GMR Genetics and Molecular Research
Online Journal
ISSN:1676-5680

Key pathways involved in prostate cancer based on gene set enrichment analysis and meta analysis

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Genet. Mol. Res. 10 (4): 3856-3887 (2011)
Received June 7, 2011
Accepted October 14, 2011
Published December 14, 2011
DOI http://dx.doi.org/10.4238/2011.December.14.10

ABSTRACT. Prostate cancer is one of the most common male malignant neoplasms; however, its causes are not completely understood. A few recent studies have used gene expression profiling of prostate cancer to identify differentially expressed genes and possible relevant pathways. However, few studies have examined the genetic mechanics of prostate cancer at the pathway level to search for such pathways. We used gene set enrichment analysis and a meta-analysis of six independent studies after standardized microarray preprocessing, which increased concordance between these gene datasets. Based on gene set enrichment analysis, there were 12 down- and 25 up-regulated mixing pathways in more than two tissue datasets, while there were two down- and two up-regulated mixing pathways in three cell datasets. Based on the meta-analysis, there were 46 and nine common pathways in the tissue and cell datasets, respectively. Three up- and 10 down-regulated crossing pathways were

detected with combined gene set enrichment analysis and meta-analysis. We found that genes with small changes are difficult to detect by classic univariate statistics; they can more easily be identified by pathway analysis. After standardized microarray preprocessing, we applied gene set enrichment analysis and a meta-analysis to increase the concordance in identifying biological mechanisms involved in prostate cancer. The gene pathways that we identified could provide insight concerning the development of prostate cancer.

Key words: Prostate cancer; Gene set enrichment analysis; Meta-analysis

INTRODUCTION

Prostate cancer (PC) is one of the most common male malignant neoplasms in the world, and its incidence has increased year by year in China (Liang et al., 2007). Although large-scaled studies have been involved in prostate cancer, the mechanism involved still remained completely unclear until now. In order to reveal this mystery, a few recently reported studies have been developed using gene expression profiling of PC to identify differentially expressed genes from several to hundreds (Endo et al., 2009; Nadiminty et al., 2010), but these studies only focused on the individual gene. Prostate cancer is a complex disease and involves a number of gene interactions. Singling out and explaining individual genes on a list with a thousand important genes is still very difficult.

The major challenge for genome-wide RNA expression analysis is not to obtain gene expression profiles, but to extract a biological insight from the results (Subramanian et al., 2005). Of course, genome-wide expression analysis with DNA microarray have been used to identify predefined biological pathways associated with the phenotypic variations for many researches (Nanni et al., 2006; Chandran et al., 2007; Wallace et al., 2008). However, the confirmed biological pathways from these methods only represent a very small part of the entire range of pathways involved in prostate cancer.

To resolve this conflict, Mootha et al. (2003) described a method-Gene Set Enrichment Analysis (GSEA) which has been recognized as the most well-known and effective approach to gene set analysis. These authors have used it to identify predefined gene sets which showed significant differences in expression between normal and patient's samples. Subsequently, Subramanian et al. (2005) improved the methodology and specifically introduced the method of how to use GSEA.

GSEA which is based on the predefined sets of genes that usually derived from functional annotation or from results of prior experiments, can identify more subtle changes of gene expression, because the biggest advantage of GSEA is that the statistical results are obtained from groups or pathways rather than individual gene. Over the years, GSEA had been gradually applied to some areas (Suarez-Farinas et al., 2010). In addition, meta-analysis as a standard statistical method has become more widespread and has been applied in many fields. In this study, after a standardized microarray preprocessing for all the expression datasets, GSEA and a meta analysis were used to find the mixing pathways which provided a systematic insight into the pathways that changed during the mechanism of PC.

MATERIAL AND METHODS

Datasets

The gene expression profiling studies about prostate cancer were searched from GEO (http://www.ncbi.nlm.nih.gov/geo/), and ArrayExpress (http://www.ebi.ac.uk/ arrayexpress/). Any data that met the following conditions was selected for inclusion: 1) the data was about genome-wide RNA expression; 2) the complete microarray raw or normalized data was effective; 3) the data provided a comparison between prostate cancer patients and controls; 4) Three or more samples were contained in the data.

Finally, we found five gene expression datasets which met the above criteria. In dataset GSE3868, two samples were removed because they were human prostate hyperplasia primary samples, and the other twenty-eight samples were all included in the processing. In dataset GSE6919 with U95 Version 2, 25 patients with metastatic prostate tumor samples in paratracheal lymph node and 63 patients with normal prostate tissue adjacent to the tumor were not included in the research. We summarized all the detailed information about the datasets, such as the first author or contributor, microarray platform, sample type, sample size, and they are shown in Table 1.

Table 1. Characteristics of datasets selected in the studies.

First author or contributor	Chip	GEO accession	Experimental design	Classification	Probs	Number of samples	
						Disease	Normal
Yegnasubramanian S (Yegnasubramanian et al., 2008)	U133 A	GSE12348	unpaired, cells	prostate cancer	22K	6	3
Wallace TA (Wallace et al., 2008)	U133A 2.0	GSE6956	unpaired, tissues	prostate cancer	22K	69	20
Nanni S (Nanni et al., 2006)	U133A	GSE3868	unpaired, cells	prostate cancer	22K	23	5
Chandran UR (Yu et al., 2004; Chandran et al., 2007)	U95 Version 2	GSE6919	unpaired tissues	Prostate tumor	12K	65	18
Vellaichamy A (Vellaichamy et al., 2009)	U133 Plus 2.0	GSE17044	unpaired, cells	prostate cancer cells	54K	3	3

Paried = compare prostate cancer to normal controls from the same patients with prostate cancer; Unparied = compare prostate cancer from men with prostate cancer to normal controls from men without prostate cancer; cells = human prostate cancer cells samples.

Data processing of standardized microarray preprocessing

Software packages developed in version 2.10.1 of Bioconductor (Mootha et al., 2003) were applied for data preprocessing. The Robust Multichip Averaging (RMA) algorithm in the affy conductor package was used for each affymetrix raw dataset to calculate background adjusted, normalized and log2 probe-set intensities. The affy U133A normalizations shown in GSE3868 was also retained for further analysis. We selected genes which could be mapped to any explicit KEGG pathway for the further analysis of GSEA and meta-analysis. The measure of variability was within the interquartile range (IQR) and a cut-off was set up to remove IQR values under 0.5 for all the remaining genes. If one gene was targeted for multiple probe sets, we retained the probe set with the largest variability. Pathway analysis of each dataset was performed independently.

Data processing of GSEA

GSEA performed using the Category version 2.10.1 package (Mootha et al., 2003). The gene sets represented by more than 10 genes were retained. The Student's-t-test statistical score was implemented in each pathway and the mean of the genes was calculated. A permutation test with 1000 times was used to identify the significantly changed pathways and p-value was less than or equaled to 0.05.

Data processing of meta-analysis

To obtain the common gene sets for the datasets regarding prostate tissues or cells independently from the above remaining genes of each dataset, we then calculated the chi-square value of each gene based on the formula according to Brown (1975):

$$X^2 = -2\sum_{i=1}^{K} \log_e p^i$$

and a cut-off was also set up to remove chi-square values under 0.05 for all the surplus genes which were used to obtain the pathways of the KEGG from DAVID Bioinformatics Resources 6.7 (http://david.abcc.ncifcrf.gov/). *K* is the number of datasets.

RESULTS

Re-analyzing each dataset to produce differentially expressed pathways

The five inclusion datasets contain 166 prostate cancer cases and 49 controls. All the datasets were implemented with a common GSEA method. For each separate analysis, the significant pathways and the genes were also obtained with GSEA and the detailed information about the analysis results are shown in Table 2.

In our studies, experimental design of 2 datasets (Chandran et al., 2007; Wallace, 2008) was related to prostate cancer tissues, while the other three datasets (Nanni et al., 2006; Yegnasubramanian et al., 2008; Vellaichamy et al., 2009) were related to prostate cancer cells. Finally, we found that the consistent pathways were separate in tissue and cell from GSEA and the meta-analysis result.

Table 2. Summary of each dataset used in the re-analysis and the number of differentially expressed pathways in gene set enrichment analysis (GSEA).

Studies	Number of patients	Number of controls	Number of genes after pre-processing	Number of pathways have genes >10	Up-regulated pathways	Down-regulated pathways
GSE17044	3	3	2421	219	0	0
GSE12348	6	3	2184	217	38	30
GSE3868	23	5	3814	216	6	17
GSE6956	69	20	2214	214	93	10
GSE6919 U95 Version 2	65	18	1810	213	72	1

Common significant pathways obtained from two prostate cancer tissue datasets by GSEA

There were 1 up and 53 down-regulated pathways that existed in 2 prostate cancer tissues datasets, the details can be seen in Additional Table 1. The up-regulated pathway concerned genetic information processing and translation. Most of the representative pathways in down-regulated pathways were associated with metabolism, biosynthesis, signal transduction, cell communication and organismal systems.

Common significant pathways obtained from three prostate cancer cell datasets by GSEA

Except for prostate cancer tissues, datasets regarding prostate cancer cells were also added to our studies. For single datasets analysis, there was no up or down-regulated pathway detected in GSE17044. The reason may be that there was only a limited number of samples available. There were 38 up- and 30 down-regulatory pathways in GSE12348, and 6 and 17 in GSE3868. Also, there were four mixing pathways including 2 up and 2 down-regulated pathways from these 2 datasets. The details are shown in Additional Table 2.

Common significant pathways obtained from these prostate cancer datasets by meta-analysis

To further identify the results, we obtained common significant pathways and genes from these datasets by meta-analysis. In total, there were 1905 significant genes and 39 common pathways in two tissues datasets. Most of these pathways concernedCancers, Cardiovascular Diseases, Cell Communication, Signal Transduction, Cellular Processes, Environmental Information Processing, Human Diseases and Organismal Systems. The details are shown in Additional Table 3. Otherwise, 131 significant genes and 9 common pathways were identified in the three cell datasets. The main pathways concerned Lipid Metabolism and Amino Acid Metabolism. The results are shown in Additional Table 4.

Common crossing significant pathways between the results of GSEA and meta-analysis

To search the intersection pathways, a comparative analysis was made independently between the common significant pathways of GSEA and meta-analysis in cancer tissues or cells. Finally, 15 consistent pathways were obtained in tissue datasets and the details are shown in Additional Table 5. In this table, the pathways were primarily concerned metabolism, environmental information processing, signal transduction, signaling molecules and interaction, human diseases, cancers. However, no consistent pathways were detected in cell datasets.

mRNA expression in human prostate cancers tissue

In order to improve the above results, we searched for a dataset which was able to show the experience according to prostate carcinoma *vs* normal tissue using the publically

available ONCOMINE cancer gene expression microarray database (Singh et al., 2002). The platform for this dataset is U95Av2 arrays (Affymetrix). The sample included 50 normal and 52 tumor prostate tissues. The raw data was downloaded from (http://www.broadinstitute.org/cgi-bin/cancer/publications/pub_paper.cgi?mode=view&paper_id=75). We also used the same GSEA program to enrich the pathways. Finally, we enriched 27 up-regulated and 66 down-regulated pathways. The results are shown in Additional Table 6. Except for two pathways, which is glycolysis/gluconeogenesis, starch and sucrose metabolism, the other 13 pathways as shown in Additional Table 5 were included in these enriched pathways.

DISCUSSION

PC is one of the most serious diseases and its mechanism still remains completely unclear. No single theory can provide a perfect definition for all the different cases of prostate cancer. The genome-wide microarrays can locate gene families and pathways which show a consistent alteration in a disease state. Pathway analysis is a valid method to reduce a major deviation and can obtain interesting common genes and pathways by mixing differently expressed genes from different datasets. Therefore, we can apply the pathway analysis to search for genes which are difficult to detect by univariate statistical analysis because of their subtle change. Gene set enrichment analysis and a meta-analysis were applied to five datasets to extract biological insights involved in prostate cancer. Our findings suggest that most of the pathways and genes that affect prostate cancer were accordant. In our study, according to functional classification, we discussed several differentially expressed pathways and genes among crossing pathways as shown in Additional Table 5 and which suggest the role of these pathways and genes in prostate cancer.

Environmental information processing

Environmental information processing includes membrane transport, signal transduction, signaling molecules and interaction etc. In our findings, signal transduction, signaling molecules and interaction are common functions in positive pathways. Signal transduction is related to cell proliferation, differentiation and apoptosis. Because most of the signaling molecules and interaction are involved in the processing of signal transduction, signaling molecules and interaction connect closely with signal transduction and may play an important role in the course of prostate cancer. Currently, numerous studies have been applied to explore signal transduction to understand the biological mechanism of prostate cancer (Skvortsova et al., 2008; Aalinkeel et al., 2010). The mitogen-activated protein kinase (MAPK) signaling pathway in our studies which belongs to signal transduction is related to various cellular functions. The MAPK cascade is a highly conserved module that is involved in various cellular functions, including cell proliferation, differentiation and migration (Takeda and Ichijo, 2002). A number of genes expression in this pathway have been reported to be related with prostate cancer i.e. CD14(+) cells exhibiting reduced expression of HLA-DR molecules in PCa patients. These cells suppress immune cell function *in vitro* and, therefore, immunotherapy protocols for PCa patients must be factored into the design (Vuk-Pavlovic et al., 2010). MYC oncogene overexpression induces prostatic intraepithelial neoplasia and loss of Nkx3.1 in mouse luminal epithelial cells (Iwata et al., 2010). Overexpression of NF-kappaB2/p52

enhances androgen-sensitive LNCaP human prostate cancer cell growth and clonogenic ability in androgen-deprived condition *in vitro*. NF-kappaB2/p52 induced androgen-independent growth occurs via protecting LNCaP cells from apoptotic cell death and cell cycle arrest induced by androgen-deprivation. Adenoviral mediated NF-kappaB2/p52 expression in LNCaP cells enhances tumor growth in intact male nude mice and induces tumor growth in castrated male nude mice, suggesting that overexpression of NF-kappaB2/p52 induces androgen-independent growth of androgen-sensitive LNCaP cells (Nadiminty et al., 2008). CD44+ cells possess stem cell characteristics and highly expressed genes known to be important in stem cell maintenance. In addition, they have shown a strong tumorigenic potential in the clonogenic assay and soft agar colony formation assay (Lee et al., 2011).

Cellular processes and cell communication

Except for signal transduction and signaling molecules and interaction, cellular processes and cell communication are also a way of obtaining information transmission between cells. Many junctions among cells are the structural characteristics of smooth muscle and become a channel connected cytoplasm in order to transmit cellular information. Numerous recent studies suggest that the disruption of cell-cell adhesion may be a key mechanism associated with calcitonin (CT)-stimulated prostate cancer progression and metastasis (Shah et al., 2008). Gap junction has been considered to be an important part of junctional communication in the prostate morphogenesis and oncogenesis (Mitra et al., 2006) and may also play a pivotal role in invasion and migration of prostate cancer cells (Tate et al., 2006). The idea that focal adhesion is related to cell movement suggests focal adhesion which may be involved in the development and metastasis of tumors. Recent studies have tested the hypothesis (Franzen et al., 2009). Epithelial tight junctions are composed of at least three types of transmembrane protein. The transmembrane proteins mediate cell adhesion and are thought to constitute the intramembrane and paracellular diffusion barriers (Balda and Matter, 2003). Cell growth, reproduction, differentiation and apoptosis are involved in signal transduction of cell transmembrane. Therefore, the factors which affect signal transduction of cell transmembrane will possibly interrupt the function of normal cells. The actin cytoskeleton participates in many fundamental processes including the regulation of cell shape, motility, and adhesion. The remodeling of the actin cytoskeleton is dependent on actin binding proteins, which organize actin filaments into specific structures that allow them to perform various specialized functions (Revenu et al., 2004). Therefore, cell communication may be a possible significant factor for an insight into the biological mechanism of prostate cancer.

