyrosine kinase activity | 9 | 3 | 6.46E-05 | 8.40E-04 | NRG1,NRG3,EGF |
| 1 | organ development positive | 9 | 3 | 6.46E-05 | 8.40E-04 | NRG2,NRG3,NRG4 |
| 1 | chemotaxis | 27 | 4 | 8.46E-05 | 1.10E-03 | FGF7,FGF8,PDGFB,FGF10 |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of interleukin-2 biosynthetic process | 10 | 3 | 8.81E-05 | 1.15E-03 | CD86,CD80,CD28 |
| 1 | positive regulation of protein phosphorylation | 91 | 6 | 1.23E-04 | 1.50E-03 | AKT2,AKT1,INSR,FGF19,PRR5,ERBB4 |

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|---|---|---|---|---|---|---|
| 1 | secretion by lung epithelial cell involved in lung growth regulation of endothelial cell | 2 | 2 | 1.36E-04 | 1.50E-03 | FGF7,FGF10 |
| 1 | chemotaxis to fibroblast growth | 2 | 2 | 1.36E-04 | 1.50E-03 | FGF1,FGF4 |

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| | factor | | | | | |
| 1 | positive regulation of hyaluronan biosynthetic process negative regulation | 2 | 2 | 1.36E-04 | 1.50E-03 | PDGFB,EGF |
| 1 | of phosphatidylin | 2 | 2 | 1.36E-04 | 1.50E-03 | PDGFB,PDGFA |

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| 1 | ositol biosynthetic process fibroblast growth factor receptor signaling pathway involved in orbitofrontal cortex devel | 2 | 2 | 1.36E-04 | 1.50E-03 | FGFR2,FGFR1 |

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|---|---|---|---|---|---|---|
| | opment | | | | | |
| 1 | cellular response to molecule of fungal origin positive regulation of endothelial cell | 2 | 2 | 1.36E-04 | 1.50E-03 | CLEC7A,SYK |
| 1 | | 2 | 2 | 1.36E-04 | 1.50E-03 | FGF16,FGF18 |

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|---|---|---|---|---|---|---|
| 1 | chemotaxis to fibroblast growth factor mammary gland bud formation negative regulation of cardiac muscle tissue development | 2 | 2 | 1.36E-04 | 1.50E-03 | FGFR2,FGF10 |
| 1 | | 2 | 2 | 1.36E-04 | 1.50E-03 | FGF3,FGF8 |

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| | nt | | | | | |
| 1 | fibroblast growth factor receptor signaling pathway involved in mammary gland specification | 2 | 2 | 1.36E-04 | 1.50E-03 | FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| 1 | branch elongation involved in salivary gland morphogenesis mesenchymal cell differentiation involved in lung developme | 2 | 2 | 1.36E-04 | 1.50E-03 | FGFR2,FGF10 |
| 1 | | 2 | 2 | 1.36E-04 | 1.50E-03 | FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| | nt | | | | | |
| 1 | chemorepulsion involved in interneuron migration from the subpallium to the cortex | 2 | 2 | 1.36E-04 | 1.50E-03 | NRG1,NRG3 |
| 1 | positive regulation of | 12 | 3 | 1.50E-04 | 1.65E-03 | PDGFB,PDGFA,INS |

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|---|---|---|---|---|---|---|
| | protein autophosphorylation | | | | | |
| 1 | T cell activation positive regulation of vascular endothelial growth factor receptor signaling path | 35 | 4 | 2.27E-04 | 2.50E-03 | CD86,CD80,CLEC7A,FYN |
| 1 | | 14 | 3 | 2.36E-04 | 2.60E-03 | FGF9,FGF18,FGF10 |

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|---|---|---|---|---|---|---|
| | way | | | | | |
| 1 | positive regulation of Ras protein signal transduction | 15 | 3 | 2.89E-04 | 3.04E-03 | FGF10,NRG1,KITLG |
| 1 | positive regulation of gamma-d | 3 | 2 | 3.04E-04 | 3.04E-03 | SYK,LCK |

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| 1 | elta T cell differentiation leukocyte activation involved in immune response positive regulation of cell proliferation by VEG | 3 | 2 | 3.04E-04 | 3.04E-03 | CLEC7A,SYK |
| 1 | | 3 | 2 | 3.04E-04 | 3.04E-03 | PDGFRB,PDGFRA |

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| 1 | F-activated platelet derived growth factor receptor signaling pathway corticotropin hormone secreting cell differentiation | 3 | 2 | 3.04E-04 | 3.04E-03 | FGF2,FGF8 |

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|---|---|---|---|---|---|---|
| 1 | regulation of endothelial cell proliferation | 3 | 2 | 3.04E-04 | 3.04E-03 | FGF16,FGF18 |
| 1 | ventricular zone neuroblast division | 3 | 2 | 3.04E-04 | 3.04E-03 | FGFR2,FGFR1 |
| 1 | negative regulation of secretion | 3 | 2 | 3.04E-04 | 3.04E-03 | NRG1,EGF |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of granulocyte macrophage colony-stimulating factor biosynthetic process | 3 | 2 | 3.04E-04 | 3.04E-03 | CD80,SYK |
| 1 | metanephric glomerular | 3 | 2 | 3.04E-04 | 3.04E-03 | PDGFRB,PDGFRA |

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|---|---|---|---|---|---|---|
| 1 | capillary formation | 39 | 4 | 3.41E-04 | 3.07E-03 | CD19,SYK,LCK,MAPK1 |
| 1 | B cell receptor signaling pathway | 71 | 5 | 3.43E-04 | 3.08E-03 | ITGAM,ITGB2,SYK,SRC,PTPN11 |
| 1 | integrin-mediated signaling pathway | 16 | 3 | 3.48E-04 | 3.13E-03 | LCK,KIT,ERBB4 |
| | positive regulation of tyrosine | | | | | |

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|---|---|---|---|---|---|---|
| | phosphorylation of Stat5 protein | | | | | |
| 1 | cell migration | 156 | 7 | 3.50E-04 | 3.15E-03 | PDGFRB,PTK6,FGFR4,FGFR1,PDPK1,ERBB4,FYN |
| 1 | ERK 1 and ERK 2 cascade | 17 | 3 | 4.15E-04 | 3.73E-03 | FGF10,MAPK1,EGF |
| 1 | embryonic digestive tract morphogenesis | 17 | 3 | 4.15E-04 | 3.73E-03 | PDGFRA,FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| 1 | embryonic pattern specification mammary gland development regulation of ERK 1 and ERK 2 cascade | 17 | 3 | 4.15E-04 | 3.73E-03 | FGFR2,FGF10,ERBB4 |
| 1 | | 18 | 3 | 4.90E-04 | 4.31E-03 | IRS1,IRS2,NRG1 |
| 1 | | 18 | 3 | 4.90E-04 | 4.31E-03 | FRS2,FGFR2,SYK |
| 1 | aging | 119 | 6 | 5.12E-04 | 4.31E-03 | CD86,FGF2,AKT1,KL,GRB2,LCK |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of epithelial cell proliferation involved in lung morphogenesis | 4 | 2 | 5.38E-04 | 4.31E-03 | FGF7,FGFR2 |
| 1 | thyroid-stimulating hormone-secreting | 4 | 2 | 5.38E-04 | 4.31E-03 | FGF2,FGF8 |

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|---|---|---|---|---|---|---|
| | cell differentiation | | | | | |
| 1 | mesenchymal cell proliferation | 4 | 2 | 5.38E-04 | 4.31E-03 | FGF4,FGF7 |
| 1 | lacrimal gland development regulation | 4 | 2 | 5.38E-04 | 4.31E-03 | FGFR2,FGF10 |
| 1 | of early endosome to late | 4 | 2 | 5.38E-04 | 4.31E-03 | SRC,MAPK1 |

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|---|---|---|---|---|---|---|
| 1 | endosome transport positive regulation of cerebellar granule cell precursor proliferation | 4 | 2 | 5.38E-04 | 4.31E-03 | FGF2,EGF |
| 1 | JAK-STAT cascade involved | 19 | 3 | 5.72E-04 | 4.58E-03 | IRS1,IRS2,MAPK1 |

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|---|---|---|---|---|---|---|
| | in growth hormone signaling pathway | | | | | |
| 1 | organ morphogenesis positive regulation of | 80 | 5 | 5.87E-04 | 4.69E-03 | EREG,PDGFA,FGF16,FGFR2,SYK |
| 1 | transcription, DNA-dependent | 406 | 11 | 5.89E-04 | 4.71E-03 | CD86,CD80,FGF7,PDGFB,FGF23,INSR,FGF10,DNM2,ERBB4,MAPK1,EGF |
| 1 | heart devel | 125 | 6 | 6.61E-04 | 5.29E-03 | PDGFB,TP53BP2,FGF19,GAB1,ERBB4,PTPN11 |

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|---|---|---|---|---|---|---|
| | opment | | | | | |
| | cellular | | | | | |
| | response to | | | | | |
| 1 | peptide hormone stimulus | 20 | 3 | 6.64E-04 | 5.31E-03 | LCK,SRC,FYN |
| | cell proliferation | | | | | |
| 1 | regulation of protein | 288 | 9 | 7.05E-04 | 5.64E-03 | IRS2,FGF5,FGF6,AKT1,SYK,GAB1,NRG1,ERBB4,KITLG |
| 1 | phosphatase type 2A | 21 | 3 | 7.64E-04 | 5.86E-03 | PPP2R1B,PPP2R1A,PPP2R5D |

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|---|---|---|---|---|---|---|
| | activity | | | | | |
| 1 | skeletal system morphogenesis positive regulation | 21 | 3 | 7.64E-04 | 5.86E-03 | PDGFRB,FGFR2,FGFR1 |
| 1 | of gene expression activation-induced cell death of T cells | 180 | 7 | 8.11E-04 | 5.86E-03 | FGF2,FGF8,FGF9,PDGFB,CD28,FGFR4,LCK |
| 1 | | 5 | 2 | 8.36E-04 | 5.86E-03 | AKT1,RPS6 |

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|---|---|---|---|---|---|---|
| 1 | embryo development ending in birth or egg hatching peripheral nervous system | 5 | 2 | 8.36E-04 | 5.86E-03 | FGF2,TP53BP2 |
| 1 | myelin maintenance | 5 | 2 | 8.36E-04 | 5.86E-03 | AKT2,AKT1 |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of T cell receptor signaling pathway | 5 | 2 | 8.36E-04 | 5.86E-03 | LCK,TRAT1 |
| 1 | epithelial cell proliferation | 5 | 2 | 8.36E-04 | 5.86E-03 | FGF10,KIT |
| 1 | phosphate ion homeostasis | 5 | 2 | 8.36E-04 | 5.86E-03 | FGF23,FGFR4 |

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|---|---|---|---|---|---|---|
| 1 | T cell proliferation involved in immune response | 5 | 2 | 8.36E-04 | 5.86E-03 | CD86,RPS6 |
| 1 | retina vasculature development in camera-type eye | 5 | 2 | 8.36E-04 | 5.86E-03 | PDGFRB,PDGFRA |
| 1 | regulation of multicellul | 23 | 3 | 9.91E-04 | 6.94E-03 | FGFR2,PIK3CA,PTPN11 |

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|---|---|---|---|---|---|---|
| | ar organism growth hair follicle morphogenesis regulation of | | | | | |
| 1 | | 23 | 3 | 9.91E-04 | 6.94E-03 | FGF7,FGFR2,FGF10 |
| 1 | cell migration epithelial cell proliferation involved in | 54 | 4 | 1.14E-03 | 7.19E-03 | AKT2,AKT1,GAB1,ERBB4 |
| 1 | | 6 | 2 | 1.20E-03 | 7.19E-03 | FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| 1 | salivary gland morphogenesis prostate epithelial cord arborization involved in prostate glandular acinus morphogenesis | 6 | 2 | 1.20E-03 | 7.19E-03 | FRS2,FGFR2 |

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|---|---|---|---|---|---|---|
| 1 | regulation of phosphatidylinositol 3-kinase activity cellular response to granulocyte | 6 | 2 | 1.20E-03 | 7.19E-03 | PIK3R3,PIK3R2 |
| 1 | macrophage colony-stimulating factor | 6 | 2 | 1.20E-03 | 7.19E-03 | AKT1,MAPK1 |

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|---|---|---|---|---|---|---|
| | stimulus | | | | | |
| 1 | mesenchymal cell differentiation positive regulation | 6 | 2 | 1.20E-03 | 7.19E-03 | FGFR2,FGFR1 |
| 1 | of respiratory burst | 6 | 2 | 1.20E-03 | 7.19E-03 | INSR,INS |
| 1 | cellular response to platelet-der | 6 | 2 | 1.20E-03 | 7.19E-03 | PDGFRB,SRC |

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|---|---|---|---|---|---|---|
| | ived growth factor stimulus positive regulation of | | | | | |
| 1 | keratinocyte proliferation positive regulation of | 6 | 2 | 1.20E-03 | 7.19E-03 | FGF7,FGF10 |
| 1 | cyclin-dependent | 6 | 2 | 1.20E-03 | 7.19E-03 | AKT1,FGF10 |

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|---|---|---|---|---|---|---|
| | protein kinase activity involved in G1/S | | | | | |
| 1 | programmed cell death | 6 | 2 | 1.20E-03 | 7.19E-03 | KIT,KITLG |
| 1 | cell activation | 6 | 2 | 1.20E-03 | 7.19E-03 | PDGFRA,PDGFA |
| 1 | bud elongation involved in | 6 | 2 | 1.20E-03 | 7.19E-03 | FGFR2,FGF10 |

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|---|---|---|---|---|---|---|
| | lung branching | | | | | |
| 1 | bone development positive regulation of cell growth negative regulation of extrinsic apoptotic signaling | 25 | 3 | 1.26E-03 | 7.55E-03 | FGF8,PDGFA,FGFR2 |
| 1 | | 57 | 4 | 1.39E-03 | 8.34E-03 | AKT1,NRG1,HBEGF,INS |
| 1 | | 26 | 3 | 1.41E-03 | 8.44E-03 | AKT1,FGF10,NRG1 |

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|---|---|---|---|---|---|---|
| 1 | pathway in absence of ligand | 99 | 5 | 1.50E-03 | 9.03E-03 | FGF1,FGF3,FGF8,EREG,FGF18 |
| 1 | anatomical structure morphogenesis positive regulation of reactive oxygen species meta | 27 | 3 | 1.57E-03 | 9.39E-03 | PDGFRB,PDGFB,GRB2 |

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|---|---|---|---|---|---|---|
| | bolic process | | | | | |
| 1 | synaptic vesicle transport positive regulation of protein localization at cell surface | 7 | 2 | 1.62E-03 | 9.73E-03 | FGFR2,DNM2 |
| 1 | | 7 | 2 | 1.62E-03 | 9.73E-03 | NRG1,ERBB4 |
| 1 | lens fiber | 7 | 2 | 1.62E-03 | 9.73E-03 | FRS2,FGFR2 |

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|---|---|---|---|---|---|---|
| 1 | cell development glucose metabolic process | 101 | 5 | 1.64E-03 | 9.85E-03 | IRS2,AKT2,AKT1,PIK3CA,INS |
| 1 | peptidyl-threonine phosphorylation | 28 | 3 | 1.74E-03 | 0.0104 | AKT1,PDPK1,MAPK1 |
| 1 | male gonad development | 63 | 4 | 2.00E-03 | 0.012 | FGF9,INSR,KIT,KITLG |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of canonical Wnt receptor signaling pathway | 107 | 5 | 2.11E-03 | 0.0126 | FGF2,FGF9,FGFR2,FGF10,SRC |
| 1 | positive regulation of insulin receptor signaling path | 8 | 2 | 2.11E-03 | 0.0126 | IRS1,INS |

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|---|---|---|---|---|---|---|
| | way | | | | | |
| 1 | organ growth positive regulation | 8 | 2 | 2.11E-03 | 0.0126 | FGFR2,PTPN11 |
| 1 | of glycolysis | 8 | 2 | 2.11E-03 | 0.0126 | INSR,INS |
| 1 | phosphatidylinositol-3-phosphate biosynthetic process | 8 | 2 | 2.11E-03 | 0.0126 | PIK3R3,PIK3R2 |

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|---|---|---|---|---|---|---|
| 1 | lung development receptor | 64 | 4 | 2.11E-03 | 0.0127 | FGF1,FGF2,FGF18,FGFR2 |
| 1 | internalization positive | 31 | 3 | 2.31E-03 | 0.0139 | GRB2,SYK,DNM2 |
| 1 | regulation of chemotaxis | 9 | 2 | 2.65E-03 | 0.015 | PDGFRB,PDGFB |
| 1 | branching involved in labyrinthine layer | 9 | 2 | 2.65E-03 | 0.015 | GRB2,FGFR2 |

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|---|---|---|---|---|---|---|
| | morphogenesis | | | | | |
| 1 | positive regulation of lipid biosynthetic process | 9 | 2 | 2.65E-03 | 0.015 | AKT1,INS |
| 1 | positive regulation of epidermal growth factor-activ | 9 | 2 | 2.65E-03 | 0.015 | EREG,EGF |

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|---|---|---|---|---|---|---|
| | ated receptor activity | | | | | |
| 1 | response to fluid shear stress | 9 | 2 | 2.65E-03 | 0.015 | AKT1,PDGFRB |
| 1 | lung morphogenesis | 9 | 2 | 2.65E-03 | 0.015 | FGF8,MAPK1 |
| 1 | ovarian follicle development | 34 | 3 | 3.00E-03 | 0.015 | FGF7,KIT,KITLG |
| 1 | digestive tract development | 34 | 3 | 3.00E-03 | 0.015 | PDGFA,FGFR2,KIT |

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| | nt | | | | | |
| 1 | negative regulation of anoikis | 10 | 2 | 3.26E-03 | 0.0163 | PIK3CA,SRC |
| 1 | keratinocyte proliferation positive regulation | 10 | 2 | 3.26E-03 | 0.0163 | EREG,FGF10 |
| 1 | of protein localization to nucle | 10 | 2 | 3.26E-03 | 0.0163 | AKT1,INS |

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| | us | | | | | |
| 1 | male sex determination | 10 | 2 | 3.26E-03 | 0.0163 | FGF9,INSR |
| 1 | limb bud formation | 10 | 2 | 3.26E-03 | 0.0163 | FGFR2,FGF10 |
| 1 | cardiac myofibril assembly regulation | 10 | 2 | 3.26E-03 | 0.0163 | PDGFRB,PDGFRA |
| 1 | of actin cytoskeleton organ | 37 | 3 | 3.79E-03 | 0.019 | PDGFRB,PDGFA,MLST8 |

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|---|---|---|---|---|---|---|
| | ization | | | | | |
| 1 | insulin-like growth factor receptor signaling pathway negative regulation of cardiac muscle cell apoptotic | 11 | 2 | 3.92E-03 | 0.0196 | IRS1,AKT1 |
| 1 | | 11 | 2 | 3.92E-03 | 0.0196 | PDPK1,NRG1 |

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|---|---|---|---|---|---|---|
| | process | | | | | |
| 1 | mesonephros development | 11 | 2 | 3.92E-03 | 0.0196 | FGF8,FGF10 |
| 1 | peptidyl-serine phosphorylation | 77 | 4 | 4.08E-03 | 0.0204 | AKT1,PDGFB,SYK,MAPK1 |
| 1 | neural crest cell migration | 38 | 3 | 4.09E-03 | 0.0204 | FGF19,ERBB4,KITLG |
| 1 | substantia nigra devel | 38 | 3 | 4.09E-03 | 0.0204 | FGF2,FGF9,MAPKAP1 |

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|---|---|---|---|---|---|---|
| | opment | | | | | |
| | mammary | | | | | |
| | gland | | | | | |
| 1 | alveolus | 12 | 2 | 4.64E-03 | 0.0232 | ERBB4,EGF |
| | development | | | | | |
| | outflow | | | | | |
| | tract | | | | | |
| 1 | septum | 12 | 2 | 4.64E-03 | 0.0232 | FGF8,FGFR2 |
| | morphogenesis | | | | | |
| | glial | | | | | |
| | cell | | | | | |
| 1 | differentiation | 12 | 2 | 4.64E-03 | 0.0232 | FGF2,FGF5 |
| 1 | regulation of | 12 | 2 | 4.64E-03 | 0.0232 | CD28,LCK |

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|---|---|---|---|---|---|---|
| 1 | defense response to virus by virus Fc-gamma receptor signaling pathway involved in phagocytosis | 188 | 6 | 5.04E-03 | 0.0249 | PIK3R2,GRB2,SYK,PIK3CA,SRC,MAPK1 |
| 1 | actin cytoskeleton reorg | 41 | 3 | 5.04E-03 | 0.0249 | FGF7,FGF10,KIT |

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|---|---|---|---|---|---|---|
| | anization | | | | | |
| 1 | TOR signaling cascade | 13 | 2 | 5.41E-03 | 0.0249 | RPS6,RICTOR |
| 1 | aorta morphogenesis | 13 | 2 | 5.41E-03 | 0.0249 | FGF8,PDGFRB |
| 1 | positive regulation of cellular protein metabolic process | 13 | 2 | 5.41E-03 | 0.0249 | AKT1,INS |

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|---|---|---|---|---|---|---|
| 1 | regulation of peptidyl-tyrosine phosphorylation positive regulation of | 13 | 2 | 5.41E-03 | 0.0249 | PDGFRB,PDGFA |
| 1 | calcium ion import stimulatory | 13 | 2 | 5.41E-03 | 0.0249 | PDGFRB,PDGFB |
| 1 | C-type lectin recep | 86 | 4 | 6.00E-03 | 0.0249 | CLEC7A,SYK,PDPK1,SRC |

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| | tor signaling pathway positive regulation of | | | | | |
| 1 | signal transduction regulation of | 44 | 3 | 6.12E-03 | 0.0249 | CD80,AKT2,TP53BP2 |
| 1 | translation regulation of | 44 | 3 | 6.12E-03 | 0.0249 | AKT2,RPS6KA2,AKT1 |
| 1 | sequence-specifi | 14 | 2 | 6.25E-03 | 0.0249 | SYK,MAPK1 |

