

Figure S1. Representative H&E and immunohistochemistry staining of AFP, HepPar-1, and PDEC GF in hepatocellular carcinoma tissues. Scale bars represent 40 μ m. AFP, α -fetoprotein; HepPar-1, hepatocyte paraffin-1; PDEC GF, platelet-derived endothelial cell growth factor; H&E, hematoxylin and eosin.

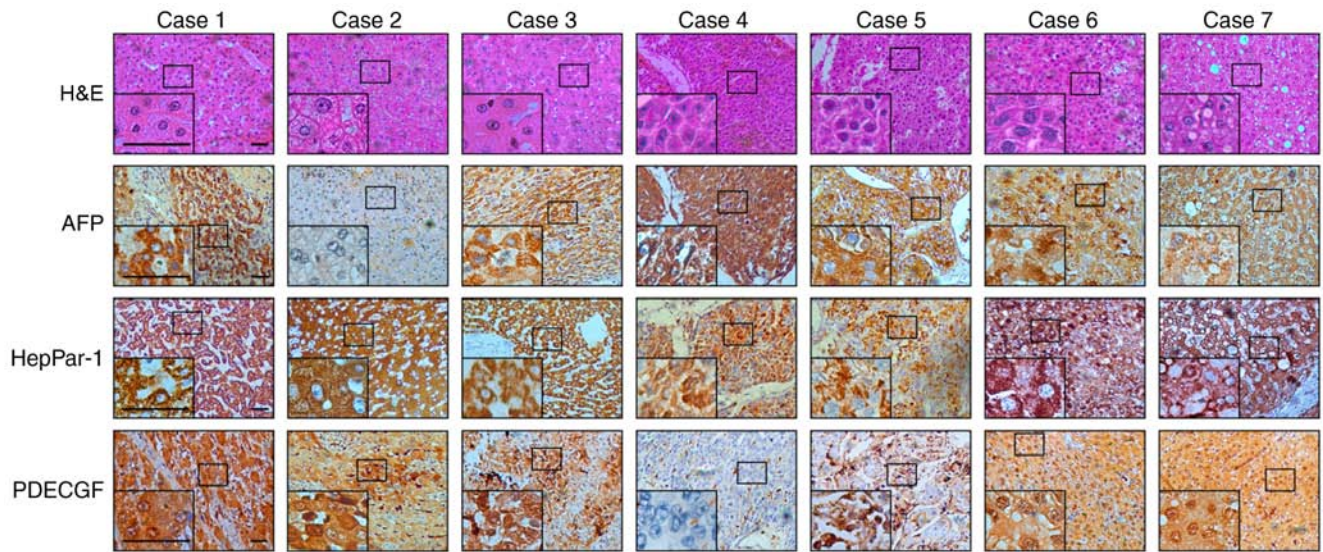


Figure S2. Vioplots for distribution of signal intensity of lncRNA-mRNA microarray. Red bars stood for mRNA. LncRNAs from the microarray data were divided into 6 types and presented in different color bars in the plot, including bidirectional (blue), exonic antisense (yellow), exonic sense (green), intergenic (pink), intronic antisense (purple) and intronic sense (grey), respectively. The left (A) displayed mean expression level of mRNA and lncRNA; while the right (B) presented standard error expression of mRNA and lncRNA. Lnc, long noncoding.