Metabolism pathways

The metabolism pathways in our study were mainly focused on lipid metabolism, amino acid metabolism and xenobiotics biodegradation and metabolism. It has been recently confirmed that genes and proteins involved in cellular metabolism play a crucial part in the development and progression of PC (Pettazzoni et al., 2011; Ouyang et al., 2011). Glycolysis/Gluconeogenesis pathway belongs to the lipid metabolism. Glycolysis is the process of converting glucose into pyruvate and generating small amounts of adenosine-5'-triphosphate (energy) and nicotinamide adenine dinucleotide. It can produce important precursor metabo-

lites. The gene PGK1 in this pathway has been reported to be significantly differentially expressed between laser microdissected malignant versus benign clinical samples of prostate tissue (Romanuik et al., 2009). Uridine diphosphate (UDP)-glucose dehydrogenase (UGDH) in the amino acid metabolism pathway was found to be significantly differentially expressed in our analysis, and can also catalyze the oxidation of UDP-glucose to yield UDP-glucuronic acid which is a precursor for synthesis of glycosaminoglycans and proteoglycans that promote aggressive PC progression (Huang et al., 2010). Drug metabolism - cytochromes P450 was also observed in our search for pathways. The cytochromes P450 (CYPs) are key enzymes in cancer formation and cancer treatment. They mediate the metabolic activation of numerous precarcinogens and participate in the inactivation and activation of anticancer drugs. Therefore, this pathway may have a relationship with the mechanism of resistance to chemotherapy drugs in prostate cancer. In the finding genes of this pathway, *CYP3A4* and *CYP3A5* expression is related to androgen metabolism (Rebbeck et al., 2008). Meta-analysis studies show that measurement of *GSTP1* promoter methylation in plasma, serum, or urine samples may complement PSA screening for prostate cancer diagnosis (Wu et al., 2011).

Endocrine system

The insulin signaling pathway in our study belongs to both the organismal and endocrine systems. Most of the positive genes in this pathway have been reported to be related to prostate cancer. Insulin binding to its receptor results in the tyrosine phosphorylation of insulin receptor substrates (IRS) by the insulin receptor tyrosine kinase. Signal transduction proteins interact with IRS including GRB2. GRB2 is part of the cascade including SOS, RAS, RAF, and MEK that lead to activation of MAPK and mitogenic response in the form of gene transcription. FASN can act as a prostate cancer oncogene in the presence of AR and then *FASN* exerts its oncogenic effect by inhibiting the intrinsic pathway of apoptosis (Migita e t al., 2009). Expression of p66(Shc) protein correlates with proliferation of human prostate cancer cells (Veeramani et al., 2005). Increasing mTOR activity and protein synthesis did not translate into enhanced cell proliferation rates. However, the lack of TSC2 resulted in a survival advantage when cells were exposed to hypoxia. Protection against hypoxia-induced cell death due to TSC2 deficiency is rapamycin-resistant, suggesting that TSC2 affects an apoptotic pathway. Tumors derived from TSC2 wild-type cells exhibited a growth delay compared with TSC2-deficient tumors, indicating that enhancing mTOR activity is advantageous in the initial phase of tumor growth (Kaper et al., 2006).

Other pathways and genes

As shown in Additional Table 3, except for the above pathways, the remaining pathways all belong to the classification of human diseases and cancers. Most of genes in these pathways can be enriched in the above pathways. Smad3 in chronic myeloid leukemia pathway is an important gene for prostate cancer and this has widely been reported in the literature. Smad3 has been shown to be the essential mediator of most Smad-dependent TGF-beta responses, including control of gene expression, cell growth, apoptosis, and tumor suppression (Yang et al., 2009). Deregulated/enhanced expression and activation of AR in prostate carcinomas may intercept the tumor suppressor function of TGF-β through transcriptional suppres-

sion of Smad3 (Song et al., 2010).

CONCLUSION

The pathogenesis of PC is quite complicated. We were able to gain an insight into the mechanisms by focusing on gene sets or pathways rather than on individual genes. In our research, many consistent biological mechanisms involved in PC were identified by GSEA and meta-analysis after a standardized microarray preprocessing, which were original in terms of their connection to PC (as obtained from the current literature). In addition, the enriched pathways can be improved by a tissue dataset from the Oncomine database. Further studies about the specific role and interactions of the genes included in related pathways are needed to improve the understanding of prostate cancer.

ACKNOWLEDGMENTS

In this research, we had a great amount of help. During writing and running the program, Zhao Hongbo, Zhang Jiange, etc., provided substantial assistance. Research supported by the National Natural Science Foundation of China (grant #81060213), Guangxi Natural Science Foundation (Grant #2011GXNSFB018100).

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SUPPLEMENTARY MATERIAL

Additional Table 1. Common significant pathways obtained from 2 prostate cancer tissue datasets by GSEA up-regulated pathways.

Pathway	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
03010	Ribosome	Genetic information processing and translation	0.01	36	RPL23P6, RPL27A, RPL29P11, RPL29P12, RPL29P26, RPL29P9, RPL31P17, RPL31P49, RPL38, RPL5P1, RPL5P34, RPS11P5, RPS19P3, RPS28, RPS28P6, RPS28P9, RPS2P11, RPS2P12, RPS2P17, RPS2P20, RPS2P5, RPS2P51, RPS2P55, RPS2P8, RPl27, RPl14, RPl23, RPl28, RPl29, RPl31, RPl5, RPS11, RPS 19, RPS 2, RPS 20, RPS 21

Additional Table 2. Common significant pathways obtained from 3 prostate cancer cell datasets by GSEA up-regulated pathways.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
00260	Glycine, serine and threonine metabolism	Amino acid metabolism	0.008	11	C8orf62; Gamt; MAOA; PHGDH; PSAT1; PSPH; PSPHL; SHMT2; dld; gcat; srr
04120	Ubiquitin mediated proteolysis	sorting and degradation	0.008	65	ANAPC5; CUL5; CUL7; Fbxo2; Fbxw11; HERC2; HUWE1; ITCH; KLHL9; LOC100132973; LOC730429; NEDD4; PIAS1; PIAS2; RBX1; SAE1; SMURF1; SMURF2; STUB1; TCEB1; Tceb2; Trip12; UBA2; UBA6; UBE2A; UBE2C; UBE2D3P; UBE2E1; UBE2G2; UBE2I; UBE2J1; UBE2MP1; UBE2N; UBE3B; UBE3C; UBR5; Uba1; Uba7; Ube2e3; Ube2h; Ube2l6; Ube2m; Ube2q1; Ube2s; Ube3a; Ube4b; WWP1; WWP2; btrc; cul3; cul4a; erc4; keap1; grn1; prpf19; rnf7; trim32; uba3; ube2b; ube2d2; ube2d3; ube2d4; ube2g1; ube2l3; ube4a

Additional Table 3. Common significant pathways obtained from 2 prostate cancer tissue datasets by meta-analysis.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Include genes
04510	Focal adhesion	Environmental Information Processing; Signal Transduction	1.63E-07	59	TLN1, PTEN, AKT1, ACTG1, CDC42, PAK3, PAK4, ILK, SHC1, ZYX, PIK3CG, ROCK2, ACTN1, FLNC, FLNA, PPP1CA, CCND1, CCND2, JUN, MAPK3, PDGFRA, MYL7, CAV2, CAV1, GRB2, TNC, ITGB4, ITGB3, ITGB1, LAMB4, PTK2, RAC3, ITGB8, BCL2, SOS2, COL6A2, COL6A1, PIK3R3, THBS1, THBS3, FN1, ACTB, COL4A2, FLT1, COL4A1, TNXA, MET, RAF1, HGF, KDR, VWF, LAMA4, ITGA6, ITGA5, LAMA5, ITGA7, RAP1A, CRK, MYLK
05220	Chronic myeloid leukemia	Chronic myeloid leukemia	3.65E-04	24	PIK3CG, CTBP2, BCR, GRB2, MAP2K2, TGFBR2, TGFB3, SMAD3, RAF1, PTPN11, AKT1, CCND1, HDAC1, SOS2, MAPK3, MDM2, SHC1, ABL1, PIK3R3, RUNX1, IKBKB, CRK, MYC, CHUK
04520	Adherens junction	Cellular Processes; Cell Communication	5.55E-04	24	ACTB, PTPRB, PARD3, PTPRF, BAIAP2, MET, TGFBR2, SMAD3, LEF1, ACTN1, CTNND1, CDH1, SNAI2, CTNNA1, IQGAP1, FARP2, ACTG1, CDC42, TJP1, CSNK2A1, RAC3, PVRL2, MAPK3, SSX2IP
04512	ECM-receptor interaction	Environmental Information Processing; Signaling Molecules and Interaction	8.63E-04	25	TNC, ITGB4, ITGB3, ITGB1, SDC2, LAMB4, GP5, CD44, ITGB8, COL6A2, COL6A1, SV2A, AGRN, THBS1, THBS3, FN1, COL4A2, COL4A1, TNXA, VWF, LAMA4, ITGA6, ITGA5, LAMA5, ITGA7
05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Environmental Information Processing; Signaling Molecules and Interaction	0.001158	23	ACTB, ITGB4, CACNB1, LEF1, ACTN1, GJA1, ITGB3, CTNNA1, ITGB1, JUP, ACTG1, DES, SGCG, ATP2A2, ITGA6, ITGA5, ITGB8, DMD, ITGA7, DSP, CACNA1D, SGCA, SGCB
03040	Spliceosome	Spliceosome	0.001238	33	CHERP, U2AF2, LSM6, TRA2A, SNRPB2, SR140, SART1, HNRNPA3, TCERG1, HNRNPK, SFRS5, DHX38, DDX23, HSPA2, PRPF8, PCBP1, LSM3, SNRNP70, ACIN1, RBM25, PRPF40A, BCAS2, SNRPA1, SFRS1, DDX5, PRPF4, HNRNPA1, SFRS3, HNRNPU, SNRPA, PUF60, SNRPG, BAT1
05210	Colorectal cancer	Environmental Information Processing; Signaling Molecules and Interaction	0.002051	24	PIK3CG, DVL3, MSH3, GRB2, CYCS, TGFBR2, MET, TGFB3, SMAD3, LEF1, RAF1, DVL1, AKT1, FOS, CCND1, RAC3, JUN, BCL2, SOS2, MAPK3, PDGFRA, PIK3R3, MYC, AXIN1
05213	Endometrial cancer	Environmental Information Processing; Signaling Molecules and Interaction	0.002683	17	PIK3CG, MAP2K2, GRB2, LEF1, RAF1, CDH1, FOXO3, CTNNA1, PTEN, AKT1, CCND1, ILK, MAPK3, SOS2, PIK3R3, MYC, AXIN1
05221	Acute myeloid leukemia	Human Diseases; Cancers	0.00354	18	PIK3CG, MAP2K2, GRB2, PML, LEF1, RAF1, STAT3, AKT1, JUP, CCND1, SOS2, MAPK3, RARA, RUNX1, IKBKB, PIK3R3, MYC, CHUK
04722	Neurotrophin signaling pathway	Organismal Systems; Nervous System	0.003847	31	GRB2, FOXO3, MAGED1, AKT1, CDC42, BCL2, SOS2, GAB1, SHC1, CAMK2B, SH2B1, CSK, PIK3R3, ARHGDIA, PIK3CG, NTF3, MAP2K2, RAF1, PRKCD, IRS1, PTPN11, ATF4, RPS6KA1, JUN, MAPK3, RAP1A, ABL1, IKBKB, CRK, CALM1, NGF

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Additional Table 3. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Include genes
05211	Renal cell carcinoma	Environmental Information Processing; Signaling Molecules and Interaction	0.005404	20	PIK3CG, MAP2K2, GRB2, MET, TGFB3, RAF1, HGF, ARNT, PTPN11, AKT1, CDC42, PAK3, JUN, PAK4, GAB1, SOS2, MAPK3, RAP1A, PIK3R3, CRK
04810	Regulation of actin cytoskeleton	Organismal Systems; Development	0.005587	47	MYL7, FGF7, MRAS, ITGAE, ITGB4, IQGAP2, RDX, FGF12, ITGB3, PIP5K1A, GNG12, ITGB1, IQGAP1, ACTG1, CDC42, PTK2, EZR, ITGB8, GSN, RAC3, PAK3, PAK4, SOS2, MSN, PIK3R3, CSK, FGF2, FN1, PIK3CG, ACTB, ROCK2, MAP2K2, BAIAP2, RAF1, ACTN1, MYH9, PPP1CA, ITGA6, ITGA5, RRAS2, MAPK3, ITGA7, PDGFRA, CRK, MYLK, CD14, F2R
04530	Tight junction	Environmental Information Processing; Signaling Molecules and Interaction	0.006753	32	MYL7, CLDN7, PARD3, OCLN, GNAI2, CLDN4, CLDN3, MRAS, CLDN5, CASK, PTEN, LLGL2, ACTG1, AKT1, CDC42, CTTN, CSNK2A1, PPP2CB, ACTB, PPP2R1A, SYMPK, PARD6B, INADL, ACTN1, MYH9, CSDA, CTNNA1, PRKCD, TJP1, EPB41L1, RRAS2, JAM3
05130	Pathogenic Escherichia coli infection	Metabolism; Biosynthesis of Other Secondary Metabolites	0.007283	17	ACTB, ARHGEF2, OCLN, ROCK2, TUBB2C, CDH1, ITGB1, ACTG1, CDC42, CTTN, EZR, KRT18, TUBA3C, TUBA4A, TUBA1A, ABL1, CD14
04910	Insulin signaling pathway	Human Diseases; Infectious Diseases	0.00756	32	PHKA2, GRB2, RHOQ, PDE3B, AKT1, PPP1R3C, SOS2, FASN, GYS1, GYS2, SHC1, PRKAA1, PIK3R3, SREBF1, PIK3CG, PTPRF, PHKG1, MAP2K2, PRKAB2, ACACA, FBP1, RAF1, IRS1, PPP1CA, PYGM, PYGL, MAPK3, TSC2, RHEB, IKBKB, CRK, CALM1
05222	Small cell lung cancer	Human Diseases; Cancers	0.009791	22	PIK3CG, CKS1B, FHIT, COL4A2, COL4A1, CYCS, ITGB1, PTEN, AKT1, LAMB4, PTK2, CCND1, LAMA4, ITGA6, LAMA5, BCL2, IKBKB, PIK3R3, MYC, CHUK, TRAF4, FN1
05200	Pathways in cancer	Metabolism; Metabolism of Cofactors and Vitamins	0.011061	65	FGF7, TGFB3, FGF12, NFKB2, PTEN, AKT1, CDC42, FOS, RARA, WNT6, TPR, MYC, FGF2, CHUK, PIK3CG, PLD1, CTBP2, BCR, CYCS, LEF1, CTNNA1, DAPK1, JUP, CCND1, JUN, MAPK3, PDGFRA, MDM2, GSTP1, KS1B, GRB2, PML, CDH1, ITGB1, ARNT, LAMB4, PTK2, RAC3, BCL2, SOS2, PIK3R3, RUNX1, TRAF4, AXIN1, FN1, DVL3, COL4A2, COL4A1, MSH3, KLK3, MAP2K2, MET, TGFBR2, SMAD3, RAF1, HGF, STAT3, DVL1, LAMA4, HDAC1, ITGA6, LAMA5, IKBKB, ABL1, CRK
05410	Hypertrophic cardiomyopathy (HCM)	Human Diseases; Infectious Diseases	0.01124	22	ACTB, ACTC1, PRKAB2, ITGB4, TGFB3, CACNB1, ITGB3, TPM2, ITGB1, ACTG1, DES, SGCG, ATP2A2, ITGA6, ITGA5, ITGB8, DMD, ITGA7, PRKAA1, CACNA1D, SGCA, SGCB
05414	Dilated cardiomyopathy	Human Diseases; Infectious Diseases	0.01412	23	ACTB, ACTC1, ADCY6, ITGB4, TGFB3, CACNB1, ITGB3, TPM2, ITGB1, ACTG1, DES, SGCG, ATP2A2, ITGA6, ITGA5, ITGB8, PLN, DMD, ITGA7, GNAS, CACNA1D, SGCA, SGCB