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|---|---|---|---|---|---|---|
| | c DNA binding transcription factor activity | | | | | |
| 1 | response to wounding | 45 | 3 | 6.51E-03 | 0.0249 | FGF7,PDGFB,PDGFA |
| 1 | phosphatidylinositol biosynthetic process | 45 | 3 | 6.51E-03 | 0.0249 | PIK3R3,PIK3R2,PIK3CA |
| 1 | stem cell maint | 45 | 3 | 6.51E-03 | 0.0249 | FGF4,FGFR1,KIT |

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|---|---|---|---|---|---|---|
| 1 | enance inner ear morphogenesis | 45 | 3 | 6.51E-03 | 0.0249 | FGF9,FGFR2,FGFR1 |
| 1 | megakaryocyte development | 15 | 2 | 7.13E-03 | 0.0249 | KIT,PTPN11 |
| 1 | gastrulation | 15 | 2 | 7.13E-03 | 0.0249 | FGF8,RPS6 |
| 1 | regulation of lipid metabolic process | 15 | 2 | 7.13E-03 | 0.0249 | IRS2,FGFR4 |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of blood vessel endothelial cell migration | 15 | 2 | 7.13E-03 | 0.0249 | AKT1,PDGFB |
| 1 | cellular response to reactive oxygen species | 15 | 2 | 7.13E-03 | 0.0249 | PDGFRA,SRC |

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|---|---|---|---|---|---|---|
| 1 | signal transduction involved in regulation of gene expression | 15 | 2 | 7.13E-03 | 0.0249 | FGF5,FGF8 |
| 1 | hemopoiesis regulation | 47 | 3 | 7.33E-03 | 0.0249 | PDGFB,LCK,KIT |
| 1 | cell proliferation | 146 | 5 | 7.74E-03 | 0.0249 | PTK6,LCK,KIT,SRC,FYN |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of calcium-mediated signaling | 16 | 2 | 8.07E-03 | 0.0249 | SYK,TRAT1 |
| 1 | labyrinthine layer blood vessel development | 16 | 2 | 8.07E-03 | 0.0249 | AKT1,MAPK1 |
| 1 | nitric oxide metabolic proce | 16 | 2 | 8.07E-03 | 0.0249 | AKT1,DNM2 |

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| | ss | | | | | |
| 1 | protein localization at cell surface | 16 | 2 | 8.07E-03 | 0.0249 | FGF7,FGF10 |
| 1 | central nervous system morphogenesis | 1 | 1 | 8.30E-03 | 0.0249 | ERBB4 |
| 1 | tear secretion | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |

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|---|---|---|---|---|---|---|
| 1 | fibroblast growth factor receptor signaling pathway involved in hemopoiesis regulation of mesenchymal stem cell differ | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | PDGFRA |

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|---|---|---|---|---|---|---|
| | entiation | | | | | |
| 1 | regulation of lymphocyte activation | 1 | 1 | 8.30E-03 | 0.0249 | LCK |
| 1 | metanephric glomerular mesangial cell development | 1 | 1 | 8.30E-03 | 0.0249 | PDGFB |

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|---|---|---|---|---|---|---|
| 1 | glycogen cell differentiation involved in embryonic placenta development abortive | 1 | 1 | 8.30E-03 | 0.0249 | AKT1 |
| 1 | mitotic cell cycle | 1 | 1 | 8.30E-03 | 0.0249 | PTPN11 |

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|---|---|---|---|---|---|---|
| 1 | motogenic signaling involved in postnatal olfactory bulb interneuron migration | 1 | 1 | 8.30E-03 | 0.0249 | FGFR1 |
| 1 | urothelial cell proliferation | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | mast cell proliferatio | 1 | 1 | 8.30E-03 | 0.0249 | KIT |

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|---|---|---|---|---|---|---|
| | n | | | | | |
| 1 | primary follicle stage vitamin E | 1 | 1 | 8.30E-03 | 0.0249 | EREG |
| 1 | metabolic process regulation of | 1 | 1 | 8.30E-03 | 0.0249 | CYP4F2 |
| 1 | osteoblast proliferation negative | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |
| 1 | regulation of | 1 | 1 | 8.30E-03 | 0.0249 | PTPN11 |

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|---|---|---|---|---|---|---|
| 1 | growth hormone secretion negative regulation of T cell anergy dendritic cell | 1 | 1 | 8.30E-03 | 0.0249 | CD86 |
| 1 | cytokine production | 1 | 1 | 8.30E-03 | 0.0249 | KIT |

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| 1 | fibroblast growth factor receptor signaling pathway involved in negative regulation of apoptotic process in bone marrow | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |

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|---|---|---|---|---|---|---|
| 1 | metanephric glomerular mesangial cell proliferation involved in metanephros development | 1 | 1 | 8.30E-03 | 0.0249 | PDGFRB |
| 1 | mesenchymal-epithelial cell | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |

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|---|---|---|---|---|---|---|
| | signaling involved in lung development coronal suture morphogenesis | | | | | |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |
| 1 | microvillus organization positive | 1 | 1 | 8.30E-03 | 0.0249 | PTPN11 |
| 1 | regulation of | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |

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|---|---|---|---|---|---|---|
| 1 | hair follicle cell proliferation alpha-beta T cell activation | 1 | 1 | 8.30E-03 | 0.0249 | INS |
| 1 | semicircular canal fusion regulation of | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | arachidonic acid secretion | 1 | 1 | 8.30E-03 | 0.0249 | SYK |

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|---|---|---|---|---|---|---|
| 1 | detection of yeast | 1 | 1 | 8.30E-03 | 0.0249 | CLEC7A |
| 1 | regulation of superoxide anion generation | 1 | 1 | 8.30E-03 | 0.0249 | SYK |
| 1 | positive regulation of meiotic cell cycle | 1 | 1 | 8.30E-03 | 0.0249 | INSR |
| 1 | oogenesis stage | 1 | 1 | 8.30E-03 | 0.0249 | RPS6 |

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|---|---|---|---|---|---|---|
| 1 | cardiac muscle cell myoblast differentiation | 1 | 1 | 8.30E-03 | 0.0249 | NRG1 |
| 1 | submandibular salivary gland formation | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | lateral sprouting from an epithelium | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |

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|---|---|---|---|---|---|---|
| 1 | angiogenesis involved in coronary vascular morphogenesis | 1 | 1 | 8.30E-03 | 0.0249 | FGF2 |
| 1 | lung proximal/distal axis specification | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | positive regulation of | 1 | 1 | 8.30E-03 | 0.0249 | EREG |

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| 1 | cytokine biosynthetic process cardiac muscle tissue regeneration positive regulation of | 1 | 1 | 8.30E-03 | 0.0249 | ERBB4 |
| 1 | inflammatory response to antig | 1 | 1 | 8.30E-03 | 0.0249 | CD28 |

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|---|---|---|---|---|---|---|
| | enic stimu lus | | | | | |
| 1 | positi ve regul ation of meta nephr ic mese nchy mal cell migra tion | 1 | 1 | 8.30E -03 | 0.02 49 | PDGFB |
| 1 | negat ive regul ation of cortis ol | 1 | 1 | 8.30E -03 | 0.02 49 | PTPN11 |

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|---|---|---|---|---|---|---|
| | secretion | | | | | |
| 1 | regulation of extrinsic apoptotic signaling pathway in absence of ligand | 1 | 1 | 8.30E-03 | 0.0249 | FGFR1 |
| 1 | cellular response to carbon mono | 1 | 1 | 8.30E-03 | 0.0249 | DNM2 |

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|---|---|---|---|---|---|---|
| | xide | | | | | |
| 1 | branch elongation involved in ureteric bud branching regulation of glomerular mesangial cell proliferation | 1 | 1 | 8.30E-03 | 0.0249 | FGF1 |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | PDGFA |

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|---|---|---|---|---|---|---|
| 1 | bronchiole morphogenesis metanephric mesenchymal cell migration positive regulation of brown fat cell proliferation | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | PDGFRB |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | FGF16 |

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|---|---|---|---|---|---|---|
| 1 | regulation of caveolin-mediated endocytosis | 1 | 1 | 8.30E-03 | 0.0249 | SRC |
| 1 | cell migration involved in coronary angiogenesis | 1 | 1 | 8.30E-03 | 0.0249 | PDGFRB |
| 1 | positive regulation of | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |

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|---|---|---|---|---|---|---|
| 1 | white fat cell proliferation cellular response to progesterone stimulus cell migration involved in mesendoderm migration | 1 | 1 | 8.30E-03 | 0.0249 | SRC |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | FGF8 |

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|---|---|---|---|---|---|---|
| 1 | platelet-derived growth factor receptor-alpha signaling pathway | 1 | 1 | 8.30E-03 | 0.0249 | PDGFRA |
| 1 | metanephros morphogenesis | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |

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|---|---|---|---|---|---|---|
| 1 | fibroblast growth factor receptor signaling pathway involved in positive regulation of cell proliferation in bone marrow | 1 | 1 | 8.30E-03 | 0.0249 | FGFR2 |

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|---|---|---|---|---|---|---|
| 1 | positive regulation of lymphotoxin A biosynthetic process | 1 | 1 | 8.30E-03 | 0.0249 | CD86 |
| 1 | positive regulation of urothelial cell proliferation | 1 | 1 | 8.30E-03 | 0.0249 | FGF10 |
| 1 | mesonephr | 1 | 1 | 8.30E-03 | 0.0249 | FGF1 |

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|---|---|---|---|---|---|---|
| | ic epithelium development negative regulation of elastin biosynthetic process | | | | | |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | HBEGF |
| | regulation of branching involved in | | | | | |
| 1 | | 1 | 1 | 8.30E-03 | 0.0249 | PDGFA |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | salivary gland morphogenesis by epithelial-mesenchymal signaling positive regulation of interleukin-4 biosynthetic proce | 1 | 1 | 8.30E-03 | 0.0249 | CD86 |

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|---|---|---|---|---|---|---|
| | ss | | | | | |
| 1 | growth factor dependent regulation of satellite cell proliferation | 1 | 1 | 8.30E-03 | 0.0249 | FGF2 |
| 1 | pallium development | 1 | 1 | 8.30E-03 | 0.0249 | FGF8 |
| 1 | embryonic | 17 | 2 | 9.06E-03 | 0.0272 | KIT,KITLG |

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|---|---|---|---|---|---|---|
| 1 | hemopoiesis positive regulation of nitric-oxide synthase activity positive regulation of smooth muscle cell migra | 17 | 2 | 9.06E-03 | 0.0272 | AKT1,INS |
| 1 | | 17 | 2 | 9.06E-03 | 0.0272 | PDGFRB,PDGFB |

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|---|---|---|---|---|---|---|
| | tion | | | | | |
| 1 | thyroid gland development | 17 | 2 | 9.06E-03 | 0.0272 | FGF8,FGF10 |
| 1 | adrenal gland development | 17 | 2 | 9.06E-03 | 0.0272 | PDGFRB,INSR |
| 1 | cartilage condensation | 17 | 2 | 9.06E-03 | 0.0272 | FGF4,FGF6 |
| 1 | negative regulation of prote | 17 | 2 | 9.06E-03 | 0.0272 | AKT1,INS |

| | | | | | | |
|---|---|---|---|---|---|---|
| | olysis | | | | | |
| 1 | phosphatidylinositol 3-kinase cascade regulation of nitric-oxide synthase activity | 17 | 2 | 9.06E-03 | 0.0272 | IRS1,PIK3R2 |
| 1 | | 17 | 2 | 9.06E-03 | 0.0272 | AKT1,DNM2 |

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|---|---|---|---|---|---|---|
| 2 | negative regulation of apoptotic process | 395 | 40 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC2,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2 |
| 2 | antigen processing and presentation of exogenous peptide antigen via MHC | 58 | 34 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| | class I, TAP-dependent | | | | | |
| 2 | Ras protein signal transduction | 192 | 36 | 1.11E-16 | 9.99E-16 | CDKN1A,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | anaphase-promoting complex-dependent proteasomal ubiquitin-dependent protein catabolic process | 63 | 37 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,SKP2,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,FZR1,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | proteasomal ubiquitin-i | 23 | 19 | 1.11E-16 | 9.99E-16 | PSMA5,PSMA6,PSMA3,PSMA4,PSMA1,PSMA2,PSME4,PSMB11,PSMA7,PSMB10,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB2,PSMB1,PSMB8,PSMB9 |

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|---|---|---|---|---|---|---|
| | ndependent protein catabolic process | | | | | |
| 2 | axon guidance | 439 | 36 | 1.11E-16 | 9.99E-16 | GSK3B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | antigen processing and presentation of | 80 | 34 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| | peptide antigen via MHC class I | | | | | |
| 2 | stimulatory C-type lectin receptor signaling pathway | 86 | 39 | 1.11E-16 | 9.99E-16 | UBE2D2,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,FBXW11,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2,MAP3K14 |

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|---|---|---|---|---|---|---|
| 2 | insulin receptor signaling pathway | 239 | 35 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | negative regulation of canonical Wnt receptor signaling pathway | 120 | 36 | 1.11E-16 | 9.99E-16 | GSK3B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | MAPK cascade | 209 | 36 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2,MAP3K14 |
| 2 | small GTPase mediated signal transduction | 522 | 36 | 1.11E-16 | 9.99E-16 | CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | activation of MAPKK activity | 181 | 36 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2,MAP3K14 |
| 2 | polyamine metabolic process | 61 | 32 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | nerve growth factor receptor signaling pathway | 312 | 39 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2 |
| 2 | G1/S transition of mitotic cell cycle | 112 | 44 | 1.11E-16 | 9.99E-16 | CDKN1A,CDKN1B,CKS1B,PSMD9,PSMD6,PSMD7,PSMD4,CCND1,PSMD5,PSMD2,PSMD3,PSMD1,SKP2,CDC25A,PSMA5,PSMA4,CDC34,CCNE2,CCNE1,PSME3,PSME1,PSME2,UBA52,PSMD10,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMB6,PSMB7,PSMB4,PSMB5,ORC1,PSMB1,PSMF1,RPS27A,CDC6,PSMB8,PSMB9,WEE1,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | cellular nitrogen compound metabolic process | 134 | 32 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | programmed cell death | 120 | 35 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | apoptotic process | 483 | 37 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,IGFBP3,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,TNIP2,PSMC2 |
| 2 | regulation of cellular amino acid metabolic process | 39 | 32 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | antigen processing and presentation of exogenous peptide antigen via MHC class I | 62 | 34 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | positive regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 54 | 36 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,FZR1,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | innate immune response | 800 | 50 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,UBE2D2,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,IKBKE,FBXW11,RBX1,PSMA5,PSMA4,TRAF3,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,RELB,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKB2,NFKBIA,PSMC3,PSMC4,TNIP2,PSMC2,MAP3K14,NFKBIB |
| 2 | positive regulation of canonical Wnt receptor signaling path | 107 | 35 | 1.11E-16 | 9.99E-16 | GSK3B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| | way | | | | | |
| 2 | mitotic cell cycle | 334 | 48 | 1.11E-16 | 9.99E-16 | CDKN1A,CDKN1B,GMNN,CKS1B,PSMD9,PSMD6,PSMD7,PSMD4,CCND1,PSMD5,PSMD2,PSMD3,PSMD1,SKP2,FBXW11,CDC25A,PSMA5,PSMA4,CCNE2,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,FZR1,PSMB5,ORC1,PSMB1,PSMF1,RPS27A,CDC6,PSMB8,PSMB9,WEE1,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | NIK/NF-kappa B cascade | 49 | 41 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,IKBKE,FBXW11,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,RELB,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKB2,PSMC3,PSMC4,PSMC2,MAP3K14 |
| 2 | gene expression | 758 | 34 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | tumor necrosis factor-mediated signaling pathway | 119 | 39 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,FBXW11,PSMA5,PSMA4,TRAF3,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2,MAP3K14 |
| 2 | Fc-epsilon receptor signaling pathway | 369 | 42 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,UBE2D2,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,FBXW11,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest | 48 | 36 | 1.11E-16 | 9.99E-16 | CDKN1A,CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | viral reproduction | 431 | 37 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2 |
| 2 | regulation of mRNA stability | 75 | 34 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | negative regulation of ubiquitin-protein | 52 | 32 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME1,PSME2,UBA52,PSMD10,PSMD12,PSMD11,PSMD14,PSMD13,PSMB6,PSMB7,PSMB4,FZR1,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | ligase activity involved in mitotic cell cycle regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 57 | 36 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,FZR1,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | protein polyubiquitination | 111 | 39 | 1.11E-16 | 9.99E-16 | UBE2D2,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,SKP2,FBXW11,PSMA5,PSMA4,CDC34,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC2,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | fibroblast growth factor receptor signaling pathway | 234 | 38 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

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|---|---|---|---|---|---|---|
| 2 | regulation of apoptotic process | 196 | 38 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,SKP2,PSMA5,PSMA4,TRAF3,PSME3,PSME4,PSME1,PSME2,UBA52,BIRC3,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2,MAP3K14 |
| 2 | vascular endothelial growth factor receptor signaling pathway | 220 | 35 | 1.11E-16 | 9.99E-16 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | proteasomal ubiquitin-dependent protein catabolic process | 133 | 24 | 1.11E-16 | 9.99E-16 | PSMD6,PSMD2,PSMD1,FBXW11,RBX1,PSMA5,PSMA6,PSMA3,PSMA4,CDC34,PSMA1,PSMA2,PSMB11,PSMA7,PSMB10,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB2,PSMB1,PSMB8,PSMB9 |
| 2 | epidermal growth factor receptor signaling pathway | 250 | 38 | 1.11E-16 | 9.99E-16 | GSK3B,CDKN1A,CDKN1B,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,RBX1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | T cell receptor signaling pathway | 116 | 38 | 1.11E-16 | 9.99E-16 | UBE2D2,PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,FBXW11,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,CUL1,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,NFKBIA,PSMC3,PSMC4,PSMC2 |
| 2 | small molecule metabolic process | 1229 | 34 | 4.60E-12 | 4.14E-11 | PSMD9,PSMD6,PSMD7,PSMD4,PSMD5,PSMD2,PSMD3,PSMD1,PSMA5,PSMA4,PSME3,PSME4,PSME1,PSME2,UBA52,PSMD10,PSMB11,PSMD12,PSMD11,PSMD14,PSMD13,PSMA8,PSMB6,PSMB7,PSMB4,PSMB5,PSMB1,PSMF1,RPS27A,PSMB8,PSMB9,PSMC3,PSMC4,PSMC2 |
| 2 | TRIF-dependent toll-like receptor signa | 58 | 10 | 2.80E-11 | 2.52E-10 | UBE2D2,IKBKE,FBXW11,UBA52,BIRC3,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ling path way | | | | | |
| 2 | MyD88-independent toll-like receptor signaling pathway | 60 | 10 | 3.89E-11 | 3.50E-10 | UBE2D2,IKBKE,FBXW11,UBA52,BIRC3,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |
| 2 | toll-like receptor 3 signaling pathway | 63 | 10 | 6.21E-11 | 5.59E-10 | UBE2D2,IKBKE,FBXW11,UBA52,BIRC3,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | positive regulation of RNA polymerase II transcriptional preinitiation complex assembly | 11 | 6 | 3.46E-10 | 2.77E-09 | PSMC5,PSMC6,PSMC3,PSMC4,PSMC1,PSMC2 |
| 2 | toll-like receptor 4 signaling path | 76 | 10 | 3.75E-10 | 3.00E-09 | UBE2D2,IKBKE,FBXW11,UBA52,BIRC3,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | way | | | | | |
| 2 | toll-like receptor signaling pathway | 84 | 10 | 9.72E-10 | 7.77E-09 | UBE2D2,IKBKE,FBXW11,UBA52,BIRC3,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |
| 2 | ubiquitin-dependent protein catabolic process | 73 | 8 | 9.34E-08 | 7.36E-07 | UBE2D2,PSMD9,PSMD3,SKP1,PSMD11,PSMD14,PSMF1,PSMC2 |
| 2 | toll-like receptor 10 signa | 49 | 7 | 1.05E-07 | 7.36E-07 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ling path way toll-like receptor 5 signaling pathway | | | | | |
| 2 | I-kappaB kinase/NF-kappaB cascade | 49 | 7 | 1.05E-07 | 7.36E-07 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |
| 2 | toll-like receptor TLR6:TLR2 | 52 | 7 | 1.57E-07 | 1.10E-06 | UBA52,BIRC3,RELB,RPS27A,NFKB2,TNIP2,MAP3K14 |
| 2 | | 55 | 7 | 2.28E-07 | 1.59E-06 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

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|---|---|---|---|---|---|---|
| 2 | signaling pathway toll-like receptor TLR1:TLR2 signaling pathway | 55 | 7 | 2.28E-07 | 1.59E-06 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |
| 2 | toll-like receptor 9 signaling pathway | 55 | 7 | 2.28E-07 | 1.59E-06 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | regulation of cyclin-dependent protein kinase activity | 34 | 6 | 2.63E-07 | 1.84E-06 | CDKN1A,CDKN1B,CKS1B,CDC25A,CCNE2,CDC6 |
| 2 | toll-like receptor 2 signaling pathway | 57 | 7 | 2.89E-07 | 2.02E-06 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |
| 2 | MyD88-dependent toll-li | 64 | 7 | 6.23E-07 | 4.36E-06 | FBXW11,UBA52,CUL1,RPS27A,NFKBIA,TNIP2,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ke receptor signaling pathway positive regulation of | | | | | |
| 2 | endopeptidase activity ER-associated | 9 | 4 | 7.68E-07 | 4.61E-06 | PSME3,PSME1,PSME2,PSMD14 |
| 2 | protein catabolic process | 43 | 6 | 1.02E-06 | 6.11E-06 | PSMC5,PSMC6,PSMC3,PSMC4,PSMC1,PSMC2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | proteasome regulatory particle assembly | 3 | 3 | 1.81E-06 | 1.08E-05 | PSMD9,PSMD5,PSMD10 |
| 2 | G2/M transition of mitotic cell cycle | 112 | 8 | 2.26E-06 | 1.36E-05 | CDKN1A,SKP2,FBXW11,CDC25A,UBA52,CUL1,RPS27A,WEE1 |
| 2 | SCF-dependent proteasomal ubiquitin-d | 32 | 5 | 4.91E-06 | 2.95E-05 | BTRC,SKP2,FBXW11,RBX1,CUL1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | epen dent protei n catab olic proce ss protei n | | | | | |
| 2 | geran ylger anyla tion | 6 | 3 | 1.42E -05 | 8.53 E-05 | CHM,RABGGTB,RABGGTA |
| 2 | prote asom e asse mbly | 6 | 3 | 1.42E -05 | 8.53 E-05 | PSMD4,PSMD11,PSMD13 |
| 2 | cytop lasmi c seque sterin g of NF-k | 6 | 3 | 1.42E -05 | 8.53 E-05 | PSMD10,NFKBIA,NFKBIB |