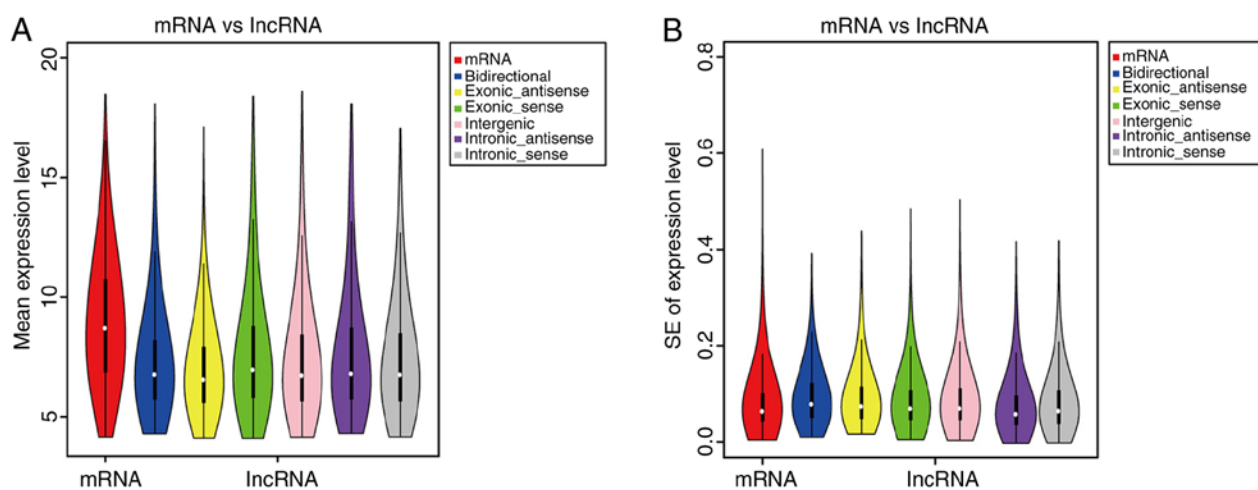


Figure S3. PCA and heatmap visualization for lncRNA plus mRNA and miRNA microarrays. (A) PCA analysis and heatmap view for lncRNAs. (B) PCA analysis and heatmap view for mRNAs.

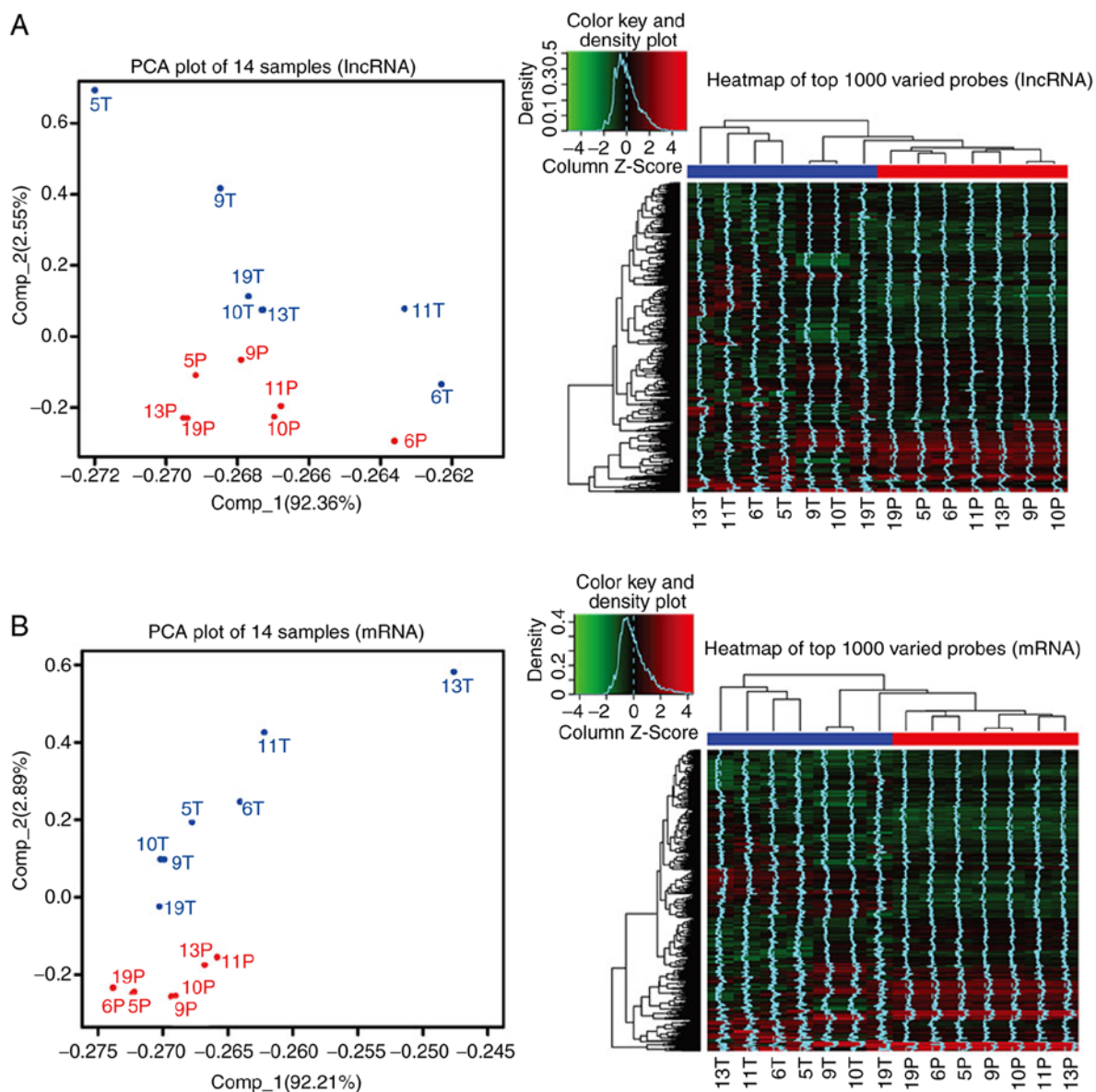


Figure S3. Continued. (C) PCA analysis and heatmap view for the combination analysis of mRNAs and lncRNAs. (D) PCA analysis and heatmap view for miRNAs. PCNA, Principle component analysis; lnc, long noncoding; miRNA, microRNA.