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Additional Table 3. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Include genes
04540	Gap junction	Organismal Systems; Sensory System	0.018837	22	GNAI2, MAP2K2, GRB2, ADCY6, TUBB2C, GJA1, RAF1, LPAR1, ITPR3, GRM1, ITPR1, ITPR2, TJP1, CSNK1D, SOS2, MAPK3, PDGFRA, TUBA3C, TUBA4A, GNAS, TUBA1A, HTR2A
04130	SNARE interactions in vesicular transport	Organismal Systems; Nervous System	0.019212	12	STX6, STX8, STX4, STX12, STX2, STX16, VAMP5, GOSR2, VAMP3, GOSR1, VAMP2, SNAP23
05012	Parkinson's disease	Organismal Systems; Nervous System	0.020499	29	NDUFB3, UQCRC1, NDUFB6, NDUFB8, COX7B, UCHL1, PINK1, NDUFS7, NDUFS5, NDUFS4, ATP5O, NDUFS2, ATP5J, COX7A1, SLC25A4, SLC25A6, NDUFA6, CYCS, VDAC2, UBE2L3, COX6C, VDAC1, SDHB, UBA1, PPID, SDHD, ATP5C1, SLC18A2, UQCRB
04020	Calcium signaling pathway	Human Diseases; Cancers	0.025932	37	PHKA2, ERBB4, TNNC2, ERBB3, EDNRA, ADRB3, ATP2B3, ATP2B4, PDE1C, PPP3CB, PPP3CC, CAMK2B, PTGER3, SLC25A4, PHKG1, SLC25A6, ITPR3, VDAC2, GRM1, ITPR1, ITPR2, VDAC1, P2RX4, ADRB2, PLCE1, ATP2A2, PPID, PLN, PDGFRA, AVPR1A, TBXA2R, NAS, CACNA1D, MYLK, CALM1, HTR2A, F2R
00010	Glycolysis / Gluconeogenesis	Metabolism; Lipid Metabolism	0.026651	16	ALDOA, LDHB, LDHA, PFKL, ALDOB, PGAM1, ADH5, FBP1, ALDH3B2, ADH1B, ADH1A, GPI, ALDH1B1, PGM1, PGK1, GAPDH, ENO1
04012	ErbB signaling pathway	Environmental Information Processing; Signal Transduction	0.028142	21	PIK3CG, ERBB4, ERBB3, MAP2K2, GRB2, RAF1, AKT1, PTK2, PAK3, JUN, PAK4, GAB1, SOS2, MAPK3, SHC1, CAMK2B, ABL1, NRG1, PIK3R3, CRK, MYC
05215	Prostate cancer	Human Diseases; Cancers	0.035202	21	PIK3CG, KLK3, MAP2K2, GRB2, LEF1, RAF1, PTEN, AKT1, ATF4, CCND1, BCL2, SOS2, MAPK3, PDGFRA, CREB3L1, MDM2, SRD5A2, IKBKB, PIK3R3, CHUK, GSTP1
00500	Starch and sucrose metabolism	Metabolism; Amino Acid Metabolism	0.039195	12	GPI, GBE1, PYGM, ENPP1, PYGL, PGM1, GAA, UGDH, GYS1, GYS2, UGT2A1, UGP2
04070	Phosphatidylinositol signaling system	Environmental Information Processing; Signal Transduction	0.041133	18	PIK3CG, INPP1, INPPL1, PI4KA, PI4KB, PIP5K1A, OCRL, ITPR3, CDS1, PTEN, ITPR1, ITPR2, PLCE1, DGKD, SYNJ2, INPP4A, PIK3R3, CALM1
04662	B cell receptor signaling pathway	Organismal Systems; Immune System	0.046124	18	PIK3CG, IFITM1, MAP2K2, GRB2, RAF1, AKT1, FOS, RAC3, JUN, SOS2, APK3, PPP3CB, PPP3CC, IKBKB, PIK3R3, NFATC3, CHUK, BLNK
05416	Viral myocarditis	Human Diseases; Cardiovascular Diseases	0.054462	17	ACTB, CAV1, CYCS, HLA-C, MYH9, CXADR, EIF4G1, ACTG1, CCND1, EIF4G3, SGCG, RAC3, CD40LG, DMD, ABL1, SGCA, SGCB
04010	MAPK signaling pathway	Environmental Information Processing; Signal Transduction	0.063862	50	MEF2C, FGF7, TGFB3, FGF12, NFKB2, AKT1, FOS, CDC42, MYC, FGF2, CHUK, IL1A, FLNC, FLNA, JUN, RRAS2, MAPK3, PDGFRA, HSPB1, PLA2G6, MAP3K13, NGF, PPP5C, GRB2, MRAS, CACNB1, GNG12, HSPA2, ELK4, RAC3, SOS2, JUND, PPP3CB, PPP3CC, NTF3, TAOK2, MAP2K2, TGFBR2, NF1, NR4A1, RAF1, ATF4, DUSP3, DUSP1, RPS6KA1, RAP1A, IKBKB, CRK, CACNA1D, CD14

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Additional Table 3. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Include genes
04670	Leukocyte transendothelial migration	Organismal Systems; Immune System	0.064448	25	CLDN7, MYL7, OCLN, CLDN4, GNAI2, CLDN3, CLDN5, CTNND1, ITGB1, ACTG1, CDC42, PTK2, EZR, CXCR4, MSN, PIK3R3, ACTB, PIK3CG, ROCK2, ACTN1, CTNNA1, PTPN11, PECAM1, RAP1A, JAM3
00030	Pentose phosphate pathway	Metabolism; Carbohydrate Metabolism	0.066747	8	ALDOA, GPI, PFKL, ALDOB, PGM1, PGD, FBP1, TKT
00982	Drug metabolism - cytochrome P450	Metabolism; Xenobiotics Biodegradation and Metabolism	0.068111	15	CYP3A4, CYP3A5, CYP3A7, CYP2D6, ADH5, ALDH3B2, ADH1B, ADH1A, MGST3, CYP2A13, FMO5, GSTM3, AOX1, UGT2A1, GSTO1, GSTP1
04144	Endocytosis	Cellular Processes; Transport and Catabolism	0.070117	36	PARD3, CLTB, ERBB4, RAB5B, RAB5C, ERBB3, PIP5K1A, CHMP2B, CDC42, ADRB3, AP2B1, HSPA2, CXCR4, SH3GLB1, RAB11A, NEDD4L, AGAP1, IQSEC1, SH3GL3, PARD6B, PLD1, FLT1, RAB4A, MET, TGFBR2, PSD4, HLA-C, KDR, RAB31, AP2A2, ADRB2, NEDD4, PDGFRA, MDM2, DNM2, F2R
05214	Glioma	Human Diseases; Cancers	0.076149	15	PIK3CG, MAP2K2, GRB2, RAF1, PTEN, AKT1, CCND1, MAPK3, SOS2, PDGFRA, MDM2, SHC1, CAMK2B, PIK3R3, CALM1
00020	Citrate cycle (TCA cycle)	Metabolism; Carbohydrate Metabolism	0.078707	9	SDHB, IDH3G, SDHD, CS, IDH2, IDH3B, ACLY, OGDH, MDH2
04610	Complement and coagulation cascades	Organismal Systems; Immune System	0.079678	16	MBL2, C7, CR1, MASP2, F13A1, F8, C1R, F13B, VWF, FGG, F5, F3, CD59, TFPI, CFD, F2R
05218	Melanoma	Human Diseases; Cancers	0.097175	16	PIK3CG, FGF7, MAP2K2, MET, RAF1, CDH1, FGF12, HGF, PTEN, AKT1, CCND1, MAPK3, PDGFRA, MDM2, PIK3R3, FGF2

Additional Table 4. Common significant pathways obtained from 3 prostate cancer cell datasets by meta-analysis.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
00330	Arginine and proline metabolism	Amino Acid Metabolism	0.002131	7	ODC1, PYCR1, GOT1, P4HA2, GLUD2, GLUD1, GAMT
00900	Terpenoid backbone biosynthesis	Amino Acid Metabolism	0.005931	4	FDPS, PMVK, ACAT2, ACAT1
00100	Steroid biosynthesis	Cancers	0.00854	4	TM7SF2, DHCR24, FDFT1, SC4MOL
00071	Fatty acid metabolism	Cell Growth and Death	0.018304	5	ACADVL, ACAA2, LOC648603, ACAT2, ACAT1, DCI
00072	Synthesis and degradation of ketone bodies	Lipid Metabolism	0.020758	3	BDH2, ACAT2, ACAT1
00250	Alanine, aspartate and glutamate metabolism	Lipid Metabolism	0.043597	4	GOT1, GLUD2, GLUD1, ASNS
05200	Pathways in cancer	Lipid Metabolism	0.074605	14	CKS1B, MET, SMAD3, ITGA3, FZD4, STAT3, FOS, CDKN1A, LAMA3, SLC2A1, KX3-1, FAS, WNT7A, MYC
04115	p53 signaling pathway	Metabolism of Other Amino Acids	0.095163	5	CDKN1A, TP53I3, SERPINB5, FAS, ADD45A
00471	D-Glutamine and D-glutamate metabolism	Metabolism of Terpenoids and Polyketides	0.098434	2	GLUD2, GLUD1

Additional Table 5. Common crossing significant pathways between the results of GSEA and meta-analysis about prostate cancer tissues.

Pathway entry	Pathway names	Classification	Number of genes expressed in the pathways	Included genes
00010	Glycolysis/ Gluconeogenesis	Metabolism; Lipid Metabolism	6	ADH1A, ADH1B, ADH5, ALDH1B1, ALDH3B2, PGK1
00050	Starch and sucrose metabolism	Metabolism; Amino Acid Metabolism	5	GAA, PYGL, PYGM, UGDH, UGP2
00982	Drug metabolism	Metabolism; Xenobiotics Biodegradation and Metabolism	11	ADH1A, ADH1B, ADH5, ALDH3B2, AOX1, CYP3A4, CYP3A5, FMO5, GSTM3, GSTO1, GSTP1
04010	MAPK signaling pathway	Environmental Information Processing; Signal Transduction	17	CD14, CHUK, DUSP1, DUSP3, FLNA, FLNC, FOS, GRB2, JUND, MEF2C, MYC, NF1, NFKB2, NR4A1, PPP3CC, RRAS2, TGFB3
04510	Focal adhesion	Environmental Information Processing; Signal Transduction	28	BCL2, CAV2, CCND1, CCND2, COL6A1, COL6A2, FLNA, FLNC, FLT1, GRB2, ILK, ITGA5, ITGA7, ITGB3, ITGB4, KDR, LAMA5, MET, MYLK, PAK4, PIK3R3, ROCK2, SHC1, SOS2, TLN1, TNC, TNXA, ZYX
04512	ECM-receptor interaction	Environmental Information Processing; Signaling Molecules and Interaction	12	AGRN, CD44, COL6A1, COL6A2, ITGA5, ITGA7, ITGB3, ITGB4, LAMA4, LAMA5, SDC2, TNC
04530	Tight junction	Environmental Information Processing; Signaling Molecules and Interaction	9	CASK, CLDN3, CLDN4, CLDN5, INADL, MYH9, RKCD, RRAS2, SYMPK
04540	Gap junction	Cellular Processes; Cell Motility	8	CSNK1D, GJA1, GRB2, ITPR1, ITPR2, ITPR3, TUBA4A, TUBB2C
04810	Regulation of actin cytoskeleton	Cellular Processes; Cell Motility	15	BAIAP2, CD14, EZR, IQGAP1, IQGAP2, ITGA5, ITGA7, ITGB3, ITGB4, MYH9, MYLK, PAK4, PIK3R3, ROCK2, RRAS2
04910	Insulin signaling pathway	Organismal Systems; Endocrine System	11	CALM1, FASN, GRB2, IRS1, PDE3B, PIK3R3, PRKAA1, PYGL, PYGM, SHC1, TSC2
05200	Pathways in cancer	Human Diseases; Cancers	19	ABL1, BCL2, CCND1, CDH1, CHUK, CTBP2, DAPK1, FOS, GRB2, GSTP1, JUP, KLK3, LAMA4, LAMA5, MYC, NFKB2, PIK3R3, TGFB3, TRAF4
05211	Renal cell carcinoma	Human Diseases; Cancers	5	GRB2, PAK4, PIK3R3, PTPN11, TGFB3
05214	Glioma	Human Diseases; Cancers	5	CALM1, CCND1, GRB2, PIK3R3, SHC1
05220	Chronic myeloid leukemia	Human Diseases; Cancers	11	ABL1, CCND1, CHUK, CTBP2, GRB2, MYC, PIK3R3, PTPN11, SHC1, SMAD3, TGFB3
05221	Acute myeloid leukemia	Human Diseases; Cancers	6	CCND1, CHUK, GRB2, JUP, MYC, PIK3R3
05222	Small cell lung cancer	Human Diseases; Cancers	9	BCL2, CCND1, CHUK, FHIT, LAMA4, LAMA5, MYC, PIK3R3, TRAF4