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|---|---|---|---|---|---|---|
| 2 | appa B DNA -dependent DNA replication initiation stress-activated | 21 | 4 | 2.13E-05 | 1.28E-04 | CDC34,CCNE2,ORC1,CDC6 |
| 2 | MAPK cascade regulation of | 46 | 5 | 2.78E-05 | 1.39E-04 | FBXW11,UBA52,CUL1,RPS27A,TNIP2 |
| 2 | transcription from RNA poly | 23 | 4 | 3.02E-05 | 1.51E-04 | UBE2D2,RBX1,UBA52,RPS27A |

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|---|---|---|---|---|---|---|
| | mera se II prom oter in respo nse to hypo xia positi ve regul ation of | | | | | |
| 2 | I-kap paB kinas e/NF-kapp aB casca de positi ve regul ation | 127 | 7 | 5.16E-05 | 2.58E-04 | IKBKE,UBA52,BIRC2,BIRC3,RPS27A,TNIP2,MAP3K14 |
| 2 | | 2 | 2 | 1.10E-04 | 5.51E-04 | CDC34,PSMC6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | of inclusion body assembly regulation | | | | | |
| 2 | of necrotic cell death | 13 | 3 | 1.39E-04 | 6.96E-04 | UBA52,BIRC3,RPS27A |
| 2 | re-entry into mitotic cell cycle | 3 | 2 | 2.47E-04 | 1.23E-03 | GSK3B,CCND1 |
| 2 | regulation of necroptosis | 3 | 2 | 2.47E-04 | 1.23E-03 | BIRC2,BIRC3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | regulation of toll-like receptor signaling pathway | 3 | 2 | 2.47E-04 | 1.23E-03 | BIRC2,BIRC3 |
| 2 | regulation of proteasomal protein catabolic process | 41 | 4 | 2.76E-04 | 1.38E-03 | PSME3,PSME1,PSME2,PSMD14 |
| 2 | programmed | 17 | 3 | 3.05E-04 | 1.52E-03 | UBA52,BIRC3,RPS27A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | necrotic cell death | | | | | |
| 2 | necroptosis | 19 | 3 | 4.21E-04 | 2.10E-03 | UBA52,BIRC3,RPS27A |
| 2 | regulation of cell cycle | 89 | 5 | 5.85E-04 | 2.92E-03 | SKP2,CDC25A,CCNE1,BIRC2,WEE1 |
| 2 | Notch signaling pathway | 141 | 6 | 7.06E-04 | 2.92E-03 | CDKN1B,CCND1,RBX1,UBA52,CUL1,RPS27A |
| 2 | positive regulation of type I interferon produ | 53 | 4 | 7.19E-04 | 2.92E-03 | UBA52,RPS27A,NFKBIA,NFKBIB |

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|---|---|---|---|---|---|---|
| | ction | | | | | |
| 2 | nucleotide-excision repair, DNA damage recognition regulation of tumor | 23 | 3 | 7.30E-04 | 2.92E-03 | RBX1,UBA52,RPS27A |
| 2 | necrosis factor-mediated signaling | 25 | 3 | 9.28E-04 | 3.71E-03 | UBA52,BIRC3,RPS27A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | pathway | | | | | |
| 2 | DNA damage response, detection of DNA damage | 28 | 3 | 1.28E-03 | 5.13E-03 | RBX1,UBA52,RPS27A |
| 2 | nucleotide-excision repair, DNA incision | 28 | 3 | 1.28E-03 | 5.13E-03 | RBX1,UBA52,RPS27A |

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|---|---|---|---|---|---|---|
| 2 | negative regulation of type I interferon production | 30 | 3 | 1.56E-03 | 6.24E-03 | IKBKE,UBA52,RPS27A |
| 2 | protein ubiquitination | 292 | 8 | 1.62E-03 | 6.49E-03 | UBE2D2,SKP2,FBXW11,RBX1,CDC34,TRAF3,BIRC3,CUL1 |
| 2 | cellular protein modification process | 67 | 4 | 1.70E-03 | 6.78E-03 | UBE2D2,RABGGTA,CDC34,UBA52 |
| 2 | protein | 9 | 2 | 2.16E-03 | 8.63E-03 | RBX1,UBA3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | neddylation | 76 | 4 | 2.67E-03 | 0.0107 | GSK3B,UBA52,CUL1,RPS27A |
| 2 | circadian rhythm | 251 | 7 | 2.88E-03 | 0.0115 | CKS1B,CCND1,CDC25A,CCNE2,FZR1,CDC6,WEE1 |
| 2 | cell division | 11 | 2 | 3.19E-03 | 0.0128 | UBA52,RPS27A |
| 2 | viral protein processing | 39 | 3 | 3.27E-03 | 0.0131 | RBX1,UBA52,RPS27A |
| 2 | translesion synthesis | 12 | 2 | 3.78E-03 | 0.0151 | CDKN1A,CCND1 |
| 2 | response to organic nitrogen | 12 | 2 | 3.78E | 0.01 | CDKN1A,CDKN1B |
| 2 | mitot | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ic cell cycle arrest positive regulation of | | | -03 | 51 | |
| 2 | cyclin-dependent protein kinase activity regulation of | 12 | 2 | 3.78E-03 | 0.0151 | CCND1,PSMD10 |
| 2 | type I interferon produ | 13 | 2 | 4.41E-03 | 0.0164 | UBA52,RPS27A |

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|---|---|---|---|---|---|---|
| | ction | | | | | |
| 2 | blastocyst development negative regulation of cyclin-dependent protein kinase activity | 13 | 2 | 4.41E-03 | 0.0164 | PSMC3,PSMC4 |
| 2 | error-free transl | 14 | 2 | 5.09E-03 | 0.0164 | CDKN1A,CDKN1B |
| 2 | | 14 | 2 | 5.09E-03 | 0.0164 | UBA52,RPS27A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | esion synthesis cellular | | | | | |
| 2 | response to hypoxia | 93 | 4 | 5.43E-03 | 0.0164 | UBE2D2,RBX1,UBA52,RPS27A |
| 2 | global genome nucleotide-excision repair | 47 | 3 | 5.48E-03 | 0.0164 | RBX1,UBA52,RPS27A |
| 2 | response to corticosterone stimulus | 15 | 2 | 5.82E-03 | 0.0175 | CDKN1A,CCND1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | error-prone translesion synthesis positive regulation of | 15 | 2 | 5.82E-03 | 0.0175 | UBA52,RPS27A |
| 2 | protein catabolic process negative regulation of | 50 | 3 | 6.49E-03 | 0.0195 | GSK3B,CDKN1B,FZR1 |
| 2 | DNA replication | 17 | 2 | 7.40E-03 | 0.0222 | GMNN,CDC6 |
| 2 | virio | 17 | 2 | 7.40E | 0.02 | UBA52,RPS27A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | n | | | -03 | 22 | |
| 2 | asse mbly regul ation of cystei ne-ty pe endo pepti dase activi ty super ior temp oral gyrus devel opme nt | 1 | 1 | 7.47E -03 | 0.02 24 | BIRC3 |
| 2 | | 1 | 1 | 7.47E -03 | 0.02 24 | GSK3B |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | canonical Wnt receptor signaling pathway involved in positive regulation of apoptotic process | 1 | 1 | 7.47E-03 | 0.0224 | GSK3B |
| 2 | regulation of RIG-I | 1 | 1 | 7.47E-03 | 0.0224 | BIRC3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | signaling pathway | | | | | |
| 2 | fat cell differentiation | 53 | 3 | 7.61E-03 | 0.0228 | GSK3B,CCND1,PSMB8 |
| 2 | nucleotide-excision repair, DNA gap filling | 18 | 2 | 8.26E-03 | 0.0248 | UBA52,RPS27A |
| 2 | response to X-ray | 18 | 2 | 8.26E-03 | 0.0248 | CDKN1A,CCND1 |
| 2 | positive regulation | 108 | 4 | 9.08E-03 | 0.0273 | UBA52,RPS27A,NFKBIA,NFKBIB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | of NF-kappa B transcription factor activity negative regulation | | | | | |
| 2 | of phosphorylation | 19 | 2 | 9.16E-03 | 0.0275 | CDKN1A,CDKN1B |
| 2 | Notch receptor processing | 19 | 2 | 9.16E-03 | 0.0275 | UBA52,RPS27A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | regulation of transcription involved in G1/S phase of mitotic cell cycle | 19 | 2 | 9.16E-03 | 0.0275 | ORC1,CDC6 |
| 3 | MyD88-independent toll-like receptor signaling | 60 | 29 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,MAPKAPK3,IRF3,TRAF6,IRF7,TLR4,TLR3,LY96,NOD1,NOD2,TANK,RELA,IRAK2,RIPK1,CD14,FADD,MAP2K7,MAP2K6,SARM1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | pathway | | | | | |
| 3 | toll-like receptor TLR6:TLR2 signaling pathway activation of | 55 | 28 | 1.11E-16 | 3.33E-15 | IKBKG,CD36,MAP3K7,MAP2K4,CHUK,RIPK2,TIRAP,TLR1,MAPKAPK3,TRAF6,PELI1,TLR6,UBE2V1,TLR4,TLR2,PELI2,LY96,NOD1,NOD2,RELA,IRAK2,CD14,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | MAPK activity | 90 | 16 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,MAP2K3,RIPK2,MAPKAPK3,TRAF6,IL1B,TLR4,NOD1,NOD2,IRAK2,MAP2K6,SAA1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | toll-like receptor 4 signaling pathway | 76 | 40 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,LBP,CD36,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,TIRAP,TLR1,MAPKAPK3,IRF3,TRAF6,PELI1,IRF7,TLR6,UBE2V1,TLR4,TLR3,TLR2,PELI2,LY96,NOD1,NOD2,TANK,RELA,IRAK1,IRAK2,RIPK1,CD14,FADD,MAP2K7,MAP2K6,MAP3K1,SARM1,TAB3,TAB2,TAB1 |
| 3 | TRIF-dependent toll-like receptor signaling pathway | 58 | 28 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,MAPKAPK3,IRF3,TRAF6,IRF7,TLR4,TLR3,LY96,NOD1,NOD2,TANK,RELA,IRAK2,RIPK1,CD14,FADD,MAP2K7,MAP2K6,TAB3,TAB2,TAB1 |
| 3 | I-kappaB kinase/NF-kappaB | 52 | 22 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,MAP3K7,TICAM2,RIPK3,CHUK,RIPK2,TIRAP,TRAF6,TLR4,TLR3,LY96,TANK,RELA,IRAK2,RIPK1,CD14,CARD9,NFKB1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | cascade | | | | | |
| 3 | positive regulation of interleukin-6 production | 38 | 12 | 1.11E-16 | 3.33E-15 | PYCARD,LBP,CD36,TICAM2,RIPK2,IL1B,TLR4,TLR3,TLR2,NOD1,NOD2,CARD9 |
| 3 | apoptotic process | 483 | 27 | 1.11E-16 | 3.33E-15 | HMGB1,PYCARD,CASP10,CASP1,CASP2,IKBKG,MAP3K7,MAP2K4,TICAM2,RIPK2,IRF3,IL1B,TLR4,TLR3,TLR2,LY96,NOD1,RIPK1,CD14,FADD,BID,MAP2K7,MAP2K6,LY86,TNFRSF10B,TNFRSF10A,FAS |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | toll-like receptor 10 signaling pathway | 49 | 22 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,MAP2K4,CHUK,RIPK2,MAPKAPK3,TRAF6,PELI1,TLR10,UBE2V1,TLR5,PELI2,NOD1,NOD2,RELA,IRAK2,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | innate immune response | 800 | 58 | 1.11E-16 | 3.33E-15 | HMGB1,ECSIT,PYCARD,TBK1,CASP10,IKBKG,LBP,CD36,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,CD180,TIRAP,TLR1,MAPKAPK3,IRF3,TRAF6,IL1B,PELI1,IRF7,TLR10,TLR6,UBE2V1,TLR5,TLR4,TLR3,CARD11,TLR2,DHX9,PELI2,LY96,NOD1,NLRC4,NOD2,TANK,AGER,MALT1,RELA,IRAK2,S100A12,RIPK1,CD14,FADD,MAP2K7,MAP2K6,MAP3K1,CARD9,LY86,S100B,NFKB1,SARM1,SAA1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | toll-like receptor 5 signaling pathway positive regulation of NF-kappa B transcription factor activity | 49 | 22 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,MAP2K4,CHUK,RIPK2,MAPKAPK3,TRAF6,PELI1,TLR10,UBE2V1,TLR5,PELI2,NOD1,NOD2,RELA,IRAK2,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | | 108 | 28 | 1.11E-16 | 3.33E-15 | PYCARD,PIDD1,IKBKG,MAP3K7,RIPK3,CHUK,RIPK2,IRAK3,TIRAP,TRAF6,IL1B,UBE2V1,TLR4,TLR3,CARD11,TLR2,NOD1,NLRC4,NOD2,AGER,MALT1,RELA,IRAK2,S100A12,RIPK1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | inflammatory response | 310 | 29 | 1.11E-16 | 3.33E-15 | HMGB1,PYCARD,TBK1,IKBKG,TICAM2,CHUK,RIPK2,CD180,TIRAP,TLR1,IL1B,TLR10,TLR6,TLR5,TLR3,TLR2,LY96,NOD1,NLRC4,AGER,RELA,IRAK2,S100A12,CD14,TNFRSF10C,LY86,TNFRSF10B,TNFRSF10A,TNFRSF10D |
| 3 | positive regulation of I-kappaB kinase/NF-kappaB cascade | 127 | 29 | 1.11E-16 | 3.33E-15 | TBK1,CASP10,IKBKG,CD36,MAP3K7,TICAM2,CHUK,RIPK2,TIRAP,IRF3,TRAF6,IL1B,PELI1,TLR6,UBE2V1,CARD11,PELI2,NOD1,NOD2,MALT1,RELA,S100A12,RIPK1,FADD,CARD9,TNFRSF10B,S100B,TAB2,MYD88 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | toll-like receptor TLR1:TLR2 signaling pathway positive regulation of | 55 | 28 | 1.11E-16 | 3.33E-15 | IKBKG,CD36,MAP3K7,MAP2K4,CHUK,RIPK2,TIRAP,TLR1,MAPKAPK3,TRAF6,PELI1,TLR6,UBE2V1,TLR4,TLR2,PELI2,LY96,NOD1,NOD2,RELA,IRAK2,CD14,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | tumor necrosis factor production | 40 | 16 | 1.11E-16 | 3.33E-15 | HMGB1,PYCARD,LBP,CD36,RIPK2,TIRAP,TLR4,TLR3,TLR2,LY96,NOD1,NOD2,RIPK1,CD14,FADD,CARD9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | stress-activated MAPK cascade MyD88-dependent toll-like receptor signaling pathway | 46 | 16 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,MAP2K4,CHUK,RIPK2,MAPKAPK3,TRAF6,NOD1,NOD2,IRAK2,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | nucleotide-binding oligomerization | 64 | 32 | 1.11E-16 | 3.33E-15 | IKBKG,CD36,MAP3K7,MAP2K4,CHUK,RIPK2,IRAK3,TIRAP,TLR1,MAPKAPK3,TRAF6,PELI1,TLR10,TLR6,UBE2V1,TLR5,TLR4,TLR2,PELI2,LY96,NOD1,NOD2,RELA,IRAK2,CD14,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1,MYD88 |
| 3 | | 21 | 14 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,CHUK,RIPK2,TRAF6,UBE2V1,NOD1,NOD2,IRAK2,MAP2K6,CARD9,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | domain containing signaling pathway toll-like receptor 3 signaling pathway toll-like receptor 2 signaling pathway | 63 | 29 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,MAPKAPK3,IRF3,TRAF6,IRF7,TLR4,TLR3,LY96,NOD1,NOD2,TANK,RELA,IRAK2,RIPK1,CD14,FADD,MAP2K7,MAP2K6,SARM1,TAB3,TAB2,TAB1 |
| 3 | | 57 | 28 | 1.11E-16 | 3.33E-15 | IKBKG,CD36,MAP3K7,MAP2K4,CHUK,RIPK2,TIRAP,TLR1,MAPKAPK3,TRAF6,PELI1,TLR6,UBE2V1,TLR4,TLR2,PELI2,LY96,NOD1,NOD2,RELA,IRAK2,CD14,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | toll-like receptor 9 signaling pathway | 55 | 21 | 1.11E-16 | 3.33E-15 | IKBKG,MAP3K7,MAP2K4,CHUK,RIPK2,MAPKAPK3,TRAF6,PELI1,IRF7,UBE2V1,PELI2,NOD1,NOD2,RELA,IRAK2,MAP2K7,MAP2K6,MAP3K1,TAB3,TAB2,TAB1 |
| 3 | nucleotide-binding domain, leucine rich repeat containing receptor signaling path | 35 | 16 | 1.11E-16 | 3.33E-15 | PYCARD,IKBKG,MAP3K7,CHUK,RIPK2,TRAF6,UBE2V1,NOD1,NLRC4,NOD2,IRAK2,MAP2K6,CARD9,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | way | | | | | |
| 3 | toll-like receptor signaling pathway | 84 | 41 | 1.11E-16 | 3.33E-15 | TBK1,IKBKG,LBP,CD36,MAP3K7,MAP2K4,TICAM2,RIPK3,CHUK,RIPK2,TIRAP,TLR1,MAPKAPK3,IRF3,TRAF6,PELI1,IRF7,TLR10,TLR6,UBE2V1,TLR5,TLR4,TLR3,TLR2,PELI2,LY96,NOD1,NOD2,TANK,RELA,IRAK2,RIPK1,CD14,FADD,MAP2K7,MAP2K6,MAP3K1,SARM1,TAB3,TAB2,TAB1 |
| 3 | JNK cascade | 44 | 12 | 4.44E-16 | 1.29E-14 | IKBKG,MAP3K7,MAP2K4,RIPK2,TRAF6,NOD1,NOD2,IRAK2,MAP2K7,TAB3,TAB2,TAB1 |
| 3 | stimulatory C-type lectin receptor | 86 | 14 | 1.55E-15 | 4.20E-14 | PYCARD,IKBKG,MAP3K7,CHUK,TRAF6,IL1B,UBE2V1,CARD11,MALT1,RELA,CARD9,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | signaling pathway activation of cysteine-type endopeptidase activity involved in apoptotic signaling pathway | 15 | 9 | 2.22E-15 | 5.77E-14 | TICAM2,TLR4,TLR3,LY96,RIPK1,CD14,FADD,TNFRSF10B,TNFRSF10A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of interleukin-8 production | 25 | 10 | 3.22E-15 | 8.05E-14 | LBP,TIRAP,IL1B,TLR5,TLR4,TLR3,TLR2,NOD2,RIPK1,FADD |
| 3 | positive regulation of JNK cascade | 51 | 11 | 9.97E-14 | 2.49E-12 | HMGB1,PYCARD,RIPK2,TIRAP,IL1B,TLR4,TLR3,NOD1,NOD2,RIPK1,CARD9 |
| 3 | activation of cysteine-type endopepti | 74 | 12 | 1.96E-13 | 4.69E-12 | PYCARD,PIDD1,CASP10,CASP2,NOD1,NLRC4,RIPK1,FADD,BID,CRADD,TNFRSF10B,TNFRSF10A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | dase activity involved in apoptotic process activation of NF-kappa B-inducing kinase activity | | | | | |
| 3 | | 15 | 8 | 2.16E-13 | 4.98E-12 | IKBKG,MAP3K7,TRAF6,TLR6,TLR3,MALT1,TNFRSF10B,TNFRSF10A |
| 3 | cellular response to mech | 59 | 11 | 4.74E-13 | 1.04E-11 | CASP2,MAP2K4,IL1B,TLR5,TLR4,TLR3,FADD,MAP3K1,CRADD,TNFRSF10B,TNFRSF10A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | anical stimulus cellular response to lipoteichoic acid cell surface receptor signaling pathway | 9 | 7 | 5.28E-13 | 1.16E-11 | LBP,CD36,RIPK2,TIRAP,TLR4,TLR2,CD14 |
| 3 | response to lipopolysaccharide | 236 | 17 | 5.85E-13 | 1.23E-11 | CASP10,IKBKG,CD36,MAP3K7,CHUK,TIRAP,MAPKAPK3,LY96,AGER,RIPK1,CD14,FADD,TNFRSF10B,TNFRSF10A,TAB3,TAB2,TAB1 |
| 3 | | 144 | 14 | 1.56E-12 | 3.13E-11 | LBP,CHUK,IRAK3,TIRAP,MAPKAPK3,PELI1,TLR4,LY96,NOD2,SOCS1,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | tumor necrosis factor-mediated signaling pathway | 119 | 13 | 2.49E-12 | 4.98E-11 | PYCARD,IKBKG,MAP3K7,CHUK,RIPK1,FADD,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D,TAB3,TAB2,TAB1 |
| 3 | lipopolysaccharide-mediated signaling pathway | 22 | 8 | 4.46E-12 | 8.47E-11 | LBP,RIPK2,IRF3,IL1B,TLR4,TLR2,LY96,IRAK2 |
| 3 | positive regulation of | 22 | 8 | 4.46E-12 | 8.47E-11 | HMGB1,TBK1,RIPK2,IRF3,IRF7,TLR4,TLR3,TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | interferon-beta production positive regulation of type I interferon production | 53 | 10 | 5.13E-12 | 9.23E-11 | TBK1,IKBKG,RIPK3,CHUK,IRF3,IRF7,DHX9,RELA,RIPK1,CD14 |
| 3 | programmed cell death | 120 | 12 | 5.03E-11 | 9.05E-10 | HMGB1,TICAM2,RIPK3,TLR4,TLR3,LY96,RIPK1,CD14,FADD,BID,TNFRSF10B,TNFRSF10A |
| 3 | extrinsic apoptotic signaling | 47 | 9 | 5.50E-11 | 9.34E-10 | TICAM2,TLR4,TLR3,LY96,RIPK1,CD14,FADD,TNFRSF10B,TNFRSF10A |

| | | | | | | |
|---|---|---|---|---|---|---|
| | pathway | | | | | |
| 3 | regulation of cytokine secretion | 9 | 6 | 6.40E-11 | 1.09E-09 | TLR1,TLR10,TLR6,TLR5,TLR4,SOCS1 |
| 3 | defense response to Gram-positive bacterium | 53 | 9 | 1.57E-10 | 2.51E-09 | TBK1,LBP,CD36,RIPK2,TIRAP,TLR2,NOD1,NOD2,CARD9 |
| 3 | positive regulation of interferon- | 12 | 6 | 3.54E-10 | 5.66E-09 | HMGB1,TBK1,RIPK2,IRF3,IRF7,TLR4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | alpha production | | | | | |
| 3 | positive regulation of interleukin-12 production | 24 | 7 | 4.66E-10 | 7.45E-09 | CD36,RIPK2,TIRAP,TLR4,TLR3,TLR2,NOD2 |
| 3 | T cell receptor signaling pathway | 116 | 11 | 5.87E-10 | 8.81E-09 | IKBKG,MAP3K7,CHUK,RIPK2,TRAF6,BTK,UBE2V1,CARD11,MALT1,RELA,TAB2 |
| 3 | cellular response to lipop | 88 | 10 | 6.73E-10 | 1.01E-08 | PYCARD,LBP,CD36,TICAM2,CD180,TRAF6,TLR5,TLR4,RELA,CD14 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | olysaccharide induction of apoptosis via death domain receptors positive regulation of interleukin-6 biosynthetic proce | 27 | 7 | 1.04E-09 | 1.57E-08 | FADD,BID,CRADD,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D |
| 3 | | 7 | 5 | 1.89E-09 | 2.64E-08 | TIRAP,TLR1,TRAF6,IL1B,TLR6 |