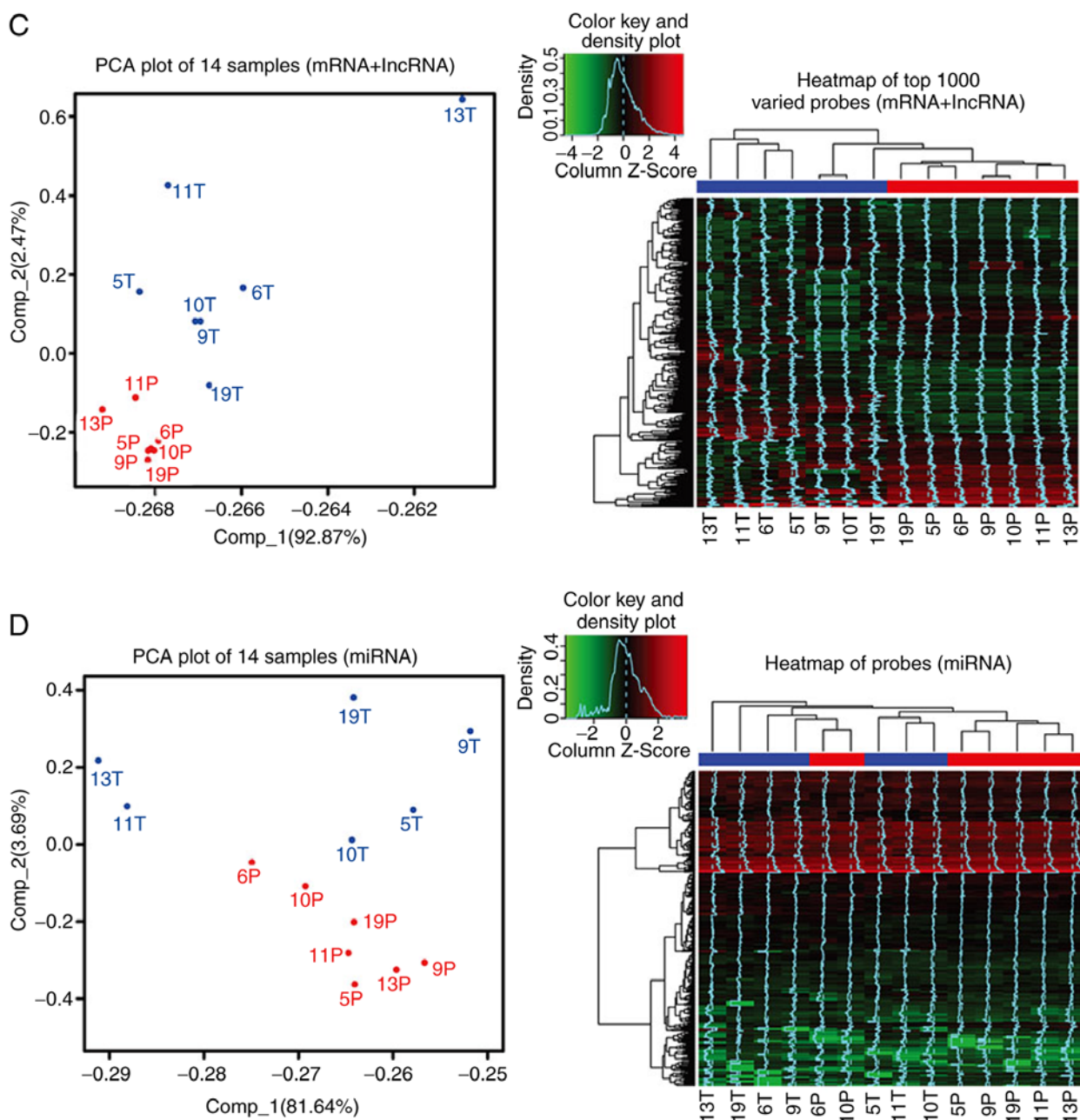


Figure S4. GSEA plots visualized for the enrichment analysis of all mRNA. Based on the value of fold-change, three most remarkably pathways were displayed, which were (A) cell cycle, (B) G2/M checkpoints and (C) cell cycle mitotic, respectively. GSEA, Gene Set Enrichment Analysis.

