

Title

An Integrated Analysis Reveals Ciliary Abnormalities in Antrochoanal Polyps

Authors

Xiaoxue Zi^{1*}, Yang Peng^{2*}, Yiran Zang¹, Shiyong Chen², Mengshi Li³, Kena Yu¹, Xu Liang¹, Peng Jin^{1†}, Deyun Wang⁴, Li Shi¹

1. Department of Otolaryngology, The Second Hospital of Shandong University, Jinan, Shandong, China
2. State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, First Affiliated Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, Guangdong, China
3. State Key Laboratory of Respiratory Disease, Department of Respiratory Pathology, Guangzhou Institute of Respiratory Health, National Clinical Research Center for Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China
4. Department of Otolaryngology, National University of Singapore, National University Health System, Singapore, Singapore

*: These authors contributed equally to this paper

†: Corresponding author

Methods

RNA sequencing (RNA-seq) and data processing

1. Sample collection and preparation

(1) RNA quantification and qualification

① RNA degradation and contamination was monitored on 1% agarose gels.

② RNA purity was checked using the NanoPhotometer® spectrophotometer (IMPLEN, CA, USA).

③ RNA integrity was assessed using the RNA Nano 6000 Assay Kit of the Bioanalyzer 2100 system (Agilent Technologies, CA, USA).

(2) Library preparation for Transcriptome sequencing

A total amount of 1 µg RNA per sample was used as input material for the RNA sample preparations. Sequencing libraries were generated using NEBNext® Ultra™ RNA Library Prep Kit for Illumina® (NEB, USA) following manufacturer's recommendations and index codes were added to attribute sequences to each sample. Briefly, mRNA was purified from total RNA using poly-T oligo-attached magnetic beads. Fragmentation was carried out using divalent cations under elevated temperature in NEBNext First Strand Synthesis Reaction Buffer(5X). First strand cDNA was synthesized using random hexamer primer and M-MuLV Reverse Transcriptase (RNase H). Second strand cDNA synthesis was subsequently performed using DNA Polymerase I and RNase H. Remaining overhangs were converted into blunt ends via exonuclease/polymerase activities. After adenylation of 3' ends of

DNA fragments, NEBNext Adaptor with hairpin loop structure were ligated to prepare for hybridization. In order to select cDNA fragments of preferentially 250~300 bp in length, the library fragments were purified with AMPure XP system (Beckman Coulter, Beverly, USA). Then 3 µl USER Enzyme (NEB, USA) was used with size-selected, adaptor-ligated cDNA at 37°C for 15 min followed by 5 min at 95 °C before PCR. Then PCR was performed with Phusion High-Fidelity DNA polymerase, Universal PCR primers and Index (X) Primer. At last, PCR products were purified (AMPure XP system) and library quality was assessed on the Agilent Bioanalyzer 2100 system.

(3) Clustering and sequencing (Genchem Experimental Department)

The clustering of the index-coded samples was performed on a cBot Cluster Generation System using TruSeq PE Cluster Kit v3-cBot-HS (Illumina) according to the manufacturer's instructions. After cluster generation, the library preparations were sequenced on an Illumina Novaseq platform and 150 bp paired-end reads were generated.

2. Data Analysis

(1) Quality control

Raw data (raw reads) of fastq format were firstly processed through in-house perl scripts. In this step, clean data (clean reads) were obtained by removing reads containing adapter, reads containing ploy-N and low quality reads from raw data. At the same time, Q20, Q30 and GC content the clean data were calculated. All the downstream analyses were based on the clean data with high quality.

(2) Reads mapping to the reference genome

Reference genome and gene model annotation files were downloaded from genome website directly. Index of the reference genome was built using Hisat2 v2.0.5 and paired-end clean reads were aligned to the reference genome using Hisat2 v2.0.5.

We selected Hisat2 as the mapping tool for that Hisat2 can generate a database of splice junctions based on the gene model annotation file and thus a better mapping result than other non-splice mapping tools.

(3) Novel transcripts prediction

The mapped reads of each sample were assembled by StringTie (v1.3.3b) (Mihaela Pertea et al. 2015) in a reference-based approach. StringTie uses a novel network flow algorithm as well as an optional de novo assembly step to assemble and quantitate fulllength transcripts representing multiple splice variants for each gene locus.

(4) Quantification of gene expression level

FeatureCounts v1.5.0-p3 was used to count the reads numbers mapped to each gene. And then FPKM of each gene was calculated based on the length of the gene and reads count mapped to this gene. FPKM, expected number of Fragments Per Kilobase of transcript sequence per Millions base pairs sequenced, considers the effect of sequencing depth and gene length for the reads count at the same time, and is currently the most commonly used method for estimating gene expression levels.