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|---|---|---|---|---|---|---|
| | ss | | | | | |
| 3 | programmed necrotic cell death positive regulation of | 17 | 6 | 2.78E-09 | 3.89E-08 | RIPK3,IRF3,RIPK1,FADD,TNFRSF10B,TNFRSF10A |
| 3 | interferon-gamma production | 36 | 7 | 7.44E-09 | 1.04E-07 | PYCARD,TICAM2,RIPK2,IL1B,TLR4,CD14,FADD |
| 3 | I-kappaB phos | 10 | 5 | 1.11E-08 | 1.44E-07 | MAP3K7,CHUK,TLR4,TLR3,TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | phorylation regulation of apoptotic process positive regulation of apoptotic process | 196 | 12 | 1.19E-08 | 1.55E-07 | CASP8,CASP1,MAP3K8,MAP2K3,CARD11,BCL10,MALT1,MAP2K6,MAP3K1,CARD9,TNFRSF10B,SARM1 |
| 3 | | 249 | 13 | 1.80E-08 | 2.34E-07 | HMGB1,PYCARD,PIDD1,CASP2,RIPK2,TRAF6,IL1B,NLRC4,RIPK1,FADD,BID,MAP2K6,S100B |
| 3 | cellular response to diacyl bacterial | 4 | 4 | 2.22E-08 | 2.89E-07 | CD36,TLR6,TLR2,CD14 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | lipopeptide | | | | | |
| 3 | negative regulation of growth of symbiont in host response to exogenous dsRNA defense response to bacterium | 15 | 5 | 8.17E-08 | 9.81E-07 | LBP,CD36,TIRAP,TLR2,NOD2 |
| 3 | | 31 | 6 | 9.47E-08 | 1.14E-06 | RIPK2,IRAK3,IRF3,TLR3,NOD2,CARD9 |
| 3 | | 80 | 8 | 9.87E-08 | 1.18E-06 | TLR6,TLR5,TLR4,TLR3,NOD1,NLRC4,NOD2,S100A12 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | interleukin-1 beta secretion positive regulation of | 7 | 4 | 2.05E-07 | 2.46E-06 | CD36,TLR6,TLR4,NLRC4 |
| 3 | toll-like receptor 4 signaling pathway | 7 | 4 | 2.05E-07 | 2.46E-06 | LBP,TICAM2,TIRAP,PELI1 |
| 3 | Fc-epsilon receptor signaling path | 369 | 14 | 2.42E-07 | 2.67E-06 | IKBKG,MAP3K7,MAP2K4,CHUK,TRAF6,UBE2V1,CARD11,MALT1,RELA,MAP2K7,MAP3K1,TAB3,TAB2,TAB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | way | | | | | |
| 3 | necroptosis positive regulation | 19 | 5 | 2.61E-07 | 2.87E-06 | RIPK3,RIPK1,FADD,TNFRSF10B,TNFRSF10A |
| 3 | of chemokine production | 19 | 5 | 2.61E-07 | 2.87E-06 | LBP,RIPK2,TLR4,TLR3,TLR2 |
| 3 | signal transduction | 858 | 21 | 2.74E-07 | 3.01E-06 | PYCARD,PIDD1,MAP2K4,RIPK3,RIPK2,TICAM1,SIGIRR,TLR1,MAPKAPK3,IL1B,TLR6,TLR3,TLR2,NOD1,TANK,MAP2K7,MAP2K6,TNFRSF10C,TNFRSF10A,TNFRSF10D,FAS |
| 3 | positive regulation of lipop | 8 | 4 | 3.48E-07 | 3.83E-06 | CD180,TRAF6,LY96,LY86 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | olysaccharide-mediated signaling pathway | | | | | |
| 3 | positive regulation of ERK 1 and ERK 2 cascade | 132 | 9 | 3.72E-07 | 4.10E-06 | HMGB1,PYCARD,CD36,RIPK2,TIRAP,IL1B,TLR4,NOD1,NOD2 |
| 3 | positive regulation of interl | 11 | 4 | 1.22E-06 | 1.22E-05 | MAP3K7,RIPK2,TRAF6,MALT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | eukin-2 production positive regulation of tumor | | | | | |
| 3 | necrosis factor biosynthetic process positive | 11 | 4 | 1.22E-06 | 1.22E-05 | LBP,TLR1,TLR4,TLR2 |
| 3 | regulation of NLRP3 | 3 | 3 | 1.41E-06 | 1.41E-05 | CD36,TLR6,TLR4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | inflammasome complex assembly regulation of dendritic cell cytokine production cellular response to triacyl bacterial lipop | 3 | 3 | 1.41E-06 | 1.41E-05 | TLR4,TLR3,TLR2 |
| 3 | | 3 | 3 | 1.41E-06 | 1.41E-05 | TLR1,TLR2,CD14 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | eptide | | | | | |
| 3 | positive regulation of JUN kinase activity | 28 | 5 | 1.73E-06 | 1.73E-05 | MAP3K7,TRAF6,IL1B,TLR6,AGER |
| 3 | response to interleukin-1 | 29 | 5 | 2.05E-06 | 1.84E-05 | RIPK2,IRAK3,TRAF6,RELA,IRAK2 |
| 3 | positive regulation of inflammatory | 53 | 6 | 2.10E-06 | 1.89E-05 | TLR10,TLR4,TLR3,TLR2,AGER,S100A12 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | response | | | | | |
| 3 | positive regulation of nitric-oxide synthase biosynthetic process | 13 | 4 | 2.36E-06 | 2.13E-05 | TLR4,TLR2,NOD2,MAP2K6 |
| 3 | regulation of necrotic cell death | 13 | 4 | 2.36E-06 | 2.13E-05 | RIPK1,FADD,TNFRSF10B,TNFRSF10A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | cellular response to peptidoglycan | 4 | 3 | 3.34E-06 | 3.00E-05 | RIPK2,TLR2,NOD2 |
| 3 | Toll signaling pathway | 4 | 3 | 3.34E-06 | 3.00E-05 | PELI1,PELI3,PELI2 |
| 3 | negative regulation of tumor necrosis factor production | 33 | 5 | 3.82E-06 | 3.41E-05 | LBP,IRAK3,BPI,TLR4,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of T cell activation | 15 | 4 | 4.15E-06 | 3.41E-05 | PYCARD,MAP3K7,TRAF6,MALT1 |
| 3 | immune response | 405 | 13 | 4.26E-06 | 3.41E-05 | IKBKG,CHUK,TLR1,TLR10,BPI,TLR6,TLR4,TLR2,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D,FAS |
| 3 | positive regulation of toll-like receptor signaling pathway | 5 | 3 | 6.48E-06 | 5.19E-05 | TLR5,TLR3,TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | cellular response to muramyl dipeptide nucleotide-binding oligomerization | 5 | 3 | 6.48E-06 | 5.19E-05 | RIPK2,NOD1,NOD2 |
| 3 | domain containing 2 signaling pathway | 5 | 3 | 6.48E-06 | 5.19E-05 | RIPK2,NOD2,RELA |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | negative regulation of cysteine-type endopeptidase activity involved in apoptotic process | 67 | 6 | 7.92E-06 | 6.33E-05 | RIPK1,FADD,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D |
| 3 | detection of bacterium | 6 | 3 | 1.11E-05 | 8.92E-05 | NOD1,NLRC4,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of interleukin-12 biosynthetic process | 6 | 3 | 1.11E-05 | 8.92E-05 | TRAF6,TLR4,RELA |
| 3 | positive regulation of interferon-beta biosynthetic process | 6 | 3 | 1.11E-05 | 8.92E-05 | TBK1,TLR4,TLR3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of extrinsic apoptotic signaling pathway | 20 | 4 | 1.28E-05 | 1.02E-04 | PYCARD,RIPK1,FADD,BID |
| 3 | positive regulation of NF-kappaB import into nucleus | 21 | 4 | 1.54E-05 | 1.23E-04 | IL1B,TLR4,TLR3,TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of macrophage cytokine production | 7 | 3 | 1.76E-05 | 1.23E-04 | CD36,TLR4,TLR2 |
| 3 | positive regulation of T cell cytokine production | 7 | 3 | 1.76E-05 | 1.23E-04 | MAP3K7,TRAF6,MALT1 |
| 3 | positive regulation | 22 | 4 | 1.85E-05 | 1.29E-04 | IRF3,TLR2,CD14,SAA1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | of cytokine secretion T-helper 1 type immune response positive regulation of type I interferon-mediated signaling pathway | | | | | |
| 3 | | 8 | 3 | 2.62E-05 | 1.83E-04 | TRAF6,TLR6,TLR4 |
| 3 | | 8 | 3 | 2.62E-05 | 1.83E-04 | IRF3,IRF7,FADD |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | regulation of tumor necrosis factor-mediated signaling pathway activation of innate immune response | 25 | 4 | 3.04E-05 | 2.13E-04 | PYCARD,IKBKG,CHUK,RIPK1 |
| 3 | positive regul | 9 | 3 | 3.71E-05 | 2.59E-04 | HMGB1,PYCARD,NLRC4 |
| 3 | | 9 | 3 | 3.71E-05 | 2.59E-04 | LBP,CD36,AGER |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | ation of phagocytosis, engulfment interleukin-1-mediated signaling pathway positive regulation | 9 | 3 | 3.71E-05 | 2.59E-04 | IRAK3,TRAF6,IRAK2 |
| 3 | of reactive oxygen speci | 27 | 4 | 4.09E-05 | 2.86E-04 | CD36,RIPK3,AGER,RIPK1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | es meta bolic proce ss defen se | | | | | |
| 3 | respo nse to virus | 136 | 7 | 4.70E -05 | 3.29 E-04 | PYCARD,TBK1,IRF3,TLR3,RELA,FADD,CARD9 |
| 3 | respo nse to mura myl dipep tide negat ive regul ation | 10 | 3 | 5.06E -05 | 3.54 E-04 | NOD2,RELA,CARD9 |
| 3 | of NF-k appa B trans cripti | 60 | 5 | 6.56E -05 | 4.59 E-04 | PYCARD,IRAK3,PELI1,NOD2,IRAK2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | on factor activity positive regulation of nitric oxide biosynthetic process | | | | | |
| 3 | positive regulation of B cell proliferation | 32 | 4 | 7.86E-05 | 4.71E-04 | IL1B,TLR5,TLR4,TLR2 |
| 3 | | 33 | 4 | 8.84E-05 | 5.30E-04 | TIRAP,PELI1,TLR4,CARD11 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | cellular response to bacterial lipopeptide | 2 | 2 | 9.37E-05 | 5.62E-04 | TIRAP,TLR2 |
| 3 | positive regulation of necroptosis | 2 | 2 | 9.37E-05 | 5.62E-04 | RIPK3,RIPK1 |
| 3 | positive regulation of interleukin-1 secretion | 2 | 2 | 9.37E-05 | 5.62E-04 | HMGB1,SAA1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | detection of diacyl bacterial lipopeptide | 2 | 2 | 9.37E-05 | 5.62E-04 | TLR6,TLR2 |
| 3 | myeloid dendritic cell activation detection of | 2 | 2 | 9.37E-05 | 5.62E-04 | HMGB1,PYCARD |
| 3 | triacyl bacterial lipopeptid | 2 | 2 | 9.37E-05 | 5.62E-04 | TLR1,TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | e | | | | | |
| 3 | negative regulation of interleukin-12 production defense response to Gram-negative bacterium detection of biotic | 13 | 3 | 1.10E-04 | 6.57E-04 | IRAK3,TLR2,NOD2 |
| 3 | | 35 | 4 | 1.11E-04 | 6.64E-04 | PYCARD,LBP,BPI,TLR4 |
| 3 | | 3 | 2 | 2.10E-04 | 1.26E-03 | NOD1,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | stimulus MDA-5 signaling pathway cytokine secretion | 3 | 2 | 2.10E-04 | 1.26E-03 | IRF3,IRF7 |
| 3 | involved in immune response | 3 | 2 | 2.10E-04 | 1.26E-03 | TLR2,NOD2 |
| 3 | B cell proliferation involved in | 3 | 2 | 2.10E-04 | 1.26E-03 | CD180,TLR4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | immune response response to interleukin-12 positive regulation of interleukin-1 beta secretion negative regulation of interl | 3 | 2 | 2.10E-04 | 1.26E-03 | TICAM2,RIPK2 |
| 3 | | 18 | 3 | 2.84E-04 | 1.70E-03 | HMGB1,PYCARD,NOD2 |
| 3 | | 19 | 3 | 3.32E-04 | 1.86E-03 | IRAK3,BPI,TLR4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | eukin-6 production positive regulation of transcription from RNA polymerase II promoter | | | | | |
| 3 | | 799 | 15 | 3.57E-04 | 1.86E-03 | HMGB1,TBK1,IKBKG,CHUK,RIPK2,TRAF6,IL1B,IRF7,TLR4,TLR3,TLR2,NOD2,RELA,RIPK1,FADD |
| | negative regulation of macropha | | | | | |
| 3 | | 4 | 2 | 3.71E-04 | 1.86E-03 | IRF7,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ge apoptotic process detection of | | | | | |
| 3 | lipopolysaccharide regulation of | 4 | 2 | 3.71E-04 | 1.86E-03 | TLR4,LY96 |
| 3 | adaptive immune response type I | 4 | 2 | 3.71E-04 | 1.86E-03 | RIPK3,IRF7 |
| 3 | interferon biosyntheti | 4 | 2 | 3.71E-04 | 1.86E-03 | IRF3,IRF7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | c process NIK/NF-kappa B cascade positive regulation | | | | | |
| 3 | | 49 | 4 | 3.95E-04 | 1.98E-03 | RIPK3,CHUK,RELA,NFKB1 |
| 3 | of protein ubiquitination positive regulation | 49 | 4 | 3.95E-04 | 1.98E-03 | RIPK2,TRAF6,PELI1,MALT1 |
| 3 | of phagocyto | 21 | 3 | 4.44E-04 | 2.22E-03 | PYCARD,IL1B,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | sis | | | | | |
| 3 | response to tumor necrosis factor positive regulation of neutrophil chemotaxis activation of protein kinas | 21 | 3 | 4.44E-04 | 2.22E-03 | RIPK1,CD14,MAP2K7 |
| 3 | | 21 | 3 | 4.44E-04 | 2.22E-03 | LBP,TIRAP,IL1B |
| 3 | | 53 | 4 | 5.30E-04 | 2.65E-03 | MAP3K8,RIPK3,TRAF6,MAP3K1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | e activity | | | | | |
| 3 | response to virus | 95 | 5 | 5.41E-04 | 2.71E-03 | TBK1,IKBKG,CHUK,IRAK3,IRF7 |
| 3 | regulation of cell proliferation | 146 | 6 | 5.50E-04 | 2.75E-03 | BTK,BID,TNFRSF10C,TNFRSF10B,TNFRSF10A,TNFRSF10D |
| 3 | positive regulation of oxidoreductase activity | 5 | 2 | 5.78E-04 | 2.89E-03 | RIPK3,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | negative regulation of cytokine-mediated signaling pathway | 5 | 2 | 5.78E-04 | 2.89E-03 | IRAK3,SIGIRR |
| 3 | response to stilbenoid | 5 | 2 | 5.78E-04 | 2.89E-03 | CD36,IL1B |
| 3 | positive regulation of adaptive immune | 5 | 2 | 5.78E-04 | 2.89E-03 | PYCARD,FADD |

| | | | | | | |
|---|---|---|---|---|---|---|
| | response | | | | | |
| 3 | positive regulation of toll-like receptor 3 signaling pathway | 5 | 2 | 5.78E-04 | 2.89E-03 | TIRAP,PELI1 |
| 3 | macropinocytosis | 5 | 2 | 5.78E-04 | 2.89E-03 | PYCARD,MAPKAPK3 |
| 3 | response to peptidoglycan | 5 | 2 | 5.78E-04 | 2.89E-03 | IRAK3,CARD9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | negative regulation of insulin receptor signaling pathway | 24 | 3 | 6.52E-04 | 3.26E-03 | IL1B,RELA,SOCS1 |
| 3 | apoptotic signaling pathway | 101 | 5 | 7.12E-04 | 3.31E-03 | CASP10,CASP2,RIPK3,TRAF6,FADD |
| 3 | death-inducing signaling complex | 6 | 2 | 8.28E-04 | 3.31E-03 | RIPK1,FADD |

| | | | | | | |
|---|---|---|---|---|---|---|
| | assembly | | | | | |
| 3 | response to fungus | 6 | 2 | 8.28E-04 | 3.31E-03 | MALT1,CARD9 |
| 3 | germ cell programmed cell death | 6 | 2 | 8.28E-04 | 3.31E-03 | CASP2,IL1B |
| 3 | macrophage activation involved in immune response | 6 | 2 | 8.28E-04 | 3.31E-03 | HMGB1,LBP |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of chemokine biosynthetic process | 6 | 2 | 8.28E-04 | 3.31E-03 | IL1B,TLR3 |
| 3 | cytokine-mediated signaling pathway | 223 | 7 | 9.27E-04 | 3.71E-03 | IRAK3,IRAK4,IRF3,IL1B,IRF7,RELA,SOCS1 |
| 3 | regulation of mitotic cell | 63 | 4 | 1.00E-03 | 4.02E-03 | MAP3K8,MAP2K3,MAP2K6,MAP3K1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | cycle | | | | | |
| 3 | positive regulation of interleukin-1 beta production | 7 | 2 | 1.12E-03 | 4.49E-03 | NOD1,NOD2 |
| 3 | positive regulation of dendritic cell antigen processing and | 7 | 2 | 1.12E-03 | 4.49E-03 | NOD1,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | presentation | | | | | |
| 3 | acute-phase response activation of | 29 | 3 | 1.12E-03 | 4.49E-03 | LBP,SIGIRR,SAA1 |
| 3 | JUN kinase activity negative regulation of | 31 | 3 | 1.36E-03 | 5.43E-03 | RIPK1,MAP2K7,MAP3K1 |
| 3 | extrinsic apopt | 31 | 3 | 1.36E-03 | 5.43E-03 | PELI3,RELA,RIPK1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | otic signaling pathway glycoprotein | | | | | |
| 3 | metabolic process positive regulation of | 8 | 2 | 1.46E-03 | 5.84E-03 | IL1B,AGER |
| 3 | cysteine-type endopeptidase activity invol | 33 | 3 | 1.62E-03 | 6.49E-03 | HMGB1,PYCARD,NOD1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ved in apoptotic process extrinsic apoptotic signaling | | | | | |
| 3 | pathway in absence of ligand stress-activated | 33 | 3 | 1.62E-03 | 6.49E-03 | CASP2,IL1B,FADD |
| 3 | protein kinase | 33 | 3 | 1.62E-03 | 6.49E-03 | MAP3K8,MAP2K3,MAP2K6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | signaling cascade protein | | | | | |
| 3 | oligomerization positive regulation | 34 | 3 | 1.77E-03 | 7.06E-03 | NOD1,NOD2,MALT1 |
| 3 | of prostaglandin secretion | 9 | 2 | 1.84E-03 | 7.35E-03 | IL1B,MAP2K6 |
| 3 | macrophage activation | 9 | 2 | 1.84E-03 | 7.35E-03 | TLR1,TLR4 |
| 3 | response to | 35 | 3 | 1.92E-03 | 7.66E-03 | IL1B,CD14,MAP2K7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | heat | | | | | |
| 3 | cellular response to tumor necrosis factor positive regulation of macrophage differentiation positive regulation of | 77 | 4 | 2.08E-03 | 8.33E-03 | PYCARD,CHUK,RELA,RIPK1 |
| 3 | | 10 | 2 | 2.26E-03 | 9.04E-03 | RIPK1,FADD |
| 3 | | 10 | 2 | 2.26E-03 | 9.04E-03 | IL1B,CARD11 |

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|---|---|---|---|---|---|---|
| 3 | interleukin-2 biosynthetic process negative regulation of interleukin-17 production | 10 | 2 | 2.26E-03 | 9.04E-03 | TLR4,TLR2 |
| 3 | membrane protein intracellular doma | 10 | 2 | 2.26E-03 | 9.04E-03 | TRAF6,RELA |

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|---|---|---|---|---|---|---|
| | in proteolysis | | | | | |
| 3 | positive regulation of interleukin-6 secretion | 11 | 2 | 2.72E-03 | 0.0109 | HMGB1,PYCARD |
| 3 | defense response | 42 | 3 | 3.20E-03 | 0.0128 | NOD1,NOD2,MALT1 |
| 3 | null | 1866 | 23 | 3.34E-03 | 0.0133 | HMGB1,PIDD1,TBK1,IKBKG,LBP,CD36,MAP3K7,RIPK3,IL1B,TLR3,NOD1,NLRC4,NOD2,AGER,RELA,SOCS1,RIPK1,FADD,BID,MAP2K7,TNFRSF10B,TNFRSF10A,SARM1 |
| 3 | response to musc | 13 | 2 | 3.77E-03 | 0.0151 | CHUK,RELA |

