

Table S1: The genes that significantly related to XYZ phenome ($p < 0.05$) at Day 14

| gene | ρ | gene | ρ | gene | ρ | gene | ρ | gene | ρ |
|--------------|----------|---------|----------|---------|----------|-----------|----------|----------|----------|
| MIR147B | 0.004631 | MARK2 | 0.007058 | GOLGA6A | 0.014295 | LOC554223 | 0.015127 | CLIP2 | 0.009233 |
| FAM229A | 0.008245 | TSNARE1 | 0.001362 | SLC10A5 | 0.017705 | NOP10 | 0.005657 | XBP1 | 0.005855 |
| MED16 | 0.013121 | VMA21 | 0.001847 | EP400NL | 0.007039 | BATF3 | 0.011038 | MIR671 | 0.017784 |
| MIR4326 | 0.020243 | AK2 | 0.019519 | APOE | 0.018332 | MAML3 | 0.022283 | ZNF180 | 0.001379 |
| MIR3615 | 0.011032 | EPHB4 | 0.013341 | SKA2 | 0.003234 | GOLGA2P5 | 0.018673 | ZNF230 | 0.019404 |
| LOC100505658 | 0.008709 | EPHB6 | 0.009424 | FAM159A | 0.019032 | MAP7D1 | 0.020876 | TMEM106C | 0.009529 |
| DCDC5 | 0.013125 | TMEM218 | 0.006845 | IL4R | 0.013165 | PARVA | 0.015672 | NUP37 | 0.014656 |
| TMEM44-AS1 | 0.01706 | ALKBH3 | 0.000224 | ILF2 | 0.014656 | WDR12 | 0.01956 | C1orf50 | 0.009431 |
| MIR4635 | 0.014911 | PHACTR1 | 0.000462 | INHBB | 0.001036 | ECHDC1 | 0.000995 | THOC6 | 0.007396 |
| EGFLAM-AS4 | 0.0153 | CCZ1B | 0.016652 | INPP5A | 0.004129 | LMO3 | 0.020593 | ZXDC | 0.004855 |
| PRICKLE2-AS3 | 0.011201 | LRWD1 | 0.00192 | CD82 | 0.006009 | UNC45A | 0.021492 | CCNJL | 0.017803 |
| SERF2 | 0.002389 | GPR97 | 0.013736 | KCNA5 | 0.012903 | APOBR | 0.001563 | AIMP2 | 0.019991 |
| GDF11 | 0.015721 | ZSCAN23 | 0.011623 | B3GNT8 | 0.005683 | SLC25A40 | 0.015345 | CALCB | 0.012864 |
| SPRY2 | 0.007861 | FGF11 | 0.002819 | APITD1 | 0.013514 | PCDHGA11 | 0.003925 | MAFK | 0.005413 |
| ABCC4 | 0.015363 | FGFR4 | 0.000672 | ACAT1 | 0.006963 | PSPN | 0.005017 | TREML2 | 0.00762 |
| SPEG | 0.016244 | COPZ1 | 0.014402 | KLRB1 | 0.013426 | SUSD2 | 0.007824 | ZNF672 | 0.009208 |
| HMG20B | 0.022647 | ZFP30 | 0.006282 | C2orf82 | 0.001386 | PANX2 | 0.015518 | WDR76 | 0.020323 |
| ANAPC10 | 0.005043 | LMTK2 | 0.023037 | CDHR4 | 0.008757 | TMEM9B | 0.021714 | THOC7 | 0.00898 |
| ADARB1 | 0.019061 | PPP6R1 | 0.013295 | PROB1 | 0.002045 | PSMA6 | 0.018636 | PUS1 | 0.007775 |
| CD52 | 0.009301 | SBNO2 | 0.014799 | LRRC26 | 0.002252 | C15orf39 | 0.012121 | VWA7 | 0.01505 |
| HAX1 | 0.006178 | KDM4B | 0.009431 | ARL5C | 0.006253 | TOMM22 | 0.002075 | B9D2 | 0.001766 |
| TACC3 | 0.021022 | KDM6B | 0.001929 | LAMC1 | 0.004907 | SLC12A9 | 0.008921 | PABPN1 | 0.017566 |
| SLC30A9 | 0.004902 | METAP1 | 0.002854 | RPSA | 0.011444 | CTNNBIP1 | 0.011245 | NETO1 | 0.017831 |

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| SEMA4B | 0.002347 | JMJD6 | 0.015296 | LGALS1 | 0.000776 | INTS12 | 0.00243 | ZNF205-AS1 | 0.015283 |
| PROCR | 0.008165 | PHLPP1 | 0.003522 | ARHGDIG | 0.021795 | CAMK1D | 0.0125 | CAPZA1 | 0.022783 |
| SH2B2 | 0.003367 | BICD2 | 0.002973 | OR2A20P | 0.002584 | SMURF1 | 0.019966 | DYSF | 0.018578 |
| MYL12A | 0.019162 | ICOSLG | 0.001659 | ARL3 | 0.018774 | PSMD10 | 0.004772 | FZD7 | 0.023267 |
| RFPL2 | 0.010585 | DPY19L1 | 0.01976 | MIRLET7B | 0.001959 | SMAGP | 0.018452 | ADPGK | 0.006703 |
| KDM5B | 0.013121 | ZNF629 | 0.021046 | TBC1D3C | 0.006296 | CLK4 | 0.017819 | SF3B5 | 0.007665 |
| NOXA1 | 0.017598 | ARHGEF18 | 0.004343 | PLEKHG7 | 0.014346 | COG6 | 0.014296 | APH1B | 0.008023 |
| CPLX1 | 0.001277 | COMMD3 | 0.002145 | NUDT4P1 | 0.011463 | WDFY4 | 0.022377 | RIOK1 | 0.005116 |
| HCP5 | 0.006543 | ZFPM2 | 0.010986 | SMIM4 | 0.004406 | PRX | 0.006774 | MAD1L1 | 0.000932 |
| EHD1 | 0.021701 | ETHE1 | 0.012489 | NUTM2G | 0.003776 | GRHL3 | 0.00571 | STARD3NL | 0.012646 |
| TMED2 | 0.020624 | RIMBP2 | 0.020788 | MYH3 | 0.021661 | PTPRK | 0.018731 | TMEM133 | 0.005172 |
| UQCR11 | 0.010242 | TNPO3 | 0.008814 | MYL4 | 0.004979 | PVRL1 | 0.0015 | TAGLN2 | 0.01976 |
| CLP1 | 0.006339 | ZKSCAN5 | 0.012266 | MYL6 | 0.023126 | CXCL16 | 0.016495 | ENKD1 | 0.000632 |
| KDELR2 | 0.001537 | EID1 | 0.010741 | HNRNPM | 0.019728 | RAB6A | 0.003097 | ELMOD3 | 0.006059 |
| SMA5 | 0.005312 | MTCH2 | 0.01507 | NDUFA9 | 0.005121 | RABIF | 0.010209 | PHF6 | 0.016656 |
| WWP2 | 0.01928 | FTH1P3 | 0.015157 | NDUFS3 | 0.022163 | RAN | 0.005683 | MIEN1 | 0.015184 |
| ADAM29 | 0.006007 | EPHX4 | 0.013609 | NDUFS6 | 0.017621 | RARA | 0.015627 | UTF1 | 0.009879 |
| ADAMTS6 | 0.014751 | EHBP1L1 | 0.00458 | RERE | 0.010814 | RXFP1 | 0.020589 | C14orf142 | 0.000549 |
| PADI2 | 0.020004 | GABRA2 | 0.008003 | NFATC1 | 0.016799 | RELB | 0.017184 | KBTBD8 | 0.002484 |
| PACSIN2 | 0.006733 | ALX3 | 0.019149 | NFKB1 | 0.005641 | RNASE2 | 0.008554 | TMEM185A | 0.002342 |
| C1orf85 | 0.021984 | TBC1D22A | 0.018292 | NOTCH1 | 0.02292 | RNASE6 | 0.015478 | TNRC18 | 0.023057 |
| MGAT4B | 0.000168 | PRDX5 | 0.01713 | PNP | 0.001364 | BCL6 | 0.018636 | HINT2 | 0.020065 |
| HENMT1 | 0.011009 | ANAPC13 | 0.020255 | ROR1 | 0.003804 | RPE | 0.007212 | MCEE | 0.017173 |
| ATG4A | 0.010982 | SPEF1 | 0.004187 | COA5 | 0.006956 | RPL10 | 0.003264 | CAPS2 | 0.015014 |
| ZNF501 | 0.014479 | NIPSNAP3A | 2.88E-05 | CHAC2 | 0.012513 | RPL12 | 0.011961 | HDGFRP2 | 0.014388 |
| WDR92 | 0.017238 | NPHP4 | 0.003371 | P2RX5 | 0.021003 | RPL15 | 0.008736 | CBX2 | 0.007129 |

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| MRPL54 | 0.012908 | MYCBP | 0.022824 | PA2G4 | 0.003694 | RPL18A | 0.023057 | SFT2D3 | 0.010018 |
| ARAP1 | 0.005683 | GBAS | 0.009366 | PAX5 | 0.012856 | RPL30 | 0.01295 | TMEM25 | 0.012438 |
| CLCN4 | 0.014449 | BLOC1S1 | 0.013781 | PBX2 | 0.015778 | RPLP0 | 0.007212 | GEMIN2 | 0.005363 |
| CHCHD1 | 0.001189 | SLC17A5 | 0.007915 | ATP5C1 | 0.013426 | RPS3 | 0.016757 | RAB2B | 0.01538 |
| CPXM2 | 0.011169 | CNNM1 | 0.014752 | FIS1 | 0.000213 | RPS5 | 0.011763 | LSM10 | 0.017566 |
| CLTA | 0.018752 | PGBD2 | 0.019542 | TXNDC12 | 0.0003 | RPS6 | 0.017184 | COX14 | 0.014741 |
| GTSF1 | 0.004125 | SNORD50A | 0.015979 | APH1A | 0.000842 | RPS11 | 0.005434 | TMEM60 | 0.002269 |
| ANKRD9 | 0.007258 | AMPD2 | 0.011952 | SS18L2 | 0.015778 | RPS14 | 0.003097 | SNORD14C | 0.022023 |
| ADSSL1 | 0.012665 | FAM184B | 0.013978 | NUSAP1 | 0.01332 | RPS20 | 0.005434 | SCIN | 0.018753 |
| NTAN1 | 0.002175 | NFU1 | 0.013558 | TMEM216 | 0.015387 | RPS27 | 0.017898 | DNAH17 | 0.004158 |
| PAQR4 | 0.0142 | ERLEC1 | 0.007909 | COA4 | 0.014236 | BDNF | 0.022225 | AOC3 | 0.007194 |
| SLC38A10 | 0.016031 | CSDC2 | 0.021434 | PHF21A | 0.009095 | SAFB | 0.002024 | DYNLL1 | 0.013871 |
| TBC1D16 | 0.004897 | GLO1 | 0.012283 | TMA7 | 0.006831 | BGN | 0.020155 | IRS2 | 0.005495 |
| ALDH16A1 | 0.010888 | CECR2 | 0.018271 | ATRAID | 0.017039 | UBE2O | 0.010593 | EIF3I | 0.009941 |
| ZNF57 | 0.005116 | GNB3 | 0.008725 | TRMT112 | 0.022512 | ANKEF1 | 0.023251 | VAMP8 | 0.000471 |
| PLK3 | 0.007839 | LOC283038 | 0.021043 | UFC1 | 0.014515 | MRPS14 | 0.001396 | ACTN1 | 0.009269 |
| KLHDC7A | 0.002283 | CCDC88B | 0.010242 | CHMP5 | 0.014515 | C19orf33 | 0.019512 | TNFSF13 | 0.01697 |
| COL6A3 | 0.018191 | TTC9C | 0.004763 | CUTA | 0.004813 | BLVRB | 0.005 | CBS | 0.016029 |
| AASDH | 0.011424 | HARBI1 | 0.00327 | ATP5G1 | 0.013571 | SH3GL1 | 0.012697 | TNFRSF10C | 0.021583 |
| COX6B1 | 0.011111 | SUGT1P3 | 0.015212 | LIPT1 | 0.009205 | PLA2G2F | 0.016278 | PEX11B | 0.009865 |
| COX7B | 0.015528 | PRTG | 0.021222 | ATP6V1H | 0.004288 | CSRNP1 | 0.017065 | BANF1 | 0.004288 |
| C7orf31 | 0.010866 | HID1 | 0.004194 | FAM96B | 0.003277 | LOC646938 | 0.000525 | ST3GAL5 | 0.005705 |
| HDX | 0.022505 | UBALD2 | 0.00421 | PTRH2 | 0.015222 | ST3GAL2 | 0.01909 | EIF2B2 | 0.005748 |
| FUNDC1 | 0.007404 | HMSD | 0.020175 | ASB1 | 0.022519 | TTC23 | 0.006601 | BUD31 | 0.016442 |
| SPIN4 | 0.020635 | EPHA10 | 0.01561 | VPS29 | 0.020423 | MRPS24 | 0.023265 | NAV2 | 0.016948 |
| UBE2F | 0.008837 | LOC285074 | 0.015233 | SELT | 0.001027 | MRPS15 | 0.016985 | MVB12B | 0.001728 |

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| CSF2RB | 0.01881 | RABL3 | 0.015212 | RTEL1 | 0.022451 | MRPL32 | 0.013338 | UBE3D | 0.012379 |
| CSNK1G2 | 0.012993 | C5orf51 | 0.019705 | TM7SF3 | 0.010418 | PINK1 | 0.021246 | CCDC97 | 0.021317 |
| CSPG4 | 0.008714 | FFAR2 | 0.014751 | PENK | 0.00297 | JMJD4 | 0.013874 | TMEM263 | 0.022077 |
| PRSS36 | 0.017935 | GRK6 | 0.008554 | PEX7 | 0.018873 | KIAA0895L | 0.01419 | NFS1 | 0.006172 |
| CCDC42 | 0.000246 | GRB10 | 0.006327 | PFKFB3 | 0.002683 | PAX8-AS1 | 0.01114 | SART1 | 0.015994 |
| RUNDC1 | 0.013736 | MAGEH1 | 0.002379 | PFKL | 0.019162 | SLC11A1 | 0.019044 | RQCD1 | 0.002274 |
| NLRP4 | 0.006589 | MRPL15 | 0.011813 | ATP5J | 0.00081 | FUNDC2 | 0.020698 | SYNGR1 | 0.018538 |
| C22orf42 | 0.020743 | STXBP6 | 0.023023 | PGM5 | 0.022043 | UAP1 | 0.019256 | CD3D | 0.00911 |
| MSL3P1 | 0.005238 | GSN | 0.009999 | PIK3CD | 0.004668 | SSR2 | 0.000541 | ZNF765 | 0.016998 |
| CYP1A1 | 0.014111 | GTF2E1 | 0.012124 | STX18 | 0.014125 | STAT5A | 0.021911 | COX7A2L | 0.016599 |
| CCDC167 | 0.020206 | UBN1 | 0.003694 | PMM2 | 0.015482 | STAT5B | 0.006635 | TMSB10 | 0.001352 |
| CLEC2L | 0.022283 | TIMM22 | 0.000164 | ATP5O | 0.014468 | SNORA54 | 0.002557 | IL1RL1 | 0.02292 |
| CRYGN | 0.002613 | NENF | 0.018054 | RIPK4 | 0.008022 | SURF2 | 0.020517 | PTTG1 | 0.014043 |
| WBSCR27 | 0.010799 | OSGIN1 | 0.015398 | POLR2I | 0.002347 | TBCE | 0.004497 | STRADA | 0.017461 |
| ADRBK1 | 0.011186 | FTSJ2 | 0.003251 | POLR2J | 0.013692 | TCEB2 | 0.004029 | IMP4 | 0.021668 |
| CYP2F1 | 0.019925 | ANXA1 | 0.020939 | POLR2K | 0.005077 | PPAN-P2RY11 | 0.015468 | ATP6V1F | 0.006037 |
| TTC16 | 0.016291 | HBG2 | 0.008554 | NLE1 | 0.021977 | MIR572 | 0.015996 | NT5C1B | 0.002168 |
| CD55 | 0.015878 | HIP1 | 0.007769 | RNF186 | 0.021105 | MIR619 | 0.021003 | LOC93432 | 0.005099 |
| ZFP1 | 0.015567 | HMBS | 0.004033 | GNB1L | 0.018179 | ZEB1 | 0.020939 | SDR42E1 | 0.0056 |
| ZNF433 | 0.013041 | HMGB2 | 0.02178 | FBXL12 | 0.012823 | DYNLT1 | 0.022783 | CRIP1 | 0.009431 |
| DDT | 0.002807 | NR4A1 | 0.017527 | TMEM70 | 0.00546 | TEF | 0.012306 | PGS1 | 0.008859 |
| NLRP6 | 0.008593 | PRMT1 | 0.00474 | PPP1R1A | 0.02044 | TLE3 | 0.007167 | AATK | 0.010357 |
| ARID3A | 0.013704 | HSD17B3 | 0.013787 | SOBP | 0.006578 | TLN1 | 0.021518 | ZNF592 | 0.014468 |
| IMMP1L | 8.83E-05 | HSPA1B | 0.023057 | ATP5SL | 0.006082 | GOLGA6L7P | 0.000734 | CROCC | 0.000842 |
| OR56B4 | 0.007385 | HSPA8 | 0.018868 | SHQ1 | 0.010392 | RGPD6 | 0.01581 | TBKBP1 | 0.015493 |
| EIF2S1 | 0.00167 | HTR2A | 0.017178 | TRIM62 | 0.019392 | UBA52 | 0.001823 | RNF40 | 0.01538 |

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| SNAI3-AS1 | 0.021195 | C17orf67 | 0.018394 | NUDT15 | 0.012646 | UBB | 0.001626 | ARHGEF11 | 0.023265 |
| APLF | 0.003043 | CCDC158 | 0.015409 | CWF19L1 | 0.012823 | VAV1 | 0.016235 | GAB2 | 0.015578 |
| TIGD1 | 0.016878 | IFITM4P | 0.022318 | SLC39A9 | 0.0066 | VCP | 0.005948 | RBM8A | 0.00251 |
| KCTD6 | 0.016974 | SMCO2 | 0.019715 | LGR4 | 0.012015 | VWF | 0.022512 | CDC34 | 0.011215 |