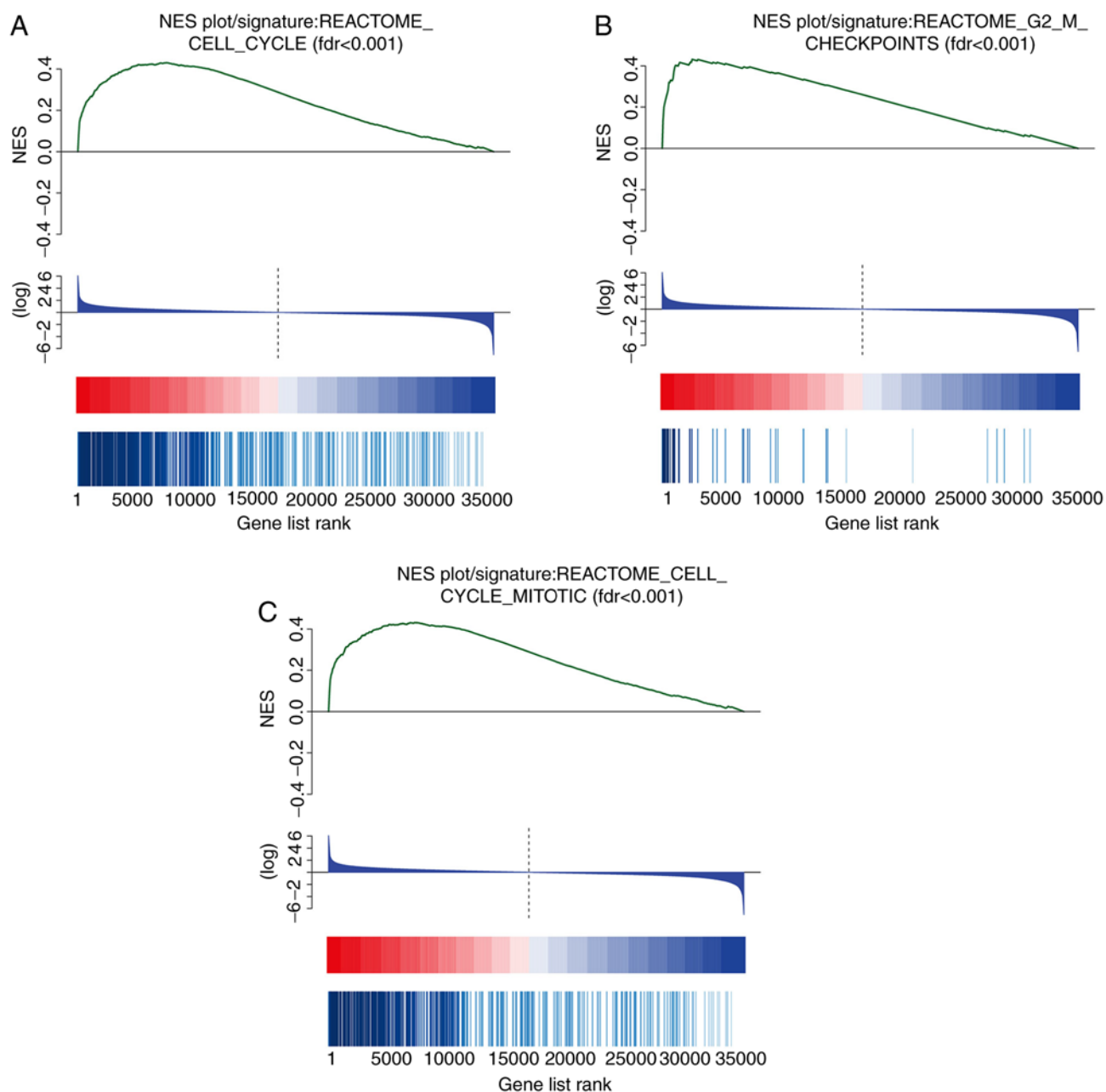


Table SI. The details of the clinical characteristics.

Case	Gender	Age	Pathological diagnosis	TNM	Cirrhosis	HBV
1	Male	57	HCC	II	+	+
2	Female	67	HCC	II	+	+
3	Male	58	HCC	II-III	+	+
4	Male	52	HCC	II	+	+
5	Female	62	HCC	III	+	+
6	Male	54	HCC	III	-	+
7	Male	27	HCC	II	+	+

HCC, hepatocellular carcinoma; TNM, tumor node and metastasis; HBV, hepatitis B virus.