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|---|---|---|---|---|---|---|
| | le stretch positive regulation of | | | | | |
| 3 | stress-activated MAPK cascade | 14 | 2 | 4.35E-03 | 0.0169 | NOD2,CARD9 |
| 3 | apoptotic mitochondrial changes | 14 | 2 | 4.35E-03 | 0.0169 | BID,MAP3K1 |

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|---|---|---|---|---|---|---|
| 3 | DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest | 48 | 3 | 4.63E-03 | 0.0169 | PIDD1,CASP2,CRADD |
| 3 | signal transduction by phosphory | 48 | 3 | 4.63E-03 | 0.0169 | MAP3K8,MAP2K3,MAP2K6 |

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|---|---|---|---|---|---|---|
| | lation | | | | | |
| 3 | peptidyl-tyrosine phosphorylation positive regulation of T cell proliferation negative regulation of osteoclast | 97 | 4 | 4.73E-03 | 0.0169 | MAP2K4,RIPK2,MAP2K7,MAP2K6 |
| 3 | | 49 | 3 | 4.91E-03 | 0.0169 | TRAF6,IL1B,CARD11 |
| 3 | | 15 | 2 | 4.97E-03 | 0.0169 | TLR4,TLR3 |

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|---|---|---|---|---|---|---|
| | differentiation | | | | | |
| 3 | cellular defense response protein | 50 | 3 | 5.19E-03 | 0.0169 | LBP,LY96,RELA |
| 3 | heteroolig omerization | 51 | 3 | 5.48E-03 | 0.0169 | RIPK3,RIPK1,FADD |
| 3 | T cell proliferation | 16 | 2 | 5.63E-03 | 0.0169 | RIPK2,MALT1 |
| 3 | lymph node development | 16 | 2 | 5.63E-03 | 0.0169 | RIPK3,FADD |

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| | nt | | | | | |
| 3 | elevation of cytosolic calcium ion concentration induction by symbiont of defense-related host nitric oxide production | 108 | 4 | 6.86E-03 | 0.0173 | HMGB1,CD36,IL1B,SAA1 |
| 3 | | 1 | 1 | 6.89E-03 | 0.0173 | TLR2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive regulation of interleukin-18-mediated signaling pathway | 1 | 1 | 6.89E-03 | 0.0173 | TICAM2 |
| 3 | TIRAP-dependent toll-like receptor 4 signaling pathway | 1 | 1 | 6.89E-03 | 0.0173 | TIRAP |

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|---|---|---|---|---|---|---|
| 3 | regulation of MyD88-independent toll-like receptor signaling pathway positive regulation of | 1 | 1 | 6.89E-03 | 0.0173 | IRF7 |
| 3 | nucleotide-binding oligomeriz | 1 | 1 | 6.89E-03 | 0.0173 | TLR4 |

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| | ation domain containing 1 signaling pathway negative regulation of | | | | | |
| 3 | branching morphogenesis of a nerve | 1 | 1 | 6.89E-03 | 0.0173 | IL1B |
| 3 | smooth muscle | 1 | 1 | 6.89E-03 | 0.0173 | IL1B |

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|---|---|---|---|---|---|---|
| 3 | adaptation regulation of activation of JAK2 kinase activity | 1 | 1 | 6.89E-03 | 0.0173 | SOCS1 |
| 3 | motor neuron apoptotic process | 1 | 1 | 6.89E-03 | 0.0173 | FADD |
| 3 | response to methylglyoxal | 1 | 1 | 6.89E-03 | 0.0173 | AGER |

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|---|---|---|---|---|---|---|
| 3 | detection of muramyl dipeptide regulation of MyD88-dependent | 1 | 1 | 6.89E-03 | 0.0173 | NOD2 |
| 3 | toll-like receptor signaling pathway | 1 | 1 | 6.89E-03 | 0.0173 | IRF7 |
| 3 | error-free postreplic | 1 | 1 | 6.89E-03 | 0.0173 | UBE2V1 |

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| | ation | | | | | |
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| 3 | activ | 1 | 1 | 6.89E-03 | 0.0173 | RIPK3 |
| | ation- | | | | | |

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| 3 | induced cell death of T cells positive regulation of interleukin-15 production | 1 | 1 | 6.89E-03 | 0.0173 | TIRAP |
| 3 | toll-like receptor 6 signaling pathway | 1 | 1 | 6.89E-03 | 0.0173 | TLR6 |

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|---|---|---|---|---|---|---|
| 3 | positive regulation of type III interferon production | 1 | 1 | 6.89E-03 | 0.0173 | TLR3 |
| 3 | polyketide metabolic process | 1 | 1 | 6.89E-03 | 0.0173 | IL1B |
| 3 | macrophage inflammatory protein-1 alpha | 1 | 1 | 6.89E-03 | 0.0173 | NOD2 |

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|---|---|---|---|---|---|---|
| | production | | | | | |
| 3 | B-1 B cell differentiation | 1 | 1 | 6.89E-03 | 0.0173 | MALT1 |
| 3 | detection of fungus | 1 | 1 | 6.89E-03 | 0.0173 | TLR4 |
| 3 | regulation of monocyte differentiation | 1 | 1 | 6.89E-03 | 0.0173 | IRF7 |

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|---|---|---|---|---|---|---|
| 3 | regulation of CD8-positive, alpha-beta cytotoxic T cell extravasation negative regulation | 1 | 1 | 6.89E-03 | 0.0173 | RIPK3 |
| 3 | of apoptotic cell clearance | 1 | 1 | 6.89E-03 | 0.0173 | HMGB1 |
| 3 | acetaldehy | 1 | 1 | 6.89E-03 | 0.0173 | RELA |

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|---|---|---|---|---|---|---|
| 3 | de metabolic process regulation of restriction endodeoxyribonuclease activity | 1 | 1 | 6.89E-03 | 0.0173 | HMGB1 |
| 3 | chloramphenicol transport | 1 | 1 | 6.89E-03 | 0.0173 | TLR2 |

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|---|---|---|---|---|---|---|
| 3 | positive regulation of macrophage tolerance induction | 1 | 1 | 6.89E-03 | 0.0173 | IRAK3 |
| 3 | response to selenite ion | 1 | 1 | 6.89E-03 | 0.0173 | AGER |
| 3 | interleukin-8 biosynthetic process | 1 | 1 | 6.89E-03 | 0.0173 | NOD1 |

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|---|---|---|---|---|---|---|
| 3 | positive regulation of immature T cell proliferation | 1 | 1 | 6.89E-03 | 0.0173 | RIPK2 |
| 3 | cellular response to sorbitol | 1 | 1 | 6.89E-03 | 0.0173 | MAP2K6 |
| 3 | plasmacytoid dendritic cell activation | 1 | 1 | 6.89E-03 | 0.0173 | HMGB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | cellular response to methotrexate positive regulation of | 1 | 1 | 6.89E-03 | 0.0173 | IL1B |
| 3 | Schwann cell differentiation type I | 1 | 1 | 6.89E-03 | 0.0173 | RELA |
| 3 | interferon production | 1 | 1 | 6.89E-03 | 0.0173 | TBK1 |
| 3 | response to interl | 1 | 1 | 6.89E-03 | 0.0173 | RIPK2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | eukin-18 positive regulation of | | | | | |
| 3 | blood micro particle formation positive regulation of | 1 | 1 | 6.89E-03 | 0.0173 | CD36 |
| 3 | prostaglandin-E synthase activity | 1 | 1 | 6.89E-03 | 0.0173 | NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | response to molecule of fungal origin positive regulation of myosin light chain kinase activity regulation of T cell | 1 | 1 | 6.89E-03 | 0.0173 | TLR2 |
| 3 | | 1 | 1 | 6.89E-03 | 0.0173 | IL1B |
| 3 | | 1 | 1 | 6.89E-03 | 0.0173 | RIPK3 |

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|---|---|---|---|---|---|---|
| | medi ated cytot oxicit y toll-li ke recep tor 1 signa ling path way negat ive regul ation of RNA poly mera se II trans cripti onal preini | | | | | |
| 3 | | 1 | 1 | 6.89E -03 | 0.01 73 | TLR1 |
| 3 | | 1 | 1 | 6.89E -03 | 0.01 73 | HMGB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | tiation complex assembly | | | | | |
| 3 | regulation of ATP:ADP antiporter activity positive regulation of | 1 | 1 | 6.89E-03 | 0.0173 | RIPK1 |
| 3 | chemokine (C-X-C motif | 1 | 1 | 6.89E-03 | 0.0173 | TIRAP |

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|---|---|---|---|---|---|---|
| | ) ligand 1 production response to acetate positive regulation of | | | | | |
| 3 | | 1 | 1 | 6.89E-03 | 0.0173 | CHUK |
| 3 | gamma-delta T cell activation positive regulation of | 1 | 1 | 6.89E-03 | 0.0173 | NOD2 |
| 3 | CD8- | 1 | 1 | 6.89E-03 | 0.0173 | FADD |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | positive, alpha-beta cytotoxic T cell extravasation regulation of oxidoreductase activity | 1 | 1 | 6.89E-03 | 0.0173 | ECSIT |
| 3 | positive regulation of interleukin-10 | 18 | 2 | 7.06E-03 | 0.0173 | TLR4,NOD2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | production | | | | | |
| 3 | cellular response to fatty acid | 18 | 2 | 7.06E-03 | 0.0173 | IL1B,AGER |
| 3 | neutrophil chemotaxis positive regulation | 57 | 3 | 7.42E-03 | 0.0173 | IL1B,S100A12,SAA1 |
| 3 | of cytokine production | 19 | 2 | 7.84E-03 | 0.0173 | PELI1,CARD11 |
| 3 | osteoclast | 19 | 2 | 7.84E-03 | 0.0173 | CHUK,TRAF6 |

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|---|---|---|---|---|---|---|
| 3 | differentiation negative regulation of interferon-gamma production | 20 | 2 | 8.64E-03 | 0.0173 | TLR4,NOD2 |
| 3 | T cell homeostasis positive regulation of activated T cell | 20 | 2 | 8.64E-03 | 0.0173 | RIPK3,FADD |
| 3 | | 20 | 2 | 8.64E-03 | 0.0173 | PYCARD,FADD |

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|---|---|---|---|---|---|---|
| | proliferation | | | | | |
| 3 | response to morphine positive regulation of release of cytochrome c from mitochondria | 21 | 2 | 9.49E-03 | 0.019 | IL1B,RELA |
| 3 | | 21 | 2 | 9.49E-03 | 0.019 | PYCARD,BID |
| 3 | type I interferon-medi | 63 | 3 | 9.73E-03 | 0.0195 | IRF3,IRF7,SOCS1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ated signaling pathway | | | | | |
| 4 | mitotic cell cycle | 334 | 26 | 1.11E-16 | 4.44E-15 | RB1,MCM7,MCM8,CETN2,MCM10,CCNA2,CCNA1,DBF4,BIRC5,MCM5,MCM6,PRIM2,ORC5,ORC4,UBB,ORC3,ORC2,E2F1,E2F2,CDT1,RPA2,POLA2,RPA3,POLE2,RPA4,MNAT1 |
| 4 | DNA replication | 110 | 20 | 1.11E-16 | 4.44E-15 | MCM7,MCM8,MCM10,POLE,DBF4,MCM3,MCM4,MCM5,MCM6,ORC5,ORC4,ORC6,ORC3,ORC2,CDT1,RPA1,RPA2,POLA2,RPA3,POLE2 |
| 4 | nucleotide-excision repair | 85 | 28 | 1.11E-16 | 4.44E-15 | CETN2,SUMO1,SUMO3,SUMO2,RNF111,PARP1,USP45,RAD23A,CHD1L,RAD23B,DDB2,DDB1,XPA,XPC,UBB,RPA2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC4,RPA3,RPA4,ERCC2,ERCC5,MNAT1 |
| 4 | DNA-dependent DNA replic | 21 | 15 | 1.11E-16 | 4.44E-15 | MCM7,MCM10,MCM5,MCM6,MCM2,PRIM2,ORC5,ORC4,CDC45,ORC2,CDC7,POLA1,POLA2,POLE2,RPA4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ation initiation | | | | | |
| 4 | global genome nucleotide-excision repair | 47 | 24 | 1.11E-16 | 4.44E-15 | CETN2,SUMO1,SUMO3,SUMO2,RNF111,PARP1,USP45,CHD1L,RAD23B,DDB2,DDB1,XPC,UBB,RPA2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC4,RPA3,ERCC2,MNAT1 |
| 4 | G1/S transition of mitotic cell cycle | 112 | 22 | 1.11E-16 | 4.44E-15 | RB1,MCM7,MCM8,MCM10,CCNA1,DBF4,MCM5,MCM6,PRIM2,ORC5,ORC4,UBB,ORC3,ORC2,E2F1,CDT1,RPA2,POLA2,RPA3,POLE2,RPA4,MNAT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | DNA repair | 303 | 26 | 1.11E-16 | 4.44E-15 | CETN2,SUMO1,SUMO3,SUMO2,RNF111,PARP1,USP45,CHD1L,RAD23B,DDB2,DDB1,XPC,UBB,RPA2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC4,RPA3,ERCC1,POLE2,ERCC2,MNAT1 |
| 4 | nucleotide-excision repair, DNA incision transcription-coupled nucleotide-excision repair | 28 | 15 | 1.11E-16 | 4.44E-15 | PARP1,CHD1L,DDB2,DDB1,UBB,RPA2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC4,RPA3,ERCC2 |
| 4 | nucleotide-excision repair | 59 | 13 | 1.11E-16 | 4.44E-15 | DDB1,UBB,RPA2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC4,RPA3,ERCC2,MNAT1 |

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|---|---|---|---|---|---|---|
| 4 | DNA strand elongation involved in DNA replication | 20 | 8 | 6.49E-13 | 2.33E-11 | MCM7,MCM8,MCM5,MCM6,PRIM2,RPA2,POLA2,RPA3 |
| 4 | mRNA capping transcription elongation | 25 | 8 | 3.78E-12 | 1.21E-10 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | from RNA polymerase I prom | 26 | 8 | 5.14E-12 | 1.54E-10 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |

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|---|---|---|---|---|---|---|
| | oter | | | | | |
| 4 | termination of RNA polymerase I transcription transcription initiation from RNA polymerase I promoter | 27 | 8 | 6.92E-12 | 1.87E-10 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | | 29 | 8 | 1.21E-11 | 3.04E-10 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | transcription from RNA polymerase I promoter positive regulation | 31 | 8 | 2.05E-11 | 4.92E-10 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | of viral transcription | 37 | 8 | 8.21E-11 | 1.81E-09 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | nucleotide-excision repair, DNA | 23 | 7 | 1.26E-10 | 2.64E-09 | CETN2,PARP1,RAD23B,DDB2,DDB1,XPC,UBB |

| | | | | | | |
|---|---|---|---|---|---|---|
| | damage recognition telomere maintenance | | | | | |
| 4 | | 42 | 8 | 2.21E-10 | 4.42E-09 | PARP1,PRIM2,RPA2,POLA2,ERCC4,RPA3,POLE2,ATM |
| | transcription initiation from RNA polymerase II promoter | | | | | |
| 4 | | 198 | 12 | 2.50E-09 | 4.50E-08 | RNF111,PARP1,UBB,E2F2,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| | negative regulation of | | | | | |
| 4 | | 62 | 8 | 4.53E-09 | 8.16E-08 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | gene expression, epigenetic transcription elongation from RNA polymerase II promoter regulation of | 65 | 8 | 6.52E-09 | 1.11E-07 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | gene expression, epigenetic | 72 | 8 | 1.43E-08 | 2.29E-07 | GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | telomere maintenance via semi-conservative replication double-strand break repair | 13 | 5 | 1.97E-08 | 2.95E-07 | PRIM2,RPA2,POLA2,RPA3,POLE2 |
| 4 | via homologous recombination | 110 | 9 | 2.31E-08 | 3.47E-07 | MCM8,SUMO1,SUMO2,PARP1,UBB,RPA2,ERCC4,RPA3,ATM |
| 4 | protein sumo | 84 | 8 | 4.64E-08 | 6.49E-07 | CETN2,SUMO1,SUMO3,SUMO2,PIAS3,PARP1,XPC,UBE2I |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ylation telomere maintenance via recombination | | | | | |
| 4 | | 17 | 5 | 7.38E-08 | 9.59E-07 | PRIM2,RPA2,POLA2,RPA3,POLE2 |
| 4 | DNA duplex unwinding | 38 | 6 | 1.32E-07 | 1.71E-06 | CHD1L,MCM5,MCM2,CDC45,GTF2H4,ERCC2 |
| 4 | DNA damage response, detection of DNA damage | 28 | 5 | 8.50E-07 | 1.02E-05 | PARP1,DDB1,UBB,RPA2,RPA3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | response to UV | 31 | 5 | 1.39E-06 | 1.67E-05 | DDB2,XPA,GTF2H2,ERCC3,ERCC4 |
| 4 | viral reproduction | 431 | 13 | 1.61E-06 | 1.93E-05 | RB1,SUMO1,DDB1,CCNA2,UBB,GTF2H1,GTF2H2,GTF2H3,GTF2H4,GTF2H5,ERCC3,ERCC2,MNAT1 |
| 4 | cellular response to xenobiotic stimulus | 4 | 3 | 2.17E-06 | 2.39E-05 | RB1,MCM7,E2F1 |
| 4 | error-prone translesion synthesis | 15 | 4 | 2.35E-06 | 2.58E-05 | UBB,RPA2,RPA3,POLE2 |
| 4 | double-strand break repair | 114 | 7 | 6.00E-06 | 6.00E-05 | SUMO1,SUMO2,PARP1,UBB,RPA2,ERCC4,RPA3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | UV-damage excision repair | 7 | 3 | 1.15E-05 | 1.15E-04 | DDB2,DDB1,XPC |
| 4 | UV protection | 7 | 3 | 1.15E-05 | 1.15E-04 | ERCC3,ERCC4,ERCC2 |
| 4 | G2/M transition of mitotic cell cycle | 112 | 6 | 6.10E-05 | 6.10E-04 | CETN2,CCNA2,CCNA1,BIRC5,UBB,MNAT1 |
| 4 | error-free translesion synthesis | 14 | 3 | 8.92E-05 | 8.03E-04 | UBB,RPA2,RPA3 |
| 4 | translesion | 39 | 4 | 9.63E-05 | 8.66E-04 | DDB1,UBB,RPA2,RPA3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | synthesis phosphorylation of RNA polymerase II C-terminal domain | 3 | 2 | 1.58E-04 | 1.42E-03 | GTF2H3,GTF2H4 |
| 4 | negative regulation of transcription involved in G1/S | 3 | 2 | 1.58E-04 | 1.42E-03 | RB1,E2F1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | phase of mitotic cell cycle nucleotide-excision repair, DNA gap filling | 18 | 3 | 1.86E-04 | 1.49E-03 | UBB,RPA2,RPA3 |
| 4 | regulation of transcription involved in G1/S | 19 | 3 | 2.18E-04 | 1.75E-03 | RB1,CCNA1,CDT1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | phase of mitotic cell cycle | | | | | |
| 4 | mismatch repair | 20 | 3 | 2.53E-04 | 2.01E-03 | XPC,RPA2,RPA3 |
| 4 | hair cell differentiation | 4 | 2 | 2.80E-04 | 2.01E-03 | ERCC3,ERCC2 |
| 4 | DNA replication, synthesis of RNA primer | 4 | 2 | 2.80E-04 | 2.01E-03 | PRIM2,PRIM1 |
| 4 | nucleic acid | 52 | 4 | 2.87E-04 | 2.01E-03 | POLE,POLA1,ERCC1,ERCC5 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | phosphodiester bond hydrolysis | | | | | |
| 4 | DNA damage checkpoint | 24 | 3 | 4.30E-04 | 3.01E-03 | E2F1,RPA4,ATM |
| 4 | DNA biosynthetic process | 24 | 3 | 4.30E-04 | 3.01E-03 | POLE,POLA1,POLA2 |
| 4 | dopamine catabolic process | 5 | 2 | 4.35E-04 | 3.05E-03 | MAOB,MAOA |
| 4 | DNA unwinding | 8 | 2 | 1.10E-03 | 7.59E-03 | MCM7,MCM6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | involved in replication regulation of cyclin-dependent protein kinase activity | | | | | |
| 4 | | 34 | 3 | 1.17E-03 | 7.59E-03 | CCNA2,GTF2H1,MNAT1 |
| 4 | proteasomal ubiquitin-dependent protei | 133 | 5 | 1.26E-03 | 7.59E-03 | RNF111,USP45,RAD23A,RAD23B,DDB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | n catabolic process | | | | | |
| 4 | base-excision repair protein | 35 | 3 | 1.27E-03 | 7.64E-03 | PARP1,RPA2,RPA3 |
| 4 | phosphorylation | 358 | 8 | 1.37E-03 | 8.24E-03 | BIRC5,GTF2H1,GTF2H2,CDK7,ERCC3,CDK4,ERCC2,MNAT1 |
| 5 | renal water homeostasis | 24 | 15 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,AVPR2,ADCY9,PRKAR1B,PRKAR1A,AVP |
| 5 | cellular response to glucagon stimu | 32 | 25 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,GNG10,GNG3,GNG2,GNG5,PRKAR2B,GNG4,PRKACG,PRKAR2A,GNG7,GNG8,GNG12,GNG11,GNG13,ADCY9,PRKAR1B,PRKAR1A,GNB1,GNB4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | lus | | | | | |
| 5 | activation of protein kinase A activity | 14 | 13 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,ADCY9,PRKAR1B,PRKAR1A |
| 5 | activation of phospholipase C activity | 51 | 17 | 1.11E-16 | 2.66E-15 | ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,ADCY9,PRKAR1B,PRKAR1A,CALM1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | cAMP biosynthetic process | 15 | 9 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,ADCY5,ADCY9 |
| 5 | nerve growth factor receptor signaling pathway | 312 | 19 | 1.11E-16 | 2.66E-15 | GSK3A,ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,BAD,ADCY9,PRKAR1B,PRKAR1A,CALM1 |
| 5 | water transport | 27 | 15 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,AVPR2,ADCY9,PRKAR1B,PRKAR1A,AVP |
| 5 | fibroblast growth factor | 234 | 19 | 1.11E-16 | 2.66E-15 | GSK3A,ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,BAD,ADCY9,PRKAR1B,PRKAR1A,CALM1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | receptor signaling pathway energy reserve metabolic process | 86 | 29 | 1.11E-16 | 2.66E-15 | ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,GNG10,GNG3,GNG2,GNG5,PRKAR2B,GNG4,PRKACG,PRKAR2A,GNG7,GNG8,GNG12,GNG11,GNG13,ADCY9,PRKAR1B,PRKAR1A,GNB1,GNB4,GNAS |
| 5 | synaptic transmission | 353 | 20 | 1.11E-16 | 2.66E-15 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,GNGT1,GNG10,GNG3,GNGT2,GNG2,GNG5,GNG4,GNG7,GNG8,GNG12,ADCY9,GNB1,CALM1 |
| 5 | signal transduction | 858 | 29 | 1.11E-16 | 2.66E-15 | ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,GNGT1,GNG10,GNG5,PRKAR2B,PRKACG,PRKAR2A,GNG12,GNG11,POMC,ADCY9,PRKAR1B,PRKAR1A,GNB2,GNB1,GNB4,GNB3,AVP,GNB5,CALM1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | small molecule metabolic process | 1229 | 30 | 1.11E-16 | 2.66E-15 | ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,CYP17A1,GNG10,GNG3,GNG2,GNG5,PRKAR2B,GNG4,PRKACG,PRKAR2A,GNG7,GNG8,GNG12,GNG11,GNG13,ADCY9,PRKAR1B,PRKAR1A,GNB1,GNB4,CALM1 |
| 5 | epidermal growth factor receptor signaling pathway | 250 | 19 | 1.11E-16 | 2.66E-15 | GSK3A,ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,BAD,ADCY9,PRKAR1B,PRKAR1A,CALM1 |
| 5 | adenylate cyclase-activating G-protein | 35 | 9 | 1.53E-14 | 3.37E-13 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,ADCY9,GNAS |