Table S2: The genes that significantly related to XYZ phenome ($p < 0.05$) at Day 30

| Gene | ρ | Gene | ρ | Gene | ρ |
|----------------|----------|-------------|----------|-----------|----------|
| SNORD121A | 0.022687 | TIMM9 | 0.008581 | SMAP1 | 0.018805 |
| C10orf131 | 0.021325 | RNU4-2 | 0.012015 | RPL36A | 0.015737 |
| TMEM221 | 0.000959 | GLUD1 | 0.021323 | MRPS12 | 0.013176 |
| SMIM6 | 0.010393 | GNG3 | 0.009899 | ACSM3 | 0.009518 |
| CLUHP3 | 0.006241 | C14orf177 | 0.017721 | CELA2A | 0.004952 |
| REXO1L2P | 0.002949 | FAM171A2 | 0.004115 | ATXN2 | 0.020163 |
| MIR4313 | 0.001961 | IAH1 | 0.022706 | SCP2 | 0.014205 |
| MIR3685 | 0.015154 | ZNF252P-AS1 | 0.018079 | VIPAS39 | 0.02253 |
| FGD5-AS1 | 0.007342 | ILDR1 | 0.02258 | SDHB | 0.001482 |
| LINC00888 | 0.01673 | GRIN1 | 0.008271 | RBKS | 0.01839 |
| INMT-FAM188B | 0.007612 | ZC3H7A | 0.017048 | SMOC2 | 0.008825 |
| BLOC1S5-TXNDC5 | 0.017909 | LINC00652 | 0.007612 | CEP170P1 | 0.011829 |
| MIA-RAB4B | 0.000942 | DROSHA | 0.00647 | CLEC7A | 0.010494 |
| FAM13A | 0.021015 | SNX12 | 0.017593 | LOC646938 | 0.018382 |
| CDK2 | 0.020831 | HDGF | 0.01641 | ARMCX5 | 0.018626 |
| RBM7 | 0.004009 | HLA-J | 0.002983 | C8orf33 | 0.019355 |
| TESK2 | 0.009258 | HMG2 | 0.004091 | SLC9A5 | 0.022161 |
| VAV3 | 0.019544 | FOXA3 | 0.000585 | SLC18A2 | 0.014318 |
| GPNMB | 0.009336 | HNRNPC | 0.00885 | SLC20A2 | 0.019433 |
| VTI1B | 0.007879 | HOXC13 | 0.011786 | SMARCE1 | 0.005464 |
| SLC19A2 | 0.012598 | HPN | 0.004866 | SPOCK1 | 0.005391 |
| CENPA | 0.00075 | TFAP2E | 0.02012 | SREBF2 | 0.018261 |
| TRIM3 | 0.006108 | CCDC36 | 0.012603 | SCARNA15 | 0.01867 |
| TXNIP | 0.013855 | KY | 0.013519 | SNORA81 | 0.005417 |
| IGF2BP1 | 0.010483 | ZKSCAN2 | 0.017445 | AURKA | 0.009741 |
| MTX2 | 0.014553 | XKR7 | 0.003245 | SULT1A2 | 0.009496 |
| EBP | 0.011857 | ACTBL2 | 0.007648 | KLF9 | 0.018765 |
| TCFL5 | 0.007714 | IFNGR1 | 0.02001 | TAF7 | 0.01294 |
| IQGAP2 | 0.011051 | FAM71F2 | 0.006358 | SNORD86 | 0.00425 |
| YWHAQ | 0.009479 | SOX2-OT | 0.020383 | SNORD89 | 0.005537 |
| DSTN | 0.016814 | IGFBP7 | 0.011762 | DYNLT3 | 0.018125 |
| RCC1 | 0.018901 | ILF2 | 0.015194 | TEC | 0.014156 |
| PRDM5 | 0.020594 | IMPG1 | 0.008902 | TFDP1 | 0.014823 |
| ZWINT | 0.010342 | KCNJ12 | 0.014996 | C1QBP | 0.003782 |
| HHLA2 | 0.015943 | KIF3C | 0.011667 | TMOD1 | 0.008758 |
| ADCY6 | 0.015846 | KRT10 | 0.002683 | KRTAP19-8 | 0.006519 |
| RNF139 | 0.022642 | LRRC75A | 0.004114 | TUFM | 0.009624 |
| GTF3C6 | 0.000856 | LINC00478 | 0.001915 | OSGIN2 | 0.014715 |
| CYP4F8 | 0.023154 | TMPRSS11F | 0.022089 | UFD1L | 0.012791 |
| LYST | 0.023158 | OR52H1 | 0.019914 | UGCG | 0.013415 |
| DDX42 | 0.008224 | CTXN2 | 0.003287 | KDM6A | 0.001656 |

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| PDAP1 | 0.021275 | LINC00938 | 0.011762 | ZNF131 | 0.022581 |
| CHRNA3 | 0.000812 | LMX1B | 0.018139 | DDX54 | 0.010974 |
| PIK3IP1 | 0.023082 | MBNL1-AS1 | 0.006468 | C2orf54 | 0.00866 |
| KLHL32 | 0.01381 | RGS7BP | 0.010452 | SEMA6D | 0.000613 |
| OSBPL9 | 0.010763 | MIR7-1 | 0.003802 | PIF1 | 0.021751 |
| FBXO32 | 0.002145 | EPCAM | 0.022718 | RPF1 | 0.016467 |
| SLC26A7 | 0.010703 | SMAD7 | 0.020945 | EPC1 | 0.010338 |
| UHRF2 | 0.009055 | MAGOH | 0.012708 | ZSCAN16 | 0.003219 |
| MED12L | 0.006014 | CD46 | 0.019743 | PTP4A2 | 0.011814 |
| CATSPER1 | 0.021739 | SMIM22 | 0.014961 | ANKRD13C | 0.015552 |
| CLC | 0.020078 | HIST2H2BF | 0.01513 | CAMK2B | 0.004038 |
| DCUN1D3 | 0.0083 | MYBPC1 | 0.001916 | COIL | 0.015754 |
| WFIKKN2 | 0.019259 | NDUFS1 | 0.016183 | CAB39L | 0.00715 |
| ATP6V1G3 | 0.00378 | NPTX1 | 0.01587 | ISCA1 | 0.021111 |
| SYT2 | 0.011438 | SERPINE1 | 0.012512 | GDF5 | 0.02091 |
| SPATA17 | 0.002983 | COPS7A | 0.02001 | RILP | 0.012914 |
| TTC32 | 0.016996 | PCDH7 | 0.012815 | DYNLRB2 | 0.020596 |
| ADORA2A | 0.017107 | FAHD2A | 0.00177 | HIST1H4E | 0.008729 |
| PIP5KL1 | 0.000395 | GLOD4 | 0.020693 | KRTAP4-12 | 0.018167 |
| UBE2F | 0.016629 | MEMO1 | 0.003593 | CASP8 | 0.002175 |
| ASB15 | 0.021525 | GAL | 0.022089 | BFSP2 | 0.005738 |
| CSNK2A2 | 0.005943 | LEF1 | 0.006541 | POLR3GL | 0.016004 |
| TMEM161B | 0.010957 | ZNF117 | 0.012299 | C9orf64 | 0.022993 |
| RAET1L | 0.005324 | ANGPT4 | 0.004556 | NTPCR | 0.006676 |
| CYP19A1 | 0.012436 | BIN2 | 0.006334 | USP38 | 0.012178 |
| HSFY2 | 0.011317 | SFMBT1 | 0.017341 | MAEL | 0.014383 |
| DBI | 0.006995 | CHMP5 | 0.021752 | PPFIBP1 | 0.006954 |
| DENND2C | 0.010981 | TMBIM4 | 0.012754 | ITGA8 | 0.00668 |
| UBXN2A | 0.012576 | CES1P1 | 0.00951 | SLC25A12 | 0.021775 |
| C10orf128 | 0.002704 | PFDN4 | 0.007893 | EIF3D | 0.022065 |
| E2F3 | 0.010763 | PIGH | 0.00735 | EIF3G | 0.020213 |
| EMR1 | 0.014771 | PKP1 | 0.022089 | B3GALNT1 | 0.010623 |
| R3HCC1 | 0.008417 | PLXNA2 | 0.002124 | URI1 | 0.018386 |
| ETS2 | 0.007678 | SETD4 | 0.002569 | GGACT | 0.022175 |
| F8 | 0.002852 | POLE3 | 0.009697 | DCAF5 | 0.021098 |
| LOC220729 | 0.011719 | ERRFI1 | 0.005341 | KSR1 | 0.021775 |
| | 43167 | INO80 | 0.005555 | KAT2B | 0.022781 |
| ALKBH3 | 0.004708 | PCSK4 | 0.020211 | SYNJ2 | 0.002245 |
| SDK1 | 0.004344 | ZNF586 | 0.013214 | NAE1 | 0.023244 |
| TMED4 | 0.020349 | ANKRD49 | 0.011358 | CPNE3 | 0.010416 |
| FGF2 | 0.021267 | TRIM68 | 0.022856 | GYG2 | 0.00064 |
| CASC3 | 0.012884 | ZDHHC4 | 0.022211 | CCND3 | 0.00301 |
| CPEB3 | 0.022237 | NADSYN1 | 0.016229 | WDR34 | 0.01807 |
| WDR47 | 0.023296 | LGI2 | 0.019251 | CCNH | 0.014771 |

| | | | | | |
|-----------|----------|--------|----------|-----------|----------|
| SNX13 | 0.001982 | YOD1 | 0.010486 | ZNF551 | 0.004921 |
| RFTN1 | 0.002839 | GNG12 | 0.010136 | MCU | 0.003364 |
| GANAB | 0.012134 | KCMF1 | 0.022052 | CCT6A | 0.020611 |
| TSPYL4 | 0.012312 | C8orf4 | 0.00378 | TCEAL8 | 0.020508 |
| ARHGEF18 | 0.019216 | MCCC1 | 0.017066 | PRPF4 | 0.019998 |
| TDRD7 | 0.015453 | PTGER2 | 0.020417 | C12orf29 | 0.015627 |
| DDAH2 | 0.010486 | MIR491 | 0.013621 | GGTLC1 | 0.015302 |
| GABARAPL1 | 0.020167 | ERMN | 0.019519 | C1orf105 | 0.018411 |
| ABL1 | 0.016571 | PTMA | 0.023158 | PXYLP1 | 0.01512 |
| ACKR1 | 0.013079 | WDR48 | 0.02131 | REEP6 | 0.017695 |
| SNX32 | 0.014883 | PTPN1 | 0.022042 | BAG5 | 0.022088 |
| MCM9 | 0.01547 | SPTBN4 | 0.004799 | CD70 | 0.005004 |
| DNAJB5 | 0.007966 | PTPN12 | 0.008411 | DOCK4 | 0.009675 |
| EGFL6 | 0.015708 | RAP2C | 0.008575 | PTDSS1 | 0.01356 |
| CHMP2B | 0.01983 | RAB6A | 0.00527 | NUP153 | 0.006177 |
| FAM32A | 0.00185 | ACTA2 | 0.01484 | NR_024132 | 0.00808 |
| DECR2 | 0.01391 | RBBP7 | 0.009845 | NR_024557 | 0.007757 |
| FAM127B | 0.020555 | ZNF350 | 0.015562 | 3-Sep | 0.003284 |

Table S3: Pathway enrichment results for chest pain at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|--|
| hsa03010 | Ribosome | -19 | 9 | 15 | FAU RPSA RPL4 RPL6 RPL10 RPL12 RPL15 RPL17 RPL18A RPL24 RPL27 RPL30 RPL29 RPL31 RPL35A RPLP0 RPS3 RPS5 RPS6 RPS9 RPS11 RPS14 RPS15 RPS20 RPS27 UBA52 MRPL15 MRPS14 MRPL14 MRPS15 |
| hsa05171 | Coronavirus disease - COVID-19 | -14 | 5.9 | 11 | FAU CXCL10 RPSA NFKB1 RPL4 RPL6 RPL10 RPL12 RPL15 RPL17 RPL18A RPL24 RPL27 RPL30 RPL29 RPL31 RPL35A RPLP0 RPS3 RPS5 RPS6 RPS9 RPS11 RPS14 RPS15 RPS20 RPS27 UBA52 VWF |
| hsa00190 | Oxidative phosphorylation | -12 | 7.4 | 11 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP6V1E1 ATP5PO COX6A1 COX6B1 COX7A2 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 UQCRB COX7A2L ATP6V1F ATP5MF ATP5MG UQCR11 |
| hsa05012 | Parkinson disease | -11 | 5 | 9.6 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 EIF2S1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 PSMA1 PSMA4 PSMA6 PSMD8 TXN UBA52 UBB UQCRB COX7A2L UQCR11 SLC39A8 PINK1 MCU |
| hsa05016 | Huntington disease | -10 | 4.3 | 8.6 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO BDNF CLTA COX6A1 COX6B1 COX7A2 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 POLR2I POLR2J POLR2K POLR2L PSMA1 PSMA4 PSMA6 PSMD8 UQCRB ULK1 COX7A2L UQCR11 |
| hsa05014 | Amyotrophic lateral sclerosis | -8.9 | 3.8 | 7.8 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 EIF2S1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 MAP2K3 PSMA1 PSMA4 PSMA6 PSMD8 UQCRB VCP ULK1 COX7A2L UQCR11 PINK1 MCU MAP1LC3B2 POM121C |
| hsa05208 | Chemical carcinogenesis - reactive oxygen species | -8.6 | 4.7 | 8.1 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 CYP2F1 MGST1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 NFKB1 UQCRB COX7A2L GSTO1 UQCR11 PRKD2 |
| hsa05022 | Pathways of | -8.5 | 3.3 | 7.4 | ATP2A3 ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO BDNF COX6A1 COX6B1 CO |

| | | | | | |
|----------|---------------------------------------|------|-----|-----|--|
| | neurodegeneration - multiple diseases | | | | X7A2 EIF2S1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 NFKB1 MAP2K3 PSMA1 PSMA4 PSMA6 PSMD8 UBA52 UBB UQCRB VCP ULK1 COX7A2L UQCR11 PINK1 MCU MAP1LC3B2 |
| hsa05010 | Alzheimer disease | -8.4 | 3.6 | 7.5 | ATP2A3 ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 EIF2S1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 NFKB1 PSMA1 PSMA4 PSMA6 PSMD8 UQCRB ULK1 COX7A2L UQCR11 APH1A SLC39A8 APH1B MCU ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 EIF2S1 L |
| hsa05020 | Prion disease | -8.3 | 4.2 | 7.7 | AMC1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 PSMA1 PSMA4 PSMA6 PSMD8 UQCRB COX7A2L UQCR11 MCU |
| hsa04714 | Thermogenesis | -8.3 | 4.5 | 7.8 | ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 MAP2K3 RPS6 UQCRB COX7A2L ATP5MF ATP5MG UQCR11 COA5 |
| hsa05415 | Diabetic cardiomyopathy | -7.1 | 4.4 | 7.2 | ATP2A3 ATP5F1B ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6A1 COX6B1 COX7A2 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 NFKB1 UQCRB COX7A2L UQCR11 |
| hsa04120 | Ubiquitin mediated proteolysis | -5.7 | 4.7 | 6.4 | CDC34 SKP1 ELOB UBA52 UBB UBE2E1 UBE2E2 UBE2H WWP2 ANAPC13 PRPF19 ANAPC2 UBE2O UBE2F |
| hsa04932 | Non-alcoholic fatty liver disease | -5.2 | 4.3 | 6 | COX6A1 COX6B1 COX7A2 EIF2S1 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 NFKB1 UQCRB COX7A2L UQCR11 |
| hsa04144 | Endocytosis | -4 | 3 | 4.7 | GRK2 CLTA FGFR4 GRK6 WIPF1 HGS CYTH1 ACAP1 ARPC2 EHD1 DNM3 EPS15L1 VPS37B VPS25 RAB11FIP4 MVB12B |
| hsa03020 | RNA polymerase | -3.2 | 7 | 5.1 | POLR2I POLR2J POLR2K POLR2L POLR1D |
| hsa03040 | Spliceosome | -2.9 | 3.2 | 4 | DHX8 HNRNPC HNRNPM SNRPD2 SART1 DDX23 SF3A1 LSM5 PRPF19 SF3B5 |
| hsa04146 | Peroxisome | -2.8 | 4 | 4.1 | PRDX1 ABCD4 PXMP2 PEX11B PRDX5 HACL1 GSTK1 |
| hsa04810 | Regulation of actin cytoskeleton | -2.6 | 2.6 | 3.5 | ACTN1 FGFR4 GSN ITGB4 LIMK2 MYH9 VAV1 LPAR2 ARPC2 SCIN FGD3 MYL12B |

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|----------|---|------|-----|-----|---|
| hsa04260 | Cardiac muscle contraction | -2.6 | 3.8 | 3.9 | ATP2A3 COX6A1 COX6B1 COX7A2 UQCRB COX7A2L UQCR11 |
| hsa05017 | Spinocerebellar ataxia | -2.5 | 3 | 3.5 | ATP2A3 PSMA1 PSMA4 PSMA6 PSMD8 ULK1 CIC ATXN10 MCU |
| hsa04137 | Mitophagy - animal | -2.4 | 3.9 | 3.7 | UBA52 UBB ULK1 FIS1 PINK1 MAP1LC3B2 |
| hsa05132 | Salmonella infection | -2.2 | 2.3 | 3 | DYNC1I2 FLNA NFKB1 MAP2K3 RPS3 SKP1 DYNLT1 TXN CYTH1 ARPC2 MYL12B ARL8A |
| hsa05166 | Human T-cell leukemia virus 1 infection | -2.1 | 2.3 | 3 | HLA-DQA1 MAD2L1 NFATC1 NFKB1 NFKB2 RAN STAT5B MAD1L1 PTTG1 ANAPC13 ANAPC2 |
| hsa04066 | HIF-1 signaling pathway | -2.1 | 3 | 3.1 | MKNK2 LDHA NFKB1 PFKFB3 PFKL RPS6 ELOB |
| hsa04623 | Cytosolic DNA-sensing pathway | -2 | 3.8 | 3.2 | CXCL10 NFKB1 POLR2K POLR2L POLR1D |
| hsa05203 | Viral carcinogenesis Retrograde | -1.9 | 2.3 | 2.8 | ACTN1 GSN H2BC5 NFKB1 NFKB2 STAT5B H4C4 MAD1L1 HDAC5 SCIN |
| hsa04723 | endocannabinoid signaling | -1.9 | 2.6 | 2.8 | GNB3 NDUFA4 NDUFA8 NDUFA9 NDUFB1 NDUFC1 NDUFS6 GNB5 |
| hsa03050 | Proteasome | -1.8 | 4.1 | 3.1 | PSMA1 PSMA4 PSMA6 PSMD8 |
| hsa00620 | Pyruvate metabolism | -1.8 | 4 | 3.1 | ACAT1 DLAT GLO1 LDHA |
| hsa00650 | Butanoate metabolism | -1.7 | 5.1 | 3.2 | ACAT1 BDH1 HADH |
| hsa04721 | Synaptic vesicle cycle | -1.6 | 3 | 2.6 | ATP6V1E1 CLTA RAB3A ATP6V1F DNM3 |
| hsa03018 | RNA degradation | -1.6 | 3 | 2.6 | CNOT2 CNOT3 PFKL CNOT9 LSM5 |
| hsa03013 | Nucleocytoplasmic transport | -1.6 | 2.6 | 2.5 | RAN SUMO2 TNPO3 THOC6 THOC7 POM121C |
| hsa00480 | Glutathione metabolism | -1.5 | 3.3 | 2.5 | MGST1 GSTO1 TXNDC12 GSTK1 |
| hsa00760 | Nicotinate and | -1.4 | 4.1 | 2.7 | PNP NADK NT5C1B |

| | | | | | |
|----------|-------------------------------------|------|-----|-----|--|
| | nicotinamide metabolism | | | | |
| hsa05131 | Shigellosis | -1.4 | 1.9 | 2.1 | ACTN1 NFKB1 SKP1 UBA52 UBB CYTH1 ARPC2 TECPR1 MYL12B MAP1LC3B2 |
| hsa04658 | Th1 and Th2 cell differentiation | -1.3 | 2.6 | 2.2 | HLA-DQA1 JAG2 NFATC1 NFKB1 STAT5B |

Table S4: Pathway enrichment results for chest distress at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|---|
| hsa03010 | Ribosome | -23 | 10 | 17 | FAU RPSA RPL3 RPL4 RPL6 RPL7 RPL7A RPL10 RPL12 RPL15 RPL17 RPL24 RPL30 RPL31 RPL34 RPL35A RPLP0 RPS3 RPS3A RPS9 RPS10 RPS14 RPS15A RPS18 RPS20 RPS24 RPS27 UBA52 RPL23 RPL35 RPL13A MRPS14 MRPS15 MRPL11 |
| hsa05171 | Coronavirus disease - COVID-19 | -19 | 7 | 14 | FAU RPSA PIK3CD PIK3R2 RPL3 RPL4 RPL6 RPL7 RPL7A RPL10 RPL12 RPL15 RPL17 RPL24 RPL30 RPL31 RPL34 RPL35A RPLP0 RPS3 RPS3A RPS9 RPS10 RPS14 RPS15A RPS18 RPS20 RPS24 RPS27 MAP3K7 UBA52 IKBK G RPL23 RPL35 RPL13A |
| hsa05012 | Parkinson disease | -8.3 | 4.2 | 7.7 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C EIF2S1 NDUFA4 NDUFA6 NDUFA8 NDUFS3 PRKACB PSMA6 UBA52 UBB UBC XBP1 COX7A2L PPIF UQC R11 TXN2 SLC39A9 MCU |
| hsa05010 | Alzheimer disease | -8.1 | 3.5 | 7.3 | APOE ATP2A3 ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C EIF2S1 NDUFA4 NDUFA6 NDUFA8 NDUFS3 PIK3CD PIK3R2 PSMA6 XBP1 FZD1 FZD8 IKBK G IRS2 COX7A2L ATG13 PPIF APC2 UQCR11 SLC39A9 MCU |
| hsa05022 | Pathways of neurodegeneration - multiple diseases | -7.7 | 3.1 | 6.9 | ATP2A3 ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C EIF2S1 HIP1 NDUFA4 NDUFA6 NDUFA8 NDUFS3 MAP2K3 PSMA6 SPTBN2 UBA52 UBB UBC XBP1 FZD1 FZD8 DNAH17 COX7A2L ATG13 PPIF APC2 UQCR11 TOMM40L MCU MAP1LC 3C |
| hsa05208 | Chemical carcinogenesis - | -7.7 | 4.4 | 7.5 | ACP1 ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C NDUFA4 NDUFA6 NDUFA8 NDUFS3 PIK3CD PIK3R2 PRKCD IKBK G COX7A2L GSTO1 PPIF UQCR11 |