Table SII. Primer sequences designed for quantitative PCR.

Gene	Forward (5'-3')	Reverse (5'-3')
ENST00000522221	CCAGGGTGTGAGAGAGTTGAC	CTCAAGGAGCAACCTGGCTA
ENST00000577319	CGCCTGTAATCCCAGCTACTT	AGGAACTTCTGCTTTGGATCAG
lnc-GADD45B-4:1	ATCCCTCCACGATGCTATCC	GAAGCCATCAGCACTTCCAAT
lnc-HACE1-6:1	GAGGAGGCGGATGTGAAACT	GGAAACTTGCTACCACTCCCA
lnc-ICOSLG-11:1	TTCTTTGAAGCCACAGTGACCC	TGTCCAGTGTTGGTGATTCCAG
GAPDH	ACCACAGTCCATGCCATCAC	TCCACCACCCTGTTGCTGTA

Table SIII. Description of the microarray probes.

Microarray types	Probes	Before filter	After filter
lncRNA plus mRNA	lncRNA	91,007	32,793
	mRNA	29,859	22,224
miRNA	miRNA	2,570	369
miRNA, microRNA; lnc, long non-coding.			

Table SIV. Summary of differentially expressed RNAs.

RNA types	Upregulation	Downregulation	NS
lncRNA	1,056	1,288	30,449
mRNA	1,171	1,516	19,537
miRNA	5	1	363

NS, not significant; miRNA, microRNA; lnc, long noncoding.

Table SV. Details for the annotation of the GO accession ID numbers involved in GO analysis.

GO accession no.	Annotation
Figure 2A (molecular function)	
Upregulation	
GO: 0048037	Cofactor binding
GO: 0001882	Nucleoside binding
GO: 0000166	Nucleotide binding
GO: 0032555	Purine ribonucleotide binding
GO: 0001883	Purine nucleoside binding
GO: 0017076	Purine nucleotide binding
GO: 0032553	Ribonucleotide binding
GO: 0030554	Adenyl nucleotide binding
GO: 0005524	ATP binding
GO: 0032559	Adenyl ribonucleotide binding
Downregulation	
GO: 0030247	Polysaccharide binding
GO: 0005539	Glycosaminoglycan binding
GO: 0008201	Heparin binding
GO: 0001871	Pattern binding
GO: 0030246	Carbohydrate binding
GO: 0019838	Growth factor binding
GO: 0046906	Tetrapyrrole binding
GO: 0009055	Electron carrier activity
GO: 0019825	Oxygen binding
GO: 0005506	Iron ion binding
GO: 0070330	Aromatase activity
GO: 0020037	Heme binding
GO: 0016712	Oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavo-protein as one donor, and incorporation of one atom of oxygen
Figure 2B (biological process)	
Upregulation	
GO: 0048285	Organelle fission
GO: 0000279	M phase
GO: 0051301	Cell division
GO: 0000087	M phase of mitotic cell cycle
GO: 0000278	Mitotic cell cycle
GO: 0000280	Nuclear division
GO: 0022402	Cell cycle process
GO: 0007049	Cell cycle
GO: 0007067	Mitosis
GO: 0051726	Regulation of cell cycle
GO: 0022403	Cell cycle phase
GO: 0006259	DNA metabolic process
GO: 0006260	DNA replication
GO: 0048878	Chemical homeostasis
Downregulation	
GO: 0002253	Activation of immune response
GO: 0002541	Activation of plasma proteins involved in acute inflammatory response
GO: 0045087	Innate immune response
GO: 0002684	Positive regulation of immune system process
GO: 0006956	Complement activation
GO: 0051604	Protein maturation
GO: 0009611	Response to wounding
GO: 0006955	Immune response
GO: 0051605	Protein maturation by peptide bond cleavage
GO: 0006958	Complement activation, classical pathway

Table SV. Continued.