| | | | | | | |
|---|---|---|---|---|---|---|
| | coupled receptor signaling pathway cAMP-mediated signaling | | | | | |
| 5 | adenylate cyclase-inhibiting G-protein coupled receptor | 27 | 8 | 1.59E-13 | 3.34E-12 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,ADCY9 |
| 5 | | 43 | 8 | 6.29E-12 | 1.19E-10 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,ADCY9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | signaling pathway | | | | | |
| 5 | innate immune response | 800 | 19 | 3.22E-11 | 5.80E-10 | GSK3A,ADCY4,ITPR1,ADCY3,ITPR2,ADCY2,ITPR3,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,BAD,ADCY9,PRKAR1B,PRKAR1A,CALM1 |
| 5 | transmembrane transport | 436 | 15 | 4.45E-11 | 7.57E-10 | ADCY4,ADCY3,ADCY2,ADCY1,ADCY8,ADCY7,ADCY6,PRKAR2B,PRKACG,PRKAR2A,AVPR2,ADCY9,PRKAR1B,PRKAR1A,AVP |
| 5 | regulation of insulin secretion | 76 | 8 | 5.46E-10 | 8.73E-09 | ITPR1,ITPR2,ITPR3,PRKAR2B,PRKACG,PRKAR2A,PRKAR1B,PRKAR1A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | negative regulation of cAMP-dependent protein kinase activity | 7 | 4 | 1.85E-08 | 2.78E-07 | PRKAR2B,PRKAR2A,PRKAR1B,PRKAR1A |
| 5 | blood coagulation | 377 | 11 | 1.42E-07 | 2.13E-06 | ITPR1,ITPR2,ITPR3,GNG2,PRKAR2B,PRKACG,PRKAR2A,PRKAR1B,PRKAR1A,GNB1,CALM1 |
| 5 | cellular response to catecholamine | 6 | 3 | 1.87E-06 | 2.61E-05 | ADCY6,GNG2,GNB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | stimulus | | | | | |
| 5 | regulation of rhodopsin mediated signaling pathway | 31 | 4 | 6.67E-06 | 8.67E-05 | GNGT1,GNB1,GNB5,CALM1 |
| 5 | rhodopsin mediated signaling pathway | 33 | 4 | 8.51E-06 | 1.03E-04 | GNGT1,GNB1,GNB5,CALM1 |
| 5 | inositol phosphate | 10 | 3 | 8.55E-06 | 1.03E-04 | ITPR1,ITPR2,ITPR3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | -mediated signaling adenylate cyclase-activating | | | | | |
| 5 | dopamine receptor signaling pathway | 10 | 3 | 8.55E-06 | 1.03E-04 | GNG2,GNB1,GNAS |
| 5 | cellular response to prostaglandin E stimu | 12 | 3 | 1.47E-05 | 1.62E-04 | ADCY6,GNG2,GNB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | lus | | | | | |
| 5 | stimulatory C-type lectin receptor signaling pathway | 86 | 5 | 2.03E-05 | 2.23E-04 | ITPR1,ITPR2,ITPR3,PRKACG,CALM1 |
| 5 | response to calcium ion | 48 | 4 | 3.65E-05 | 3.82E-04 | AHCYL1,ITPR3,BAD,CALM1 |
| 5 | platelet activation | 164 | 6 | 3.82E-05 | 3.82E-04 | ITPR1,ITPR2,ITPR3,GNG2,GNB1,CALM1 |
| 5 | G-protein coupl | 735 | 11 | 8.17E-05 | 8.17E-04 | ITPR3,GNG10,GNG3,GNGT2,GNG5,GNG4,GNG7,GNG8,GNG12,GNG11,CALM1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | ed receptor signaling pathway cardiac muscle | | | | | |
| 5 | cell apoptotic process positive regulation | 4 | 2 | 1.14E-04 | 1.03E-03 | GNGT1,GNB1 |
| 5 | of systemic arterial blood | 4 | 2 | 1.14E-04 | 1.03E-03 | AVPR2,AVP |

| | | | | | | |
|---|---|---|---|---|---|---|
| | pressure | | | | | |
| 5 | epithelial fluid transport negative regulation of urine volume | 5 | 2 | 1.78E-04 | 1.60E-03 | AHCYL1,ITPR1 |
| 5 | phototransduction, visible light | 6 | 2 | 2.55E-04 | 2.30E-03 | ADCY6,AVPR2 |
| 5 | | 85 | 4 | 3.24E-04 | 2.59E-03 | GNGT1,GNB1,GNB5,CALM1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | adenylate cyclase-modulating G-protein coupled receptor signaling pathway | 35 | 3 | 3.43E-04 | 2.74E-03 | ADCY4,ADCY2,AVPR2 |
| 5 | cellular response to ethanol | 7 | 2 | 3.46E-04 | 2.77E-03 | ITPR2,ADCY7 |
| 5 | female meiosis | 7 | 2 | 3.46E-04 | 2.77E-03 | ADCY3,PRKAR1A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | positive regulation of cAMP biosynthetic process | 38 | 3 | 4.35E-04 | 3.05E-03 | GSK3A,ADCY7,AVP |
| 5 | elevation of cytosolic calcium ion concentration | 108 | 4 | 7.92E-04 | 5.55E-03 | ITPR3,GNG3,GNB1,AVP |
| 5 | sensory perce | 13 | 2 | 1.18E-03 | 8.24E-03 | GNG13,GNB1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | ption of taste cellular iron ion homeostasis ATP hydrolysis coupled proton transport | 54 | 16 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1C1,ATP6V1C2,ATP6V1F |
| 6 | proton transport | 28 | 18 | 1.11E-16 | 3.33E-16 | ATP6V0B,ATP6V0E1,ATP6AP1,TCIRG1,ATP6V0A2,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0D1,ATP6V0E2,ATP6V1E2,ATP6V0D2,ATP6V0C,ATP6V1C1,ATP6V0A1,ATP6V1C2,ATP6V1F |
| 6 | proton transport | 36 | 12 | 1.11E-16 | 3.33E-16 | ATP6V1A,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1C1,ATP6V1F,ATP6V1B1 |

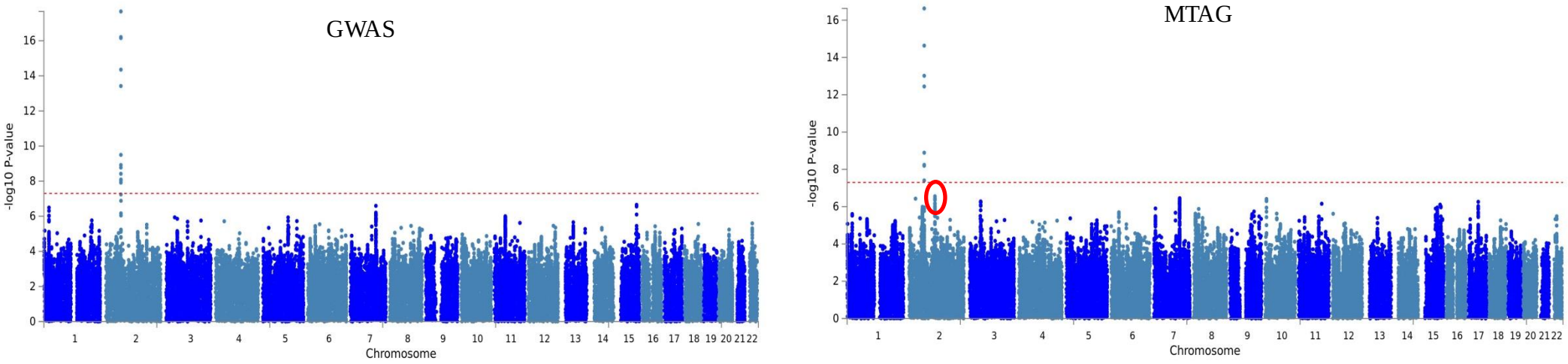
| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | phagosome maturation | 27 | 15 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1C1,ATP6V1C2,ATP6V1F |
| 6 | ion transmembrane transport | 187 | 16 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1C1,ATP6V1C2,ATP6V1F |
| 6 | transferrin transport | 25 | 16 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1C1,ATP6V1C2,ATP6V1F |
| 6 | transmembrane transport | 436 | 17 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1D,ATP6V1C1,ATP6V1C2,ATP6V1F |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | insulin receptor signaling pathway | 239 | 16 | 1.11E-16 | 3.33E-16 | ATP6V1G1,ATP6V0B,ATP6V0E1,ATP6V1G2,ATP6AP1,ATP6V1B2,ATP6V1H,ATP6V0A4,ATP6V1E1,ATP6V0E2,ATP6V1G3,ATP6V1E2,ATP6V0D2,ATP6V1C1,ATP6V1C2,ATP6V1F |
| 6 | vacuolar acidification | 10 | 8 | 1.11E-16 | 3.33E-16 | ATP6V0B,ATP6V0E1,TCIRG1,ATP6V0A2,ATP6V1H,ATP6V0A4,ATP6V0E2,ATP6V0A1 |
| 6 | vacuolar proton-transporting V-type ATPase complex asse | 4 | 4 | 1.31E-10 | 3.92E-10 | TCIRG1,ATP6V0A2,ATP6V0A4,ATP6V0A1 |

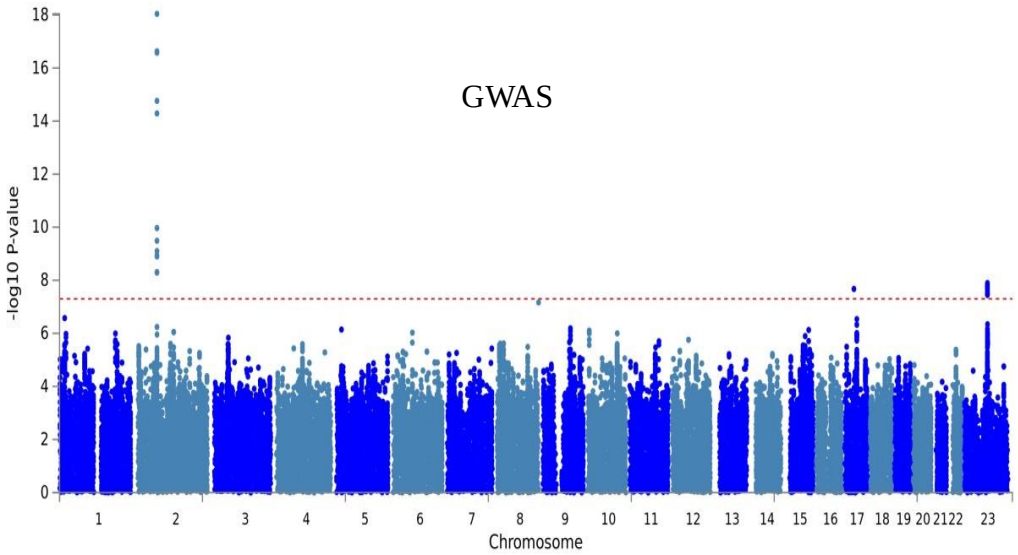
| | | | | | | |
|---|---|---|---|---|---|---|
| | mbly | | | | | |
| 6 | ATP synthesis coupled proton transport | 6 | 4 | 6.59E-10 | 1.32E-09 | TCIRG1,ATP6V0A2,ATP6V0A4,ATP6V0A1 |
| 6 | ATP metabolic process | 19 | 3 | 7.84E-06 | 1.57E-05 | ATP6V1A,ATP6V1B2,ATP6V1B1 |
| 6 | metabolic process | 284 | 4 | 2.28E-03 | 4.00E-03 | ATP6V1G1,ATP6V0E1,ATP6V1E1,ATP6V0E2 |
| 6 | pH reduction | 2 | 1 | 3.99E-03 | 4.00E-03 | ATP6AP1 |

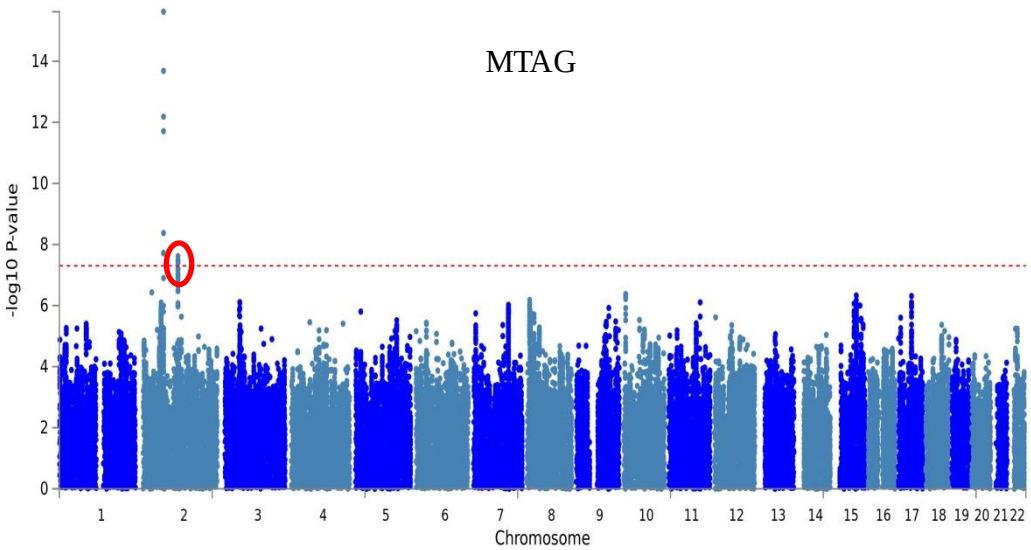
| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | establishment of organelle localization | 2 | 1 | 3.99E-03 | 4.00E-03 | ATP6AP1 |
| 6 | cell growth positive regulation | 47 | 2 | 4.00E-03 | 4.00E-03 | ATP6V0E1,ATP6V0E2 |
| 6 | of osteoclast development | 3 | 1 | 5.98E-03 | 5.98E-03 | ATP6AP1 |

**Supplementary figure 1A.** Manhattan plot of the SNP-level analysis of insomnia complaints

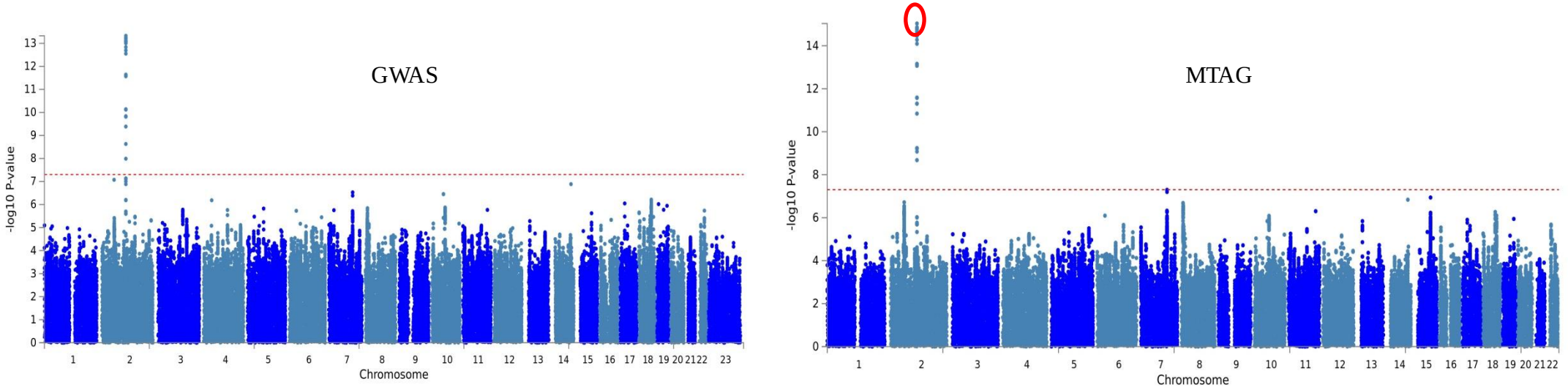


**Supplementary figure 1B.** Manhattan plot of the SNP-level analysis of insomnia symptoms

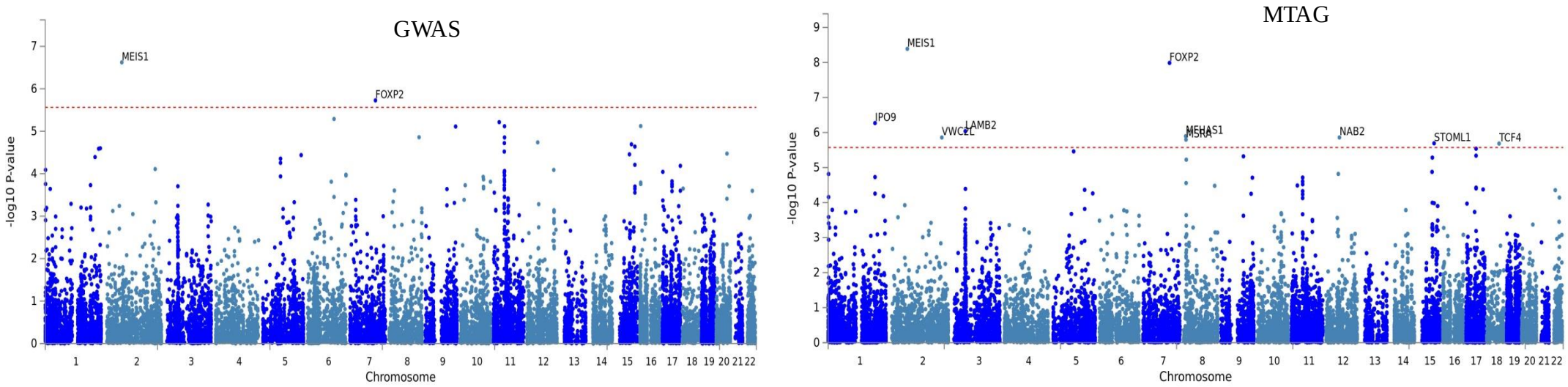


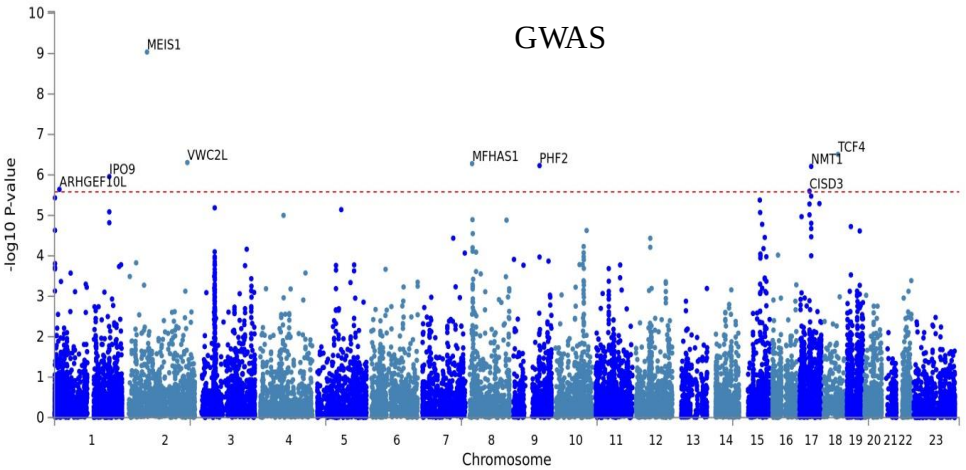
**Supplementary figure 1C.** Manhattan plot of the SNP-level analysis of sleep duration