(5) Bioinformatics analysis of the RNA-seq

Differential expression analysis between the two groups was performed using the DESeq2 R package (1.16.1). The resulting *P*-values were adjusted using the Benjamini and Hochberg's approach for controlling the false discovery rate. Genes with an adjusted *P* value <0.05 found by DESeq2 were assigned as differentially expressed. Gene Ontology (GO) enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of differentially expressed genes were implemented by the clusterProfiler R package, in which gene length bias was corrected. Terms with corrected *P* values less than 0.05 were considered significantly enriched by differential expressed genes. Gene set enrichment analysis (GSEA) is a computational method used to determine whether a predefined set of genes shows statistically significant and consistent differences between two groups of phenotypes, etc. The GSEA official software package was used for analysis.

RNA extraction and Real Time RT-PCR

Total RNA was extracted from frozen nasal tissues in RNA later by using the mirVana™ isolation kit (Applied Biosystems, Foster City, CA) and 1 µg total RNA was reverse transcribed with reversing transcription kit (Thermo, USA) based on the manufacturer's protocol. cDNA were diluted in 40µl nuclease free water. After validating the quality of cDNA, Real-time RT-PCR analysis (Mastercycler Nexus, Eppendorf, Germany) was performed to evaluate the expression levels of 9 cilia-related genes (*FOXJ1*, *DNAI1*, *DNAH9*, *RSPH1*, *RSPH9*, *RSPH4A*, *CP110*, *DNAH5*, *DNAL1*) and 8 inflammatory factors (*CCL7*, *CCL18*, *CCL20*, *CXCL6*, *CXCL8*, *IL17REL* , *IFNG* and *IL13RA2*) . Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as housekeeping genes for the tissue mRNA. Relative mRNA levels were calculated by using the comparative $2^{-\Delta\Delta Ct}$ methods, with

the housekeeping gene as the reference.

Immunofluorescence (IF) assay

To explore the expression patterns of epithelial markers and ciliary structure, including α -tubulin (1:500, ab24610) and forkhead Box J1 (FOXJ1)(1:100, Sigma HPA005714) for ciliated cells, keratin 5 (KRT5)(1:150, Biolegend 905903) for basal cell, mucin 5AC (MUC5AC) (1:100, Thermo Fisher MA5-12178)for goblet cells, DNAI1(1:100, HPA021649) for outer dynein arm, RSPH4A(1:100, HPA031196) for radial spoke. We then incubated the slides with Alexa Fluor 488-, 555-, and 647-conjugated secondary antibodies at 37 °C for 1 hour at 1:500 dilution.

Figure legends

Figure E1. Validation of the expression levels of 8 inflammatory factors in nasal mucosa between patients with ACPs (n = 17) and controls (n = 20) with qRT-PCR. Data were analyzed by Mann–Whitney 2-sided nonparametric test. Median values with range are indicated. $P < 0.05$ was statistically significant. *CCL7*, C-C motif chemokine ligand 7; *CCL18*, C-C motif chemokine ligand 18; *CCL20*, C-C motif chemokine ligand 20; *CXCL6*, C-X-C motif chemokine ligand 6; *CXCL8*, C-X-C motif chemokine ligand 8; *IFNG*, interferon gamma; *IL13RA2*, interleukin 13 receptor subunit alpha 2; *IL17REL*, interleukin 17 receptor E like. ACPs, antrochoanal polyps; qRT-PCR, quantitative reverse transcription polymerase chain reaction.

Figure E2. The correlation between *FOXJ1* and the 8 inflammatory factors in ACPs (n = 17). The mRNA expression of *FOXJ1* and *CCL7* (A), *FOXJ1* and *CCL18* (B), *FOXJ1* and *CCL20* (C), *FOXJ1* and *CXCL6* (D), *FOXJ1* and *CXCL8* (E), *FOXJ1* and *IL17REL* (F), *FOXJ1* and *IFNG* (G), *FOXJ1* and *IL13RA2* (H). The correlation analysis was performed by Spearman's correlation analysis. $P < 0.05$ was statistically significant. *FOXJ1*, forkhead box J1; *CCL7*, C-C motif chemokine ligand 7; *CCL18*, C-C motif chemokine ligand 18; *CCL20*, C-C motif chemokine ligand 20; *CXCL6*, C-X-C motif chemokine ligand 6; *CXCL8*, C-X-C motif chemokine ligand 8; *IFNG*, interferon gamma; *IL13RA2*, interleukin 13 receptor subunit alpha 2; *IL17REL*,

interleukin 17 receptor E like. ACPs, antrochoanal polyps.