GO accession no.	Annotation
GO: 0002455	Humoral immune response mediated by circulating immunoglobulin
GO: 0009611	Response to wounding
GO: 0050817	Coagulation
GO: 0042060	Wound healing
GO: 0048584	Positive regulation of response to stimulus
GO: 0002252	Immune effector process
GO: 0016485	Protein processing
GO: 0050878	Regulation of body fluid levels
GO: 0007599	Hemostasis
GO: 0007596	Blood coagulation
GO: 0006952	Defense response
GO: 0006959	Humoral immune response
GO: 0050778	Positive regulation of immune response
GO: 0002526	Acute inflammatory response
GO: 0046395	Carboxylic acid catabolic process
GO: 0055114	Oxidation reduction
GO: 0016054	Organic acid catabolic process
GO: 0009725	Response to hormone stimulus
GO: 0010033	Response to organic substance
GO: 0051384	Response to glucocorticoid stimulus
GO: 0031960	Response to corticosteroid stimulus
GO: 0048545	Response to steroid hormone stimulus

Figure 2C (cellular component)

Upregulation	
GO: 0005819	Spindle
GO: 0043233	Organelle lumen
GO: 0043228	Non-membrane-bounded organelle
GO: 0031981	Nuclear lumen
GO: 0015630	Microtubule cytoskeleton
GO: 0043232	Intracellular non-membrane-bounded organelle
GO: 0031974	Membrane-enclosed lumen
GO: 0070013	Intracellular organelle lumen
GO: 0000775	Chromosome, centromeric region
GO: 0000793	Condensed chromosome
GO: 0005694	Chromosome
GO: 0044427	Chromosomal part
GO: 0005829	Cytosol
Downregulation	
GO: 0044421	Extracellular region part
GO: 0031983	Vesicle lumen
GO: 0031093	Platelet alpha granule lumen
GO: 0005576	Extracellular region
GO: 0060205	Cytoplasmic membrane-bounded vesicle lumen
GO: 0031091	Platelet alpha granule
GO: 0005615	Extracellular space
GO: 0005887	Integral to plasma membrane
GO: 0031226	Intrinsic to plasma membrane

No., number; GO, gene ontology.

Table SVI. Details for the annotation of the pathways involved in KEGG pathway analysis.

KEGG accession no.	Annotation
Upregulation	
HSA04110	Cell cycle
REACT_152	Cell cycle, mitotic
REACT_1538	Cell cycle checkpoints
REACT_383	DNA replication
HSA03030	DNA replication
REACT_7970	Telomere maintenance
Downregulation	
HSA00232	Caffeine metabolism
HSA00830	Retinol metabolism
REACT_13433	Biological oxidations
HSA00590	Arachidonic acid metabolism
REACT_649	Phase 1 functionalization
HSA00982	Drug metabolism
REACT_6900	Signaling in immune system
HSA00071	Fatty acid metabolism
HSA00260	Glycine, serine and threonine metabolism
REACT_604	Hemostasis
HSA00380	Tryptophan metabolism
REACT_13	Metabolism of amino acids
HSA00280	Valine, leucine and isoleucine degradation
HSA00250	Alanine, aspartate and glutamate metabolism
H_COMPPATHWAY	Complement pathway
H_INTRINSIPATHWAY	Intrinsic prothrombin Activation pathway
HSA04610	Complement and coagulation cascades
No., number; KEGG, Kyoto Encyclopedia of Genes and Genomes.	

Table SVII. Overview of significantly upregulated pathways.

Category	Pathway	Count	P-value
REACTOME_PATHWAY	REACT_152: Cell Cycle, Mitotic	68	8.75×10^{-21}
KEGG_PATHWAY	hsa04110: Cell cycle	32	1.70×10^{-12}
REACTOME_PATHWAY	REACT_1538: Cell Cycle Checkpoints	27	8.30×10^{-9}
REACTOME_PATHWAY	REACT_383: DNA Replication	25	8.42×10^{-9}
KEGG_PATHWAY	hsa03030: DNA replication	14	4.66×10^{-8}
REACTOME_PATHWAY	REACT_7970: Telomere Maintenance	17	3.51×10^{-7}
KEGG_PATHWAY	hsa00240: Pyrimidine metabolism	17	9.64×10^{-5}
BIOCARTA	h_cellcycle Pathway: Cyclins and Cell Cycle Regulation	8	1.02×10^{-3}
REACTOME_PATHWAY	REACT_1698: Metablism of nucleotides	14	1.48×10^{-3}
KEGG_PATHWAY	hsa04115: p53 signaling pathway	12	1.68×10^{-3}
KEGG_PATHWAY	hsa05222: Small cell lung cancer	13	3.12×10^{-3}
REACTOME_PATHWAY	REACT_216: DNA Repair	15	7.08×10^{-3}
KEGG_PATHWAY	hsa00970: Aminoacyl-tRNA biosynthesis	8	8.57×10^{-3}
KEGG_PATHWAY	hsa04914: Progesterone-mediated oocyte maturation	12	1.06×10^{-2}
KEGG_PATHWAY	hsa04114: Oocyte meiosis	14	1.09×10^{-2}
REACTOME_PATHWAY	REACT_6850: Cdc20: Phospho-APC/C mediated degradation of Cyclin A	11	1.11×10^{-2}
KEGG_PATHWAY	hsa00230: Purine metabolism	17	1.56×10^{-2}
BIOCARTA	h_smPathway: Spliceosomal Assembly	5	1.60×10^{-2}
BIOCARTA	h_g2Pathway: Cell Cycle: G2/M Checkpoint	6	1.74×10^{-2}
KEGG_PATHWAY	hsa00480: Glutathione metabolism	8	2.44×10^{-2}
BIOCARTA	h_akap95Pathway: AKAP95 role in mitosis and chromosome dynamics	4	3.49×10^{-2}
KEGG_PATHWAY	hsa03430: Mismatch repair	5	4.15×10^{-2}
BIOCARTA	h_g1Pathway: Cell Cycle: G1/S Check Point	6	4.43×10^{-2}
KEGG_PATHWAY	hsa00051: Fructose and mannose metabolism	6	4.49×10^{-2}
KEGG_PATHWAY	hsa00630: Glyoxylate and dicarboxylate metabolism	4	5.28×10^{-2}
KEGG_PATHWAY	hsa05322: Systemic lupus erythematosus	11	6.08×10^{-2}
REACTOME_PATHWAY	REACT_8017: APC-Cdc20 mediated degradation of Nek2A	5	6.30×10^{-2}
BIOCARTA	h_p38mapkPathway: p38 MAPK Signaling Pathway	6	7.13×10^{-2}
REACTOME_PATHWAY	REACT_474: Metabolism of carbohydrates	11	9.41×10^{-2}