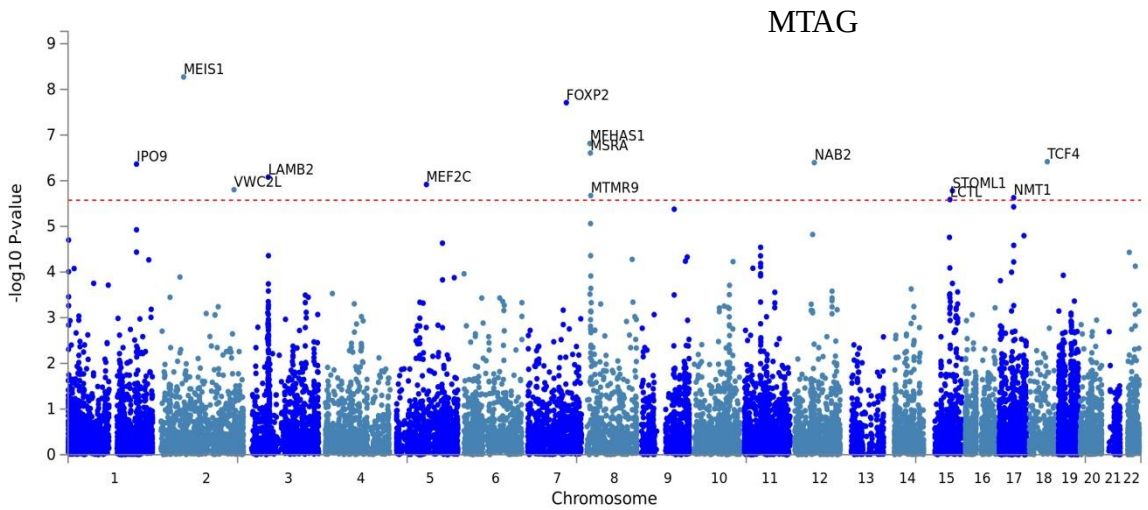


**Supplementary figure 1D.** Manhattan plot of the gene-based analysis of insomnia complaints

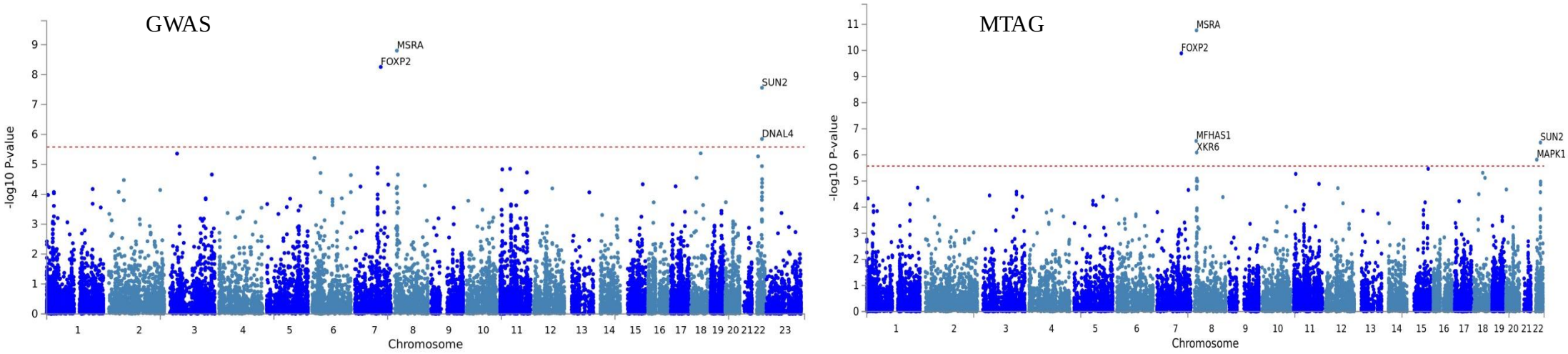


**Supplementary figure 1E.** Manhattan plot of the gene-based analysis of insomnia symptoms

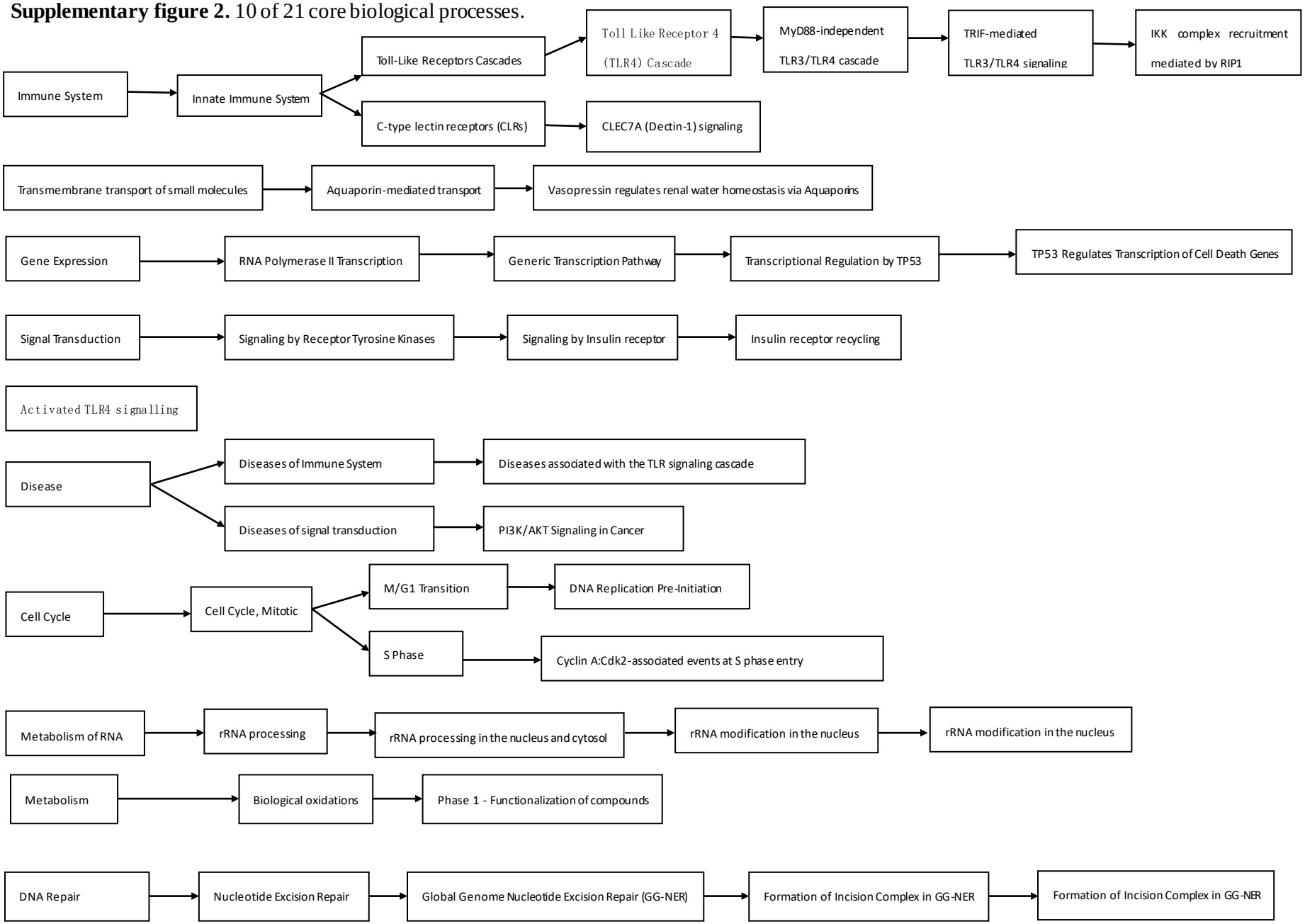


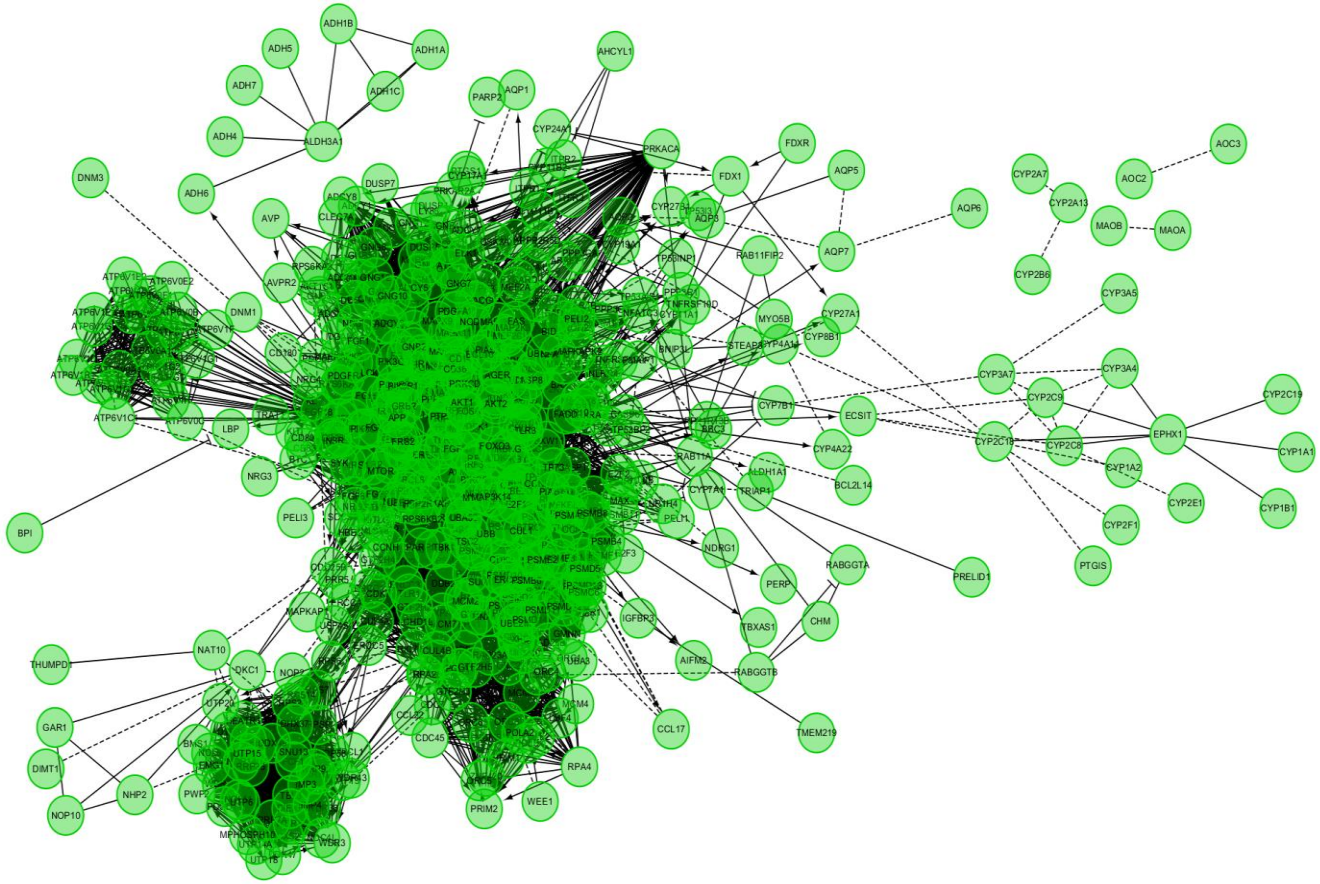
**Supplementary figure 1F.** Manhattan plot of the gene-based analysis of sleep duration



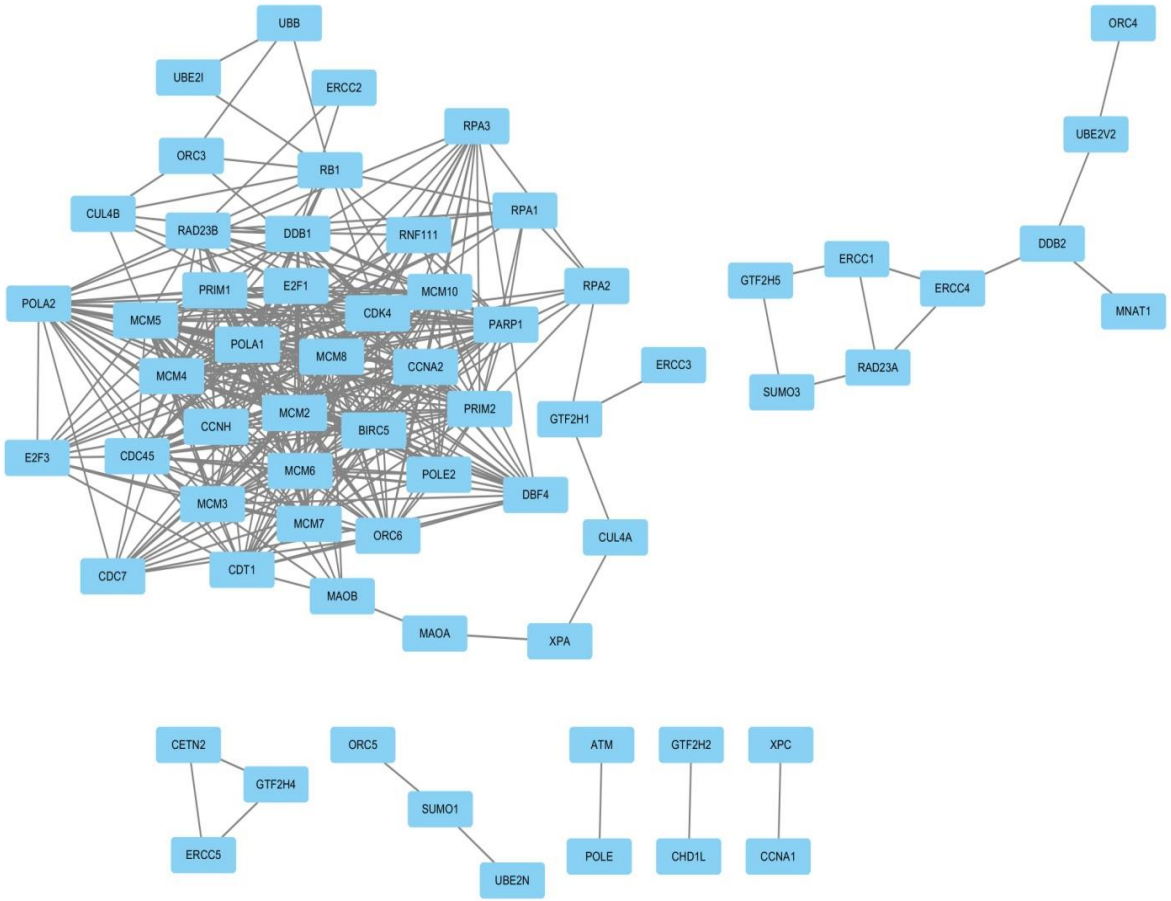
**Supplementary figure 2.** 10 of 21 core biological processes.



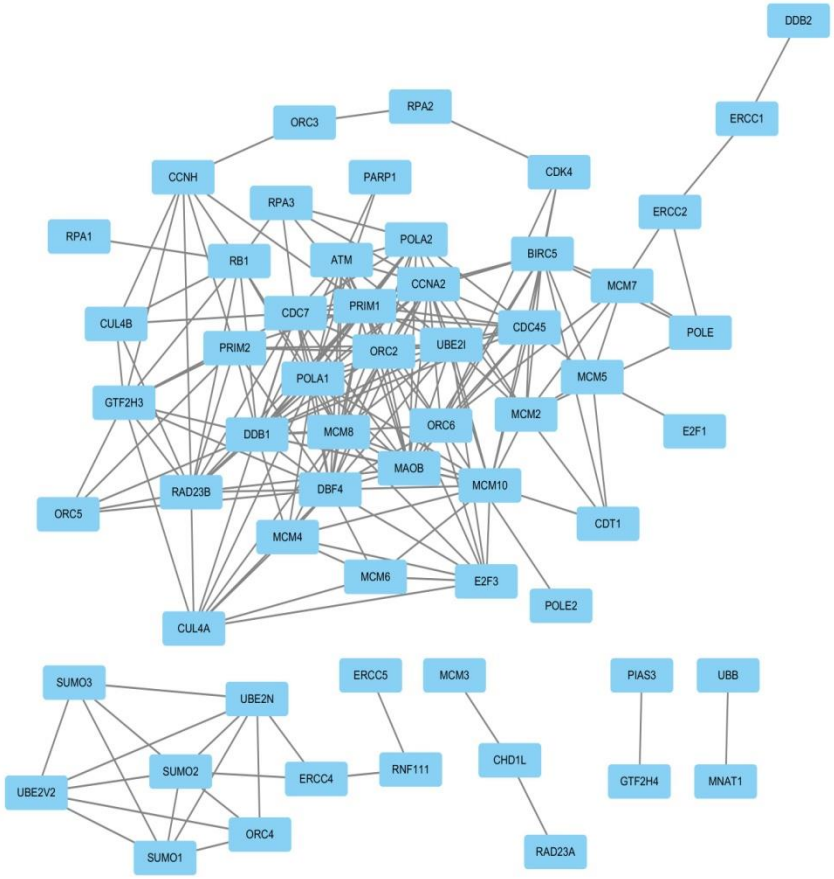
**Supplementary figure 3.** The larger molecular network by using the Reactome FI program.



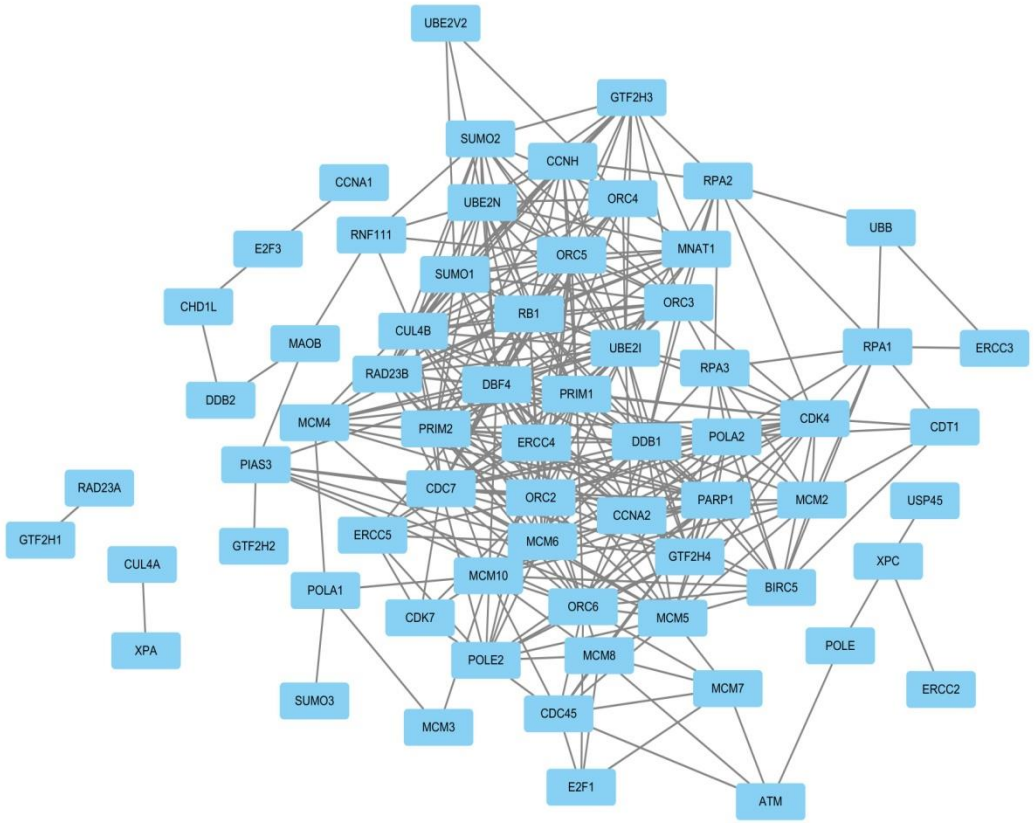
**Supplementary figure 4A.** Co-expression networks of genes in Cluster 4 in the amygdala (|R|)>0.8).



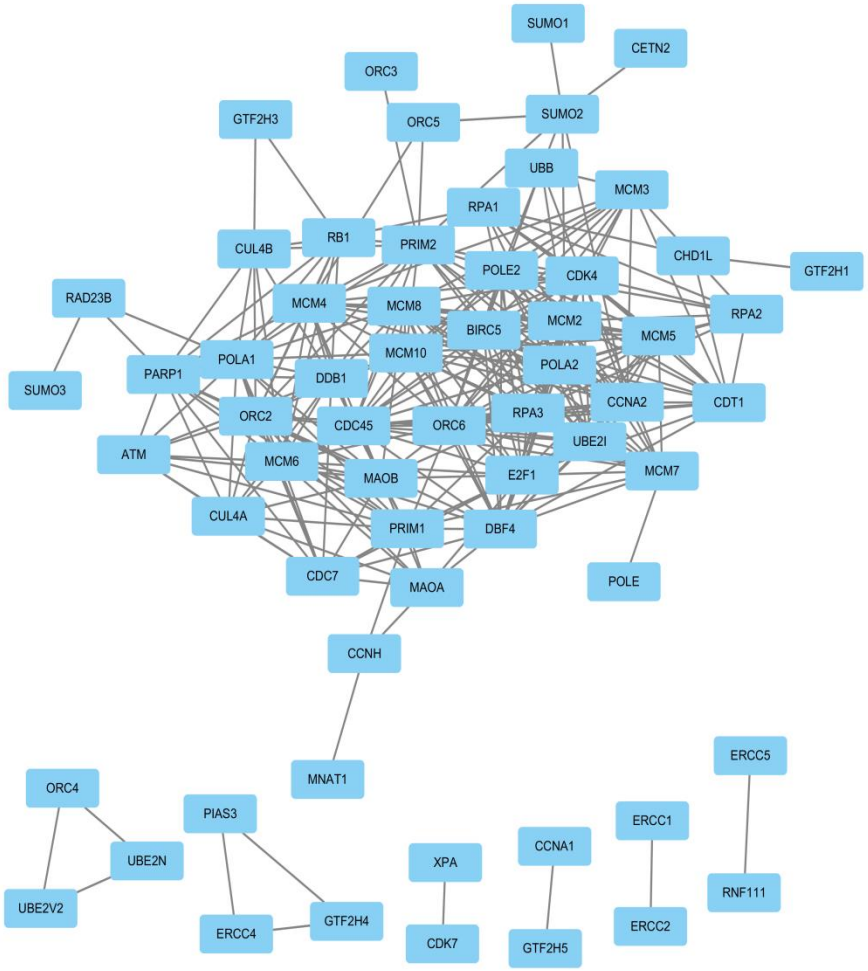
**Supplementary figure 4B.** Co-expression networks of genes in Cluster 4 in the DFC (|R|)>0.8).