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|----------|-----------------------------------|------|-----|-----|--|
| | reactive oxygen species | | | | PRKD2 |
| hsa05020 | Prion disease | -7.5 | 3.9 | 7.1 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C EIF2S1 HSPA8 NDUFA4 NDUFA6 NDUFA8 NDUFS3 NOTCH1 PIK3CD PIK3R2 PRKACB PRKCD PSMA6 COX7A2L PPIF UQCR11 MCU |
| hsa04714 | Thermogenesis | -6.7 | 4 | 6.8 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C NDUFA4 NDUFA6 NDUFA8 NDUFS3 PRKACB PRKAG1 MAP2K3 COX7A2L ATP5MF UQCR11 COA4 SIRT6 COX14 |
| hsa00190 | Oxidative phosphorylation | -6.6 | 5.2 | 7.2 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C NDUFA4 NDUFA6 NDUFA8 NDUFS3 PPA1 COX7A2L ATP5MF UQCR11 |
| hsa04932 | Non-alcoholic fatty liver disease | -6.6 | 4.8 | 7 | COX7A2 COX7B COX7C EIF2S1 MAP3K11 NDUFA4 NDUFA6 NDUFA8 NDUFS3 PIK3CD PIK3R2 PRKAG1 XBP1 IRS2 COX7A2L UQCR11 |
| hsa04120 | Ubiquitin mediated proteolysis | -6.3 | 4.9 | 6.9 | CDC34 ELOC ELOB UBA52 UBB UBC UBE2E2 CUL5 ANAPC10 WWP2 ANAPC13 ANAPC2 KLHL9 UBE2O UBE2F |
| hsa05415 | Diabetic cardiomyopathy | -6.3 | 4.1 | 6.6 | ATP2A3 ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C NDUFA4 NDUFA6 NDUFA8 NDUFS3 PIK3CD PIK3R2 PRKCD COX7A2L PPIF UQCR11 |
| hsa05014 | Amyotrophic lateral sclerosis | -5.3 | 2.9 | 5.5 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C EIF2S1 NDUFA4 NDUFA6 NDUFA8 NDUFS3 MAP2K3 PSMA6 SRSF3 XBP1 DNAH17 COX7A2L ATG13 UQCR11 TOMM40L MCU MAP1LC3C |
| hsa05016 | Huntington disease | -4.9 | 3 | 5.3 | ATP5F1C ATP5MC3 ATP5PF ATP5PO COX7A2 COX7B COX7C HIP1 NDUFA4 NDUFA6 NDUFA8 NDUFS3 POLR2D POLR2K PSMA6 DNAH17 COX7A2L ATG13 PPIF UQCR11 |
| hsa04658 | Th1 and Th2 cell differentiation | -4.5 | 5 | 5.8 | CD3D JAG2 JAK3 NFATC1 NOTCH1 NOTCH3 STAT5A STAT5B IKBKG MAML3 |
| hsa04140 | Autophagy - animal | -4.2 | 3.9 | 5.2 | EIF2S1 PIK3CD PIK3R2 PRKACB PRKCD MAP3K7 IRS2 VAMP8 ATG13 DEPTOR ATG4A MAP1LC3C |
| hsa04137 | Mitophagy - animal | -3.8 | 5.1 | 5.2 | TFE3 UBA52 UBB UBC TFEB FIS1 FUNDC1 MAP1LC3C |

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|----------|---|------|-----|-----|--|
| hsa05017 | Spinocerebellar ataxia | -3.5 | 3.6 | 4.6 | ATP2A3 PIK3CD PIK3R2 PSMA6 SPTBN2 XBP1 ATG13 PPIF CIC ATXN10 MCU |
| hsa05166 | Human T-cell leukemia virus 1 infection | -3.4 | 2.9 | 4.3 | CD3D JAK3 NFATC1 PIK3CD PIK3R2 PRKACB SPI1 STAT5A STAT5B TLN1 IKBKGA NAPC10 ANAPC13 ANAPC2 |
| hsa03040 | Spliceosome | -3.4 | 3.5 | 4.4 | HNRNPC HSPA8 MAGOH SRSF3 BUD31 RBM8A CRNKL1 PPIL1 MAGOHB SF3B5 PHF5A |
| hsa04660 | T cell receptor signaling pathway | -3.4 | 4 | 4.6 | CD3D CD8B NCK1 NFATC1 PIK3CD PIK3R2 MAP3K7 VAV1 IKBKGA |
| hsa05221 | Acute myeloid leukemia | -3.2 | 4.8 | 4.7 | PIK3CD PIK3R2 RARA SPI1 STAT5A STAT5B IKBKGA |
| hsa03020 | RNA polymerase | -3.1 | 6.8 | 5 | POLR2D POLR2K POLR3B POLR3GL POLR1F |
| hsa05135 | Yersinia infection | -3.1 | 3.4 | 4.1 | CD8B NFATC1 PIK3CD PIK3R2 MAP2K3 MAP3K7 VAV1 WAS IKBKGA ARPC1A |
| hsa05162 | Measles | -3 | 3.3 | 4.1 | CD3D EIF2S1 HSPA8 JAK3 PIK3CD PIK3R2 STAT5A STAT5B MAP3K7 IKBKGA |
| hsa04062 | Chemokine signaling pathway | -3 | 2.9 | 3.9 | GRK5 GRK6 JAK3 PIK3CD PIK3R2 PRKACB PRKCD CCL23 STAT5B VAV1 WAS IKBKGA |
| hsa04666 | Fc gamma R-mediated phagocytosis | -2.9 | 3.8 | 4.1 | LIMK2 PIK3CD PIK3R2 PRKCD VAV1 WAS GAB2 ARPC1A |
| hsa04144 | Endocytosis | -2.9 | 2.6 | 3.7 | CAPZA1 FGFR4 GRK5 GRK6 HSPA8 SH3GL1 DNAJC6 IQSEC1 ARPC1A EHD1 CHMP5 VPS37B MVB12B ARAP1 |
| hsa04330 | Notch signaling pathway | -2.8 | 4.7 | 4.2 | JAG2 NOTCH1 NOTCH3 TLE3 HEY1 MAML3 |
| hsa04213 | Longevity regulating pathway - multiple species | -2.7 | 4.5 | 4.1 | HSPA8 PIK3CD PIK3R2 PRKACB PRKAG1 IRS2 |
| hsa05170 | Human immunodeficiency virus 1 infection | -2.6 | 2.6 | 3.5 | CD3D LIMK2 NFATC1 PIK3CD PIK3R2 MAP2K3 MAP3K7 ELOC ELOB CUL5 IKBKGA AP1S2 |

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|----------|--|------|-----|-----|---|
| hsa05161 | Hepatitis B | -2.5 | 2.9 | 3.5 | JAK3 NFATC1 PCNA PIK3CD PIK3R2 MAP2K3 STAT5A STAT5B MAP3K7 IKBK |
| hsa05131 | Shigellosis | -2.5 | 2.4 | 3.4 | ACTN1 PIK3CD PIK3R2 PRKCD MAP3K7 TLN1 UBA52 UBB UBC IKBK ARPC1A TE CPR1 MAP1LC3C |
| hsa05200 | Pathways in cancer | -2.5 | 1.9 | 3.2 | CSF2RB FGFR4 GLI1 JAG2 JAK3 NOTCH1 NOTCH3 PIK3CD PIK3R2 PRKACB RARA SPI1 STAT5A STAT5B ELOC ELOB FZD1 FZD8 IKBK GSTO1 APC2 HEY1 |
| hsa05224 | Breast cancer | -2.3 | 2.8 | 3.3 | JAG2 NOTCH1 NOTCH3 PIK3CD PIK3R2 FZD1 FZD8 APC2 HEY1 |
| hsa05220 | Chronic myeloid leukemia | -2.2 | 3.7 | 3.4 | PIK3CD PIK3R2 STAT5A STAT5B IKBK GAB2 |
| hsa05340 | Primary immunodeficiency | -2 | 4.9 | 3.5 | CD3D CD8B JAK3 IKBK |
| hsa04659 | Th17 cell differentiation | -2 | 3 | 3.1 | CD3D JAK3 NFATC1 RARA STAT5A STAT5B IKBK |
| hsa03013 | Nucleocytoplasmic transport | -2 | 3 | 3.1 | EEF1A1 KPNA2 MAGO RBM8A TNPO3 MAGO THOC7 |
| hsa04066 | HIF-1 signaling pathway | -2 | 3 | 3.1 | ANGPT1 PFKFB3 PIK3CD PIK3R2 ELOC ELOB MKNK1 |
| hsa04310 | Wnt signaling pathway | -2 | 2.5 | 2.9 | NFATC1 PRKACB MAP3K7 TLE3 FZD1 FZD8 APC2 LGR4 NOTUM |
| hsa04260 | Cardiac muscle contraction | -1.9 | 3.2 | 3 | ATP2A3 COX7A2 COX7B COX7C COX7A2L UQCR11 |
| hsa04530 | Tight junction | -1.9 | 2.5 | 2.8 | ACTN1 CD1E MYL6 PCNA PRKACB PRKAG1 WAS ARPC1A F11R |
| hsa05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | -1.9 | 3.1 | 3 | CD3D NFATC1 PIK3CD PIK3R2 MAP2K3 IKBK |
| hsa04211 | Longevity regulating pathway | -1.9 | 3.1 | 3 | PIK3CD PIK3R2 PRKACB PRKAG1 IRS2 ATG13 |
| hsa05203 | Viral carcinogenesis | -1.9 | 2.3 | 2.7 | ACTN1 GTF2E1 JAK3 PIK3CD PIK3R2 PRKACB STAT5A STAT5B H2BC21 IKBK |

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|----------|--|------|-----|-----|---|
| hsa04935 | Growth hormone synthesis, secretion and action | -1.8 | 2.7 | 2.8 | PIK3CD PIK3R2 PRKACB MAP2K3 STAT5A STAT5B IRS2 |
| hsa04152 | AMPK signaling pathway | -1.8 | 2.7 | 2.8 | PFKFB3 PIK3CD PIK3R2 PRKAG1 MAP3K7 IRS2 EEF2K |
| hsa04664 | Fc epsilon RI signaling pathway | -1.8 | 3.4 | 2.9 | PIK3CD PIK3R2 MAP2K3 VAV1 GAB2 |
| hsa04919 | Thyroid hormone signaling pathway | -1.8 | 2.7 | 2.7 | ATP2A3 NOTCH1 NOTCH3 PIK3CD PIK3R2 PRKACB MED16 |
| hsa05211 | Renal cell carcinoma | -1.8 | 3.4 | 2.9 | PIK3CD PIK3R2 ELOC ELOB TFE3 |
| hsa04930 | Type II diabetes mellitus | -1.8 | 4 | 3 | PIK3CD PIK3R2 PRKCD IRS2 |
| hsa04520 | Adherens junction | -1.7 | 3.3 | 2.8 | ACP1 ACTN1 NECTIN1 MAP3K7 WAS |
| hsa05417 | Lipid and atherosclerosis | -1.7 | 2.2 | 2.5 | EIF2S1 HSPA8 NFATC1 PIK3CD PIK3R2 MAP2K3 MAP3K7 VAV1 XBP1 IKBKG |
| hsa01522 | Endocrine resistance | -1.7 | 2.8 | 2.7 | JAG2 NOTCH1 NOTCH3 PIK3CD PIK3R2 PRKACB |
| hsa05223 | Non-small cell lung cancer | -1.7 | 3.2 | 2.8 | JAK3 PIK3CD PIK3R2 STAT5A STAT5B |
| hsa04380 | Osteoclast differentiation | -1.7 | 2.5 | 2.6 | NFATC1 PIK3CD PIK3R2 SPI1 MAP3K7 IKBKG GAB2 |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications | -1.7 | 2.8 | 2.6 | NFATC1 PIK3CD PIK3R2 PRKCD STAT5A STAT5B |
| hsa00270 | Cysteine and methionine metabolism | -1.6 | 3.7 | 2.8 | GCLC MDH1 MAT2B KYAT3 |
| hsa04914 | Progesterone-mediated | -1.6 | 2.7 | 2.6 | PIK3CD PIK3R2 PRKACB ANAPC10 ANAPC13 ANAPC2 |

| | | | | | |
|----------|--|------|-----|-----|---|
| | oocyte maturation | | | | |
| hsa04625 | C-type lectin receptor signaling pathway | -1.6 | 2.7 | 2.5 | BCL3 NFATC1 PIK3CD PIK3R2 PRKCD IKBK |
| hsa04910 | Insulin signaling pathway | -1.5 | 2.4 | 2.4 | PIK3CD PIK3R2 PRKACB PRKAG1 MKNK1 IRS2 SH2B2 |
| hsa04915 | Estrogen signaling pathway | -1.5 | 2.3 | 2.4 | HSPA8 KRT12 PIK3CD PIK3R2 PRKACB PRKCD RARA |
| hsa04662 | B cell receptor signaling pathway | -1.5 | 2.8 | 2.5 | NFATC1 PIK3CD PIK3R2 VAV1 IKBK |
| hsa04923 | Regulation of lipolysis in adipocytes | -1.5 | 3.3 | 2.6 | PIK3CD PIK3R2 PRKACB IRS2 |
| hsa04141 | Protein processing in endoplasmic reticulum | -1.5 | 2.2 | 2.3 | EIF2S1 HSPA8 SSR2 XBP1 UBXN8 BAG2 TRAM1 ERLEC1 |
| hsa04668 | TNF signaling pathway | -1.5 | 2.5 | 2.3 | BCL3 PIK3CD PIK3R2 MAP2K3 MAP3K7 IKBK |
| hsa04550 | Signaling pathways regulating pluripotency of stem cells | -1.4 | 2.3 | 2.3 | FGFR4 JAK3 PIK3CD PIK3R2 FZD1 FZD8 APC2 |
| hsa04012 | ErbB signaling pathway | -1.4 | 2.7 | 2.4 | NCK1 PIK3CD PIK3R2 STAT5A STAT5B |
| hsa04670 | Leukocyte transendothelial migration | -1.4 | 2.4 | 2.3 | ACTN1 PIK3CD PIK3R2 SIPA1 VAV1 F11R |
| hsa00760 | Nicotinate and nicotinamide metabolism | -1.4 | 4 | 2.6 | PNP SIRT6 NADK |
| hsa04015 | Rap1 signaling | -1.4 | 2 | 2.1 | ANGPT1 FGFR4 PIK3CD PIK3R2 MAP2K3 SIPA1 TLN1 VAV1 PRKD2 |

| | | | | | |
|----------|---|------|-----|-----|--|
| hsa04621 | pathway NOD-like receptor signaling pathway | -1.3 | 2 | 2 | PRKCD MAP3K7 IKBK SUGT1 TXN2 NLRX1 MCU MAP1LC3C |
| hsa04623 | Cytosolic DNA-sensing pathway | -1.3 | 2.9 | 2.3 | POLR2K IKBK POLR3B POLR3GL |
| hsa05217 | Basal cell carcinoma | -1.3 | 2.9 | 2.3 | GLI1 FZD1 FZD8 APC2 |
| hsa04810 | Regulation of actin cytoskeleton | -1.3 | 1.9 | 2 | ACTN1 FGFR4 ITGB4 LIMK2 PIK3CD PIK3R2 VAV1 APC2 ARPC1A |
| hsa01240 | Biosynthesis of cofactors | -1.3 | 2.1 | 2.1 | AK2 GCLC MAT2B LIPT1 COQ3 NADK IDO2 |

Table S5: Pathway enrichment results for palpitations at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|--|
| hsa05168 | Herpes simplex virus 1 infection | -2.9 | 2.7 | 3.8 | LTA NFKBIA ZNF354A ZNF17 ZNF180 CARD9 ZNF419 ZNF442 ZNF527 ZNF160 ZNF563 ZNF565 ZNF850 |
| hsa05321 | Inflammatory bowel disease | -2.4 | 6.3 | 4.3 | IL12RB1 TGFB2 IL23A IL23R |
| hsa03022 | Basal transcription factors | -2 | 6.9 | 3.9 | GTF2B TAF11 GTF2IRD1 |
| hsa05134 | Legionellosis | -1.7 | 5.4 | 3.3 | CLK1 NFKBIA SAR1B |
| hsa04659 | Th17 cell differentiation | -1.7 | 3.8 | 2.9 | IL12RB1 NFKBIA IL23A IL23R |
| hsa04080 | Neuroactive ligand-receptor interaction | -1.6 | 2.3 | 2.5 | ADRB3 CHRNA2 GNRH2 HRH1 PLG PRSS1 NPFFR2 PATE2 |
| hsa04060 | Cytokine-cytokine | -1.6 | 2.4 | 2.5 | IL12RB1 LTA TGFB2 ACKR4 IL23A IL23R GDF6 |

receptor interaction
 hsa05164 Influenza A -1.6 3 2.6 DNAJB1|NFKBIA|PLG|PRSS1|CALCOCO2

Table S6: Pathway enrichment results for purple or dark lips at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|--|------|------------|---------|---------------------------------|
| hsa00140 | Steroid hormone biosynthesis | -3 | 8.8 | 5.3 | CYP1A1 AKR1C1 AKR1C2 HSD17B3 |
| hsa05217 | Basal cell carcinoma | -2.9 | 8.6 | 5.2 | BMP2 GADD45B AXIN2 FZD7 |
| hsa05202 | Transcriptional misregulation in cancer | -1.8 | 3.5 | 3 | CEBPA MLLT3 GADD45B ZEB1 BCL11B |
| hsa04550 | Signaling pathways regulating pluripotency of stem cells | -1.7 | 3.8 | 2.9 | INHBB REST AXIN2 FZD7 |
| hsa05224 | Breast cancer | -1.6 | 3.7 | 2.8 | GADD45B AXIN2 FZD7 SHC2 |
| hsa05226 | Gastric cancer | -1.6 | 3.6 | 2.8 | GADD45B AXIN2 FZD7 SHC2 |
| hsa05225 | Hepatocellular carcinoma | -1.4 | 3.2 | 2.5 | GADD45B AXIN2 FZD7 SHC2 |

Table S7: Pathway enrichment results for purple or dark tongue at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|--|------|------------|---------|--|
| hsa03013 | Nucleocytoplasmic transport | -3.6 | 5.6 | 5.2 | KPNB1 RAN UPF1 SUMO3 TNPO3 THOC6 KPNA7 |
| hsa04974 | Protein digestion and absorption | -2.1 | 4.2 | 3.5 | ATP1B1 COL3A1 MEP1B COL14A1 COL27A1 |
| hsa04144 | Endocytosis | -2 | 2.7 | 3 | FGFR4 HSPA1B PIP5K1A IST1 CHMP4A MVB12B WIPF2 ACTR3C |
| hsa04630 | JAK-STAT signaling pathway | -1.9 | 3.2 | 3 | CCND2 IFNA5 IL5RA IL15 PIK3CD IL20 |
| hsa04120 | Ubiquitin mediated proteolysis | -1.6 | 3 | 2.6 | CDC34 UBA52 UBOX5 UBE2S UBE2O |
| hsa04550 | Signaling pathways regulating pluripotency of stem cells | -1.6 | 3 | 2.6 | BMPR1B FGFR4 INHBB PIK3CD WNT4 |
| hsa05132 | Salmonella infection | -1.6 | 2.4 | 2.4 | DYNC1LI2 PIK3CD TXN RIPK1 ACTR1B RHOJ ACTR3C |
| hsa04623 | Cytosolic DNA-sensing pathway | -1.4 | 4.1 | 2.7 | IFNA5 POLR2L RIPK1 |
| hsa03010 | Ribosome | -1.4 | 2.7 | 2.3 | RPL3L MRPL12 UBA52 MRPL20 MRPS11 |

| | | | | | |
|----------|-----------------------|------|-----|-----|----------------------------------|
| hsa04217 | Necroptosis | -1.4 | 2.7 | 2.3 | PARP1 IFNA5 RIPK1 CHMP4A SPATA2L |
| hsa04668 | TNF signaling pathway | -1.4 | 3.1 | 2.4 | IL15 PIK3CD VEGFC RIPK1 |