KEGG, Kyoto Encyclopedia of Genes and Genomes.

Table SVIII. Overview of significantly downregulated pathways.

Category	Pathway	Count	P-value
KEGG_PATHWAY	hsa04610: Complement and coagulation cascades	36	5.74x10 ⁻²⁰
REACTOME_PATHWAY	REACT_13433: Biological oxidations	34	1.96x10 ⁻¹⁰
REACTOME_PATHWAY	REACT_13: Metabolism of amino acids	39	4.28x10 ⁻⁰⁹
REACTOME_PATHWAY	REACT_604: Hemostasis	47	3.43x10 ⁻⁰⁸
KEGG_PATHWAY	hsa00260: Glycine, serine and threonine metabolism	15	7.23x10 ⁻⁰⁸
BIOCARTA	h_intrinsic Pathway: Intrinsic Prothrombin Activation Pathway	12	1.97x10 ⁻⁰⁷
KEGG_PATHWAY	hsa00830: Retinol metabolism	18	1.46x10 ⁻⁰⁶
KEGG_PATHWAY	hsa00982: Drug metabolism	18	1.19x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00590: Arachidonic acid metabolism	17	1.21x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00380: Tryptophan metabolism	14	1.74x10 ⁻⁰⁵
BIOCARTA	h_compPathway: Complement Pathway	10	2.74x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00250: Alanine, aspartate and glutamate metabolism	12	3.08x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00280: Valine, leucine and isoleucine degradation	14	5.45x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00232: Caffeine metabolism	6	8.60x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00071: Fatty acid metabolism	13	8.96x10 ⁻⁰⁵
REACTOME_PATHWAY	REACT_649: Phase 1 functionalization	8	1.16x10 ⁻⁰⁵
REACTOME_PATHWAY	REACT_6900: Signaling in Immune system	44	1.32x10 ⁻⁰⁵
BIOCARTA	h_alternative Pathway: Alternative Complement Pathway	7	2.78x10 ⁻⁰⁵
KEGG_PATHWAY	hsa00591: Linoleic acid metabolism	10	3.89x10 ⁻⁰⁴
KEGG_PATHWAY	hsa05020: Prion diseases	11	5.38x10 ⁻⁰⁴
BIOCARTA	h_classicPathway: Classical Complement Pathway	7	1.00x10 ⁻⁰³
BIOCARTA	h_lectinPathway: Lectin Induced Complement Pathway	7	1.00x10 ⁻⁰³
BIOCARTA	h_tcapoptosis Pathway: HIV Induced T Cell Apoptosis	6	1.52x10 ⁻⁰³
BIOCARTA	h_plateletApp Pathway: Platelet Amyloid Precursor Protein Pathway	6	1.52x10 ⁻⁰³
KEGG_PATHWAY	hsa04060: Cytokine-cytokine receptor interaction	38	1.70x10 ⁻⁰³
KEGG_PATHWAY	hsa00650: Butanoate metabolism	10	1.85x10 ⁻⁰³
KEGG_PATHWAY	hsa03320: PPAR signaling pathway	15	1.96x10 ⁻⁰³
KEGG_PATHWAY	hsa00980: Metabolism of xenobiotics by cytochrome P450	13	4.56x10 ⁻⁰³
BIOCARTA	h_tcr Pathway: Lck and Fyn tyrosine kinases in initiation of TCR Activation	6	4.62x10 ⁻⁰³
KEGG_PATHWAY	hsa00640: Propanoate metabolism	9	4.82x10 ⁻⁰³