Additional Table 6A. Enriched significant pathways obtained from the publically available ONCOMINE cancer gene expression microarray database by GSEA up-regulated pathways.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
00020	Citrate cycle (TCA cycle)	Metabolism; Carbohydrate Metabolism	0.002	17	SdhB; IDH3B; ACLY; ACO2; LOC100130320; sdhD; CS; sdhC; FH; Idh3g; Mdh1; PCK1; IDH1; IDH2; pdhB; SDHA; pdhA2
00030	Pentose phosphate pathway	Metabolism; Carbohydrate Metabolism	0.000	14	GPI; Fbp1; pgm1; PGD; FBP2; pfkp; taldo1; ALDOA; Prps1l1; PRPS1; prps2; H6pd; tkt; Aldob
00190	Oxidative phosphorylation	Metabolism; Energy Metabolism	0.001	77	ATP6V0E1; Atp6v0b; ATP6V1E1; ATP6V0C; COX8A; ATP5B; NDUFA1; NDUFC1; COX6C; Uqcrh; UQCRHL; atp6v1b2; Atp6v0e2; Ndufa2; Atp5d; Atp5j; SDHA; SdhB; NDUFA5; LOC442454; LOC727947; UQCRB; COX5A; ATP5G1; ATP4B; Ndufs8; ATP6V1F; COX6B1; Atp5c1; Ndufb7; atp5h; uqcrfs1; QCRFSL1; Atp6v1a; Ndufv2; NDUFAB1; ATP6AP1; NDUFS6; atp5o; ATP5J2; OC100130320; sdhD; UQCRQ; Cox6a2; NDUFS4; ndufs3; COX4I1; ATP6V1D; COX7A1; Ndufv1; ATP5G2; Ndufa7; sdhC; ATP5G3; ATP6V1G2; Uqcrc1; Cox7a2l; Uqcrc2; COX5B; Cox6a1; Atp5a1; Ndufb5; Atp5i; Ndufb8; cyc1; Ndufs5; LOC100130794; COX7A2; Uqcr11; NDUFB1; ATP6V1G1; ATP4A; Atp12a; ATP6V0A2; Cox7b; cox17; Cox7c
00230	Purine metabolism	Metabolism; Nucleotide Metabolism	0.001	61	GUK1; PDE4C; POLD4; Adcy10; NME4; NME2; NME1-NME2; Nme1; ADCY2; entpd6; PRUNE; Nme6; Pde4a; itpa; POLR2G; POLR2H; POLR2L; Aprt; Prps1l1; PRPS1; papss1; ENTPD2; POLR2J; NT5C2; POLR2F; POLR2B; ATIC; GUCY2F; PRIM2; Pole; rrm2; LOC652797; PKM2; XDH; Pde2a; ADCY1; ada; Pold2; PDE4D; prps2; NPR1; PPAT; NME2; NME1-NME2; Nme1; paics; Pde4b; Polr2c; pold3; pde1b; PKLR; FHIT; GUCY2C; PDE8A; polr2i; GUCY1A3; Impdh2; GUCY1A2; PDE5A; Pde1c; nme3
00240	Pyrimidine metabolism	Metabolism; Nucleotide Metabolism	0.001	33	tk1; POLD4; NME4; entpd6; NME2; NME1-NME2; Nme1; Nme6; LOC100130902; TXNRD1; Pold2; cad; itpa; POLR2G; POLR2H; POLR2L; NME2; NME1-NME2; Nme1; POLR2J; NT5C2; POLR2F; uckl1; POLR2B; Polr2c; pold3; dctD; dut; PRIM2; polr2i; Pole; rrm2; nme3
00270	Cysteine and methionine metabolism	Metabolism; Amino Acid Metabolism	0.000	11	AHCYL1; mat1a; ahcY; Ldhc; LdhA; mat2a; SRM; Got2; ldhb; AMD1; bhmT
00280	Valine, leucine and isoleucine degradation	Metabolism; Amino Acid Metabolism	0.015	18	ALDH2; aldh3a2; hadh; Echs1; MUT; ACADM; hadhb; Aldh6a1; HADHA; ALDH9A1; BCAT2; HMGCS2; pccA; ALDH7A1; AUH; PCCB; Acaa1; ACADSB
00510	N-Glycan biosynthesis	Metabolism; Glycan Biosynthesis and Metabolism	0.001	14	B4GALT1; MAN1A2; DAD1; LOC151162; Mgat5; b4galt2; MAN2A1; Rpn2; RPN1; DDOST; DPM1; ST6GAL1; GANAB; ALG8
00520	Amino sugar and nucleotide sugar metabolism	Metabolism; Carbohydrate Metabolism	0.000	17	HK2P1; Hk2; GPI; UGDH; Renbp; MPI; CHIT1; cyb5r3; TSTA3; UAP1; hexA; gne; pgm1; HK3; UGP2; Pgm3; gck
00600	Sphingolipid metabolism	Metabolism; Lipid Metabolism	0.023	12	Neu1; GBA; sgpl1; sptlc1; PPAP2A; SMPD1; GALC; Ppap2b; UGCG; DEGS1; Sptlc2; ASAH1

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Additional Table 6A. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
00650	Butanoate metabolism	Metabolism; Carbohydrate Metabolism	0.024	14	ALDH5A1; ALDH2; aldh3a2; GAD2; hadh; Echs1; acsm3; ACSM1; ALDH9A1; HMGCS2; HADHA; ALDH7A1; pdhB; pdhA2
00710	Carbon fixation in photosynthetic organisms	Metabolism; Energy Metabolism	0.011	13	TPI1; TPI1P1; FBP2; PGK1; Mdh1; Got2; Fbp1; ALDOA; tkt; ME1; Aldob; LOC652797; PKM2
00970	Aminoacyl-tRNA biosynthesis	Genetic Information Processing; Translation	0.002	11	Nars; KARS; rars; iars2; Gars; farsa; AARS; SARS; eprs; Tars; iars
01061	Biosynthesis of phenylpropanoids	-	0.001	37	LOC100130320; sdhD; pgam1; eno2; HK3; sdhC; pfkp; Mdh1; ALDOA; pdhB; DHA; pdhA2; Aldob; SdhB; GPI; HK2P1; Hk2; ACLY; ACO2; PGK1; CS; Fbp1; Dhfr; Prdx6; LOC100133042; GAPDH; GAPDHL6; FH; FBP2; Got2; eno1; IDH1; taldo1; IDH2; tkt; LOC652797; PKM2
01065	Biosynthesis of alkaloids derived from histidine and purine	-	0.023	41	LOC100130320; sdhD; pgam1; eno2; HK3; sdhC; PGD; BCAT2; pfkp; Mdh1; H6pd; prps2; Prps1l1; PRPS1; ALDOA; pdhB; SDHA; pdhA2; Aldob; SdhB; IDH3B; GPI; HK2P1; Hk2; ACLY; NT5C2; ACO2; PGK1; CS; ATIC; LOC100133042; GAPDH; GAPDHL6; Idh3g; Impdh2; eno1; IDH1; IDH2; ME1; LOC652797; PKM2
01070	Biosynthesis of plant hormones	-	0.008	50	SC5DL; DHCR24; LOC100130320; sdhD; pgam1; eno2; MVD; HK3; sdhC; PGD; FDPS; pfkp; Mdh1; H6pd; prps2; Prps1l1; PRPS1; ALDOA; pdhB; SDHA; pdhA2; Aldob; SdhB; tm7sf2; mat1a; IDH3B; GPI; HK2P1; Hk2; ACLY; ACO2; PGK1; CS; mat2a; IDI1; ATIC; LOC100133042; GAPDH; GAPDHL6; HMGCS2; Idh3g; Got2; IDH1; eno1; taldo1; IDH2; tkt; EBP; LOC652797; PKM2
01100	Metabolic pathways	-	0.001	422	ATP6V0E1; HAAO; GUK1; Pla2g2a; ATP6V1E1; HSD17B2; NFKB1; aldh1a1; Pcyt1a; CYP3A4; POLR2G; GALNS; Aprt; AUH; tyr; TYRL; CHST1; Atp5j; DBH; AHCYL1; HK2P1; Hk2; papss1; POLR2F; MUT; ACO2; ACSL1; IDI1; Fbp1; gpaa1; ATP6V1F; Atp5c1; LOC100133042; GAPDH; GAPDHL6; Idh3g; ckm; QPRT; NOS1; NDUFAB1; aass; rrm2; atp5o; ATP5J2; PNLIPRP1; tk1; ODC1; OCRL; AKR1D1; PPT1; Pafah1b2; Uqcrc1; CYP2E1; dao; PTGES; ids; Sat1; nadK; FASN; Ppap2b; ITPKA; POLD4; NOS2; cd38; ptgds; HPGDS; MTMR1; AGPS; itpa; ALDH3A1; pgm1; rdh11; ST3GAL1; TPI1; TPI1P1; POLR2L; CYP4F2; atp6v1b2; SDHA; ALDH4A1; SdhB; hadh; LOC442454; LOC727947; UQCRB; PGK1; LdhA; ATP5G1; hsd17b4; AKR1B1; COX6B1; ATIC; aoc3; uqcrfs1; UQCRFSL1; PLA2G10; Ndufv2; LOC652797; PKM2; NDUFS6; MTMR6; XDH; Echs1; LOC100130320; sdhD; SRM; ada; ACSM1; cad; Cyp11b2; Aldh6a1; Galntl4; ATP6V1G2; sgpl1; Ptgs1; SCP2; Ndufs5; LOC100130794; Uqcr11; dctD; PIGC; Impdh2; tkt; ALPL; nme3; ALOX12B; DHCR24; ATP6V0C; NME2; NME1-NME2; Nme1; hpd; B3GNT2; b3gnt1; PK1; RPN1; PIGH; POLR2H; B3galt5; NDUFC1; SGSH; Ogt; ddc; PLCG2; dh1c; ADH1B; ADH1A; Aldob; NDUFA5; ALDH1A3; PLA2G1B; NOS3; PLA2G5; HADHA; CYP2C19; GLUL; IDH2; B4GALT1; UQCRQ; agxt;

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Additional Table 6A. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					GALC; ANPEP; MAN2A1; RDH16; PI4KB; ALG8; ldhb; CYP4A11; Sptlc2; ALDH2; Ndufb8; CYP2A7; ALOX12; NDUFB1; DPM1; Asmt; LTA4H; eno1; PCCB; Acaa1; cox17; ACADSB; UGDH; COX8A; ATP5B; LOC100131795; eno2; det; nnmt; NT5C2; uckl1; POLR2B; CYP19A1; dut; Rpn2; atp5h; Atp6v1a; Cyp1a2; EBP; ATP6AP1; MAOA; B3gnt3; UGT2B17; DEGS1; UAP1; ATP6V1D; ATP5G2; Atp5i; grhpr; paics; PKLR; Ptgis; HMGCS2; FH; pccA; taldo1; AKR1A1; GANAB; b3gat2; Alad; ACY1; PPAP2A; acsm3; CYP2C8; ACADM; NME4; st8sia5; Nme6; gne; PGD; PLA2G7; Atp6v0e2; H6pd; alaS2; IDO1; Aanat; PRODH2; OAT; CYP2C18; GAA; FAM164A; Ndufb7; Dhfr; PCK1; Gk2; Pole; eprs; PRODH; FUT3; ahcY; TPO; SC5DL; ALPI; PON3; Aoc2; AMD1; Ndufv1; Dhrs3; PIP4K2B; COX5B; pdhB; PPAT; mthfd2; Ndufb5; FUT5; mat1a; GUSB; ST3GAL2; ACADVL; GBA; Polr2c; COASY; IDH1; DGKZ; Khk; Cox7b; Cox7c; Atp6v0b; ALDH9A1; DDOST; ALAS1; GAD2; sorD; Ndufs8; LOC151162; Mgat5; Mthfr; Prdx6; Ldhc; FBP2; Aldh3b1; Dgkg; GLUD2; ALDH5A1; B4GALNT1; sptlc1; hexA; Hsd3b2; HK3; pfkp; gck; NME2; NME1-NME2; Nme1; PIP5K1A; GPI; INPP4A; AASDHPPT; hadhb; ADH5; ADH5P4; ATP6V1G1; CYP3A7; CKB; cyp2a6; COMT; ATP6V0A2; bhmT; MAN1A2; CYP21A2; HAO1; UGT2B15; pgam1; REV3L; NDUFA1; MVD; CHSY1; COX6C; CYP2C9; pdxK; Adh1c; ADH1B; ADH1A; GNS; Ndufa2; ALDOA; hgd; POLR2J; COX5A; CS; Aceab; Pikfyve; PRIM2; Kynu; Acsl6; Pcyt1b; ME1; DAD1; COX4I1; ndufs3; Ephx2; pigl; Ndufa7; BCAT2; UGT2B7; INPP5A; PLCB2; prps2; Atp5a1; Cox6a1; FUT4; cyc1; MPI; SMPD1; ASAH1; CYP27B1; aldh3a2; Cyp11a1; CDS1; Uqcrh; UQCRHL; Mdh1; cat; Prps1l1; PRPS1; Atp5d; IDH3B; mat2a; Pafah1b1; MAOB; arg2; UGP2; Got2; CYP17A1; Pip5k1b; cyp2a13; agl; ALOX15B; CYP11B1; NDUFS4; Cox6a2; TSTA3; Cps1; Pold2; b4galt2; ACSL3; sdhC; ATP5G3; FDPS; Alppl2; pts; CYP3A5; Uqcrc2; UGCG; ptgds; HPGDS; pdhA2; tm7sf2; ACLY; SC4MOL; CHPF; MGLL; pold3; ALOX15; polr2i; ALDH7A1; ST6GAL1; ABO; ldua; GALNT1; GALNT13; pigo
03010	Ribosome	Genetic Information Processing; Translation	0.000	218	rps20; RPL21P14; rpl21; RPL21P20; RPL21P80; RPL21P119; RPL21P128; RPL21P13; RPL21P105; RPL21P134; RPL21P93; RPL21P125; RPL21P16; RPL21P29; RPL21P28; RPL21P120; RPL21P87; RPL21P39; RPL21P98; RPL21P97; RPL21P69; RPL21P46; RPL21P37; RPL21P45; RPL21P53; RPS10P7; RPS10P11; rps10; RPS10P13; RPS10P4; RPS10P22; RPL18; rpl24; RPL24P6; rpl9; RPL9P25; RPS24; rps13; RPS13P8; RPS13P2; RPL10AP9; RPL10A; RPL10AP6; RPL37; RPS27AP11; RPS27AP12; RPS27A; RPS27AP16; RPS29P11; RPS29; RPS29P9; RPS29P3; RPS29P17; RPS29P16; rpl22; RPL22P11; RPL3; LOC65388l; RPL5P34; rpl5; RPL5P1; Rpl34; RPL38; RPS6P25; RPS6P1; RPS6; RPS7P10; RPS7P4; RPS7P11; rps7; RPL8P2; rpl8; RPLP0P6; RPLP0P2; RPLP0P3; rplP0; SNORA7B; rpl32; Snora7a; RpL30; RPL17P18; RPL17P39; RPL17P7; RPL17P20; LOC729046; RPL17P33;