Table S8: Pathway enrichment results for XYZ phenome at Day 14

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|--|
| hsa03010 | Ribosome | -10 | 7 | 10 | RPSA RPL10 RPL12 RPL15 RPL18A RPL30 RPLP0 RPS3 RPS5 RPS6 RPS11 RPS14 RPS20 RPS27 UBA52 MRPL15 MRPS14 MRPS15 MRPL32 |
| hsa05171 | Coronavirus disease - COVID-19 | -6.9 | 4.5 | 7.1 | RPSA NFKB1 PIK3CD RPL10 RPL12 RPL15 RPL18A RPL30 RPLP0 RPS3 RPS5 RPS6 RPS11 RPS14 RPS20 RPS27 UBA52 VWF |
| hsa00190 | Oxidative phosphorylation | -6.2 | 5.6 | 7.1 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B NDUFA9 NDUFS3 NDUFS6 COX7A2L ATP6V1F UQCR11 ATP6V1H |
| hsa05012 | Parkinson disease | -6 | 3.9 | 6.3 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B EIF2S1 NDUFA9 NDUFS3 NDUFS6 PSMA6 UBA52 UBB XBP1 COX7A2L UQCR11 SLC39A9 PINK1 |
| hsa05010 | Alzheimer disease | -6 | 3.3 | 6.1 | APOE ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B EIF2S1 NDUFA9 NDUFS3 NDUFS6 NFKB1 PIK3CD PSMA6 XBP1 FZD7 IRS2 COX7A2L UQCR11 APH1A SLC39A9 APH1B |
| hsa05020 | Prion disease | -5.8 | 3.8 | 6.2 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B EIF2S1 HSPA1B HSPA8 LAMC1 NDUFA9 NDUFS3 NDUFS6 NOTCH1 PIK3CD PSMA6 COX7A2L UQCR11 |
| hsa05016 | Huntington disease | -5.7 | 3.6 | 6.1 | ATP5F1C ATP5MC1 ATP5PF ATP5PO BDNF CLTA COX6B1 COX7B HIP1 NDUFA9 NDUFS3 NDUFS6 POLR2I POLR2J POLR2K PSMA6 DNAH17 COX7A2L UQCR11 |
| hsa05208 | Chemical carcinogenesis - reactive oxygen species | -5.7 | 4.2 | 6.3 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B CYP1A1 CYP2F1 NDUFA9 NDUFS3 NDUFS6 NFKB1 PIK3CD COX7A2L UQCR11 EPHX4 |
| hsa05022 | Pathways of neurodegeneration - | -5 | 2.8 | 5.2 | ATP5F1C ATP5MC1 ATP5PF ATP5PO BDNF COX6B1 COX7B EIF2S1 HI |

| | | | | | |
|----------|---|------|-----|-----|---|
| | multiple diseases | | | | P1 NDUFA9 NDUFS3 NDUFS6 NFKB1 PSMA6 UBA52 UBB VCP XBP1 FZD7 DNAH17 COX7A2L UQCR11 PINK1 |
| hsa04714 | Thermogenesis | -4.9 | 3.7 | 5.6 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B NDUFA9 NDUFS3 NDUFS6 RPS6 COX7A2L UQCR11 COA4 COX14 COA5 |
| hsa04932 | Non-alcoholic fatty liver disease | -4.8 | 4.5 | 5.8 | COX6B1 COX7B EIF2S1 NDUFA9 NDUFS3 NDUFS6 NFKB1 PIK3CD XBP1 IRS2 COX7A2L UQCR11 |
| hsa05415 | Diabetic cardiomyopathy | -4.2 | 3.7 | 5.1 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B NDUFA9 NDUFS3 NDUFS6 NFKB1 PIK3CD COX7A2L UQCR11 |
| hsa05014 | Amyotrophic lateral sclerosis | -4.1 | 2.9 | 4.7 | ATP5F1C ATP5MC1 ATP5PF ATP5PO COX6B1 COX7B EIF2S1 NDUFA9 NDUFS3 NDUFS6 PSMA6 VCP XBP1 DNAH17 COX7A2L UQCR11 PINK1 NUP37 |
| hsa04144 | Endocytosis | -3.9 | 3.2 | 4.7 | GRK2 CAPZA1 CLTA FGFR4 GRK6 HSPA1B HSPA8 SH3GL1 EHD1 CHMP5 VPS29 SMURF1 MVB12B ARAP1 |
| hsa05166 | Human T-cell leukemia virus 1 infection | -3.9 | 3.4 | 4.7 | CD3D NFATC1 NFKB1 PIK3CD RAN RELB STAT5A STAT5B TLN1 MAD1L1 PTTG1 ANAPC10 ANAPC13 |
| hsa04120 | Ubiquitin mediated proteolysis | -3.7 | 4.1 | 4.9 | CDC34 ELOB UBA52 UBB ANAPC10 WWP2 ANAPC13 SMURF1 UBE2O UBE2F |
| hsa04658 | Th1 and Th2 cell differentiation | -3.7 | 5 | 5.1 | CD3D IL4R NFATC1 NFKB1 NOTCH1 STAT5A STAT5B MAML3 |
| hsa04659 | Th17 cell differentiation | -2.6 | 3.8 | 3.8 | CD3D IL4R NFATC1 NFKB1 RARA STAT5A STAT5B |
| hsa05162 | Measles | -2.5 | 3.3 | 3.7 | CD3D EIF2S1 HSPA1B HSPA8 NFKB1 PIK3CD STAT5A STAT5B |
| hsa05134 | Legionellosis | -2.5 | 5.1 | 4.1 | HSPA1B HSPA8 NFKB1 VCP CLK4 |
| hsa04330 | Notch signaling pathway | -2.5 | 4.9 | 4 | NOTCH1 TLE3 APH1A MAML3 APH1B |
| hsa05221 | Acute myeloid leukemia | -2.2 | 4.3 | 3.6 | NFKB1 PIK3CD RARA STAT5A STAT5B |
| hsa04137 | Mitophagy - animal | -2.1 | 4 | 3.4 | UBA52 UBB FIS1 PINK1 FUNDC1 |
| hsa04510 | Focal adhesion | -2.1 | 2.6 | 3 | ACTN1 COL6A3 LAMC1 PIK3CD TLN1 VAV1 VWF MYL12A PARVA |
| hsa05203 | Viral carcinogenesis | -2 | 2.6 | 3 | ACTN1 GSN GTF2E1 NFKB1 PIK3CD STAT5A STAT5B MAD1L1 SCIN |

| | | | | | |
|----------|--|------|-----|-----|--|
| hsa05220 | Chronic myeloid leukemia | -2 | 3.8 | 3.3 | NFKB1 PIK3CD STAT5A STAT5B GAB2 |
| hsa03013 | Nucleocytoplasmic transport | -2 | 3.2 | 3.1 | RAN RBM8A TNPO3 NUP37 THOC6 THOC7 |
| hsa04066 | HIF-1 signaling pathway | -1.9 | 3.2 | 3 | NFKB1 PFKFB3 PFKL PIK3CD RPS6 ELOB |
| hsa05417 | Lipid and atherosclerosis | -1.9 | 2.4 | 2.8 | CYP1A1 EIF2S1 HSPA1B HSPA8 NFATC1 NFKB1 PIK3CD VAV1 XBP1 |
| hsa03040 | Spliceosome | -1.9 | 2.8 | 2.8 | HSPA1B HSPA8 HNRNPM BUD31 SART1 RBM8A SF3B5 |
| hsa04260 | Cardiac muscle contraction | -1.8 | 3.3 | 2.9 | COX6B1 COX7B MYL4 COX7A2L UQCR11 |
| hsa04150 | mTOR signaling pathway | -1.7 | 2.6 | 2.7 | GRB10 PIK3CD RPS6 FZD7 ATP6V1F ATP6V1H STRADA |
| hsa04062 | Chemokine signaling pathway | -1.7 | 2.4 | 2.6 | GRK2 GNB3 GRK6 NFKB1 PIK3CD STAT5B VAV1 CXCL16 |
| hsa00051 | Fructose and mannose metabolism | -1.7 | 5.3 | 3.3 | PFKFB3 PFKL PMM2 |
| hsa05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | -1.7 | 3.3 | 2.8 | CD3D NFATC1 NFKB1 PIK3CD BATF3 |
| hsa03020 | RNA polymerase | -1.7 | 5.1 | 3.2 | POLR2I POLR2J POLR2K |
| hsa04151 | PI3K-Akt signaling pathway | -1.7 | 2 | 2.4 | BDNF COL6A3 FGFR4 GNB3 NR4A1 IL4R LAMC1 NFKB1 PIK3CD RPS6 VWF PHLPP1 |
| hsa04213 | Longevity regulating pathway - multiple species | -1.7 | 3.7 | 2.9 | HSPA1B HSPA8 PIK3CD IRS2 |
| hsa04666 | Fc gamma R-mediated phagocytosis | -1.6 | 3 | 2.6 | GSN PIK3CD VAV1 GAB2 SCIN |
| hsa04141 | Protein processing in endoplasmic reticulum | -1.5 | 2.4 | 2.4 | EIF2S1 HSPA1B HSPA8 SSR2 VCP XBP1 ERLEC1 |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications | -1.5 | 2.9 | 2.5 | NFATC1 NFKB1 PIK3CD STAT5A STAT5B |
| hsa05207 | Chemical carcinogenesis - receptor activation | -1.5 | 2.2 | 2.3 | BCL6 CYP1A1 NFKB1 PIK3CD STAT5A STAT5B EPHX4 MIRLET7B |
| hsa04917 | Prolactin signaling pathway | -1.5 | 3.3 | 2.6 | NFKB1 PIK3CD STAT5A STAT5B |
| hsa04660 | T cell receptor signaling pathway | -1.5 | 2.8 | 2.4 | CD3D NFATC1 NFKB1 PIK3CD VAV1 |
| hsa04625 | C-type lectin receptor signaling | -1.5 | 2.8 | 2.4 | PLK3 NFATC1 NFKB1 PIK3CD RELB |

| | pathway | | | | |
|----------|---------------------------|------|-----|-----|--------------------------------|
| hsa04721 | Synaptic vesicle cycle | -1.3 | 3 | 2.3 | CLTA ATP6V1F CPLX1 ATP6V1H |
| hsa01200 | Carbon metabolism | -1.3 | 2.5 | 2.2 | ACAT1 PFKL RPE ADPGK MCEE |
| hsa01240 | Biosynthesis of cofactors | -1.3 | 2.3 | 2.1 | AK2 HMBS PMM2 NFS1 LIPT1 ADSS1 |

Table S9: Pathway enrichment results for chest pain at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|--------------------------------------|
| hsa04360 | Axon guidance | -2.5 | 5.2 | 4.1 | CFL1 EFNA4 RHOD SEMA6D PARD6G |
| hsa04080 | Neuroactive ligand-receptor interaction | -1.9 | 3.2 | 3 | AVP CHRNA1 CHRNA3 GRIN1 GABRR3 UTS2B |
| hsa04015 | Rap1 signaling pathway | -1.6 | 3.6 | 2.8 | EFNA4 GRIN1 DOCK4 PARD6G |
| hsa04142 | Lysosome | -1.5 | 4.3 | 2.8 | HYAL2 ABCB9 PLA2G15 |

Table S10: Pathway enrichment results for chest distress at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|---|
| hsa04014 | Ras signaling pathway | -3 | 4 | 4.3 | ETS2 GNG3 GRIN1 KITLG PRKACG REL KSR1 RASSF5 |
| hsa05203 | Viral carcinogenesis | -2.7 | 4 | 4 | CDC20 DDB1 HPN JAK1 NFKBIA PRKACG REL |
| hsa04610 | Complement and coagulation cascades | -2.2 | 5.5 | 3.8 | C4A C8B F8 SERPINE1 |
| hsa04144 | Endocytosis | -2.2 | 3.2 | 3.3 | ARRB1 CXCR4 CYTH3 SH3KBP1 VPS26B CHMP4B PIP5KL1 |
| hsa04062 | Chemokine signaling pathway | -2.2 | 3.6 | 3.4 | ARRB1 FOXO3 GNG3 NFKBIA PRKACG CXCR4 |
| hsa04140 | Autophagy - animal | -2.1 | 4.1 | 3.5 | LAMP1 PRKACG IRS2 MLST8 EIF2AK4 |
| hsa05030 | Cocaine addiction | -2.1 | 7.1 | 4 | GRIN1 PRKACG PPP1R1B |
| hsa03040 | Spliceosome | -2 | 4 | 3.3 | SF3A1 SF3B2 DDX42 WBP11 CTNNBL1 |
| hsa04713 | Circadian entrainment | -2 | 4.8 | 3.5 | GNG3 GRIN1 PER1 PRKACG |
| hsa05166 | Human T-cell leukemia virus 1 infection | -1.9 | 3.1 | 3 | CDC20 E2F3 ETS2 JAK1 NFKBIA PRKACG |
| hsa05163 | Human cytomegalovirus infection | -1.9 | 3.1 | 2.9 | E2F3 GNG3 JAK1 NFKBIA PRKACG CXCR4 |
| hsa03013 | Nucleocytoplasmic transport | -1.8 | 4.3 | 3.2 | SUMO3 CASC3 XPO7 POM121C |
| hsa04213 | Longevity regulating pathway - multiple species | -1.8 | 5.6 | 3.4 | FOXO3 PRKACG IRS2 |
| hsa04724 | Glutamatergic synapse | -1.8 | 4.1 | 3.1 | GNG3 GRIN1 PRKACG SLC38A3 |
| hsa04726 | Serotonergic synapse | -1.8 | 4 | 3 | APP GNG3 HTR2B PRKACG |

| | | | | | |
|----------|--|------|-----|-----|--|
| hsa05031 | Amphetamine addiction | -1.7 | 5.1 | 3.1 | GRIN1 PRKACG PPP1R1B |
| hsa05223 | Non-small cell lung cancer | -1.6 | 4.8 | 3 | E2F3 FOXO3 RASSF5 |
| hsa04926 | Relaxin signaling pathway | -1.6 | 3.6 | 2.8 | ARRB1 GNG3 NFKBIA PRKACG |
| hsa04728 | Dopaminergic synapse | -1.6 | 3.5 | 2.7 | ARRB1 GNG3 PRKACG PPP1R1B |
| hsa05162 | Measles | -1.5 | 3.3 | 2.6 | CSNK2A2 JAK1 NFKBIA EIF2AK4 |
| hsa04371 | Apelin signaling pathway | -1.5 | 3.3 | 2.6 | GNG3 SERPINE1 PRKACG PRKCE |
| hsa04151 | PI3K-Akt signaling pathway | -1.5 | 2.3 | 2.3 | AREG FOXO3 GNG3 JAK1 KITLG PRL MLST8 |
| hsa04211 | Longevity regulating pathway | -1.4 | 3.9 | 2.6 | FOXO3 PRKACG IRS2 |
| hsa05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | -1.4 | 3.9 | 2.6 | CSNK2A2 JAK1 NFKBIA |
| hsa04727 | GABAergic synapse | -1.4 | 3.9 | 2.6 | GNG3 PRKACG SLC38A3 |
| hsa04010 | MAPK signaling pathway | -1.4 | 2.4 | 2.2 | AREG ARRB1 KITLG PRKACG TAOK3 CACNA2D4 |
| hsa05032 | Morphine addiction | -1.4 | 3.8 | 2.5 | ARRB1 GNG3 PRKACG |
| hsa04218 | Cellular senescence | -1.3 | 3 | 2.3 | E2F3 FOXO3 SERPINE1 RASSF5 |
| hsa05160 | Hepatitis C | -1.3 | 3 | 2.3 | E2F3 JAK1 NFKBIA EIF2AK4 |

Table S11: Pathway enrichment results for palpitations at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|--|------|------------|---------|---|
| hsa05152 | Tuberculosis | -7.6 | 6.7 | 8.3 | CAMK2A CAMK2G CASP8 FCGR3B IFNGR2 IL10RB LAMP2 PP3R1 MAPK13 RAF1 TLR4 TLR6 TLR9 TIRAP |
| hsa05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | -5 | 7.8 | 6.9 | IFNGR2 PPP3R1 MAPK13 RAF1 TLR4 CD274 TLR9 TIRAP |
| hsa04218 | Cellular senescence | -4.1 | 5 | 5.4 | CCND3 CDKN2A HLA-C CXCL8 NBN PPP3R1 MAPK13 RAF1 MCU |
| hsa05132 | Salmonella infection | -3.8 | 3.8 | 4.8 | CASP8 CXCL8 PAK1 MAPK13 RAF1 TLR4 TLR6 RIPK3 TLR9 ACTR3B TIRAP |

| | | | | | |
|----------|---|------|-----|-----|--|
| hsa05142 | Chagas disease | -3.7 | 5.9 | 5.4 | CASP8 IFNGR2 CXCL8 MAPK13 TLR4 TLR6 TLR9 |
| hsa04620 | Toll-like receptor signaling pathway | -3.7 | 5.8 | 5.3 | CASP8 CXCL8 MAPK13 TLR4 TLR6 TLR9 TIRAP |
| hsa05417 | Lipid and atherosclerosis | -3.7 | 4 | 4.8 | CAMK2A CAMK2G CASP8 ICAM1 CXCL8 PPP3R1 MAPK13 TLR4 TLR6 TIRAP |
| hsa05163 | Human cytomegalovirus infection | -3.5 | 3.8 | 4.6 | CASP8 CDKN2A GNG3 HLA-C CXCL8 IL10RB PPP3R1 MAPK13 RAF1 SP1 |
| hsa04613 | Neutrophil extracellular trap formation | -3.4 | 4.1 | 4.6 | FCGR3B FPR2 MAPK13 RAF1 SELPLG TLR4 H4C5 H4-16 H2BC18 |
| hsa05200 | Pathways in cancer | -3.3 | 2.6 | 4 | CAMK2A CAMK2G CASP8 CCND3 CDKN2A FGF7 GNG3 IFNGR2 CXCL8 IL15RA JAK3 RAF1 SP1 TGFA RALBP1 DAPK2 |
| hsa04217 | Necroptosis | -3.3 | 4.4 | 4.6 | CAMK2A CAMK2G CASP8 IFNGR2 JAK3 TLR4 RIPK3 CHMP1B |
| hsa04650 | Natural killer cell mediated cytotoxicity | -3.1 | 4.6 | 4.5 | FCGR3B HLA-C ICAM1 IFNGR2 PAK1 PPP3R1 RAF1 |
| hsa05219 | Bladder cancer | -2.9 | 8.4 | 5.2 | CDKN2A CXCL8 RAF1 DAPK2 |
| hsa04140 | Autophagy - animal | -2.9 | 4.3 | 4.2 | LAMP2 RAF1 DAPK2 GABARAPL1 WIPI1 SUPT20H VMP1 |
| hsa04360 | Axon guidance | -2.9 | 3.8 | 4.1 | CAMK2A CAMK2G PAK1 PPP3R1 RAF1 SEMA7A PLXNC1 LRR C4 |
| hsa04621 | NOD-like receptor signaling pathway | -2.9 | 3.8 | 4.1 | CASP8 DEFA3 CXCL8 MAPK13 TLR4 RIPK3 GABARAPL1 MCU |
| hsa05214 | Glioma | -2.7 | 5.8 | 4.5 | CAMK2A CAMK2G CDKN2A RAF1 TGFA |
| hsa05167 | Kaposi sarcoma-associated herpesvirus infection | -2.7 | 3.6 | 3.9 | CASP8 GNG3 HLA-C ICAM1 CXCL8 PPP3R1 MAPK13 RAF1 |
| hsa05144 | Malaria | -2.6 | 6.9 | 4.5 | ICAM1 CXCL8 TLR4 TLR9 |
| hsa05203 | Viral carcinogenesis | -2.6 | 3.4 | 3.7 | CASP8 CCND3 CDKN2A HLA-C JAK3 H4C5 H4-16 H2BC18 |
| hsa05161 | Hepatitis B | -2.5 | 3.7 | 3.8 | CASP8 CXCL8 JAK3 MAPK13 RAF1 TLR4 TIRAP |
| hsa04012 | ErbB signaling pathway | -2.5 | 5.1 | 4.1 | CAMK2A CAMK2G PAK1 RAF1 TGFA |
| hsa05170 | Human immunodeficiency virus 1 infection | -2.5 | 3.3 | 3.6 | CASP8 GNG3 HLA-C PAK1 PPP3R1 MAPK13 RAF1 TLR4 |
| hsa05164 | Influenza A | -2.4 | 3.5 | 3.6 | CASP8 CCND3 ICAM1 IFNGR2 CXCL8 RAF1 TLR4 |