KEGG_PATHWAY	hsa00330: Arginine and proline metabolism	12	4.85x10 ⁻⁰³
KEGG_PATHWAY	hsa04062: Chemokine signaling pathway	28	5.17x10 ⁻⁰³
KEGG_PATHWAY	hsa04270: Vascular smooth muscle contraction	19	7.05x10 ⁻⁰³
KEGG_PATHWAY	hsa04020: Calcium signaling pathway	25	1.61x10 ⁻⁰²
REACTOME_PATHWAY	REACT_602: Metabolism of lipids and lipoproteins	22	1.65x10 ⁻⁰²
KEGG_PATHWAY	hsa00270: Cysteine and methionine metabolism	8	2.39x10 ⁻⁰²
BIOCARTA	h_eicosanoid Pathway: Eicosanoid Metabolism	7	2.47x10 ⁻⁰²
KEGG_PATHWAY	hsa00983: Drug metabolism	9	2.88x10 ⁻⁰²
KEGG_PATHWAY	hsa04640: Hematopoietic cell lineage	14	3.23x10 ⁻⁰²
KEGG_PATHWAY	hsa00350: Tyrosine metabolism	9	3.26x10 ⁻⁰²
KEGG_PATHWAY	hsa00340: Histidine metabolism	7	3.47x10 ⁻⁰²
BIOCARTA	h_CSKPathway: Activation of Csk by cAMP-dependent Protein Kinase Inhibits Signaling through the T Cell Receptor	6	3.52x10 ⁻⁰²
BIOCARTA	h_tsp1Pathway: TSP-1 Induced Apoptosis in Microvascular Endothelial Cell	4	3.55x10 ⁻⁰²
KEGG_PATHWAY	hsa00360: Phenylalanine metabolism	6	3.64x10 ⁻⁰²
KEGG_PATHWAY	hsa00072: Synthesis and degradation of ketone bodies	4	3.64x10 ⁻⁰²
KEGG_PATHWAY	hsa00910: Nitrogen metabolism	6	4.33x10 ⁻⁰²
BIOCARTA	h_amiPathway: Acute Myocardial Infarction	5	5.03x10 ⁻⁰²
BIOCARTA	h_ghrelinPathway: Ghrelin: Regulation of Food Intake and Energy Homeostasis	5	5.50x10 ⁻⁰²
BIOCARTA	h_nktPathway: Selective expression of chemokine receptors during T-cell polarization	7	5.50x10 ⁻⁰²
REACTOME_PATHWAY	REACT_474: Metabolism of carbohydrates	14	5.76x10 ⁻⁰²
KEGG_PATHWAY	hsa00400: Phenylalanine, tyrosine and tryptophan biosynthesis	3	6.27x10 ⁻⁰²
KEGG_PATHWAY	hsa04666: Fc gamma R-mediated phagocytosis	14	6.41x10 ⁻⁰²
BIOCARTA	h_Ccr5Pathway: Pertussis toxin-insensitive CCR5 Signaling in Macrophage	5	6.43x10 ⁻⁰²

Table SVIII. Continued.

Category	Pathway	Count	P-value
REACTOME_PATHWAY	REACT_15518: Transmembrane transport of small molecules	8	6.49×10^{-02}
BIOCARTA	h_methioninepathway:Catabolic Pathways for Methionine, Isoleucine, Threonine and Valine	3	6.58×10^{-02}
KEGG_PATHWAY	hsa05340: Primary immunodeficiency	7	7.69×10^{-02}
BIOCARTA	h_ctl Pathway: CTL mediated immune response against target cells	5	8.03×10^{-02}
KEGG_PATHWAY	hsa00310: Lysine degradation	8	8.13×10^{-02}
BIOCARTA	h_etsPathway: METS effect on Macrophage Differentiation	5	9.79×10^{-02}
KEGG_PATHWAY	hsa00140: Steroid hormone biosynthesis	8	9.81×10^{-02}
KEGG, Kyoto Encyclopedia of Genes and Genomes.			