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Additional Table 6A. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					RPL17P34; RPL17P9; RPL17P22; RpL17; RPL17P36; RPS9P4; rps9; RPL27A; rps12; RPS12P11; RPS12P4; RPS12P9; rps17; RPL12P6; RPL12P32; RPL12P14; rpl12; RPL12P2; RPL12P35; RPL12P19; RPS15AP12; RPS15AP24; RPS15AP11; RPS15AP17; RPS15AP19; RPS15A; rps19; RPS19P3; RPS28P6; RPS28; RPS28P9; rpl28; RPS4Y1; RPL31P17; rpl31; RPL31P49; RPL19P12; rpl19; Fau; rps23; RPL15P18; RPL15P17; RPL15P7; RPL15; RPL15P3; RPL15P22; RPL35P2; RPL35P1; rpl35; RPS8P10; RPS8P8; rps8; rps21; RPL41; RPL37A; Rpl27; RPL23AP65; RPL23AP44; RPL23AP43; RPL23AP63; RPL23AP75; RPL23AP37; Rpl23a; RPS15P5; rps15; rpl11; rplp1; Rps5; rpl23; RPL23P6; RPL7P20; RPL7; RPL7P32; RPL7P24; RPL7P23; RPL7P26; RPL7P16; RPS2P17; rps2; RPS2P55; RPS2P8; RPS2P20; RPS2P11; RPS2P12; RPS2P5; RPS2P51; RPL13; RPL13P12; rpl14; RPS25; RPS25P8; rpl4; RPL4P4; RPL4P5; RPS16P10; RPS16P1; rps16; rps11; RPS11P5; RPL29P11; RPL29P9; RPL29P26; rpl29; RPL29P12; rps3; RPS3P3; RPS27P13; RPS27P19; RPS27P29; RPS27P6; rps27; RPS27P7; RPS27P21; RPS27P9; RPS27P23; RPL6P27; rpl6; RPL6P19; RPL6P10; LOC100130107; RPS3AP5; RPS3AP49; LOC100131699; RPS3AP47; rps3a; RPS18P12; rps18; RPS18P5; RPL36AL; RPS4XP13; rps4x; RPS4XP6
03050	Proteasome	Genetic Information Processing; Folding, Sorting and Degradation	0.001	33	Psmd11; Psme4; PSMB5; psmd3; Psma3; psmd7; PSMB10; psmb7; psmc3; PSMD13; PSMD1; SHFM1; psmc1; LOC643668; PSMD8; PSMB3; PSMA1; Psma4; psmA2; PSMC2; psmc4; LOC652826; PSMD2; PSMD14; PSMD4; PSME2; PSME1; psmb8; psmb2; PSMC5; PSMB4; Psmc6; psmb1
03410	Base excision repair	Genetic Information Processing; Replication and Repair	0.001	13	pcnA; MBD4; lig3; parp1; POLD4; pold3; OGG1; mpg; HMGB1; HMGB1L10; Pole; Pold2; Apex1
04120	Ubiquitin mediated proteolysis	Genetic Information Processing; Folding, Sorting and Degradation	0.000	46	UBE2N; UBR5; LOC730429; FZR1; HUWE1; BIRC3; LOC100132973; TCEB1; UBE2I; mdm2; ANAPC5; Trip12; btrc; ube2d2; WWP1; Tceb2; park2; DDB1; cdc20; UBE2E1; Ube3a; WWP2; Skp2; ppil2; birc2; UBE2D1; Uba1; UBE2J1; vhl; Nedd4l; Cblb; ube2l3; ube4a; UBE2G2; mgrn1; ANAPC13; CDC16; UBE3B; Socs1; PIAS1; UBA2; uba3; SKP1; Fbxw11; Ube2s; SIAH1
04142	Lysosome	Cellular Processes; Transport and Catabolism	0.009	55	Atp6v0b; ATP6V0C; CD164; CTSL1; lamp1; CTSB; SGSH; GALNS; SLC11A1; GNS; Cltb; ACP2; TPP1; Gga2; lipA; CTSZ; GAA; ctsf; ap3s1; CTSH; ATP6AP1; CTSD; fucA1; LGMN; CD63; CTSG; CLTA; GALC; LAPTM5; PLA2G15; PPT1; hexA; Neu1; AP3B2; ABCA2; PSAP; Ap3d1; GUSB; Abcb9; Laptm4b; GBA; LAMP3; AP1S1; SMPD1; ids; Ctsk; ASAH1; Sort1; CTSE; AP1B1; Idua; ATP6V0A2; LAPTM4A; lamp2; gm2a
05010	Alzheimer's disease	Human Diseases; Neurodegenerative Diseases	0.001	104	Cacna1f; NOS2; COX8A; BID; ATP5B; CYCS; IL1B; CAPN1; NDUFA1; Calml3; TNF; Bad; NDUFC1; APOE; LOC100129500; Apaf1; COX6C; Uqcrh; UQCRHL; Ndufa2; CAPN2; Atp5d; Atp5j; SDHA; GRIN2A; SdhB; NDUFA5;

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Additional Table 6A. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					CALM3; CALM2; CALM1; LOC442454; LOC727947; UQCRB; COX5A; ATP5G1; CALM3; CALM2; CALM1; Ndufs8; RYR3; ppp3ca; COX6B1; Atp5c1; Ndufb7; NOS3; atp5h; LOC100133042; GAPDH; GAPDHL6; uqcrfs1; UQCRFSL1; grin2c; APP; Cacna1d; Ndufv2; CASP8; NOS1; NDUFAB1; ADAM10; NDUFS6; atp5o; mapt; LOC100130320; sdhD; UQCRQ; NDUFS4; Cox6a2; ndufs3; COX4I1; ATP2A2; COX7A1; Cdk5r1; ATP5G2; Ndufv1; Ndufa7; sdhC; Fas; chp2; ATP5G3; PLCB2; Uqcrc1; Cox7a2l; Uqcrc2; CACNA1S; COX5B; Cox6a1; Atp5a1; Ndufb5; Ndufb8; cyc1; Ndufs5; LOC100130794; COX7A2; Uqcr11; NDUFB1; LOC100131098; CACNA1C; ITPR1; PPP3CC; Nae1; Psen1; Cox7b; GNAQ; Cox7c
05012	Parkinson's disease	Human Diseases; Neurodegenerative Diseases	0.001	82	COX8A; ATP5B; CYCS; NDUFA1; NDUFC1; Apaf1; park2; COX6C; Uqcrh; UQCRHL; Ndufa2; Atp5d; Atp5j; SDHA; SdhB; NDUFA5; PARK7; LOC442454; LOC727947; UQCRB; COX5A; ATP5G1; Uba1; SLC25A6; UBE2J1; HTRA2; Ndufs8; COX6B1; Atp5c1; Ndufb7; UBE2G2; atp5h; uqcrfs1; UQCRFSL1; slc6a3; Ndufv2; NDUFAB1; NDUFS6; atp5o; LOC100130320; sdhD; UQCRQ; Cox6a2; NDUFS4; ndufs3; COX4I1; SLC25A5; SLC25A5P8; COX7A1; RPS27AP11; RPS27AP12; RPS27A; RPS27AP16; Ndufv1; ATP5G2; vdac2; Ndufa7; sdhC; ATP5G3; Uqcrc1; Cox7a2l; Uqcrc2; COX5B; Cox6a1; Atp5a1; Ndufb5; Ndufb8; cyc1; Ndufs5; LOC100130794; VDAC1P1; VDAC1; COX7A2; Uqcr11; SLC18A1; ube2l3; NDUFB1; SLC18A2; VDAC3; Cox7b; Cox7c; SLC25A4
05016	Huntington's disease	Human Diseases; Neurodegenerative Diseases	0.001	100	COX8A; ATP5B; CYCS; CREB3L2; NDUFA1; NRF1; CREB1; Hap1; POLR2G; NDUFC1; POLR2H; Apaf1; COX6C; Grm5; POLR2L; Uqcrh; UQCRHL; Ndufa2; Atp5d; Atp5j; HDAC2; SDHA; Cltb; SdhB; DNAH3; POLR2J; NDUFA5; POLR2F; tp53; LOC442454; LOC727947; UQCRB; POLR2B; COX5A; ATP5G1; SLC25A6; Ndufs8; COX6B1; Atp5c1; Ndufb7; atp5h; uqcrfs1; UQCRFSL1; DLG4; BAX; Ndufv2; CASP8; NDUFAB1; SOD1; GPX1; NDUFS6; atp5o; CLTA; LOC100130320; sdhD; UQCRQ; NDUFS4; Cox6a2; ndufs3; COX4I1; SLC25A5; SLC25A5P8; COX7A1; AP2S1; ATP5G2; Ndufv1; vdac2; Ndufa7; sdhC; ATP5G3; AP2M1; PLCB2; Uqcrc1; Cox7a2l; Uqcrc2; COX5B; Cox6a1; Atp5a1; Ndufb5; tgm2; Ndufb8; cyc1; Ndufs5; LOC100130794; VDAC1P1; VDAC1; COX7A2; Uqcr11; Polr2c; DCTN2; sp1; NDUFB1; Hdac1; polr2i; ITPR1; VDAC3; Cox7b; GNAQ; Cox7c; SLC25A4
05110	Vibrio cholerae infection	Human Diseases; Infectious Diseases	0.001	30	ATP6V0E1; Atp6v0b; Gnas; muc2; ATP6V0C; ATP6V1E1; ACTG1; ATP6V1D; CFTR; Arf1; ATP6V1G2; SEC61B; Prkca; PLCG2; atp6v1b2; PRKACA; Atp6v0e2; PRKCB; KDELR1; ATP6V1F; KDELR2; PRKCG; ATP6V1G1; Atp6v1a; Pdia4; KCNQ1; ACTB; ATP6V0A2; sec61g; ATP6AP1
05130	Pathogenic *Escherichia coli* infection	Human Diseases; Infectious Diseases	0.010	35	CDH1; YWHAZ; ncl; KRT18P19; KRT18; KRT18P26; cttn; ACTG1; TUBB2C; Rhoa; Prkca; ywhaq; Tubb4; tubb2b; NCK2; ABL1; TUBA4A; CTNNB1; WAS; LOC399942; TUBA1B; Tubb2a; EZR; LOC100129652; Cdc42; CDC42P2; Ocln; LOC647859; WASL; ACTB; MC1R; tubb3; TUBA3E; ARPC5; Itgb1