| | | | | | |
|----------|--|------|-----|-----|--|
| hsa05150 | Staphylococcus aureus infection | -2.3 | 4.5 | 3.7 | DEFA3 FCGR3B FPR2 ICAM1 SELPLG |
| hsa04666 | Fc gamma R-mediated phagocytosis | -2.3 | 4.5 | 3.7 | FCGR3B INPP5D PAK1 RAF1 ACTR3B |
| hsa05202 | Transcriptional misregulation in cancer | -2.1 | 3.2 | 3.2 | BCL6 DEFA3 EYA1 CXCL8 CDK14 SP1 KDM6A |
| hsa04625 | C-type lectin receptor signaling pathway | -2.1 | 4.2 | 3.5 | CASP8 PAK1 PPP3R1 MAPK13 RAF1 |
| hsa04720 | Long-term potentiation | -2.1 | 5.2 | 3.7 | CAMK2A CAMK2G PPP3R1 RAF1 |
| hsa04514 | Cell adhesion molecules | -2.1 | 3.5 | 3.3 | HLA-C ICAM1 SELPLG MPZL1 CD274 LRRC4 |
| hsa04664 | Fc epsilon RI signaling pathway | -2.1 | 5.1 | 3.7 | ALOX5AP INPP5D MAPK13 RAF1 |
| hsa05130 | Pathogenic Escherichia coli infection | -2.1 | 3.1 | 3.2 | CASP8 CXCL8 PAK1 MAPK13 TLR4 ACTR3B TIRAP |
| hsa05223 | Non-small cell lung cancer | -2 | 4.8 | 3.5 | CDKN2A JAK3 RAF1 TGFA |
| hsa05145 | Toxoplasmosis | -2 | 3.9 | 3.3 | CASP8 IFNGR2 IL10RB MAPK13 TLR4 |
| hsa04725 | Cholinergic synapse | -2 | 3.8 | 3.3 | CAMK2A CAMK2G GNG3 KCNJ2 KCNQ2 |
| hsa04115 | p53 signaling pathway | -2 | 4.7 | 3.5 | CASP8 CCND3 CDKN2A COP1 |
| hsa00260 | Glycine, serine and threonine metabolism | -2 | 6.5 | 3.8 | ALAS1 AOC2 AOC3 |
| hsa04630 | JAK-STAT signaling pathway | -1.9 | 3.2 | 3 | CCND3 IFNGR2 IL10RB IL15RA JAK3 RAF1 |
| hsa05133 | Pertussis | -1.9 | 4.6 | 3.4 | CXCL8 MAPK13 TLR4 TIRAP |
| hsa05212 | Pancreatic cancer | -1.9 | 4.6 | 3.4 | CDKN2A RAF1 TGFA RALBP1 |
| hsa05140 | Leishmaniasis | -1.9 | 4.5 | 3.3 | FCGR3B IFNGR2 MAPK13 TLR4 |
| hsa04310 | Wnt signaling pathway | -1.9 | 3.1 | 3 | CAMK2A CAMK2G CCND3 PPP3R1 DAAM2 SOST |
| hsa05166 | Human T-cell leukemia virus 1 infection | -1.8 | 2.7 | 2.8 | CCND3 CDKN2A HLA-C ICAM1 IL15RA JAK3 PPP3R1 |
| hsa04926 | Relaxin signaling pathway | -1.8 | 3.4 | 2.9 | ACTA2 GNG3 MAPK13 RAF1 RFXFP2 |
| hsa04068 | FoxO signaling pathway | -1.7 | 3.3 | 2.9 | BCL6 FOXO4 MAPK13 RAF1 GABARAPL1 |
| hsa04014 | Ras signaling pathway | -1.7 | 2.6 | 2.7 | FGF7 GNG3 FOXO4 PAK1 RAF1 TGFA RALBP1 |
| hsa04658 | Th1 and Th2 cell differentiation | -1.7 | 3.8 | 2.9 | IFNGR2 JAK3 PPP3R1 MAPK13 |
| hsa04151 | PI3K-Akt signaling pathway | -1.6 | 2.2 | 2.5 | CCND3 FGF7 GNG3 IBSP ITGB6 JAK3 RAF1 TGFA TLR4 |
| hsa04912 | GnRH signaling pathway | -1.6 | 3.7 | 2.8 | CAMK2A CAMK2G MAPK13 RAF1 |
| hsa05162 | Measles | -1.6 | 3.1 | 2.7 | CASP8 CCND3 JAK3 TLR4 TLR9 |

| | | | | | |
|----------|--|------|-----|-----|-------------------------------------|
| hsa04936 | Alcoholic liver disease | -1.6 | 3 | 2.6 | CASP8 CXCL8 MAPK13 TLR4 TIRAP |
| hsa01522 | Endocrine resistance | -1.6 | 3.5 | 2.7 | CDKN2A MAPK13 RAF1 SP1 |
| hsa05134 | Legionellosis | -1.5 | 4.6 | 2.9 | CASP8 CXCL8 TLR4 |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications | -1.5 | 3.5 | 2.7 | ICAM1 CXCL8 MAPK13 THBD |
| hsa05169 | Epstein-Barr virus infection | -1.5 | 2.6 | 2.4 | CASP8 CCND3 HLA-C ICAM1 JAK3 MAPK13 |
| hsa04370 | VEGF signaling pathway | -1.5 | 4.4 | 2.8 | PPP3R1 MAPK13 RAF1 |
| hsa04145 | Phagosome | -1.5 | 2.8 | 2.5 | FCGR3B HLA-C LAMP2 TLR4 TLR6 |
| hsa05416 | Viral myocarditis | -1.5 | 4.3 | 2.8 | CASP8 HLA-C ICAM1 |
| hsa05205 | Proteoglycans in cancer | -1.5 | 2.5 | 2.4 | CAMK2A CAMK2G PAK1 MAPK13 RAF1 TLR4 |
| hsa04660 | T cell receptor signaling pathway | -1.5 | 3.3 | 2.6 | PAK1 PPP3R1 MAPK13 RAF1 |
| hsa04064 | NF-kappa B signaling pathway | -1.5 | 3.3 | 2.6 | ICAM1 CXCL8 TLR4 TIRAP |
| hsa04921 | Oxytocin signaling pathway | -1.5 | 2.8 | 2.4 | CAMK2A CAMK2G KCNJ2 PPP3R1 RAF1 |
| hsa04922 | Glucagon signaling pathway | -1.4 | 3.2 | 2.5 | CAMK2A CAMK2G PPP3R1 PPP4R3C |
| hsa04659 | Th17 cell differentiation | -1.4 | 3.2 | 2.5 | IFNGR2 JAK3 PPP3R1 MAPK13 |
| hsa04066 | HIF-1 signaling pathway | -1.4 | 3.2 | 2.5 | CAMK2A CAMK2G IFNGR2 TLR4 |
| hsa04668 | TNF signaling pathway | -1.4 | 3.1 | 2.4 | CASP8 ICAM1 MAPK13 RIPK3 |
| hsa04810 | Regulation of actin cytoskeleton | -1.4 | 2.4 | 2.2 | FGF7 ITGB6 PAK1 RAF1 ACTR3B FGD3 |
| hsa05031 | Amphetamine addiction | -1.3 | 3.8 | 2.5 | CAMK2A CAMK2G PPP3R1 |
| hsa05211 | Renal cell carcinoma | -1.3 | 3.8 | 2.5 | PAK1 RAF1 TGFA |
| hsa05120 | Epithelial cell signaling in Helicobacter pylori infection | -1.3 | 3.7 | 2.5 | CXCL8 PAK1 MAPK13 |
| hsa04622 | RIG-I-like receptor signaling pathway | -1.3 | 3.7 | 2.5 | CASP8 CXCL8 MAPK13 |
| hsa04722 | Neurotrophin signaling pathway | -1.3 | 2.9 | 2.3 | CAMK2A CAMK2G MAPK13 RAF1 |

Table S12: Pathway enrichment results for purple or dark lips at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|---|------|------------|---------|--|
| hsa05014 | Amyotrophic lateral sclerosis | -16 | 3.1 | 10 | ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CASP3 COX6C COX7A2 COX7B COX7C EIF2S1 HNRNPA1 HNRNPA2B1 KIF5B NCBP1 NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NUP88 PIK3C3 PPP3CB PPP3CC PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 RAB5A SDHA SDHB SRSF7 SOD1 VDAC1 TUBA1A BECN1 COX7A2L EIF2AK3 MATR3 NUP58 RB1CC1 PSMD6 NUP153 ALYREF DCTN6 UQCR11 TARDBP CHMP2B TBK1 NUP54 CYCS ATG2B WDR41 NUP107 DERL1 SEH1L DNAL1 TOMM40L C9orf72 |
| hsa05020 | Prion disease | -14 | 3.2 | 9.6 | SLC25A5 ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CASP3 COX6C COX7A2 COX7B COX7C CREB1 ATF2 CSNK2A2 EIF2S1 FYN HSPA8 KIF5B NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 PIK3CA PPP3CB PPP3CC PRKACB MAPK3 PRNP PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 SDHA SDHB SOD1 VDAC1 VDAC2 VDAC3 TUBA1A COX7A2L EIF2AK3 PSMD6 UQCR11 CYCS |
| hsa05022 | Pathways of neurodegeneration - multiple diseases | -14 | 2.6 | 9.1 | SLC25A5 FAS ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CALM2 CAMK2D CASP3 CASP7 COX6C COX7A2 COX7B COX7C CSNK2A2 CTNNB1 EIF2S1 KIF5B KRAS ATXN3 NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NRAS PIK3C3 PPP3CB PPP3CC PRKCB MAPK3 PRNP PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 RAB5A RPS27A SDHA SDHB SOD1 VDAC1 VDAC2 VDAC3 TUBA1A AXIN2 BECN1 COX7A2L EIF2AK3 RB1CC1 PSMD6 DCTN6 UQCR11 FRAT2 TARDBP CHMP2B TBK1 CYCS ATG2B WDR41 DERL1 DNAL1 TOMM40L WNT3A CSNK1A1L C9orf72 |
| hsa05010 | Alzheimer disease | -14 | 2.8 | 9.2 | SLC25A5 FAS ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CALM2 |

| | | | | | |
|----------|--------------------|-----|-----|-----|---|
| hsa05016 | Huntington disease | -14 | 3.1 | 9.3 | CASP3 CASP7 COX6C COX7A2 COX7B COX7C CSNK2A2 CTNNA1 EIF2S1 KIF5B KRAS NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 SLC11A2 NRAS PIK3C3 PIK3CA PPP3CB PPP3CC MAPK3 PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 SDHA SDHB ADAM17 VDAC1 VDAC2 VDAC3 TUBA1A AXIN2 BECN1 NAE1 COX7A2L EIF2AK3 RB1CC1 PSMD6 UQCR11 FRAT2 CYCS ATG2B SLC39A9 SLC39A10 WNT3A CSNK1A1L SLC25A5 ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CASP3 COX6C COX7A2 COX7B COX7C CREB1 HDAC2 KIF5B NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NRF1 PIK3C3 POLR2B POLR2D POLR2H POLR2K PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 REST SDHA SDHB SOD1 TFAM VDAC1 VDAC2 VDAC3 TUBA1A BECN1 COX7A2L TBPL1 RB1CC1 PSMD6 DCTN6 UQCR11 CYCS ATG2B DNAL1 DHX15 HNRNPA1 HNRNPC HSPA8 MAGOH NCBP1 SNU13 PLRG1 SRSF1 SRSF7 TRA2B SNRPF SRSF9 SNRNP40 DHX38 RBM8A ALYREF SMNDC1 BCAS2 SRSF10 SRSF8 SNRNP27 NCBP2 SF3B3 SF3B1 LSM5 RBMX CRNKL1 CDC40 SF3B6 LSM8 PRPF38B PRPF40A RBM22 RBM25 PHF5A RBM17 ISY1-RAB43 SLC25A5 ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CALM2 CAMK2D CASP3 COX6C COX7A2 COX7B COX7C EIF2S1 GNAI3 KIF5B NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NFE2L2 SLC11A2 PRKACB PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 RPS27A SDHA SDHB SOD1 VDAC1 VDAC2 VDAC3 TUBA1A COX7A2L EIF2AK3 PSMD6 UQCR11 CYCS SLC39A9 SLC39A10 FAU RPL5 RPL6 RPL7 RPL15 RPL17 RPL24 RPL27 RPL30 RPL31 RPL34 RPL35A RPL39 RPS3A RPS6 RPS7 RPS10 RPS15A RPS17 RPS18 RPS20 RPS21 RPS23 RPS27 RPS27A RPS29 RPL23 RPL35 RPS27L RSL24D1 MRPL30 MRPL16 MRPL20 MRPS1 |
| hsa03040 | Spliceosome | -14 | 4.2 | 9.9 | |
| hsa05012 | Parkinson disease | -13 | 3.2 | 9.3 | |
| hsa03010 | Ribosome | -11 | 3.7 | 8.7 | |

| | | | | | |
|----------|--------------------------------|------|-----|-----|---|
| hsa04120 | Ubiquitin mediated proteolysis | -9.8 | 3.6 | 8.1 | 4 MRPS11 RPL36A-HNRNPH2 BIRC2 UBE2K MDM2 NEDD4 RPS27A SKP1 ELOC UBE2D2 UBE2E1 UBE2I UBE2N UBE3A CUL4B CUL3 CUL2 UBA3 UBE4A RNF7 UBE3C UBA2 SAE1 WWP1 FBXW11 ANAPC13 HERC4 ANAPC4 UBR5 UBA6 UBE2W FBXW7 KLHL9 UBE2FCTSL EIF2S1 HMGB1 IGBP1 KRAS NRAS PIK3C3 PIK3CA PPP2CA PPP2CB PRKA A1 PRKACB PRKCQ MAPK3 RHEB MAP3K7 UVRAG BECN1 EIF2AK3 RB1CC1 R RAS2 MRAS TBK1 SH3GLB1 ATG2B WDR41 ATG3 RAB33B ATG4C ATG4A C9orf72 |
| hsa04140 | Autophagy - animal | -9.3 | 3.5 | 7.8 | ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO COX6C COX7A2 COX7B COX7C COX15 NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 SDHA SDHB COX7A2L ATP6V1G1 ATP5MG UQCR11 PPA2 ATP6V1D CYCS ATP6V1E2 ATP6V1C2 FAU IFNA13 IL6ST OAS2 PIK3CA PRKCB MAPK3 RPL5 RPL6 RPL7 RPL15 RPL17 RPL24 RPL27 RPL30 RPL31 RPL34 RPL35A RPL39 RPS3A RPS6 RPS7 RPS10 RPS15A RPS17 RPS18 RPS20 RPS21 RPS23 RPS27 RPS27A RPS29 ADAM17 MAP3K7 RPL23 RPL35 TBK1 RPS27L IRAK4 RSL24D1 RPL36A-HNRNPH2 |
| hsa00190 | Oxidative phosphorylation | -9.2 | 3.6 | 7.8 | ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO BMP8B COX6C COX7A2 COX7B COX7C COX15 CREB1 ATF2 KRAS NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NRAS PRKAA1 PRKACB PRKAG1 RHEB RPS6 SDHA SDHB SMARCE1 COX7A2L ATP5MG UQCR11 PRKAG2 COA1 COX14 COX20 NDUFAF8 |
| hsa05171 | Coronavirus disease - COVID-19 | -8.9 | 2.8 | 7.3 | BIRC2 ARF6 RHOG RHOH CASP3 CASP7 CDC42 CTNNB1 DYNC1I2 HSP90AA1 KIF5B M6PR PIK3C3 PIK3CA MAPK3 PTPRC RAB5A RALA SKP1 MAP3K7 DYNLT3 TUBA1A RIPK2 TNFRSF10B CYTH1 ABI1 ARPC2 MYL12A EXOC5 DCTN6 LY96 IRAK4 SNX9 CYCS ARL8B EXOC2 ELMO2 RILP MYL12B TIRAP SNX33 |
| hsa04714 | Thermogenesis | -8.4 | 2.8 | 7 | EEF1A1 TNPO1 MAGOH NCBP1 NUP88 RAN SUMO3 SUMO2 UBE2I SUMO1 NUP |
| hsa05132 | Salmonella infection | -8 | 2.7 | 6.7 | |
| hsa03013 | Nucleocytoplasmic | -7.4 | 3.6 | 6.9 | |

| | | | | | |
|----------|---|------|-----|-----|--|
| | transport | | | | 58 RBM8A NUP153 ALYREF IPO8 IPO7 NCBP2 XPO7 NMD3 PHAX NUP54 NUP107 THOC7 SEH1L |
| hsa05208 | Chemical carcinogenesis - reactive oxygen species | -7.4 | 2.7 | 6.5 | ABL1 ABL2 ACP1 SLC25A5 ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO COX6C COX7A2 COX7B COX7C KRAS NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 NFE2L2 NRAS PIK3CA MAPK3 PTPN1 SDHA SDHB SOD1 VDAC1 VDAC2 VDAC3 COX7A2L UQCR11 PRKD3 |
| hsa05017 | Spinocerebellar ataxia | -7.3 | 3.2 | 6.6 | SLC25A5 GTF2B ATXN3 OPA1 PIK3C3 PIK3CA PRKCB PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 VDAC1 VDAC2 VDAC3 BECN1 TBPL1 RB1CC1 PSMD6 PUM2 ATXN10 CYCS ATG2B |
| hsa03015 | mRNA surveillance pathway | -7 | 3.7 | 6.7 | MAGOH NCBP1 PPP1CB PPP1CC PPP2CA PPP2CB PPP2R2A PPP2R5C RNGTT RB |
| hsa03050 | Proteasome | -6.4 | 4.9 | 6.8 | M8A ALYREF HBS1L NUDT21 CPSF6 NCBP2 TARDBP DAZAP1 PPP2R3B PCF11 PPP2R3C PAPOLG BCL2L2-PABPN1 |
| hsa04141 | Protein processing in endoplasmic reticulum | -6.1 | 2.7 | 5.8 | PSMA1 PSMA2 PSMA3 PSMA5 PSMA6 PSMA7 PSMC6 PSMD1 PSMD4 PSMD9 PSME2 PSMD6 PSME4 POMP |
| hsa04932 | Non-alcoholic fatty liver disease | -6 | 2.8 | 5.8 | AMFR EIF2S1 DNAJA1 HSPA8 HSP90AA1 ATXN3 NFE2L2 SKP1 SSR3 SEC62 UBE2D2 UFD1 MBTPS1 EIF2AK3 BAG2 SEC24D DNAJA2 SEC24B ERP29 UBXN4 TRAM1 SEC61G ERLEC1 YOD1 NGLY1 SAR1A DNAJC1 DERL1 STT3B |
| hsa05415 | Diabetic cardiomyopathy | -6 | 2.5 | 5.7 | FAS CASP3 CASP7 CDC42 COX6C COX7A2 COX7B COX7C EIF2S1 NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 PIK3CA PRKAA1 PRKAG1 SDHA SDHB COX7A2L EIF2AK3 UQCR11 PRKAG2 CYCS |
| hsa04144 | Endocytosis | -5.6 | 2.3 | 5.3 | SLC25A5 ATP5F1A ATP5F1B ATP5F1E ATP5PB ATP5MC3 ATP5PO CAMK2D COX6C COX7A2 COX7B COX7C NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 PIK3CA PPP1CB PPP1CC PRKCB SDHA SDHB VDAC1 VDAC2 VDAC3 COX7A2L TBC1D4 UQCR11 |
| | | | | | ARF4 ARF6 CAPZA1 CAPZA2 CDC42 HSPA8 KIF5B MDM2 NEDD4 RAB4A RAB5A SNX1 SNX4 USP8 CYTH1 VPS26A ARPC2 STAM2 WWP1 RAB11FIP2 WASHC4 |