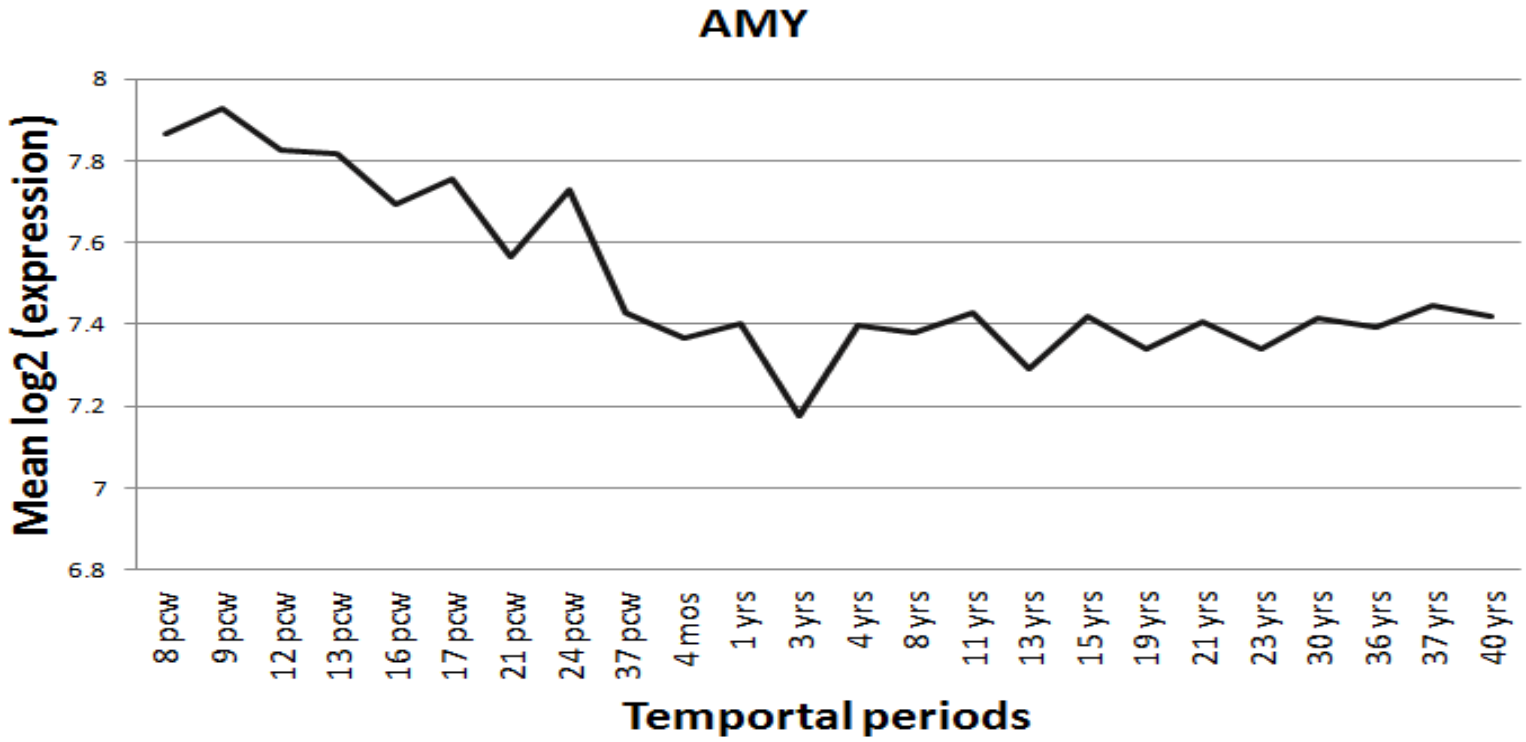
**Supplementary figure 4C.** Co-expression networks of genes in Cluster 4 in the ITC (|R|)>0.8).



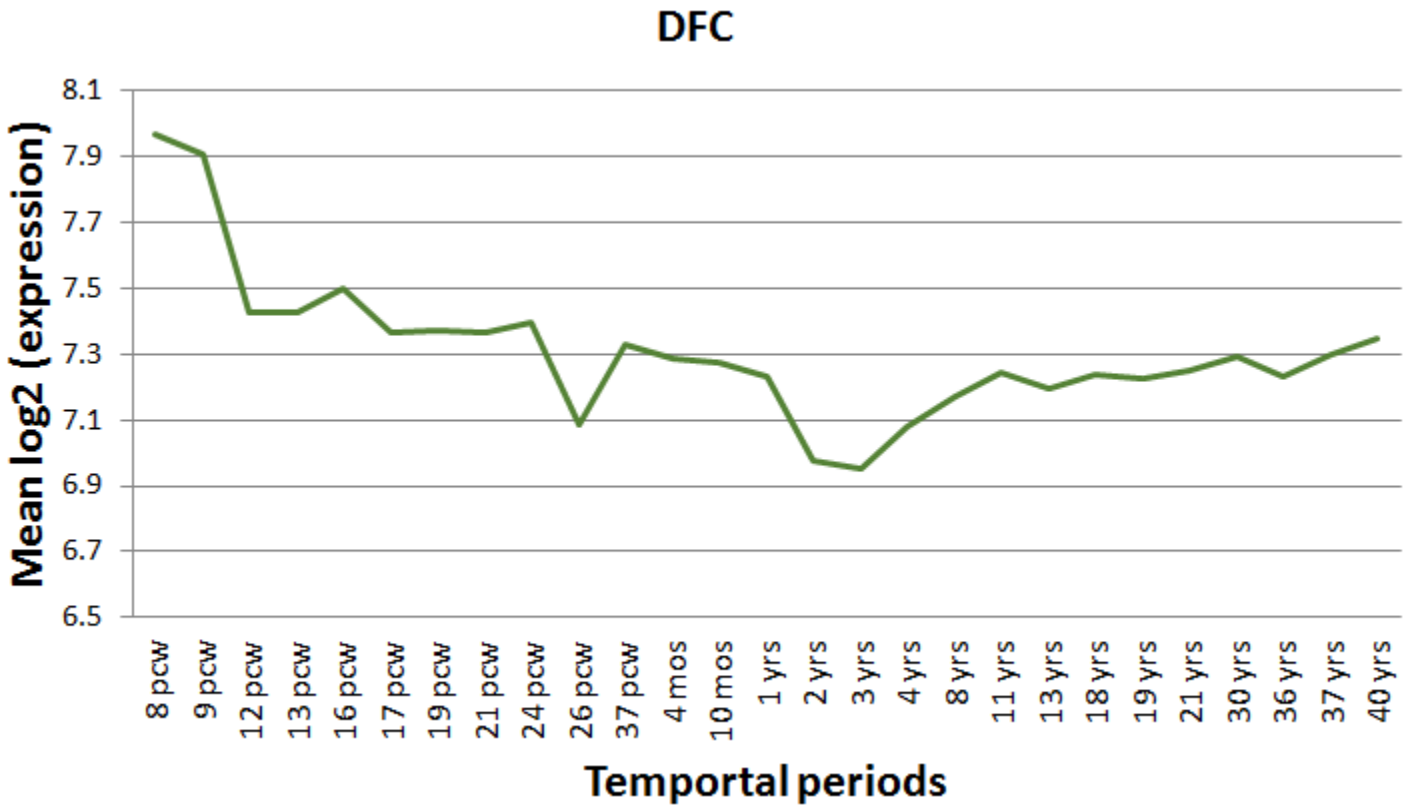
**Supplementary figure 4D.** Co-expression networks of genes in Cluster 4 in the MFC (|R|)>0.8).



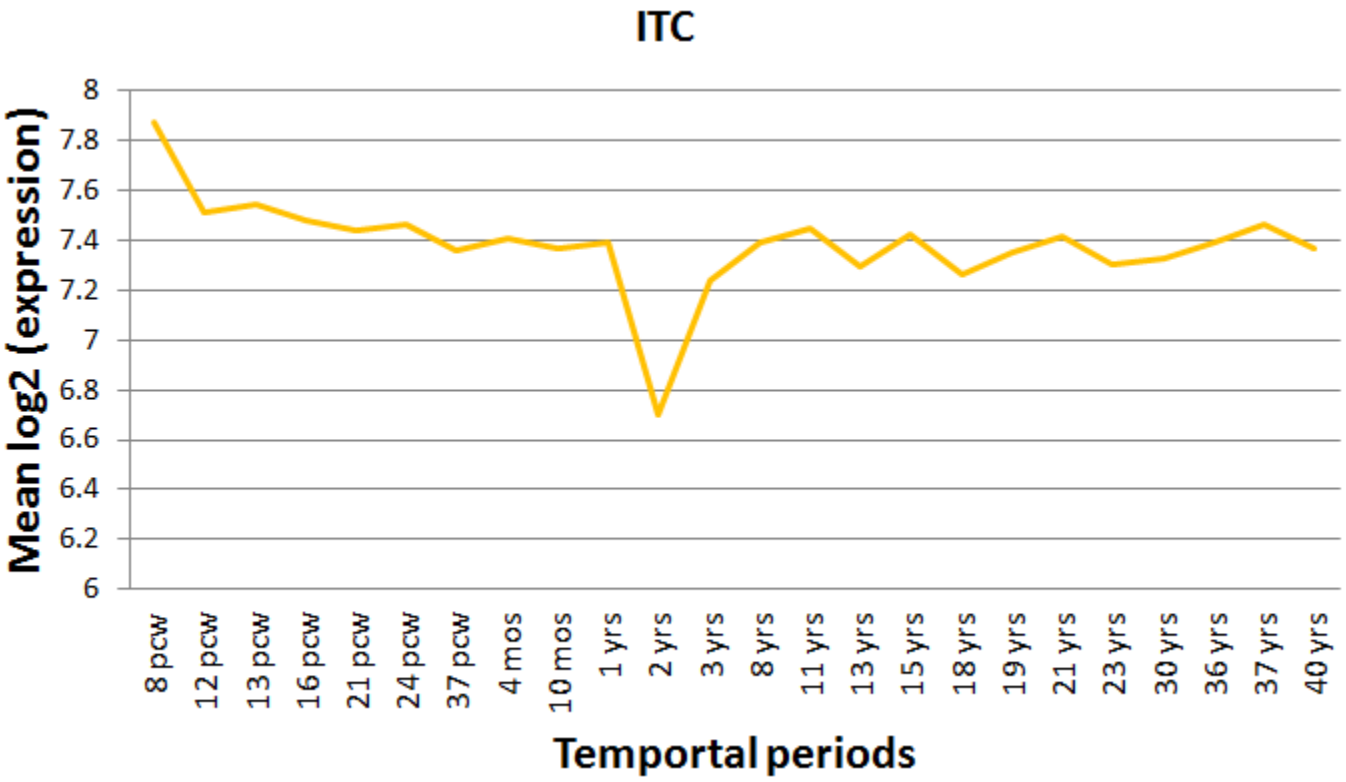
**Supplementary figure 5. A)** The average expression level of genes in Cluster 4 with the AMY in different temporal steps.



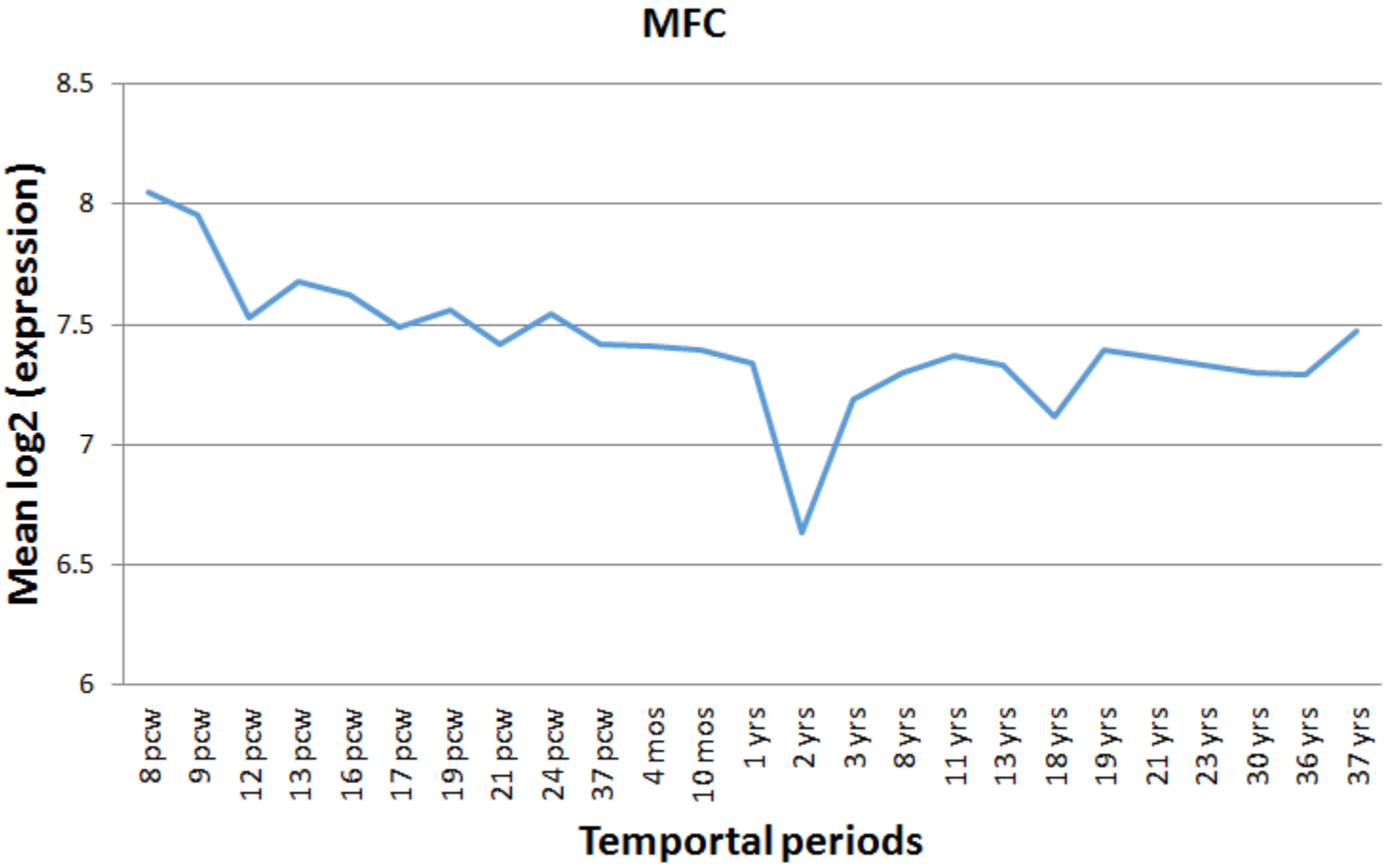
**B)** The average expression level of genes in Cluster 4 with the DFC in different temporal steps.



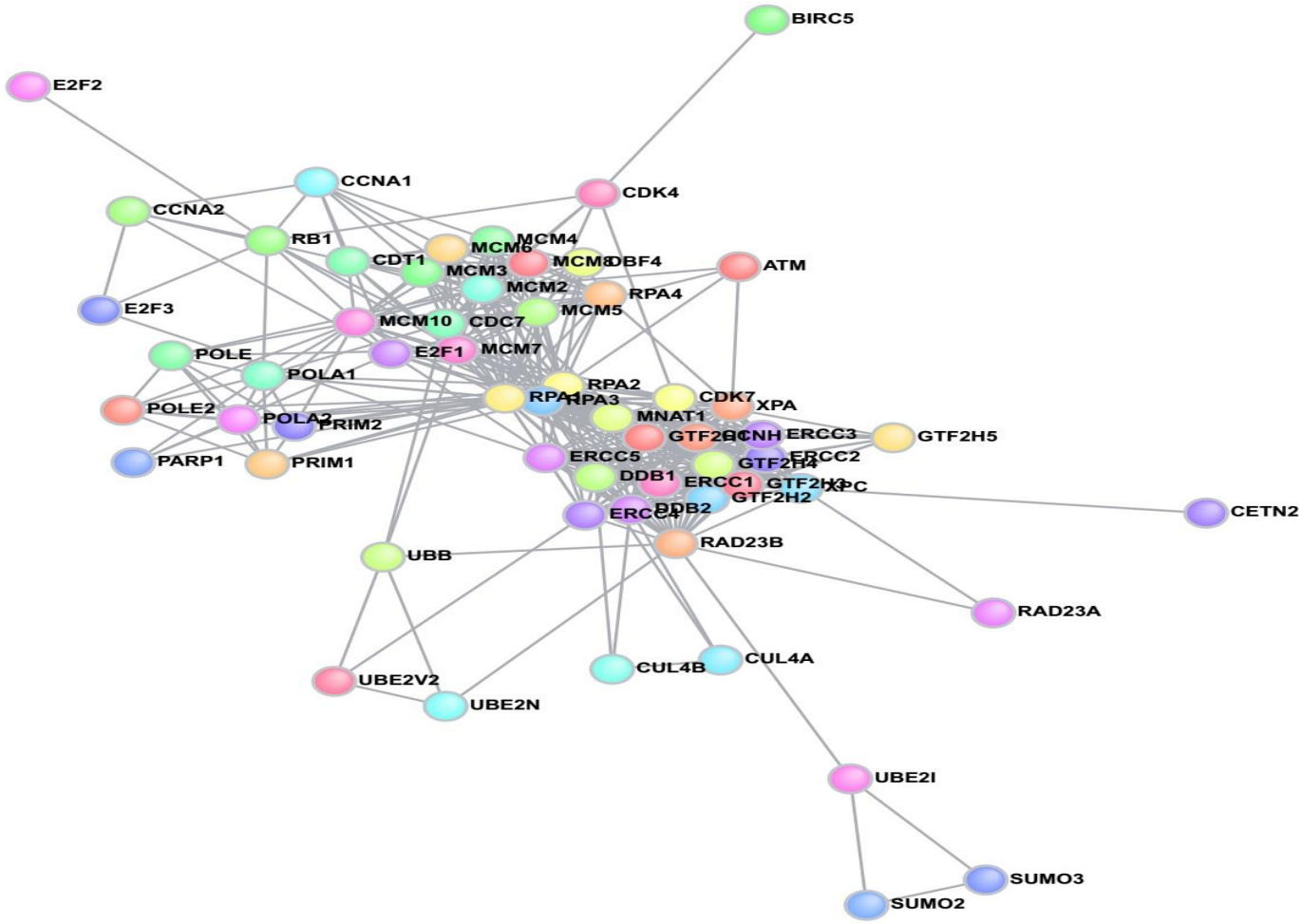
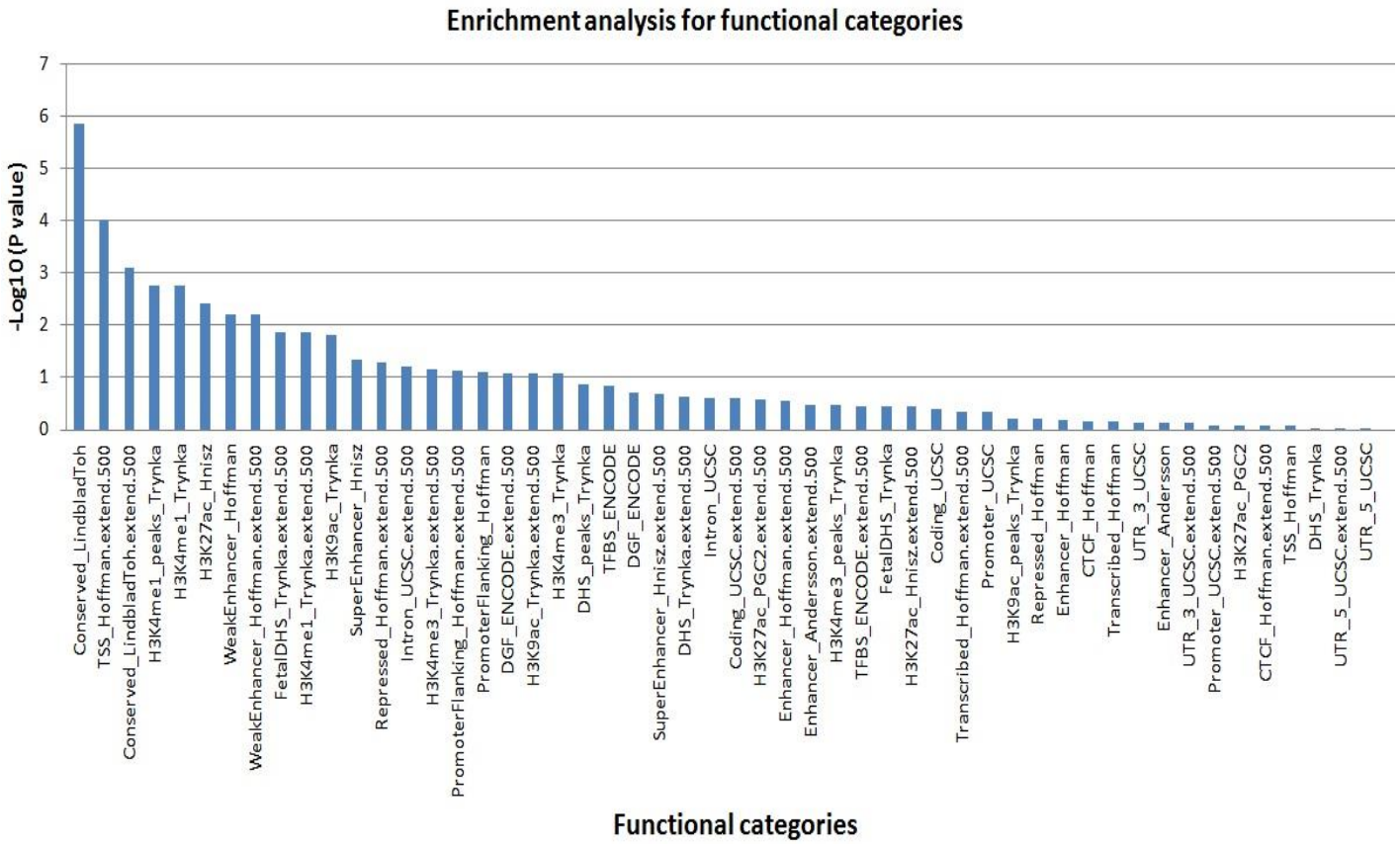
**C)** The average expression level of genes in Cluster 4 with the ITC in different temporal steps.



**D)** The average expression level of genes in Cluster 4 with the MFC in different temporal steps.



**Supplementary figure 6.** protein protein interaction for 72 genes in cluster 4 across DAPPLE program.



**Supplementary Figure 7.** Enrichment analysis for insomnia using the 52 functional categories.