Additional Table 6B. Down-regulated pathways.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
00052	Galactose metabolism	Metabolism; Carbohydrate Metabolism	0.000	13	B4GALT1; Lct; pgm1; HK2P1; Hk2; HK3; UGP2; pfkp; GAA; LALBA; AKR1B1; gck; b4galt2
00350	Tyrosine metabolism	Metabolism; Amino Acid Metabolism	0.011	29	TPO; Wbscr22; ALDH1A3; MAOA; Aoc2; LOC284889; hpd; dct; MAOB; ADH5; ADH5P4; ech1; ALDH3A1; aoc3; ddc; Aldh3b1; COMT; Got2; tyr; TYRL; Adh1c; ADH1B; ADH1A; Adh1c; ADH1B; ADH1A; LCMT2; DBH; hgd
00562	Inositol phosphate metabolism	Metabolism; Carbohydrate Metabolism	0.008	18	ITPKA; INPP4A; PIK3CD; OCRL; PIK3CG; Pikfyve; ITPK1; Aldh6a1; PIP4K2B; Pik3cb; TPI1; TPI1P1; PI4KB; INPP5A; PLCG2; PLCB2; Pip5k1b; PIP5K1A
00590	Arachidonic acid metabolism	Metabolism; Lipid Metabolism	0.000	29	ALOX12B; ALOX15B; Pla2g2a; CYP2C8; Ephx2; ptgds; HPGDS; CYP4F2; CYP2C9; GPX4; ptgds; HPGDS; CYP4A11; PTGS2; gpX3; GPX2; CYP2E1; PTGES; Ptgs1; CYP2C18; PLA2G1B; ALOX12; ALOX15; Ptgis; PLA2G5; PLA2G10; CYP2C19; LTA4H; GPX1
00591	Linoleic acid metabolism	Metabolism; Lipid Metabolism	0.005	14	CYP2E1; Pla2g2a; CYP2C18; CYP2C8; PLA2G1B; ALOX15; CYP3A4; PLA2G5; PLA2G10; CYP3A7; CYP2C19; CYP2C9; CYP3A5; Cyp1a2
00830	Retinol metabolism	Metabolism; Metabolism of Cofactors and Vitamins	0.001	29	CYP2A7; UGT2B15; CYP2C18; CYP2C8; CYP1A1; UGT2B17; aldh1a1; Dhrs3; ADH5; ADH5P4; CYP3A4; rdh11; RDH16; CYP3A7; Cyp26a1; cyp2a6; UGT2B7; CYP2C19; CYP2C9; CYP3A5; Cyp1a2; Adh1c; ADH1B; ADH1A; Adh1c; ADH1B; ADH1A; cyp2a13; CYP4A11
00980	Metabolism of xenobiotics by cytochrome P450	Metabolism; Xenobiotics Biodegradation and Metabolism	0.000	36	CYP2C8; UGT2B15; GSTM5; UGT2B17; ALDH3A1; CYP3A4; UGT2B7; CYP2C9; GSTO1; CYP3A5; Adh1c; ADH1B; ADH1A; Adh1c; ADH1B; ADH1A; GSTA4; CYP2E1; ALDH1A3; CYP2C18; gsta1; gstA2; CYP1A1; GSTM3; CYP2F1; Mgst3; ADH5; ADH5P4; GSTP1; CYP3A7; Aldh3b1; CYP2C19; GSTT1; Cyp1a2; mgst2; CYP1B1
00982	Drug metabolism - cytochrome P450	Metabolism; Xenobiotics Biodegradation and Metabolism	0.000	40	MAOA; CYP2C8; UGT2B15; GSTM5; UGT2B17; ALDH3A1; CYP3A4; UGT2B7; CYP2C9; GSTO1; CYP3A5; Adh1c; ADH1B; ADH1A; Adh1c; ADH1B; ADH1A; GSTA4; CYP2E1; CYP2A7; ALDH1A3; CYP2C18; gsta1; gstA2; cyp2d6; FMO1; GSTM3; Mgst3; MAOB; ADH5; ADH5P4; GSTP1; CYP3A7; cyp2a6; Aldh3b1; CYP2C19; Cyp1a2; GSTT1; mgst2; cyp2a13
00983	Drug metabolism - other enzymes	Metabolism; Xenobiotics Biodegradation and Metabolism	0.005	17	GUSB; XDH; uckl1; tk1; CYP2A7; UGT2B15; UGT2B17; CES1; itpa; CYP3A4; CYP3A7; cyp2a6; UGT2B7; Impdh2; CYP3A5; tpmT; cyp2a13
03320	PPAR signaling pathway	Organismal Systems; Endocrine System	0.016	32	RPS27AP11; RPS27AP12; RPS27A; RPS27AP16; fabp3; ; ACADM; slc27a2; aqp7; Cpt1b; CHKB; PPARA; ACSL3; ILK; Pltp; FADS2; RXRG; CYP4A11; DBI; APOC3; PLIN1; SCP2; ACSL1; Fabp6; Fabp7; ADIPOQ; HMGCS2; RXRA; PCK1; Gk2; Acsl6; Acaa1; ME1
04010	MAPK signaling pathway	Environmental Information Processing; Signal Transduction	0.001	138	Cacna1f; map2k6; Rap1b; ACVR1B; dusp6; FLNB; Pdgfb; Pla2g2a; Dusp7; PPM1A; NFATC4; IL1B; NFKB1; MAP4K1; DUSP1; mapk8; RASGRF1; PTPN7; FGF5; LOC407835; Map2k2; FLNC; tp53; Tgfbr2; FGF18; MAP3K5;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					PLA2G1B; Map2k5; MYC; ppp3ca; TGFB3; PRKCG; PLA2G5; FGF2; Fgf3; RAF1; mapt; MAPK10; DUSP9; SOS1; ptprr; NFKB2; CRKL; Srf; Stk3; Pdgfrb; Fas; chp2; CACNB4; FOS; Prkca; elk1; MAP3K7; CACNB2; RRAS2; LOC100133211; Gadd45b; KIAA1549; tab2; MAP3K13; Rasgrp2; FGF4; LOC100131098; CACNA1C; PPP3CC; RAPGEF2; LOC100133567; CACNG1; NR4A1; DUSP3; FGF8; FGF9; rac1; STMN1; relA; Gadd45g; FASLG; GADD45A; dusp5; TNF; Pak2; TAOK3; NF1; akt1; FLNA; PRKACA; rasgrp3; MAPKAPK2; RPS6KA2; LOC100127984; Kras; CACNA1E; Jun; MAP3K4; PLA2G10; Cacna1d; CACNG3; Il1r1; HSPA8; Mapk8ip2; CACNA1G; FGFR2; MEF2C; ATF4; ATF4C; pdgfra; mapkapk3; JUND; tgfbr1; Hspa1l; NTRK1; Mapk14; Mapk11; CACNB1; Fgfr1; CACNA1S; PRKCB; MAX; ELK4; akt2; TGFB1; Rras; HSPA1A; HSPA1B; fgf12; Cdc42; CDC42P2; MKNK2; ikbkg; Gna12; Cacna2d1; Hspb1; HSPBL2; NTRK2; SOS2; Fgf7; LOC100132771; FGF7P2
04012	ErbB signaling pathway	Environmental Information Processing; Signal Transduction	0.015	47	CAMK2G; MAPK10; gab1; TGFA; Pak3; PIK3CD; SOS1; PIK3CG; CRKL; PIK3R3; Pak2; Bad; Prkca; akt1; SHC1; PLCG2; elk1; mapk8; Erbb3; PRKCB; LOC407835; Map2k2; Nrg2; NCK2; ABL1; RPS6KB1; akt2; KIAA1549; Camk2a; Camk2b; Erbb4; Kras; CDKN1A; Cblb; Stat5b; MYC; CDKN1B; Jun; PRKCG; SHC2; Pik3cb; SHC3; PIK3R2; SOS2; RAF1; NRG1; Erbb2
04020	Calcium signaling pathway	Environmental Information	0.013	98	CAMK2G; Cacna1f; SLC8A2; Tacr1; ITPKA; BDKRB2; P2RX1; NOS2; HTR4; cd38; ADCY2; Agtr1; HTR6; P2RX6; Calml3; HTR7; LHCGR; ADRA1A; HTR2A; PLCG2; Grm5; MYLK; PRKACA; camk4; GRIN2A; CALM3; CALM2; CALM1; EDNRA; atp2b4; CALM3; CALM2; CALM1; SLC25A6; Trpc1; Erbb4; CCKAR; RYR3; ppp3ca; NOS3; CACNA1E; P2rx5; PRKCG; ATP2B2; grin2c; gnal; Cacna1d; GRM1; CCKBR; AVPR1B; NOS1; SLC8A1; grpr; CACNA1G; Gnas; ADCY1; Atp2b3; DRD5; SLC25A5; SLC25A5P8; pdgfra; ATP2A2; tbxa2r; PTGER3; Ntsr1; P2RX4; vdac2; Pdgfrb; chp2; PTAFR; Prkca; Erbb3; PLCB2; CACNA1S; PRKCB; TACR3; Adrb3; VDAC1P1; VDAC1; Camk2a; ATP2B1; Camk2b; ADRA1D; pde1b; LOC100131098; CACNA1C; PPP3CC; ITPR1; Phkb; VDAC3; CHRM3; adra1b; ADRB2; GNA11; GNAQ; Pde1c; Erbb2; SLC25A4
04060	Cytokine-cytokine receptor interaction	Environmental Information Processing; Signaling Molecules and Interaction	0.022	119	csf1; IFNA6; ACVR1B; eda; Pdgfb; IL10RA; IL1B; CCL14; CCL15; Tnfsf11; IL18RAP; LEP; CSF3; CXCR6; CCR2; Tgfbr2; CXCR3; TNFSF9; CSF2RB; CCL4L1; CCL4L2; CXCL1; TGFB3; LEPR; TNFRSF25; csf3r; CCR7; CCL3; Il5; TPO; ccl1; Cxcl3; il10; CCL22; ZFP91; CNTF; Zfp91-Cntf; Ccl2; PRLR; Tnfrsf4; INHBC; Pdgfrb; Fas; CD40LG; il2rg; IL8; Hgf; lta; Il5ra; FLT1; Il24; Ifna14; CCR1; IFNW1; TNFSF4; IFNA4; IL13; CXCL5; Il3; Vegfb; CXCL2; XCL2; LTBR; CXCR2; CD27; FLT3; Inhbb; LOC652799; LOC653882; KIT; IL9R; EPOR; IFNGR2; FASLG; IL4; OSMR; TNF; IL6ST; CXCL12;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					Il18r1; IFNA21; CCR9; INHBA; Ifna10; Ccl27; TNFRSF21; GDF5; IFNA5; IL17A; Cd70; CXCR5; Il1r1; gh2; il1rap; IFNGR1; ccr4; TNFSF10; TNFRSF8; IL7R; CCL5; pdgfra; IL6; CCL23; Cxcr1; ctf1; tgfbr1; Tnfrsf11a; MET; CXCR4; Il10rb; EPO; TGFB1; IL23A; CCL16; VEGFA; CCL13; ifna2; TNFRSF10C; TNFRSF17
04062	Chemokine signaling pathway	Organismal Systems; Immune System	0.020	83	JAK3; rac1; Rap1b; relA; foxo3b; FOXO3; PRKCD; Pard3; ADCY2; PIK3CG; NFKB1; CCL14; CCL15; Rhoa; akt1; SHC1; CXCL12; ADRBK1; PRKACA; CXCR6; CCR2; CCR9; Ccl27; CXCR3; WAS; Kras; CCL4L1; CCL4L2; CXCL1; gng5; SHC2; tiam1; CXCR5; Pik3cb; SHC3; PXN; gnb2; GNB1; CCR7; RAF1; LOC100128155; CCL3; DOCK2; NFKBIA; ccr4; ccl1; Cxcl3; ADCY1; CCL5; SOS1; PIK3CD; Cxcr1; CCL23; CCL22; CRKL; Ccl2; STAT1; PIK3R3; IL8; gng7; PLCB2; PRKCB; CXCR4; akt2; STAT2; KIAA1549; CCR1; Stat5b; CXCL5; CCL16; Stat3; CCL13; Cdc42; CDC42P2; Rasgrp2; CXCL2; ikbkg; XCL2; WASL; PIK3R2; CXCR2; gnb3; SOS2
04070	Phosphatidylinositol signaling system	Environmental Information Processing; Signal Transduction	0.000	31	ITPKA; PIK3CD; PIK3CG; OCRL; CDS1; Calml3; PIK3R3; ITPK1; PIP4K2B; Prkca; PI4KB; PLCG2; INPP5A; PLCB2; PRKCB; PIP5K1A; CALM3; CALM2; CALM1; CALM3; CALM2; CALM1; INPP4A; Pikfyve; PRKCG; Pik3cb; ITPR1; PIK3R2; DGKZ; Pip5k1b; Dgkg
04115	p53 signaling pathway	Cellular Processes; Cell Growth and Death	0.006	34	Gadd45g; EI24; GADD45A; BID; CCND1; CYCS; mdm2; MDM4; Fas; Apaf1; Thbs1; LOC651610; ATM; SERPINB5; LOC648152; LOC651921; ATR; CCNB2; Cdk6; Gadd45b; GTSE1; tp53; CCND2; igfbp3; CDKN1A; TSC2; CCNG2; BAX; SERPINE1; Igf1; CASP8; SFN; rrm2; SIAH1
04140	Regulation of autophagy	Cellular Processes; Transport and Catabolism	0.014	13	Ifna14; BECN1; Ifna10; IFNA6; GABARAP; ifna2; GABARAPL2; IFNA4; IFNA21; GABARAPL3; GABARAPL1; IFNA5; Ulk2
04150	mTOR signaling pathway	Environmental Information Processing; Signal Transduction	0.002	24	RPS6KB1; HIF1A; RPS6P25; RPS6P1; RPS6; akt2; KIAA1549; ddit4; EIF4B; EIF4BP7; PIK3CD; RPS6KA2; LOC100127984; PIK3CG; TSC2; VEGFA; Vegfb; PIK3R3; rheb; Pik3cb; akt1; Igf1; PIK3R2; Ulk2
04270	Vascular smooth muscle contraction	Organismal Systems; Circulatory System	0.000	63	Cacna1f; PRKCD; Pla2g2a; prkcq; ADCY2; Agtr1; Calml3; ARHGEF12; ADRA1A; Rhoa; MYLK; PRKACA; LOC407835; Map2k2; Gna13; CALM3; CALM2; CALM1; EDNRA; CALM3; CALM2; CALM1; PLA2G1B; PTGIR; PRKCG; PLA2G5; PLA2G10; PPP1R12B; RAMP1; Cacna1d; AVPR1B; RAF1; MYH11; ADCY1; Gnas; Ppp1cc; PPP1R12A; MYL6B; Ppp1ca; Prkca; Prkce; acta2; PLCB2; CACNA1S; NPR1; CYP4A11; PRKCB; KIAA1549; ADRA1D; ARHGEF11; Actg2; CALD1; LOC100131098; CACNA1C; Gna12; ITPR1; GUCY1A3; adra1b; GNA11; GUCY1A2; GNAQ; KCNMA1; MYL9
04310	Wnt signaling pathway	Environmental Information	0.000	59	CAMK2G; rac1; csnk1a1; CCND1; NFATC4; btrc; SFRP4; Rhoa; Ctbp1;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					Il18r1; IFNA21; CCR9; INHBA; Ifna10; Ccl27; TNFRSF21; GDF5; IFNA5; IL17A; Cd70; CXCR5; Il1r1; gh2; il1rap; IFNGR1; ccr4; TNFSF10; TNFRSF8; IL7R; CCL5; pdgfra; IL6; CCL23; Cxcr1; ctf1; tgfbr1; Tnfrsf11a; MET; CXCR4; Il10rb; EPO; TGFB1; IL23A; CCL16; VEGFA; CCL13; ifna2; TNFRSF10C; TNFRSF17
04062	Chemokine signaling pathway	Organismal Systems; Immune System	0.020	83	JAK3; rac1; Rap1b; relA; foxo3b; FOXO3; PRKCD; Pard3; ADCY2; PIK3CG; NFKB1; CCL14; CCL15; Rhoa; akt1; SHC1; CXCL12; ADRBK1; PRKACA; CXCR6; CCR2; CCR9; Ccl27; CXCR3; WAS; Kras; CCL4L1; CCL4L2; CXCL1; gng5; SHC2; tiam1; CXCR5; Pik3cb; SHC3; PXN; gnb2; GNB1; CCR7; RAF1; LOC100128155; CCL3; DOCK2; NFKBIA; ccr4; ccl1; Cxcl3; ADCY1; CCL5; SOS1; PIK3CD; Cxcr1; CCL23; CCL22; CRKL; Ccl2; STAT1; PIK3R3; IL8; gng7; PLCB2; PRKCB; CXCR4; akt2; STAT2; KIAA1549; CCR1; Stat5b; CXCL5; CCL16; Stat3; CCL13; Cdc42; CDC42P2; Rasgrp2; CXCL2; ikbkg; XCL2; WASL; PIK3R2; CXCR2; gnb3; SOS2
04070	Phosphatidylinositol signaling system	Environmental Information Processing; Signal Transduction	0.000	31	ITPKA; PIK3CD; PIK3CG; OCRL; CDS1; Calml3; PIK3R3; ITPK1; PIP4K2B; Prkca; PI4KB; PLCG2; INPP5A; PLCB2; PRKCB; PIP5K1A; CALM3; CALM2; CALM1; CALM3; CALM2; CALM1; INPP4A; Pikfyve; PRKCG; Pik3cb; ITPR1; PIK3R2; DGKZ; Pip5k1b; Dgkg
04115	p53 signaling pathway	Cellular Processes; Cell Growth and Death	0.006	34	Gadd45g; EI24; GADD45A; BID; CCND1; CYCS; mdm2; MDM4; Fas; Apaf1; Thbs1; LOC651610; ATM; SERPINB5; LOC648152; LOC651921; ATR; CCNB2; Cdk6; Gadd45b; GTSE1; tp53; CCND2; igfbp3; CDKN1A; TSC2; CCNG2; BAX; SERPINE1; Igf1; CASP8; SFN; rrm2; SIAH1
04140	Regulation of autophagy	Cellular Processes; Transport and Catabolism	0.014	13	Ifna14; BECN1; Ifna10; IFNA6; GABARAP; ifna2; GABARAPL2; IFNA4; IFNA21; GABARAPL3; GABARAPL1; IFNA5; Ulk2
04150	mTOR signaling pathway	Environmental Information Processing; Signal Transduction	0.002	24	RPS6KB1; HIF1A; RPS6P25; RPS6P1; RPS6; akt2; KIAA1549; ddit4; EIF4B; EIF4BP7; PIK3CD; RPS6KA2; LOC100127984; PIK3CG; TSC2; VEGFA; Vegfb; PIK3R3; rheb; Pik3cb; akt1; Igf1; PIK3R2; Ulk2
04270	Vascular smooth muscle contraction	Organismal Systems; Circulatory System	0.000	63	Cacna1f; PRKCD; Pla2g2a; prkcq; ADCY2; Agtr1; Calml3; ARHGEF12; ADRA1A; Rhoa; MYLK; PRKACA; LOC407835; Map2k2; Gna13; CALM3; CALM2; CALM1; EDNRA; CALM3; CALM2; CALM1; PLA2G1B; PTGIR; PRKCG; PLA2G5; PLA2G10; PPP1R12B; RAMP1; Cacna1d; AVPR1B; RAF1; MYH11; ADCY1; Gnas; Ppp1cc; PPP1R12A; MYL6B; Ppp1ca; Prkca; Prkce; acta2; PLCB2; CACNA1S; NPR1; CYP4A11; PRKCB; KIAA1549; ADRA1D; ARHGEF11; Actg2; CALD1; LOC100131098; CACNA1C; Gna12; ITPR1; GUCY1A3; adra1b; GNA11; GUCY1A2; GNAQ; KCNMA1; MYL9

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
04310	Wnt signaling pathway	Environmental Information Processing; Signal Transduction	0.000	59	CAMK2G; rac1; csnk1a1; CCND1; NFATC4; btrc; SFRP4; Rhoa; Ctbp1; DAAM1; mapk8; Lef1; WNT2B; PRKACA; CTBP2; PPP2CB; PPP2R1A; tp53; APC2; nfatc1; CTNNB1; NFAT5; Nfatc3; LY6G5B; CSNK2B; Chd8; wnt2; ppp3ca; MYC; Jun; PRKCG; WNT11; Sfrp1; SKP1; wnt8b; Fbxw11; tbl1x; SIAH1; CSNK1E; MAPK10; FZD7; smad4; chp2; FOSL1; Prkca; MAP3K7; PLCB2; PPP2R5C; PRKCB; CCND2; Camk2a; Camk2b; PPP2CA; ppp2r1b; wnt10b; mmp7; SMAD3; PPP3CC; Psen1
04340	Hedgehog signaling pathway	Environmental Information Processing; Signal Transduction	0.001	17	CSNK1E; csnk1a1; BMP6; wnt2; wnt10b; btrc; IHH; BMP5; ZIC2; Gli3; WNT11; CSNK1D; WNT2B; Fbxw11; wnt8b; PRKACA; Smo
04350	TGF-beta signaling pathway	Environmental Information Processing; Signal Transduction	0.000	36	Inhbb; ACVR1B; thbs4; BMP6; TNF; tgfbr1; smad4; INHBC; Thbs1; Rhoa; e2f4; id1; Rbl1; LEFTY2; Id3; RPS6KB1; Ltbp1; INHBA; PPP2CB; PPP2R1A; Tgfbr2; TGFB1; GDF5; sp1; ppp2r1b; PPP2CA; LEFTY1; MYC; TGFB3; BMP5; RBL2; SMAD3; SKP1; E2f5; pitx2; SMAD9
04360	Axon guidance	Organismal Systems; Development	0.001	51	rac1; ephb1; NFATC4; SEMA4D; Pak2; ARHGEF12; efna2; Dpysl2; PLXNB3; Rhoa; EFNA5; CXCL12; EFNB2; sema3f; SEMA3C; ABL1; nfatc1; NFAT5; Nfatc3; Slit2; Kras; ppp3ca; EFNA1; EPHB6; RND1; efnb1; Ntng1; Itgb1; slit1; Pak3; EFNA3; SEMA7A; Efnb3; chp2; MET; EPHA4; L1cam; EPHA2; CXCR4; NCK2; Unc5b; CFL1; SEMA4F; Epha5; ephb2; Cdc42; CDC42P2; SEMA5A; PPP3CC; plxnb2; UNC5C
04370	VEGF signaling pathway	Environmental Information Processing; Signal Transduction	0.012	41	rac1; Pla2g2a; PIK3CD; PIK3CG; mapkapk3; NFATC4; PIK3R3; Bad; chp2; Mapk14; Mapk11; Prkca; akt1; PLCG2; LOC407835; Map2k2; PRKCB; PTGS2; MAPKAPK2; akt2; nfatc1; NFAT5; Nfatc3; Kras; PLA2G1B; ppp3ca; VEGFA; NOS3; Cdc42; CDC42P2; PRKCG; SHC2; PLA2G5; PLA2G10; Pik3cb; PPP3CC; Hspb1; HSPBL2; PXN; PIK3R2; RAF1
04510	Focal adhesion	Cellular Processes; Cell Communication	0.000	114	Col6a3; Rap1b; FLNB; ITGA5; itga6; Pdgfb; Chad; CCND1; PIK3CG; myl2; ACTG1; BCL2; Rhoa; SHC1; mapk8; RASGRF1; vwf; FLNC; birc2; CTNNB1; MYL12A; MYL12B; COL11A1; LAMA1; PRKCG; SHC2; SHC3; cav1; Igf1; COL6A2; LAMC2; COL1A1; RAF1; Lama2; ZYX; LOC100128155; IBSP; Itgb1; Itgb5; MAPK10; BIRC3; thbs4; Pak3; SOS1; PIK3CD; PPP1R12A; Col4a6; CRKL; TLN1; LAMA4; PIK3R3; Pdgfrb; Ppp1ca; ITGB3; Thbs1; Prkca; Hgf; elk1; FLT1; ITGA9; IGF1R; lamb2; KIAA1549; Col11a2; Vegfb; LAMB1; actn4; vcl; COL6A1; ITGA10; CAV3; rac1; SPP1; Pak2; Bad; FLNA; akt1; MYLK; actn1; CAPN2; LAMC1; COL3A1; vtn; Jun; Pik3cb; LAMA5; ACTB; PXN; itga2b; pdgfra; Ppp1cc; MET; ILK; ITGA7; fn1; TNN; PRKCB; Itgav; GRLF1; TLN2; akt2; CCND2; VEGFA; COL1A2; Cdc42; CDC42P2; ITGA3; TNC; col4a2; Col4a1; PIK3R2; SOS2; Erbb2; MYL9