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|----------|---------------------------------------|------|-----|-----|--|
| hsa04660 | T cell receptor signaling pathway | -5.3 | 3.1 | 5.5 | ACAP2 CHMP2B SNX5 CHMP2A CHMP4A SNX12 SH3GLB1 CHMP5 VTA1 CHMP3 CHMP1B SNX6 ARAP2 VPS37A AGAP6 CD3G CD8A CDC42 MAP3K8 DLG1 FYN ITK KRAS NCK1 NRAS PIK3CA PPP3CB PPP3CC PRKCQ MAPK3 PTPRC MAP3K7 BCL10 VAV3 MALT1 |
| hsa01200 | Carbon metabolism | -5.1 | 2.9 | 5.4 | ADH5 DLAT DLD FH GLUD1 GOT1 GOT2 IDH3A MDH1 PGK1 PGK2 PRPS1 PRPS2 PSPH SDHA SDHB SHMT1 SUCLG2 SUCLA2 PSAT1 HKDC1 SLC25A5 CALM2 E2F4 ETS1 KRAS MDM2 NBN NRAS PIK3CA PPP1CB PPP1CC P |
| hsa04218 | Cellular senescence | -4.9 | 2.6 | 5.1 | PP3CB PPP3CC MAPK3 RB1 RHEB VDAC1 VDAC2 VDAC3 RRAS2 MRAS FBXW11 TRPM7 HIPK1 LIN9 |
| hsa04071 | Sphingolipid signaling pathway | -4.9 | 2.8 | 5.2 | ASAH1 FYN GNAI3 KRAS NRAS PIK3CA PPP2CA PPP2CB PPP2R2A PPP2R5C PRKCB MAPK3 ROCK1 NSMAF SGPL1 SPTLC1 GNA13 PPP2R3B PPP2R3C SGPP1 CERS6 |
| hsa00020 | Citrate cycle (TCA cycle) | -4.2 | 4.8 | 5.4 | DLAT DLD FH IDH3A MDH1 SDHA SDHB SUCLG2 SUCLA2 |
| hsa05417 | Lipid and atherosclerosis | -4.2 | 2.2 | 4.4 | FAS CALM2 CAMK2D CASP3 CASP7 CDC42 CYP2A7 EIF2S1 HSPA8 HSP90AA1 IFNA13 KRAS NFE2L2 NRAS PIK3CA PPP3CB PPP3CC MAPK3 RAP1B MAP3K7 TNFRSF10B EIF2AK3 VAV3 LY96 TBK1 IRAK4 CYCS MIB1 TIRAP |
| hsa03018 | RNA degradation | -4 | 3.1 | 4.7 | BTG1 EXOSC10 TOB1 EXOSC8 EXOSC7 MTREX LSM5 CNOT7 LSM8 XRN1 CNOT6 TENT4B PNPT1 DCP2 CNOT6L |
| hsa04070 | Phosphatidylinositol signaling system | -4 | 2.8 | 4.6 | CALM2 IMPA1 IMPA2 INPP1 INPP4A ITPK1 MTM1 OCRL PIK3C3 PIK3CA PIP4K2A PRKCB MTMR1 MTMR6 SACM1L BPNT2 PIKFYVE |
| hsa04136 | Autophagy - other | -4 | 4.5 | 5.1 | IGBP1 PIK3C3 PPP2CA PPP2CB BECN1 ATG2B ATG3 ATG4C ATG4A |
| hsa03008 | Ribosome biogenesis in eukaryotes | -3.9 | 2.7 | 4.5 | CSNK2A2 DKC1 FBL SNU13 RAN RPP38 WDR43 REXO2 GNL3 NOB1 NMD3 FCF1 UTP18 SBDS XRN1 LSG1 NOL6 SPATA5 |
| hsa00562 | Inositol phosphate metabolism | -3.9 | 3.1 | 4.6 | IMPA1 IMPA2 INPP1 INPP4A ITPK1 MTM1 OCRL PIK3C3 PIK3CA PIP4K2A MTMR1 MTMR6 SACM1L PIKFYVE |
| hsa05163 | Human cytomegalovirus | -3.8 | 2.1 | 4.2 | FAS B2M CALM2 CASP3 CCR3 CREB1 ATF2 CTNNB1 GNAI3 IFNA13 IL10RA IT |

| | | | | | |
|----------|---------------------------------------|------|-----|-----|--|
| | infection | | | | GAV KRAS MDM2 NRAS PIK3CA PPP3CB PPP3CC PRKACB PRKCB MAPK3 PTGER2 RB1 RHEB ROCK1 GNA13 GNB5 TBK1 CYCS |
| hsa05205 | Proteoglycans in cancer | -3.7 | 2.1 | 4.1 | FAS CAMK2D CASP3 CD44 CDC42 CTNNB1 CTSL EIF4B IGF2 ITGAV KRAS MDM2 PPP1R12A NRAS PIK3CA PPP1CB PPP1CC PRKACB PRKCB MAPK3 ROCK1 RPS6 TFAP4 VAV3 RRAS2 MRAS WNT3A |
| hsa04728 | Dopaminergic synapse | -3.7 | 2.4 | 4.3 | ARNTL CALM2 CAMK2D CREB1 ATF2 GNAI3 KIF5B PPP1CB PPP1CC PPP2CA PP2CB PPP2R2A PPP2R5C PPP3CB PPP3CC PRKACB PRKCB GNB5 PPP2R3B PPP2R3C |
| hsa04910 | Insulin signaling pathway | -3.5 | 2.4 | 4.1 | CALM2 EIF4E KRAS NRAS PIK3CA PPP1CB PPP1CC PRKAA1 PRKACB PRKAG1 MAPK3 PTPN1 RHEB RPS6 SHC1 FLOT1 RHOQ PRKAG2 HKDC1 SOCS4 |
| hsa05131 | Shigellosis | -3.5 | 2 | 3.9 | ARF6 CD44 CDC42 MDM2 PIK3C3 PIK3CA PRKCQ MAPK3 ROCK1 RPS27A SKP1 MAP3K7 UBE2D2 UBE2N VDAC1 BECN1 RIPK2 BCL10 CYTH1 ARPC2 MYL12A MALT1 FBXW11 TBK1 CYCS ELMO2 HKDC1 SHARPIN TIFA MYL12B |
| hsa04217 | Necroptosis | -3.5 | 2.2 | 4 | SLC25A5 BIRC2 FAS CAMK2D GLUD1 H2AZ1 HMGB1 HSP90AA1 IFNA13 IFNGR1 VDAC1 VDAC2 VDAC3 TNFRSF10B CHMP2B CHMP2A CHMP4A CHMP5 CHMP3 TRPM7 CHMP1B SHARPIN |
| hsa05203 | Viral carcinogenesis | -3.4 | 2.1 | 3.9 | CASP3 CDC42 CCR3 CREB1 ATF2 DDX3X DLG1 GTF2B GTF2E2 GTF2H3 HDAC2 IL6ST KRAS MDM2 NRAS PIK3CA PRKACB MAPK3 RASA2 RB1 UBE3A VDAC1 H4C13 KAT2B TBPL1 YWHAQ |
| hsa04137 | Mitophagy - animal | -3.4 | 2.9 | 4.2 | CSNK2A2 KRAS NRAS RPS27A BECN1 TAX1BP1 USP8 EIF2AK3 RRAS2 MRAS BCL2L13 TBK1 TOMM7 |
| hsa04919 | Thyroid hormone signaling pathway | -3.3 | 2.4 | 4 | ATP1B3 CTNNB1 HDAC2 ITGAV KRAS MDM2 NRAS PFKFB2 PIK3CA PRKACB PRKCB MAPK3 RHEB KAT2B TBC1D4 MED13 MED4 MED30 |
| hsa05130 | Pathogenic Escherichia coli infection | -3.3 | 2 | 3.8 | ABL1 FAS ARF6 CASP3 CASP7 CDC42 FYN MYO5A NCK1 MAPK3 ROCK1 MAP3K7 TMBIM6 TUBA1A TNFRSF10B CYTH1 SEC24D ABI1 ARPC2 SEC24B GNA13 TMED10 IRAK4 CYCS TIRAP |

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|----------|-----------------------------------|------|-----|-----|--|
| hsa04014 | Ras signaling pathway | -3.2 | 1.9 | 3.7 | ABL1 ABL2 ARF6 CALM2 CDC42 EFNA1 ETS1 IGF2 KRAS NF1 NRAS PIK3CA PRKACB PRKCB MAPK3 RAB5A RALA RAP1B RASA2 SHC1 KSR1 GNB5 RRAS2 MRAS RASA3 TBK1 EXOC2 PLA2G12B |
| hsa04720 | Long-term potentiation | -3.1 | 2.9 | 4 | CALM2 CAMK2D KRAS NRAS PPP1CB PPP1CC PPP3CB PPP3CC PRKACB PRKCB MAPK3 RAP1B |
| hsa05168 | Herpes simplex virus 1 infection | -3.1 | 1.6 | 3.4 | BIRC2 FAS B2M CASP3 EIF2S1 IFNA13 IFNGR1 OAS2 PIK3CA PPP1CB PPP1CC RHEB SRSF1 SRSF7 MAP3K7 ZNF12 ZNF23 ZNF124 ZNF140 ZNF223 SRSF9 EIF2B2 ZNF235 EIF2AK3 ZNF432 ALYREF ZNF443 ZNF267 SRSF8 TBK1 IRAK4 CYCS ZFP14 ZNF77 ZNF333 ZNF551 ZNF468 ZNF486 ZNF764 ZNF792 ZNF540 ZNF584 ZNF718 ZNF780A ZFP82 ZNF680 ZNF761 ZNF674 ZNF605 |
| hsa03020 | RNA polymerase | -3 | 3.8 | 4.2 | POLR2B POLR2D POLR2H POLR2K POLR1D POLR3B POLR2M POLR1B |
| hsa04114 | Oocyte meiosis | -2.9 | 2.2 | 3.6 | CALM2 CAMK2D PPP1CB PPP1CC PPP2CA PPP2CB PPP2R5C PPP3CB PPP3CC PRKACB MAPK3 SKP1 YWHAQ CPEB3 FBXW11 ANAPC13 ANAPC4 CPEB2 |
| hsa05165 | Human papillomavirus infection | -2.8 | 1.7 | 3.3 | FAS CASP3 CDC42 CREB1 CTNNB1 DLG1 HDAC2 IFNA13 ITGA1 ITGA4 ITGAV KRAS MDM2 NRAS PIK3CA PPP2CA PPP2CB PPP2R2A PPP2R5C PRKACB MAPK3 RB1 RHEB UBE3A AXIN2 TBPL1 ATP6V1G1 PPP2R3B TBK1 ATP6V1D PPP2R3C WNT3A ATP6V1E2 CSNK1A1L ATP6V1C2 |
| hsa04150 | mTOR signaling pathway | -2.8 | 2.1 | 3.5 | EIF4B EIF4E KRAS NRAS PIK3CA PRKAA1 PRKCB MAPK3 RHEB RPS6 ATP6V1G1 TBC1D7 ATP6V1D MAPKAP1 SEH1L WDR24 WNT3A ATP6V1E2 ATP6V1C2 RICTOR |
| hsa03022 | Basal transcription factors | -2.8 | 3.2 | 3.8 | CCNH GTF2B GTF2E2 GTF2H3 TAF7 TAF12 TAF13 TBPL1 TAF5L |
| hsa04662 | B cell receptor signaling pathway | -2.8 | 2.6 | 3.6 | BTK FCGR2B KRAS NRAS PIK3CA PPP3CB PPP3CC PRKCB MAPK3 BCL10 VAV3 MALT1 DAPP1 |
| hsa05170 | Human immunodeficiency virus | -2.8 | 1.9 | 3.4 | APIG1 FAS B2M CALM2 CASP3 CD3G GNAI3 IFNA13 KRAS NRAS PIK3CA PPP3CB PPP3CC PRKCB MAPK3 SKP1 MAP3K7 ELOC CUL4B RNF7 GNB5 FBXW11 T |

| | | | | | |
|----------|---|------|-----|-----|---|
| | 1 infection | | | | BK1 IRAK4 CYCS |
| hsa05169 | Epstein-Barr virus infection | -2.8 | 1.9 | 3.4 | FAS B2M BTK CASP3 CD3G CD44 CD58 HDAC2 IFNA13 MDM2 NEDD4 OAS2 PIK3CA PSMC6 PSMD1 PSMD4 RB1 MAP3K7 SAP30 PSMD6 TBK1 IRAK4 CYCS SA P30L |
| hsa05160 | Hepatitis C | -2.8 | 2.1 | 3.4 | FAS CASP3 CTNNB1 EIF2S1 IFNA13 EIF3E KRAS NRAS OAS2 PIK3CA PPP2CA PP2CB PPP2R2A MAPK3 RB1 EIF2AK3 YWHAQ TBK1 CYCS RSAD2 |
| hsa05152 | Tuberculosis | -2.7 | 2 | 3.4 | CALM2 CAMK2D CASP3 CREB1 FCGR2B IFNA13 IFNGR1 IL10RA PIK3C3 PPP3CB PPP3CC MAPK3 RAB5A RFX5 RIPK2 KSR1 BCL10 MALT1 IRAK4 CYCS CLEC7A TIRAP |
| hsa01230 | Biosynthesis of amino acids | -2.7 | 2.6 | 3.5 | ACY1 GOT1 GOT2 IDH3A PGK1 PGK2 PRPS1 PRPS2 PSPH SHMT1 MAT2B PSAT1 |
| hsa05167 | Kaposi sarcoma-associated herpesvirus infection | -2.7 | 1.9 | 3.3 | FAS CALM2 CASP3 CCR3 CREB1 CTNNB1 IFNA13 IFNGR1 IL6ST KRAS NRAS PIK3CA PPP3CB PPP3CC MAPK3 RB1 RPS27A BECN1 GNB5 TBK1 CYCS ATG3 |
| hsa04810 | Regulation of actin cytoskeleton | -2.6 | 1.8 | 3.2 | CDC42 ITGA1 ITGA4 ITGAE ITGAV KRAS PPP1R12A NRAS PIK3CA PIP4K2A PPP1CB PPP1CC MAPK3 ROCK1 TMSB4X ARPC2 VAV3 MYL12A GNA13 IQGAP2 RRAS2 MRAS MYL12B PIKFYVE SPATA13 |
| hsa04621 | NOD-like receptor signaling pathway | -2.6 | 1.9 | 3.2 | BIRC2 HSP90AA1 IFNA13 OAS2 PKN2 MAPK3 MAP3K7 VDAC1 VDAC2 VDAC3 RIPK2 SUGT1 CARD8 TBK1 IRAK4 TRPM7 ERBIN DHX33 SHARPIN GBP4 NEK7 NLRP6 |
| hsa04371 | Apelin signaling pathway | -2.6 | 2.1 | 3.3 | CALM2 GNAI3 KRAS NRAS NRF1 PIK3C3 PRKAA1 PRKACB PRKAG1 MAPK3 RPS6 TFAM BECN1 GNA13 GNB5 RRAS2 MRAS PRKAG2 |
| hsa05134 | Legionellosis | -2.6 | 2.8 | 3.6 | CASP3 CASP7 CLK1 EEF1A1 HSPA8 HBS1L BCL2L13 CYCS SAR1A CLK4 |
| hsa04710 | Circadian rhythm | -2.6 | 3.6 | 3.8 | ARNTL CREB1 PRKAA1 PRKAG1 SKP1 FBXW11 PRKAG2 |
| hsa05161 | Hepatitis B | -2.6 | 2 | 3.2 | FAS CASP3 CREB1 ATF2 DDX3X IFNA13 KRAS NRAS PCNA PIK3CA PRKCB MAPK3 RB1 MAP3K7 VDAC3 YWHAQ TBK1 IRAK4 CYCS TIRAP |

| | | | | | |
|----------|--|------|-----|-----|--|
| hsa05166 | Human T-cell leukemia virus 1 infection | -2.5 | 1.8 | 3.1 | SLC25A5 B2M CD3G CREB1 ATF2 DLG1 ETS1 IL15 KRAS NRAS PIK3CA PPP3CB PPP3CC PRKACB MAPK3 RAN RB1 SPI1 VDAC1 VDAC2 VDAC3 KAT2B TBPL1 ANAPC13 ANAPC4 |
| hsa05235 | PD-L1 expression and PD-1 checkpoint pathway in cancer | -2.5 | 2.4 | 3.3 | CD3G CSNK2A2 IFNGR1 KRAS NRAS PIK3CA PPP3CB PPP3CC PRKCQ MAPK3 EML4 BATF3 TIRAP |
| hsa04211 | Longevity regulating pathway | -2.5 | 2.4 | 3.3 | CREB1 ATF2 EIF4E KRAS NRAS PIK3CA PRKAA1 PRKACB PRKAG1 RHEB RB1 CC1 SESN1 PRKAG2 |
| hsa05031 | Amphetamine addiction | -2.5 | 2.6 | 3.4 | CALM2 CAMK2D CREB1 ATF2 HDAC2 PPP1CB PPP1CC PPP3CB PPP3CC PRKACB PRKCB |
| hsa00470 | D-Amino acid metabolism | -2.4 | 8.1 | 4.4 | DAO GLS SRR |
| hsa04213 | Longevity regulating pathway - multiple species | -2.3 | 2.6 | 3.2 | HDAC2 HSPA8 KRAS NRAS PIK3CA PRKAA1 PRKACB PRKAG1 SOD1 PRKAG2 |
| hsa04625 | C-type lectin receptor signaling pathway | -2.3 | 2.2 | 3.1 | CALM2 KRAS MDM2 NRAS PIK3CA PPP3CB PPP3CC MAPK3 KSR1 BCL10 MALT1 RRAS2 MRAS CLEC7A |
| hsa04261 | Adrenergic signaling in cardiomyocytes | -2.3 | 1.9 | 3 | ATP1B3 ATP2B1 CALM2 CAMK2D CREB1 ATF2 GNAI3 PPP1CB PPP1CC PPP2CA PPP2CB PPP2R2A PPP2R5C PRKACB MAPK3 SCN4B PPP2R3B PPP2R3C |
| hsa05162 | Measles | -2.2 | 2 | 3 | FAS CASP3 CD3G CSNK2A2 EIF2S1 FCGR2B HSPA8 IFNA13 CD46 OAS2 PIK3CA MAP3K7 EIF3H EIF2AK3 TBK1 IRAK4 CYCS |
| hsa04145 | Phagosome | -2.2 | 1.9 | 2.9 | CTSL DYNC1I2 FCGR2B ITGAV M6PR PIK3C3 RAB5A TUBA1A STX7 MARCO ATP6V1G1 SEC61G ATP6V1D CLEC7A RILP ATP6V1E2 PIKFYVE ATP6V1C2 |
| hsa04650 | Natural killer cell mediated cytotoxicity | -2.1 | 2 | 2.9 | FAS CASP3 CD48 FYN IFNA13 IFNGR1 KRAS NRAS PIK3CA PPP3CB PPP3CC PRKCB MAPK3 SHC1 TNFRSF10B VAV3 |
| hsa04152 | AMPK signaling | -2.1 | 2 | 2.9 | CREB1 PFKFB2 PIK3CA PPP2CA PPP2CB PPP2R2A PPP2R5C PRKAA1 PRKAG1 R |