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
04512	ECM-receptor interaction	Environmental Information Processing; Signaling Molecules and Interaction	0.000	54	Col6a3; ITGA10; ITGA5; sdc3; itga6; Chad; DAG1; SPP1; GP5; vwf; CD47; LAMC1; COL3A1; CD44; vtn; Hspg2; COL11A1; LAMA1; Sdc4; LAMA5; COL6A2; LAMC2; COL1A1; Lama2; Itgb1; GP9; IBSP; HMMR; Itgb5; sdc1; Gp1ba; thbs4; itga2b; Col4a6; LAMA4; GP1BB; ITGB3; Thbs1; ITGA7; fn1; TNN; ITGA9; Itgav; lamb2; Col11a2; SV2B; SV2A; COL1A2; ITGA3; TNC; LAMB1; col4a2; Col4a1; COL6A1
04540	Gap junction	Cellular Processes; Cell Communication	0.003	39	Gnas; ADCY1; Pdgfb; pdgfra; SOS1; ADCY2; TUBB2C; GJA1; DRD2; Pdgfrb; HTR2A; Prkca; Grm5; PLCB2; PRKACA; Tubb4; tubb2b; PRKCB; LOC407835; Map2k2; TUBA4A; LOC399942; TUBA1B; Kras; Tubb2a; Map2k5; PRKCG; ITPR1; GUCY1A3; GRM1; CSNK1D; MC1R; tubb3; SOS2; GNA11; RAF1; GUCY1A2; GNAQ; TUBA3E
04610	Complement and coagulation cascades	Organismal Systems; Immune System	0.000	31	fgb; BDKRB2; SERPING1; kng1; C4BPA; C8G; PLAUR; CFH; C1s; Cd46; FGA; TFPI; vwf; C6; proC; F3; serpind1; CD59; cfd; masp2; plg; F12; C1QB; F7; SERPINE1; CPB2; C1r; F2; C7; C9; CR1
04620	Toll-like receptor signaling pathway	Organismal Systems; Immune System	0.023	49	NFKBIA; TRAF3; map2k6; rac1; MAPK10; lbp; relA; IFNA6; CCL5; IKBKE; PIK3CD; IL6; PIK3CG; NFKB1; IL1B; SPP1; STAT1; TNF; PIK3R3; TLR6; IL8; Mapk14; Mapk11; Irak1; akt1; FOS; mapk8; MAP3K7; IFNA21; IRF5; LOC407835; Map2k2; Ifna14; Ifna10; akt2; CCL4L1; CCL4L2; tab2; IFNA4; IFNA5; CD80; Jun; RIPK1; ikbkg; Pik3cb; ifna2; PIK3R2; CASP8; CCL3
04622	RIG-I-like receptor signaling pathway	Organismal Systems; Immune System	0.009	29	NFKBIA; TRAF3; MAPK10; IFNA6; relA; DDX3Y; IKBKE; NFKB1; TNF; IL8; Mapk14; Mapk11; TRIM25; mapk8; MAP3K7; PIN1; IFNA21; SIKE1; Ifna14; Ifna10; IFNW1; IFNA4; casp10; IFNA5; RIPK1; ikbkg; ifna2; CASP8; DDX3X
04630	Jak-STAT signaling pathway	Environmental Information Processing; Signal Transduction	0.012	67	JAK3; JAK1; IL9R; IFNA6; EPOR; IFNGR2; IL10RA; OSMR; CCND1; IL4; PIK3CG; socs2; IL6ST; akt1; CSF3; LEP; IFNA21; Ifna10; CSF2RB; Cblb; IFNA5; MYC; LEPR; Socs1; Pik3cb; STAT4; PIAS1; csf3r; gh2; IFNGR1; Il5; TPO; il10; IL7R; SOS1; IL6; PIK3CD; ZFP91; CNTF; Zfp91-Cntf; STAT1; ctf1; PRLR; PIK3R3; il2rg; Il5ra; Il10rb; Ifna14; Il24; akt2; CCND2; STAT2; EPO; IFNW1; IFNA4; Stat5b; IL13; Il3; IL23A; Stat3; LOC344593; LOC442113; PTPN11; STAT6; ifna2; PIK3R2; SOS2
04640	Hematopoietic cell lineage	Organismal Systems; Immune System	0.018	53	csf1; HLA-DRA; IL9R; LOC652799; LOC653882; KIT; ITGA5; EPOR; itga6; CD33; IL4; cd38; IL1B; TNF; GP5; Gypa; CSF3; CD9; Cd19; CD44; CD59; TFRC; CD5; CD3E; CD4; csf3r; CD1C; Il1r1; CD22; GP9; Il5; TPO; IL7R; Gp1ba; itga2b; IL6; Cd2; ANPEP; CD8B; GP1BB; ITGAM; ITGB3; CD1A; FCER2; Il5ra; CD1D; CD34; EPO; Il3; ITGA3; MS4A1; CR1; FLT3
04650	Natural killer cell mediated cytotoxicity	Organismal Systems; Immune System	0.016	64	SYK; KIR2DL4; rac1; IFNA6; IFNGR2; FASLG; LCK; BID; PIK3CG; NFATC4; TNF; SHC1; Ncr1; PLCG2; Prf1; IFNA21; LOC407835; Map2k2;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					HLA-G; Ifna10; nfatc1; Nfatc3; NFAT5; Kras; ppp3ca; IFNA5; Sh3bp2; PRKCG; SHC2; HLA-A; Pik3cb; SHC3; NCR3; RAF1; micB; LOC100128155; IFNGR1; TNFSF10; KLRK1; SOS1; PIK3CD; PIK3R3; Fas; FCGR3B; chp2; Prkca; TYROBP; PRKCB; Ifna14; Cd247; ICAM1; KIAA1549; IFNA4; HLA-E; LOC344593; LOC442113; PTPN11; PPP3CC; ifna2; PIK3R2; SOS2; KIR3DS1; Kir3dl1; TNFRSF10C
04660	T cell receptor signaling pathway	Organismal Systems; Immune System	0.020	56	relA; LCK; IL4; prkcq; PIK3CG; NFATC4; NFKB1; TNF; Pak2; Rhoa; akt1; LOC407835; Map2k2; nfatc1; NFAT5; Nfatc3; Cblb; Kras; ppp3ca; GRAP2; CD3E; Pdcd1; Jun; CD4; Pik3cb; RAF1; LOC100128155; NFKBIA; Il5; il10; Pak3; PIK3CD; SOS1; PIK3R3; CD8B; CD40LG; chp2; Mapk14; Mapk11; FOS; TEC; MAP3K7; MALT1; NCK2; Cd247; akt2; Cdc42; CDC42P2; Ptprc; ikbkg; PPP3CC; BCL10; LOC646626; PIK3R2; SOS2; PDK1
04662	B cell receptor signaling pathway	Organismal Systems; Immune System	0.011	45	NFKBIA; SYK; rac1; relA; PIK3CD; SOS1; PIK3CG; NFATC4; NFKB1; Cd79a; PIK3R3; chp2; FOS; akt1; PLCG2; rasgrp3; MALT1; PRKCB; LOC407835; Map2k2; Cd19; akt2; Cd79b; nfatc1; NFAT5; Nfatc3; btk; Kras; ppp3ca; Fcgr2b; FCGR2C; Jun; CD72; ikbkg; Ifitm1; Pik3cb; PPP3CC; CD81; BCL10; LOC646626; PIK3R2; SOS2; CD22; RAF1; LOC100128155
04664	Fc epsilon RI signaling pathway	Organismal Systems; Immune System	0.009	37	SYK; Il5; rac1; map2k6; MAPK10; PRKCD; Pla2g2a; IL4; PIK3CD; SOS1; PIK3CG; TNF; PIK3R3; Mapk14; Mapk11; Prkca; akt1; PLCG2; Prkce; mapk8; PRKCB; LOC407835; Map2k2; akt2; btk; Kras; PLA2G1B; IL13; Il3; PLA2G5; PLA2G10; Pik3cb; PIK3R2; SOS2; RAF1; PDK1; LOC100128155
04666	Fc gamma R-mediated phagocytosis	Organismal Systems; Immune System	0.003	43	SYK; rac1; PRKCD; PPAP2A; PIK3CD; PIK3CG; CRKL; Gsn; PIK3R3; ampH; PIP4K2B; MARCKSL1; Prkca; akt1; PLCG2; Prkce; MARCKS; PRKCB; PIP5K1A; RPS6KB1; akt2; arpc2; WAS; DNM3; CFL1; Wasf2; Fcgr2b; FCGR2C; Cdc42; CDC42P2; Ptprc; Pikfyve; PRKCG; WASL; Pik3cb; FCGR2A; PIK3R2; RAF1; Ppap2b; Pip5k1b; ARPC5; LOC100128155; DOCK2
04670	Leukocyte transendothelial migration	Organismal Systems; Immune System	0.009	61	Rap1b; rac1; Ncf4; PIK3CG; ACTG1; myl2; TXK; CLDN3; Rhoa; PLCG2; Ctnna1; CXCL12; CTNND1; actn1; Mmp2; CLDN4; PECAM1; CTNNB1; cldn18; NOX1; MYL12A; MYL12B; EZR; LOC100129652; PRKCG; Ocln; LOC647859; Pik3cb; Cldn8; PXN; ACTB; Rapgef3; LOC100128155; Itgb1; CLDN10; cldn7; CLDN9; CYBB; PIK3CD; PIK3R3; Mapk14; msn; ITGAM; Mapk11; Prkca; CXCR4; PRKCB; GRLF1; Jam3; ICAM1; Cdc42; CDC42P2; Ctnna2; LOC344593; LOC442113; PTPN11; actn4; PIK3R2; vcl; MYL9; CD99
04720	Long-term potentiation	Organismal Systems; Nervous System	0.001	43	CAMK2G; Rap1b; ADCY1; ATF4; ATF4C; Ppp1cc; PPP1R12A; Calml3; chp2; Ppp1ca; Prkca; Grm5; PLCB2; PRKACA; PRKCB; LOC407835; Map2k2; camk4; GRIN2A; CALM3; CALM2; CALM1; KIAA1549; Camk2a; CALM3; CALM2; CALM1; Camk2b; Kras; RPS6KA2; LOC100127984; ppp3ca;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					PRKCG; LOC100131098; CACNA1C; grin2c; ITPR1; PPP3CC; GRIA1; GRM1; RAF1; Rapgef3; GNAQ
04722	Neurotrophin signaling pathway	Organismal Systems; Nervous System	0.019	80	CAMK2G; Rap1b; rac1; relA; gab1; foxo3b; FOXO3; MAGED1; PRKCD; FASLG; irs2; PIK3CG; NFKB1; YWHAH; Calml3; Bad; BCL2; Rhoa; akt1; SHC1; PLCG2; mapk8; ywhaq; LOC407835; Map2k2; camk4; ABL1; MAPKAPK2; tp53; CALM3; CALM2; CALM1; MAP3K5; CALM3; CALM2; CALM1; ARHGDIA; Kras; RPS6KA2; LOC100127984; Map2k5; Jun; SHC2; Pik3cb; BAX; SHC3; RAF1; KIDINS220; NFKBIA; YWHAZ; MAPK10; ATF4; ATF4C; SOS1; PIK3CD; CRKL; NTRK3; PIK3R3; YWHAB; NTRK1; Mapk14; Mapk11; Irak1; akt2; Camk2a; KIAA1549; Camk2b; LOC440917; YWHAE; Cdc42; CDC42P2; LOC344593; LOC442113; PTPN11; Sort1; Psen1; NTRK2; PIK3R2; SOS2; PDK1
04730	Long-term depression	Organismal Systems; Nervous System	0.003	36	Gnas; Pla2g2a; CRHR1; NOS2; Prkca; Grm5; PLCB2; Gria3; PRKCB; Gna13; LOC407835; Map2k2; IGF1R; PPP2CB; PPP2R1A; KIAA1549; Kras; PLA2G1B; ppp2r1b; PPP2CA; NOS3; PRKCG; PLA2G5; Gna12; PLA2G10; ITPR1; GRIA1; Igf1; GUCY1A3; GRM1; GNAZ; GNA11; RAF1; NOS1; GUCY1A2; GNAQ
04740	Olfactory transduction	Organismal Systems; Sensory System	0.025	26	CAMK2G; OR2J2; OR1E1; CALM3; CALM2; CALM1; GUCA1A; OR7E24; Camk2a; OR2F2; CALM3; CALM2; CALM1; Camk2b; CNGB1; OR2H2; Calml3; OR2B6; OR10H3; OR7A5; GUCA1B; gnal; OR5I1; OR2H1; PRKACA; Pde1c
04810	Regulation of actin cytoskeleton	Cellular Processes; Cell Motility	0.000	105	pfn2; IQGAP2; ITGA5; itga6; BDKRB2; Pdgfb; PIK3CG; ACTG1; myl2; Rhoa; NCKAP1; FGF5; LOC407835; Map2k2; APC2; Arhgef7; WAS; FGF18; MYL12A; MYL12B; EZR; LOC100129652; Pikfyve; FGF2; tiam1; Fgf3; RAF1; Itgb1; LOC100128155; Itgb5; Pak3; PIK3CD; SOS1; PPP1R12A; CRKL; PIK3R3; ITGAD; Pdgfrb; PIP4K2B; Ppp1ca; msn; ITGAM; ITGB3; RRAS2; LOC100133211; ITGA9; KIAA1549; CFL1; MYH9; FGF4; WASL; F2; actn4; vcl; FGF8; rdx; FGF9; pfn1; ITGA10; rac1; Gsn; ARHGEF12; Pak2; ABI2; MYLK; actn1; Gna13; CYFIP1; arpc2; fgd1; Kras; Pik3cb; PXN; ACTB; Pip5k1b; ARPC5; FGFR2; itga2b; pdgfra; Ppp1cc; Fgfr1; ITGA7; fn1; PIP5K1A; Itgav; GRLF1; IQGAP1; Ras; Wasf2; ITGA3; Cdc42; CDC42P2; fgf12; Gna12; TMSL1; TMSB4X; TMSL2; CHRM3; PIK3R2; myh10; SOS2; Fgf7; LOC100132771; FGF7P2; MYL9
04912	GnRH signaling pathway	Organismal Systems; Endocrine System	0.003	53	CAMK2G; Cacna1f; map2k6; MAPK10; cga; ADCY1; Gnas; PRKCD; Pla2g2a; ATF4; ATF4C; SOS1; ADCY2; Calml3; Mapk14; Mapk11; Prkca; elk1; mapk8; MMP14; PLCB2; PRKACA; CACNA1S; PRKCB; LOC407835; Map2k2; Mmp2; CALM3; CALM2; CALM1; Camk2a; CALM3; CALM2; CALM1; Camk2b; Kras; PLA2G1B; Cdc42; CDC42P2; Jun; MAP3K4; LOC100131098;