| | | | | | |
|----------|------------------------------------|------|-----|-----|---|
| | pathway | | | | AB2A RHEB MAP3K7 PPP2R3B PRKAG2 PPP2R3C |
| hsa00240 | Pyrimidine metabolism | -2 | 2.5 | 2.9 | DCK DCTD DUT NME1 NT5E RRM1 UMPS RRM2B CMPK1 |
| hsa05211 | Renal cell carcinoma | -2 | 2.3 | 2.9 | CDC42 ETS1 FH KRAS NRAS PIK3CA MAPK3 RAP1B ELOC CUL2 |
| hsa00900 | Terpenoid backbone biosynthesis | -2 | 3.7 | 3.2 | FNTA HMGCS1 IDI1 ICMT NUS1 |
| hsa00220 | Arginine biosynthesis | -2 | 3.7 | 3.2 | ACY1 GLS GLUD1 GOT1 GOT2 |
| hsa04210 | Apoptosis | -2 | 1.9 | 2.7 | BIRC2 FAS CASP3 CASP7 CTSC CTSL EIF2S1 IL3 KRAS NRAS PIK3CA MAPK3 TUBA1A TNFRSF10B EIF2AK3 CYCS |
| hsa05110 | Vibrio cholerae infection | -1.9 | 2.6 | 2.9 | PRKACB SLC12A2 ATP6V1G1 KDELRL2 SEC61G ATP6V1D ATP6V1E2 ATP6V1C2 |
| hsa00270 | Cysteine and methionine metabolism | -1.9 | 2.6 | 2.9 | AHCY GOT1 GOT2 LDHA MDH1 MAT2B PSAT1 ENOPH1 |
| hsa04110 | Cell cycle | -1.9 | 1.9 | 2.7 | ABL1 CCNH E2F4 HDAC2 MDM2 ORC5 PCNA RB1 SKP1 TFDP1 STAG2 YWHAQ ORC3 ANAPC13 ANAPC4 |
| hsa03430 | Mismatch repair | -1.9 | 3.5 | 3.1 | MSH6 PCNA RFC1 RPA1 RPA2 |
| hsa03060 | Protein export | -1.9 | 3.5 | 3.1 | SRP14 SEC62 SEC11A SEC61G SPCS1 |
| hsa04146 | Peroxisome | -1.9 | 2.2 | 2.7 | ABCD2 DAO PEX1 PEX6 SOD1 GNPAT PEX3 AGPS ECI2 FAR1 NUDT19 |
| hsa04350 | TGF-beta signaling pathway | -1.9 | 2.1 | 2.6 | ACVR1 BMP8B E2F4 ID2 SMAD5 PPP2CA PPP2CB MAPK3 ROCK1 SKP1 TFDP1 HJV |
| hsa01240 | Biosynthesis of cofactors | -1.8 | 1.8 | 2.5 | ALPL COX15 CPOX DLD GCH1 NME1 SHMT1 UGP2 UMPS UROD KMO MTHFD2 MAT2B PSAT1 CMPK1 PDXP COQ5 |
| hsa01524 | Platinum drug resistance | -1.8 | 2.2 | 2.7 | BIRC2 FAS CASP3 ABCC2 MSH6 MDM2 PIK3CA MAPK3 TOP2B CYCS |
| hsa04921 | Oxytocin signaling pathway | -1.8 | 1.8 | 2.5 | CALM2 CAMK2D GNAI3 KRAS PPP1R12A NRAS PPP1CB PPP1CC PPP3CB PPP3CC PRKAA1 PRKACB PRKAG1 PRKCB MAPK3 ROCK1 PRKAG2 |
| hsa04022 | cGMP-PKG signaling pathway | -1.8 | 1.7 | 2.5 | SLC25A5 ATP1B3 ATP2B1 CALM2 CREB1 ATF2 GNAI3 PPP1R12A PPP1CB PPP1CC PPP3CB PPP3CC MAPK3 ROCK1 VDAC1 VDAC2 VDAC3 GNA13 |
| hsa04010 | MAPK signaling | -1.8 | 1.5 | 2.4 | FAS CASP3 CDC42 MAP3K8 ATF2 DUSP5 EFNA1 HSPA8 IGF2 KRAS STMN1 MA |

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|----------|---|------|-----|-----|--|
| | pathway | | | | P3K4 NF1 NRAS PPM1A PPM1B PPP3CB PPP3CC PRKACB PRKCB MAPK3 RAP1B RASA2 MAP3K7 MAP3K2 RRAS2 MRAS IRAK4 |
| hsa05214 | Glioma | -1.8 | 2.1 | 2.6 | CALM2 CAMK2D KRAS MDM2 NRAS PIK3CA PRKCB MAPK3 RB1 SHC1 |
| hsa04066 | HIF-1 signaling pathway | -1.8 | 1.9 | 2.5 | CAMK2D EIF4E IFNGR1 LDHA PGK1 PGK2 PIK3CA PRKCB MAPK3 RPS6 ELOC CUL2 HKDC1 |
| hsa05164 | Influenza A | -1.7 | 1.7 | 2.4 | SLC25A5 FAS CASP3 EIF2S1 IFNA13 IFNGR1 OAS2 PIK3CA PRKCB MAPK3 VDA C1 TNFRSF10B TBK1 IRAK4 CYCS TMPRSS4 RSAD2 BCL2L2-PABPN1 |
| hsa00563 | Glycosylphosphatidylo sitol (GPI)-anchor biosynthesis | -1.7 | 3.1 | 2.8 | PIGB PIGK PIGO PIGY PIGS |
| hsa04611 | Platelet activation | -1.7 | 1.8 | 2.4 | BTK FYN GNAI3 PPP1R12A PIK3CA PPP1CB PPP1CC PRKACB MAPK3 RAP1B R OCK1 MYL12A GNA13 MYL12B |
| hsa04916 | Melanogenesis | -1.6 | 1.9 | 2.4 | CALM2 CAMK2D CREB1 CTNNB1 GNAI3 KRAS NRAS POMC PRKACB PRKCB MAPK3 WNT3A |
| hsa05135 | Yersinia infection | -1.6 | 1.8 | 2.3 | ARF6 RHOG CD8A CDC42 ITGA4 PIK3CA PKN2 MAPK3 ROCK1 MAP3K7 ARPC2 VAV3 TBK1 IRAK4 ELMO2 |
| hsa04670 | Leukocyte transendothelial migration | -1.6 | 1.8 | 2.3 | RHOH CDC42 CTNNB1 GNAI3 ITGA4 ITK PIK3CA PRKCB RAP1B ROCK1 VAV3 MYL12A MYL12B |
| hsa00620 | Pyruvate metabolism | -1.6 | 2.4 | 2.5 | ADH5 DLAT DLDD FH GLO1 LDHA MDH1 |
| hsa03420 | Nucleotide excision repair | -1.6 | 2.4 | 2.5 | CCNH GTF2H3 PCNA RFC1 RPA1 RPA2 CUL4B |
| hsa04960 | Aldosterone-regulated sodium reabsorption | -1.6 | 2.6 | 2.5 | ATP1B3 KRAS NR3C2 PIK3CA PRKCB MAPK3 |
| hsa01250 | Biosynthesis of nucleotide sugars | -1.6 | 2.6 | 2.5 | UAP1 UGP2 FPGT NANS UXS1 HKDC1 |

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|----------|--|------|-----|-----|--|
| hsa04510 | Focal adhesion | -1.6 | 1.6 | 2.2 | BIRC2 CDC42 CTNNB1 FYN ITGA1 ITGA4 ITGAV PPP1R12A PIK3CA PPP1CB PPP1CC PRKCB MAPK3 RAP1B ROCK1 SHC1 ZYX VAV3 MYL12A MYL12B |
| hsa01210 | 2-Oxocarboxylic acid metabolism | -1.6 | 3.4 | 2.7 | ACY1 GOT1 GOT2 IDH3A |
| hsa04064 | NF-kappa B signaling pathway | -1.6 | 1.9 | 2.3 | BIRC2 BTK CSNK2A2 PRKCB PRKCQ MAP3K7 UBE2I BCL10 MALT1 LY96 IRAK4 TIRAP |
| hsa00280 | Valine, leucine and isoleucine degradation | -1.6 | 2.4 | 2.4 | ACADM DLD HADH HMGCS1 HIBADH ACAD8 MCCC1 |
| hsa04370 | VEGF signaling pathway | -1.5 | 2.2 | 2.3 | CDC42 KRAS NRAS PIK3CA PPP3CB PPP3CC PRKCB MAPK3 |
| hsa04936 | Alcoholic liver disease | -1.5 | 1.7 | 2.2 | ACADM ADH5 FAS CASP3 CTNNB1 IFNA13 PRKAA1 PRKAG1 TRA2B MAP3K7 LY96 TBK1 IRAK4 PRKAG2 TIRAP |
| hsa04520 | Adherens junction | -1.5 | 2 | 2.3 | ACP1 CDC42 CSNK2A2 CTNNB1 FYN MAPK3 PTPN1 MAP3K7 FARP2 |
| hsa04730 | Long-term depression | -1.5 | 2.1 | 2.3 | GNAI3 KRAS NRAS PPP2CA PPP2CB PRKCB MAPK3 GNA13 |
| hsa05225 | Hepatocellular carcinoma | -1.5 | 1.6 | 2.1 | CTNNB1 IGF2 KRAS NFE2L2 NRAS PIK3CA PRKCB MAPK3 RB1 SHC1 SMARCE1 AXIN2 FRAT2 PBRM1 PHF10 WNT3A CSNK1A1L |
| hsa04722 | Neurotrophin signaling pathway | -1.5 | 1.8 | 2.1 | ABL1 CALM2 CAMK2D CDC42 KRAS NRAS PIK3CA MAPK3 RAP1B SHC1 RIPK2 PRDM4 IRAK4 |
| hsa04530 | Tight junction | -1.5 | 1.6 | 2.1 | CDC42 DLG1 NEDD4 PCNA PPP2CA PPP2CB PPP2R2A PRKAA1 PRKACB PRKAG1 ROCK1 TUBA1A ARPC2 MYL12A PRKAG2 RAB8B MYL12B |
| hsa04360 | Axon guidance | -1.5 | 1.6 | 2.1 | ABL1 CAMK2D CDC42 EFNA1 FYN GNAI3 KRAS NCK1 NRAS PIK3CA PPP3CB PPP3CC MAPK3 ROCK1 RYK SEMA3B MYL12A MYL12B |
| hsa04142 | Lysosome | -1.5 | 1.7 | 2.1 | AP1G1 AGA ASAH1 CTSC CLN5 CTSL FUCA2 M6PR SLC11A2 CD164 LAPTM4A GGA3 DMXL2 SLC17A5 |
| hsa04390 | Hippo signaling pathway | -1.5 | 1.6 | 2.1 | BIRC2 BMP8B CTNNB1 DLG1 ID2 PPP1CB PPP1CC PPP2CA PPP2CB PPP2R2A TP53BP2 AXIN2 LIMD1 YWHAQ FBXW11 WNT3A |
| hsa00260 | Glycine, serine and | -1.5 | 2.4 | 2.3 | DAO DLD PSPH SHMT1 PSAT1 SRR |

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|--------------------------------------|------|------------|---------|---|
| | threonine metabolism | | | | |
| hsa04931 | Insulin resistance | -1.4 | 1.8 | 2.1 | CREB1 PIK3CA PPP1CB PPP1CC PRKAA1 PRKAG1 PRKCB PRKCQ PTPN1 OGT TBC1D4 PRKAG2 |
| hsa04115 | p53 signaling pathway | -1.4 | 2 | 2.2 | FAS CASP3 MDM2 PPM1D TNFRSF10B SESN1 RRM2B CYCS ZMAT3 |
| hsa04012 | ErbB signaling pathway | -1.4 | 1.9 | 2.1 | ABL1 ABL2 CAMK2D KRAS NCK1 NRAS PIK3CA PRKCB MAPK3 SHC1 |
| hsa05210 | Colorectal cancer | -1.4 | 1.9 | 2.1 | CASP3 CTNNB1 MSH6 KRAS NRAS PIK3CA MAPK3 RALA AXIN2 CYCS |
| hsa04925 | Aldosterone synthesis and secretion | -1.4 | 1.8 | 2.1 | ATF1 ATP1B3 ATP2B1 CALM2 CAMK2D CREB1 ATF2 POMC PRKACB PRKCB PRKD3 |
| hsa04723 | Retrograde endocannabinoid signaling | -1.4 | 1.6 | 2 | GABRG2 GNAI3 NDUFA4 NDUFA9 NDUFAB1 NDUFB2 NDUFB4 NDUFB5 NDUFS3 NDUFS4 PRKACB PRKCB MAPK3 GNB5 SLC17A8 |
| hsa04668 | TNF signaling pathway | -1.3 | 1.7 | 2 | BIRC2 FAS CASP3 CASP7 MAP3K8 CREB1 ATF2 IL15 PIK3CA MAPK3 MAP3K7 BAG4 |
| hsa05220 | Chronic myeloid leukemia | -1.3 | 1.9 | 2 | ABL1 HDAC2 KRAS MDM2 NRAS PIK3CA MAPK3 RB1 SHC1 |
| hsa04215 | Apoptosis - multiple species | -1.3 | 2.5 | 2.2 | BIRC2 CASP3 CASP7 BECN1 CYCS |
| hsa04915 | Estrogen signaling pathway | -1.3 | 1.6 | 1.9 | CALM2 CREB1 ATF2 GNAI3 HSPA8 HSP90AA1 KRAS NRAS PIK3CA POMC PRKACB MAPK3 SHC1 KRT23 |

Table S13: Pathway enrichment results for purple or dark tongue at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|----------------------------------|------|------------|---------|--|
| hsa05168 | Herpes simplex virus 1 infection | -7.2 | 2.4 | 6.2 | BAK1 C5 CASP8 EIF2S1 IKKBK IRAK1 NFKB1 OAS2 OAS3 POU2F1 PPP1CB PPP1CC PTPN11 RNASEL SRSF2 SRSF6 STAT2 TAP1 ZNF8 ZNF33A ZNF43 ZNF84 ZNF90 ZNF136 ZNF175 TNFRSF14 ZNF443 ZNF544 IRAK4 ZNF571 TLR9 ZNF83 MA |

| | | | | | |
|----------|--------------------------------------|------|-----|-----|--|
| | | | | | VS ZNF471 ZNF529 ZNF250 ZNF426 ZNF557 ZNF333 ZNF587 ZNF764 ZNF641 ZNF621 ZNF699 ZNF605 |
| hsa00514 | Other types of O-glycan biosynthesis | -6 | 6.2 | 7.1 | GALNT3 B4GALT1 MFNG OGT PLOD3 C1GALT1C1 GALNT7 GALNT11 COLGALT1 B3GLCT GXYLT1 |
| hsa05164 | Influenza A | -5.7 | 3.2 | 5.8 | SLC25A6 BAK1 CASP8 EIF2S1 IKBKB KPNA1 CIITA NFKB1 OAS2 OAS3 RNASEL STAT2 XPO1 TRIM25 PABPN1 TNFRSF10B TNFRSF10A CALCOCO2 KPNA6 IRAK4 MAVS |
| hsa05132 | Salmonella infection | -5 | 2.7 | 5.2 | ARF6 BAK1 CASP8 DYNC1LI2 FLNB IKBKB IRAK1 KPNA1 M6PR NFKB1 PFN2 PIK3C2A TNFRSF10B TNFRSF10A WASL TLR6 RIPK3 ARHGEF26 VPS41 FHOD1 IRAK4 TLR9 VPS33A AHNAK2 TAB3 |
| hsa03015 | mRNA surveillance pathway | -4.1 | 3.5 | 5 | PNN PPP1CB PPP1CC PPP2CB PPP2R2A PPP2R5B PABPN1 ACIN1 PCF11 PPP2R2D PAPOLG UPF3A PABPC1L |
| hsa04371 | Apelin signaling pathway | -4.1 | 3 | 4.8 | ACTA2 APLNR MEF2A BORCS8-MEF2B MEF2D MYL4 PDE3B SLC8A2 HDAC4 MRAS PIK3R4 PRKAG2 GNG13 GNB4 CALML4 MEF2B |
| hsa05162 | Measles | -3.6 | 2.9 | 4.3 | BAK1 CASP8 CDK2 EIF2S1 FCGR2B IKBKB IRAK1 JAK3 NFKB1 OAS2 OAS3 STAT2 IRAK4 TLR9 MAVS |
| hsa04722 | Neurotrophin signaling pathway | -3.2 | 2.9 | 4.1 | ABL1 CAMK2A CRK GAB1 IKBKB IRAK1 MAP3K3 NFKB1 PDPK1 PTPN11 SH2B3 IRAK4 CALML4 |
| hsa04621 | NOD-like receptor signaling pathway | -3.2 | 2.4 | 3.9 | CASP8 IKBKB NFKB1 OAS2 OAS3 RNASEL STAT2 VDAC2 RIPK3 CARD8 IRAK4 ERBIN DHX33 MAVS MCU GBP4 TAB3 |
| hsa05160 | Hepatitis C | -3 | 2.5 | 3.8 | BAK1 CASP8 CDK2 EIF2S1 IKBKB NFKB1 OAS2 OAS3 PPP2CB PPP2R2A RNASEL STAT2 CLDN16 PPP2R2D MAVS |
| hsa05169 | Epstein-Barr virus infection | -2.7 | 2.2 | 3.5 | BAK1 BTK CASP8 CDK2 HDAC2 IKBKB IRAK1 JAK3 NFKB1 OAS2 OAS3 PSMD12 STAT2 TAP1 IRAK4 MAVS SAP30L |
| hsa00310 | Lysine degradation | -2.6 | 3.4 | 3.7 | ACAT2 EZH1 NSD2 BBOX1 PLOD3 KMT5B SMYD2 COLGALT1 |
| hsa04014 | Ras signaling pathway | -2.5 | 2.1 | 3.2 | ABL1 ARF6 EFNA1 FLT4 GAB1 IKBKB NFKB1 PTPN11 STK4 BRAP RASA4 PAK |

| | | | | | |
|----------|---|------|-----|-----|---|
| hsa05130 | Pathogenic Escherichia coli infection | -2.5 | 2.1 | 3.2 | 4 MRAS GNG13 PAK6 GNB4 PLA2G12B CALML4 ABL1 ARF6 BAK1 CASP8 IKBKB IRAK1 NCK1 NFKB1 PTPN11 TNFRSF10B TNFRSF10A WASL CLDN16 IRAK4 WIPF2 TAB3 |
| hsa00260 | Glycine, serine and threonine metabolism | -2.4 | 4 | 3.7 | ALAS2 SARDH PGAM2 SHMT1 AOC3 GCAT |
| hsa00511 | Other glycan degradation | -2.4 | 5.9 | 4.1 | FUCA2 MAN2C1 MAN2B1 GBA2 |
| hsa04142 | Lysosome | -2.4 | 2.4 | 3.2 | AP1G1 CTSE CTSO FUCA2 GALC M6PR MAN2B1 NAGLU LAPTM4A ATP6V0A2 LAMP3 NAGPA |
| hsa04261 | Adrenergic signaling in cardiomyocytes | -2.3 | 2.3 | 3.1 | CAMK2A CREB1 MYH7 MYL4 PPP1CB PPP1CC PPP2CB PPP2R2A PPP2R5B SLC8A2 TNNI3 PPP2R2D CALML4 |
| hsa05142 | Chagas disease | -2.3 | 2.6 | 3.2 | CASP8 IKBKB IRAK1 NFKB1 PPP2CB PPP2R2A TLR6 IRAK4 TLR9 PPP2R2D |
| hsa04910 | Insulin signaling pathway | -2.2 | 2.3 | 3.1 | CRK IKBKB PDE3B PDPK1 PHKA2 PPP1CB PPP1CC PYGB MKNK1 PRKAG2 PPP1R3F CALML4 |
| hsa04330 | Notch signaling pathway | -2.2 | 3.1 | 3.3 | CTBP1 HDAC2 MFNG TLE1 DTX4 DLL1 DTX3L |
| hsa05170 | Human immunodeficiency virus 1 infection | -2.2 | 2 | 2.9 | AP1G1 BAK1 CASP8 CRK IKBKB IRAK1 NFKB1 TAP1 TNFRSF1B CUL4B PAK4 IRAK4 GNG13 PAK6 GNB4 CALML4 |
| hsa04140 | Autophagy - animal | -2.1 | 2.3 | 3 | EIF2S1 PDPK1 PPP2CB ULK1 SNAP29 MRAS WIP1 PIK3R4 SUPT20H RRAGC MTMR14 ATG4C |
| hsa04130 | SNARE interactions in vesicular transport | -2.1 | 4 | 3.4 | STX16 SNAP23 SNAP29 GOSR1 STX6 |
| hsa03013 | Nucleocytoplasmic transport | -2.1 | 2.4 | 3 | KPNA1 PNN XPO1 NUP155 ACIN1 KPNA6 NUP62 SEN2 XPO4 UPF3A |
| hsa04931 | Insulin resistance | -2.1 | 2.4 | 3 | CREB1 IKBKB NFKB1 PDPK1 PPP1CB PPP1CC PTPN11 PYGB OGT PRKAG2 |
| hsa05220 | Chronic myeloid leukemia | -2.1 | 2.8 | 3.1 | ABL1 BAK1 CRK CTBP1 HDAC2 IKBKB NFKB1 PTPN11 |
| hsa05017 | Spinocerebellar ataxia | -2.1 | 2.2 | 2.9 | SLC25A6 ATXN3 PSMD12 ATXN2 VDAC2 ULK1 NOP56 AFG3L2 WIP1 PIK3R4 TWNK MCU |

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|----------|---------------------------------------|------|-----|-----|---|
| hsa00600 | Sphingolipid metabolism | -2 | 3.2 | 3.1 | GALC SGPL1 SPTLC1 GBA2 CERK ACER2 |
| hsa03040 | Spliceosome | -2 | 2.2 | 2.8 | SRSF2 SRSF6 DHX16 PRPF4 DHX38 DDX46 SMNDC1 ACIN1 PRPF40B RBMX PRPF40A RBM25 |
| hsa00512 | Mucin type O-glycan biosynthesis | -2 | 3.7 | 3.2 | GALNT3 GCNT1 C1GALT1C1 GALNT7 GALNT11 |
| hsa04022 | cGMP-PKG signaling pathway | -2 | 2.1 | 2.7 | SLC25A6 CREB1 MEF2A BORCS8-MEF2B MEF2D MYH7 PDE3B PPP1CB PPP1CC SLC8A2 VDAC2 CALML4 MEF2B |
| hsa04728 | Dopaminergic synapse | -1.9 | 2.2 | 2.7 | CAMK2A CREB1 PPP1CB PPP1CC PPP2CB PPP2R2A PPP2R5B GNG13 PPP2R2D GNB4 CALML4 |
| hsa01200 | Carbon metabolism | -1.9 | 2.3 | 2.8 | ACAT2 DLAT GOT2 PGAM2 PGK2 PRPS2 SHMT1 H6PD ADPGK PGP |
| hsa04210 | Apoptosis | -1.8 | 2.1 | 2.6 | BAK1 CASP2 CASP8 CTSO EIF2S1 IKBKB NFKB1 PDPK1 TNFRSF10B TNFRSF10A HTRA2 |
| hsa04071 | Sphingolipid signaling pathway | -1.8 | 2.2 | 2.6 | NFKB1 PDPK1 PPP2CB PPP2R2A PPP2R5B NSMAF SGPL1 SPTLC1 PPP2R2D ACER2 |
| hsa04152 | AMPK signaling pathway | -1.8 | 2.2 | 2.6 | CREB1 EEF2 PDPK1 PPP2CB PPP2R2A PPP2R5B ULK1 EEF2K PRKAG2 PPP2R2D |
| hsa04144 | Endocytosis | -1.8 | 1.8 | 2.5 | GRK2 AP2A1 ARF6 CAV1 EPS15 SNX1 WASL RNF41 STAM2 ARFGEF1 SPART RUFY2 RAB22A SNX6 RBSN WIPF2 WASHC2C |
| hsa04622 | RIG-I-like receptor signaling pathway | -1.8 | 2.6 | 2.7 | CASP8 IKBKB NFKB1 TRIM25 RNF125 MAVS DHX58 |
| hsa04620 | Toll-like receptor signaling pathway | -1.8 | 2.3 | 2.6 | CASP8 IKBKB IRAK1 IRF5 NFKB1 TLR6 IRAK4 TLR9 TOLLIP |
| hsa05152 | Tuberculosis | -1.7 | 1.9 | 2.4 | CAMK2A CASP8 CREB1 FCGR2B IRAK1 CIITA NFKB1 NFYB TLR6 ATP6V0A2 IRAK4 TLR9 CALML4 |
| hsa04922 | Glucagon signaling pathway | -1.7 | 2.2 | 2.5 | CAMK2A CREB1 PDE3B PGAM2 PHKA2 PYGB PRKAG2 CALML4 LDHAL6A |
| hsa00562 | Inositol phosphate | -1.7 | 2.5 | 2.6 | PIK3C2A PI4KB MTMR6 MINPP1 CDIPT MTMR14 ITPKC |

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|----------|---|------|-----|-----|---|
| | metabolism | | | | |
| hsa05410 | Hypertrophic cardiomyopathy | -1.7 | 2.4 | 2.5 | ITGA4 ITGAV ITGB6 MYBPC3 MYH7 SLC8A2 TNNI3 PRKAG2 |
| hsa04360 | Axon guidance | -1.7 | 1.9 | 2.4 | ABL1 CAMK2A EFNA1 NCK1 PDPK1 PTPN11 SLIT3 TRPC1 SEMA3B PAK4 SEMA4D SRGAP2 PAK6 |
| hsa03022 | Basal transcription factors | -1.6 | 2.9 | 2.6 | ERCC3 GTF2E1 MNAT1 TAF1 TAF5 |
| hsa04114 | Oocyte meiosis | -1.6 | 2 | 2.3 | CAMK2A CDK2 PPP1CB PPP1CC PPP2CB PPP2R5B SMC1A CDC16 ANAPC7 CALML4 |
| hsa05165 | Human papillomavirus infection | -1.6 | 1.6 | 2.2 | ATP6V1A BAK1 CASP8 CDK2 CREB1 FZD2 HDAC2 IKBKB ITGA4 ITGAV ITGB6 LLGL1 MFNG NFKB1 PPP2CB PPP2R2A PPP2R5B STAT2 ATP6V0A2 PPP2R2D |
| hsa04141 | Protein processing in endoplasmic reticulum | -1.5 | 1.9 | 2.2 | BAK1 EIF2S1 ATXN3 SSR3 MBTPS1 MAN1B1 SEC61A1 NPLOC4 NGLY1 ERO1B EDEM3 UBXN2A |
| hsa04070 | Phosphatidylinositol signaling system | -1.5 | 2.2 | 2.3 | PIK3C2A PI4KB DGKD MTMR6 CDIPT MTMR14 ITPKC CALML4 |
| hsa04136 | Autophagy - other | -1.5 | 3.3 | 2.6 | PPP2CB WIPI2 PIK3R4 ATG4C |
| hsa03420 | Nucleotide excision repair | -1.5 | 2.8 | 2.5 | ERCC3 MNAT1 RFC2 XPC CUL4B |
| hsa00280 | Valine, leucine and isoleucine degradation | -1.5 | 2.8 | 2.4 | ACAT2 HADHB HMGCS1 MCCC1 MCCC2 |
| hsa05417 | Lipid and atherosclerosis | -1.5 | 1.7 | 2.1 | CAMK2A CASP8 EIF2S1 IKBKB IRAK1 NFKB1 PDPK1 POU2F1 VAV2 TNFRSF10B TNFRSF10A TLR6 IRAK4 CALML4 |
| hsa04218 | Cellular senescence | -1.5 | 1.9 | 2.1 | SLC25A6 CDK2 FOXO1 NFKB1 PPP1CB PPP1CC RBBP4 VDAC2 MRAS MCU CALML4 |
| hsa05135 | Yersinia infection | -1.5 | 1.9 | 2.2 | ARF6 CRK IKBKB IRAK1 ITGA4 NFKB1 VAV2 WASL IRAK4 WIPF2 |
| hsa04217 | Necroptosis | -1.4 | 1.8 | 2.1 | SLC25A6 CAMK2A CASP8 JAK3 PYGB STAT2 VDAC2 TNFRSF10B TNFRSF10A RIPK3 H2AW |
| hsa05144 | Malaria | -1.4 | 2.6 | 2.3 | GYPC HBA1 HBA2 HBB TLR9 |

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|----------|--|------|-----|-----|--|
| hsa00010 | Glycolysis / Gluconeogenesis | -1.4 | 2.4 | 2.2 | DLAT PGAM2 PGK2 MINPP1 ADPGK LDHAL6A |
| hsa04012 | ErbB signaling pathway | -1.4 | 2.2 | 2.2 | ABL1 CAMK2A CRK GAB1 NCK1 PAK4 PAK6 |
| hsa04510 | Focal adhesion | -1.4 | 1.7 | 2 | CAV1 CRK FLNB FLT4 ITGA4 ITGAV ITGB6 PDPK1 PPP1CB PPP1CC VAV2 PAK4 PAK6 |
| hsa04120 | Ubiquitin mediated proteolysis | -1.4 | 1.9 | 2 | TRIM37 UBB UBA7 CUL4B CDC16 HERC4 FZR1 ANAPC7 UBA6 UBE2Z |
| hsa04660 | T cell receptor signaling pathway | -1.4 | 2 | 2.1 | IKBKB NCK1 NFKB1 PDCD1 PDPK1 VAV2 PAK4 PAK6 |
| hsa04064 | NF-kappa B signaling pathway | -1.4 | 2 | 2.1 | BTK IKBKB IRAK1 NFKB1 TRIM25 CARD10 IRAK4 TAB3 |
| hsa05031 | Amphetamine addiction | -1.3 | 2.3 | 2.1 | CAMK2A CREB1 HDAC2 PPP1CB PPP1CC CALML4 |
| hsa05211 | Renal cell carcinoma | -1.3 | 2.3 | 2.1 | CRK GAB1 PTPN11 PAK4 PAK6 FLCN |
| hsa05205 | Proteoglycans in cancer | -1.3 | 1.7 | 1.9 | ANK3 CAMK2A CAV1 FLNB FZD2 GAB1 ITGAV PDPK1 PPP1CB PPP1CC PTPN11 VAV2 MRAS |
| hsa00900 | Terpenoid backbone biosynthesis | -1.3 | 3.6 | 2.4 | ACAT2 FNTA HMGCS1 |
| hsa00230 | Purine metabolism | -1.3 | 1.9 | 2 | ADSS2 AMPD3 GUK1 HPRT1 PDE3B PDE7A PPAT PRPS2 PAICS |
| hsa04110 | Cell cycle | -1.3 | 1.9 | 2 | ABL1 CDK2 HDAC2 ZBTB17 SMC1A CDC16 DBF4 FZR1 ANAPC7 |
| hsa05143 | African trypanosomiasis | -1.3 | 2.9 | 2.2 | HBA1 HBA2 HBB TLR9 |
| hsa00250 | Alanine, aspartate and glutamate metabolism | -1.3 | 2.9 | 2.2 | ADSS2 GOT2 PPAT DDO |

Table S14: Pathway enrichment results for XYZ phenome at Day 30

| GO | Description | LogP | Enrichment | Z-score | genes |
|----------|-------------|------|------------|---------|---------------------------------------|
| hsa04110 | Cell cycle | -3.6 | 5.6 | 5.2 | ABL1 CCND3 CCNH CDK2 E2F3 TFDP1 YWHAQ |

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|----------|---|------|-----|-----|--|
| hsa04725 | Cholinergic synapse | -3 | 5.4 | 4.6 | ADCY6 CAMK2B CHRNA3 GNG3 KCNJ12 GNG12 |
| hsa05203 | Viral carcinogenesis | -3 | 4 | 4.2 | CASP8 CCND3 CDK2 HPN H4C5 KAT2B YWHAQ H2BC18 |
| hsa04114 | Oocyte meiosis | -2.7 | 4.6 | 4.2 | ADCY6 CAMK2B CDK2 AURKA YWHAQ CPEB3 |
| hsa04014 | Ras signaling pathway | -2.6 | 3.5 | 3.8 | ABL1 ETS2 FGF2 GNG3 GRIN1 KSR1 ANGPT4 GNG12 |
| hsa05200 | Pathways in cancer | -2.6 | 2.5 | 3.4 | ABL1 ADCY6 CAMK2B CASP8 CCND3 CDK2 E2F3 FGF2 GNG3 IFNGR1 PTGER2 LEF1 GNG12 |
| hsa05034 | Alcoholism | -2.6 | 3.8 | 3.8 | ADORA2A GNG3 GRIN1 SLC18A2 H4C5 GNG12 H2BC18 |
| hsa04713 | Circadian entrainment | -2.5 | 5.2 | 4.2 | ADCY6 CAMK2B GNG3 GRIN1 GNG12 |
| hsa05167 | Kaposi sarcoma-associated herpesvirus infection | -2.5 | 3.6 | 3.7 | CASP8 E2F3 FGF2 GNG3 IFNGR1 LEF1 GNG12 |
| hsa04390 | Hippo signaling pathway | -2.3 | 3.9 | 3.6 | CCND3 SMAD7 SERPINE1 GDF5 YWHAQ LEF1 |
| hsa04015 | Rap1 signaling pathway | -2.3 | 3.4 | 3.4 | ADCY6 ADORA2A FGF2 GRIN1 DOCK4 VAV3 ANGPT4 |
| hsa04217 | Necroptosis | -2.3 | 3.8 | 3.6 | CAMK2B CASP8 GLUD1 IFNGR1 CHMP2B CHMP5 |
| hsa04115 | p53 signaling pathway | -2.2 | 5.5 | 3.9 | CASP8 CCND3 CDK2 SERPINE1 |
| hsa04727 | GABAergic synapse | -1.9 | 4.5 | 3.3 | ADCY6 GNG3 GABARAPL1 GNG12 |
| hsa05162 | Measles | -1.9 | 3.6 | 3.1 | CASP8 CCND3 CDK2 CSNK2A2 CD46 |
| hsa04371 | Apelin signaling pathway | -1.9 | 3.6 | 3.1 | ACTA2 ADCY6 GNG3 SERPINE1 GNG12 |
| hsa03040 | Spliceosome | -1.8 | 3.4 | 3 | HNRNPC MAGOH PRPF4 DDX42 RNU4-2 |
| hsa04914 | Progesterone-mediated oocyte maturation | -1.7 | 4 | 3 | ADCY6 CDK2 AURKA CPEB3 |
| hsa04934 | Cushing syndrome | -1.7 | 3.3 | 2.8 | ADCY6 CAMK2B CDK2 E2F3 LEF1 |
| hsa04218 | Cellular senescence | -1.7 | 3.2 | 2.8 | CCND3 CDK2 E2F3 SERPINE1 MCU |
| hsa04024 | cAMP signaling pathway | -1.6 | 2.7 | 2.6 | ADCY6 ADORA2A CAMK2B GRIN1 PTGER2 VAV3 |
| hsa04066 | HIF-1 signaling pathway | -1.6 | 3.7 | 2.8 | CAMK2B IFNGR1 SERPINE1 ANGPT4 |
| hsa05166 | Human T-cell leukemia virus 1 infection | -1.6 | 2.7 | 2.6 | ADCY6 CCND3 CDK2 E2F3 ETS2 KAT2B |

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|----------|---|------|-----|-----|---|
| hsa05163 | Human cytomegalovirus infection | -1.6 | 2.7 | 2.6 | ADCY6 CASP8 E2F3 GNG3 PTGER2 GNG12 |
| hsa04151 | PI3K-Akt signaling pathway | -1.6 | 2.3 | 2.4 | CCND3 CDK2 FGF2 GNG3 ITGA8 YWHAQ ANGPT4 GNG12 |
| hsa04724 | Glutamatergic synapse | -1.6 | 3.5 | 2.7 | ADCY6 GNG3 GRIN1 GNG12 |
| hsa05031 | Amphetamine addiction | -1.5 | 4.4 | 2.8 | CAMK2B GRIN1 SLC18A2 |
| hsa04520 | Adherens junction | -1.5 | 4.3 | 2.8 | CSNK2A2 PTPN1 LEF1 |
| hsa05152 | Tuberculosis | -1.5 | 2.8 | 2.4 | CAMK2B CASP8 IFNGR1 KSR1 CLEC7A |
| hsa04926 | Relaxin signaling pathway | -1.4 | 3.1 | 2.4 | ACTA2 ADCY6 GNG3 GNG12 |
| hsa04971 | Gastric acid secretion | -1.4 | 4 | 2.6 | ADCY6 CAMK2B SLC26A7 |
| hsa04144 | Endocytosis | -1.4 | 2.4 | 2.2 | CHMP2B SNX12 CHMP5 SMAP1 PIP5KL1 SNX32 |
| hsa04728 | Dopaminergic synapse | -1.4 | 3.1 | 2.4 | CAMK2B GNG3 SLC18A2 GNG12 |
| hsa05022 | Pathways of neurodegeneration - multiple diseases | -1.3 | 1.9 | 2 | CAMK2B CASP8 CSNK2A2 GRIN1 NDUFS1 ATXN2 SDHB CHMP2B MCU |
| hsa05012 | Parkinson disease | -1.3 | 2.3 | 2.1 | ADORA2A CAMK2B NDUFS1 SDHB SLC18A2 MCU |

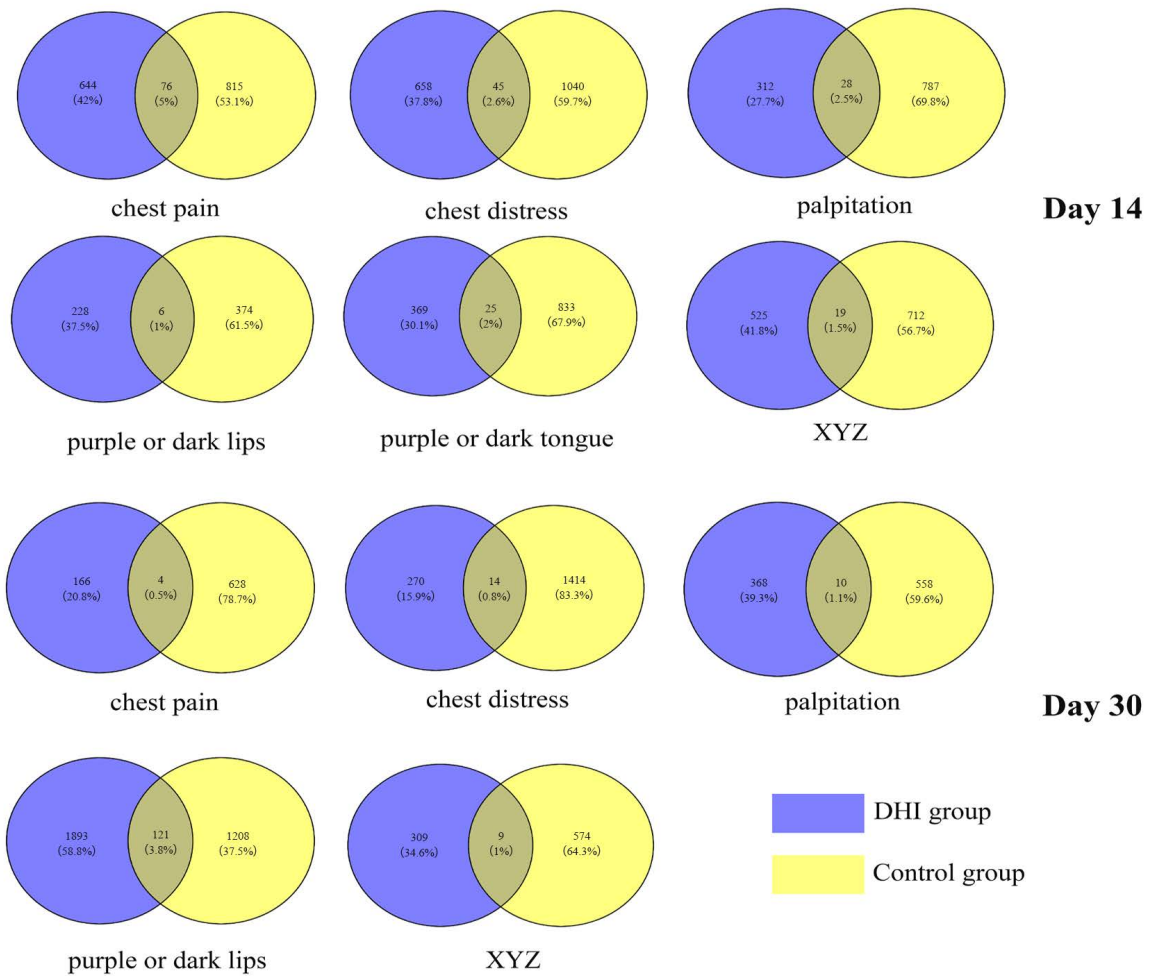


Figure S1: Comparison of the number of PARGS between DHI and control group