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
					CACNA1C; PLA2G5; PLA2G10; ITPR1; Cacna1d; FSHB; SOS2; RAF1; GNA11; GNRH2; GNAQ
04916	Melanogenesis	Organismal Systems; Endocrine System	0.000	41	CAMK2G; LOC652799; LOC653882; KIT; Gnas; ADCY1; FZD7; ADCY2; CREB3L2; POMC; dct; Calml3; CREB1; Prkca; Lef1; tyr; TYRL; PLCB2; WNT2B; PRKACA; LOC407835; Map2k2; PRKCB; CALM3; CALM2; CALM1; CTNNB1; Camk2a; CALM3; CALM2; CALM1; Camk2b; Kras; wnt2; wnt10b; PRKCG; WNT11; wnt8b; RAF1; GNAQ;
04930	Type II diabetes mellitus	Human Diseases; Metabolic Diseases	0.022	31	CACNA1G; MAPK10; PRKCD; PIK3CD; irs2; SLC2A2; PIK3CG; TNF; PIK3R3; socs2; HK3; Prkce; mapk8; ABCC8; gck; INSR; HK2P1; Hk2; PKLR; CACNA1E; ADIPOQ; LOC100131098; CACNA1C; SLC2A4; Pik3cb; Socs1; Cacna1d; PIK3R2; pdx1; LOC652797; PKM2; Asip
05020	Prion diseases	Human Diseases; Neurodegenerative Diseases	0.000	21	PRNP; LOC400750; HSPA5; CCL5; HSPA1A; HSPA1B; IL6; Ncam1; IL1B; C8G; C1QB; BAX; elk1; C7; C9; PRKACA; SOD1; C6; LAMC1; LOC407835; Map2k2
05200	Pathways in cancer	Human Diseases; Cancers	0.000	174	CDH1; ACVR1B; KLK3; Pdgfb; itga6; LOC100132973; TCEB1; CCND1; PIK3CG; NFKB1; NCOA4; BCL2; Rhoa; Ctbp1; Ctnna1; PLCG2; mapk8; foxo1; WNT2B; CTBP2; RXRG; HDAC2; LOC407835; Map2k2; FGF5; Cdk6; ABL1; birc2; E2F1; tp53; Tgfbr2; APC2; CTNNB1; FGF18; bcr; CDKN1A; Cblb; MYC; TGFB3; NOS3; LAMA1; PRKCG; FGF2; WNT11; Igf1; Fgf3; csf3r; LAMC2; wnt8b; CASP8; NOS1; RAF1; Lama2; Itgb1; Smo; ZBTB16; Hsp90b1; NFKBIA; MAPK10; RET; BIRC3; SOS1; PIK3CD; Col4a6; Msh2; NFKB2; CRKL; PIK3R3; LAMA4; Fas; Pdgfrb; IL8; FOS; Prkca; Hgf; HSP90AA2; HSP90AA1; TPM3; RB1; HIF1A; IGF1R; lamb2; KIAA1549; vhl; Stat5b; CDKN1B; Vegfb; ETS1; FGF4; Ctnna2; E2f2; Ar; LAMB1; GSTP1; Brca2; RXRA; FGF8; FLT3; FGF9; JAK1; rac1; Traf1; LOC652799; LOC653882; KIT; relA; FASLG; TGFA; NOS2; BID; RALGDS; CYCS; mdm2; Tceb2; Bad; RALBP1; LOC100129773; akt1; Runx1; Lef1; LAMC1; Mmp2; Skp2; Kras; wnt2; Jun; BAX; Pik3cb; Gli3; PIAS1; LAMA5; PAX8; TRAF3; FGFR2; pdgfra; itga2b; IL6; FZD7; HSP90AB1; STAT1; tgfbr1; NTRK1; smad4; ARNT; MET; Fgfr1; fn1; PRKCB; MAX; PTGS2; CCNA1; Itgav; akt2; TGFB1; wnt10b; Stat3; VEGFA; fgf12; Cdc42; CDC42P2; ITGA3; ikbkg; Hdac1; FH; col4a2; SMAD3; Col4a1; RUNX1T1; PIK3R2; SOS2; Erbb2; Fgf7; LOC100132771; FGF7P2
05210	Colorectal cancer	Human Diseases; Cancers	0.003	41	rac1; MAPK10; ACVR1B; pdgfra; CCND1; RALGDS; SOS1; PIK3CD; FZD7; PIK3CG; CYCS; Msh2; tgfbr1; PIK3R3; Pdgfrb; smad4; Bad; BCL2; FOS; akt1; MET; mapk8; Lef1; IGF1R; akt2; tp53; APC2; Tgfbr2; TGFB1; KIAA1549; CTNNB1; Kras; MYC; TGFB3; Jun; BAX; Pik3cb; SMAD3; PIK3R2; SOS2; RAF1

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
05211	Renal cell carcinoma	Human Diseases; Cancers	0.015	42	rac1; Rap1b; gab1; Pdgfb; TGFA; LOC100132973; TCEB1; Pak3; PIK3CD; SOS1; PIK3CG; CRKL; PIK3R3; Pak2; Tceb2; ARNT; akt1; MET; Hgf; LOC407835; Map2k2; HIF1A; akt2; TGFB1; KIAA1549; vhl; Kras; VEGFA; TGFB3; Vegfb; Cdc42; CDC42P2; ETS1; Jun; LOC344593; LOC442113; PTPN11; FH; Pik3cb; PIK3R2; SOS2; RAF1
05212	Pancreatic cancer	Human Diseases; Cancers	0.000	43	JAK1; rac1; MAPK10; relA; ACVR1B; TGFA; CCND1; RALGDS; PIK3CD; PIK3CG; NFKB1; STAT1; tgfbr1; PIK3R3; smad4; RALBP1; LOC100129773; Bad; akt1; mapk8; RB1; Cdk6; E2F1; akt2; tp53; TGFB1; Tgfbr2; KIAA1549; Kras; VEGFA; TGFB3; Vegfb; Stat3; Cdc42; CDC42P2; E2f2; ikbkg; Pik3cb; SMAD3; Brca2; PIK3R2; RAF1; Erbb2
05214	Glioma	Human Diseases; Cancers	0.001	45	CAMK2G; TGFA; Pdgfb; pdgfra; CCND1; PIK3CD; SOS1; PIK3CG; mdm2; Calml3; PIK3R3; Pdgfrb; Prkca; akt1; SHC1; PLCG2; RB1; PRKCB; LOC407835; Map2k2; Cdk6; IGF1R; E2F1; CALM3; CALM2; CALM1; akt2; tp53; KIAA1549; Camk2a; CALM3; CALM2; CALM1; Camk2b; Kras; CDKN1A; PRKCG; E2f2; SHC2; Pik3cb; SHC3; Igf1; PIK3R2; SOS2; RAF1
05215	Prostate cancer	Human Diseases; Cancers	0.000	51	NFKBIA; relA; KLK3; FGFR2; TGFA; Pdgfb; ATF4; ATF4C; pdgfra; CCND1; SOS1; PIK3CD; PIK3CG; mdm2; NFKB1; CREB3L2; HSP90AB1; CREB1; PIK3R3; Pdgfrb; Bad; BCL2; akt1; Lef1; foxo1; Fgfr1; HSP90AA2; HSP90AA1; RB1; LOC407835; Map2k2; IGF1R; E2F1; akt2; tp53; KIAA1549; CTNNB1; Kras; CDKN1A; CDKN1B; E2f2; ikbkg; Ar; Pik3cb; GSTP1; Igf1; PIK3R2; SOS2; RAF1; Erbb2; Hsp90b1
05217	Basal cell carcinoma	Human Diseases; Cancers	0.008	12	tp53; Gli3; APC2; WNT11; CTNNB1; Lef1; FZD7; WNT2B; wnt8b; wnt10b; wnt2; Smo
05218	Melanoma	Human Diseases; Cancers	0.001	41	FGF9; CDH1; Pdgfb; pdgfra; CCND1; PIK3CD; PIK3CG; mdm2; PIK3R3; Pdgfrb; Bad; akt1; MET; Hgf; Fgfr1; RB1; FGF5; LOC407835; Map2k2; Cdk6; IGF1R; E2F1; akt2; tp53; KIAA1549; FGF18; Kras; CDKN1A; fgf12; FGF4; E2f2; FGF2; Pik3cb; Fgf3; Igf1; PIK3R2; RAF1; FGF8; Fgf7; LOC100132771; FGF7P2
05219	Bladder cancer	Human Diseases; Cancers	0.002	20	CDH1; E2F1; tp53; KIAA1549; CCND1; CDKN1A; Kras; mdm2; MYC; VEGFA; Vegfb; E2f2; IL8; Thbs1; RAF1; RB1; Mmp2; LOC407835; Map2k2; Erbb2
05220	Chronic myeloid leukemia	Human Diseases; Cancers	0.003	52	relA; ACVR1B; CCND1; PIK3CG; mdm2; NFKB1; Bad; Ctbp1; Runx1; akt1; SHC1; CTBP2; HDAC2; LOC407835; Map2k2; Cdk6; ABL1; E2F1; tp53; Tgfbr2; bcr; Cblb; CDKN1A; Kras; MYC; TGFB3; SHC2; Pik3cb; SHC3; RAF1; NFKBIA; PIK3CD; SOS1; CRKL; tgfbr1; PIK3R3; smad4; RB1; akt2; TGFB1; KIAA1549; Stat5b; CDKN1B; Hdac1; LOC344593; LOC442113; PTPN11; ikbkg; E2f2; SMAD3; PIK3R2; SOS2

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Additional Table 6B. Continued.

Pathway entry	Pathway names	Classification	P value	Number of genes expressed in the pathways	Included genes
05221	Acute myeloid leukemia	Human Diseases; Cancers	0.014	33	LOC652799; LOC653882; KIT; relA; CCND1; PIK3CD; SOS1; PIK3CG; NFKB1; PIK3R3; Bad; Runx1; akt1; Lef1; LOC407835; Map2k2; RPS6KB1; CCNA1; akt2; KIAA1549; Kras; Pim2; Stat5b; MYC; Stat3; ikbkg; Pik3cb; RUNX1T1; PIK3R2; SOS2; RAF1; ZBTB16; FLT3
05222	Small cell lung cancer	Human Diseases; Cancers	0.000	53	Traf1; relA; itga6; NOS2; CCND1; PIK3CG; CYCS; NFKB1; BCL2; Apaf1; akt1; LAMC1; RXRG; Skp2; Cdk6; birc2; E2F1; tp53; MYC; NOS3; LAMA1; Pik3cb; PIAS1; LAMA5; LAMC2; NOS1; Lama2; Itgb1; NFKBIA; TRAF3; BIRC3; itga2b; PIK3CD; Col4a6; PIK3R3; LAMA4; fn1; RB1; MAX; PTGS2; Itgav; akt2; lamb2; CDKN1B; ITGA3; FHIT; E2f2; ikbkg; LAMB1; col4a2; RXRA; Col4a1; PIK3R2
05223	Non-small cell lung cancer	Human Diseases; Cancers	0.002	32	foxo3b; FOXO3; TGFA; CCND1; PIK3CD; SOS1; PIK3CG; PIK3R3; Bad; Prkca; akt1; PLCG2; RXRG; RB1; LOC407835; Map2k2; PRKCB; Cdk6; E2F1; akt2; tp53; KIAA1549; Kras; FHIT; PRKCG; E2f2; Pik3cb; RXRA; PIK3R2; RAF1; SOS2; Erbb2
05310	Asthma	Human Diseases; Immune System Diseases	0.023	16	Il5; HLA-DOB; HLA-DRA; RNASE3; il10; HLA-DQB1; LOC100133583; IL4; IL13; Il3; TNF; CD40LG; EPX; hla-dpa1; HLA-DPB1; HLA-DOA
05320	Autoimmune thyroid disease	Human Diseases; Immune System Diseases	0.017	30	Il5; HLA-DOB; TPO; HLA-DRA; IFNA6; cga; il10; FASLG; HLA-DQB1; LOC100133583; IL4; Tshb; Fas; CD40LG; TSHR; hla-dpa1; Prf1; IFNA21; HLA-DPB1; HLA-G; Ifna14; Ifna10; IFNA4; IFNA5; CD80; HLA-E; HLA-A; ifna2; HLA-F; HLA-DOA
05340	Primary immunodeficiency	Human Diseases; Immune System Diseases	0.013	19	Cd19; JAK3; Rag2; Ciita; RAG1; rfxank; IL7R; LCK; TAP2; btk; ada; Cd79a; CD3E; Ptprc; CD8B; CD40LG; ikbkg; il2rg; CD4
05410	Hypertrophic cardiomyopathy (HCM)	Human Diseases; Cardiovascular Diseases	0.000	49	ITGA10; Itgb5; Cacna1f; ITGA5; itga6; MYBPC3; itga2b; lmna; ATP2A2; IL6; DAG1; myl2; ACTG1; dmd; TNF; LOC643634; CACNB4; ITGB3; CACNB1; Myl3; SGCA; ITGA7; CACNA1S; TPM3; CACNB2; tpm2; ITGA9; Itgav; Myh7; DES; TPM1; PRKAB2; TGFB1; TTN; TGFB3; ITGA3; Actc1; LOC100131098; CACNA1C; Cacna2d1; sgcg; Igf1; Cacna1d; CACNG3; ACTB; CACNG1; Lama2; Itgb1; SLC8A1
05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Human Diseases; Cardiovascular Diseases	0.000	41	ITGA10; Itgb5; Cacna1f; ITGA5; itga6; itga2b; ATP2A2; lmna; DAG1; ACTG1; GJA1; dmd; CACNB4; ITGB3; CACNB1; Ctnna1; SGCA; Lef1; actn1; ITGA7; CACNA1S; CACNB2; ITGA9; Itgav; DES; CTNNB1; ITGA3; Ctnna2; LOC100131098; CACNA1C; Cacna2d1; sgcg; CACNG3; Cacna1d; ACTB; CACNG1; actn4; dsp; Lama2; Itgb1; SLC8A1