Figures

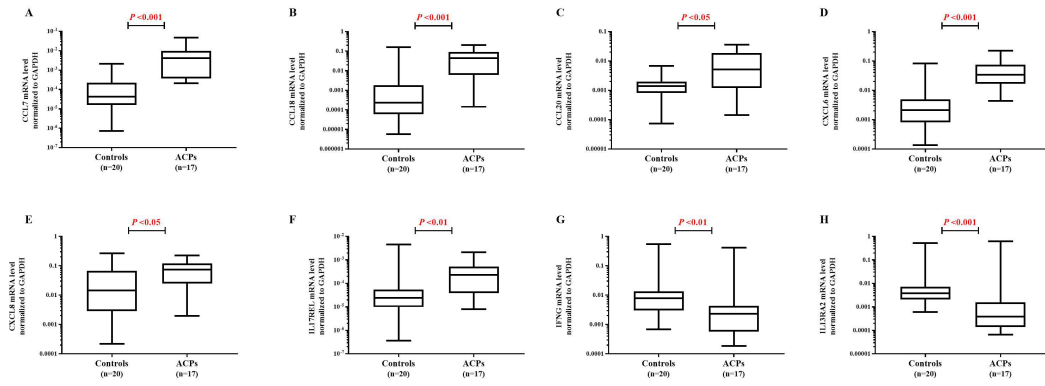


Figure E1

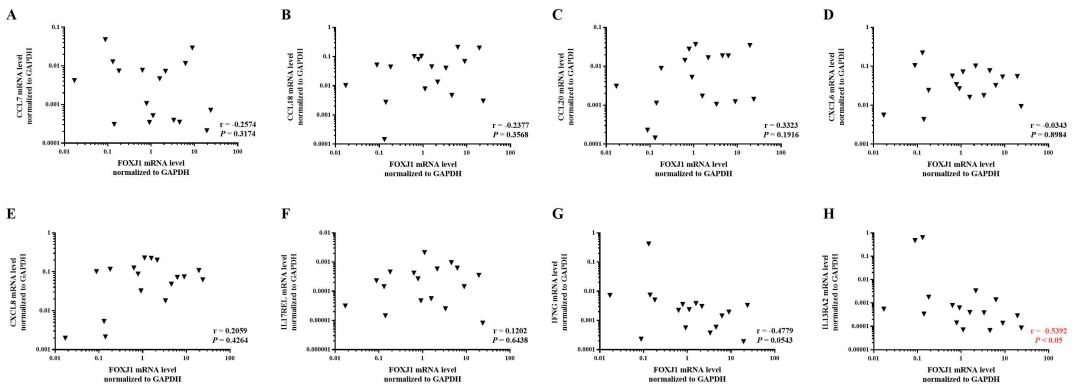


Figure E2

Table E1. The top 20 upregulated and downregulated DEGs.

	Gene Symbol	Gene ID	log2 (ACPs / UPs)	adj. <i>P</i> value (ACPs / UPs)	Chromosome	Start	End
Downregulated DEGs							
	MUC7	4589	-16.62403564	1.70E-21	NC_000004.12	70430492	70482997
	BPIFB3	359710	-15.88696536	4.26E-50	NC_000020.11	33055331	33073637
	PRB1	5542	-15.71601318	3.05E-21	NC_000012.12	11351823	11355590
	C6orf58	352999	-15.28704964	2.54E-71	NC_000006.12	127577174	127591818
	CRISP3	10321	-15.1386356	1.06E-42	NC_000006.12	49727376	49744455
	DMBT1	1755	-13.95930464	1.00E-192	NC_000010.11	122560660	122643817
	SMR3B	10879	-13.59233573	7.21E-09	NC_000004.12	70383078	70390244
	PRB4	5545	-13.43509282	1.64E-35	NC_000012.12	11307081	11310435
	PRB3	5544	-13.36374034	6.58E-33	NC_000012.12	11265914	11269707
	STATH	6779	-13.13359364	5.59E-41	NC_000004.12	69995931	70002456
	GP2	2813	-12.79103618	1.32E-39	NC_000016.10	20309574	20327805
	BPIFB2	80341	-12.39163063	3.87E-91	NC_000020.11	33007578	33023709
	SMR3A	26952	-11.6716528	2.18E-37	NC_000004.12	70360776	70367158
	SOX10	6663	-11.38613416	1.60E-84	NC_000022.11	37970134	37985352
	LPO	4025	-11.2407978	4.01E-151	NC_000017.11	58238426	58268518
	PRR4	11272	-10.78902303	1.50E-62	NC_000012.12	10845849	10849476
	CHRM1	1128	-10.74419971	5.98E-32	NC_000011.10	62908675	62921861
	LTF	4057	-10.70473896	3.07E-109	NC_000003.12	46413625	46508535
	ODAM	54959	-10.34076232	6.02E-68	NC_000004.12	70195728	70204576
	PPP1R1B	84152	-10.12426203	1.01E-128	NC_000017.11	39626735	39637032

**Upregulated
DEGs**

NKX3-2	579	5.909269643	1.24E-06	NC_000004.12	13540830	13544490
S100A8	6279	5.921946067	3.14E-13	NC_000001.11	153390032	153422583
ALPK2	115701	5.93646603	2.87E-12	NC_000018.10	58481247	58629357
MARCO	8685	6.026617329	3.71E-10	NC_000002.12	118942169	118994664
KRTAP1-5	83895	6.053316954	2.80E-04	NC_000017.11	41026026	41027202
MCEMP1	199675	6.119031945	6.93E-08	NC_000019.10	7676063	7761701
SLURP2	432355	6.145396965	4.71E-09	NC_000008.11	142764338	142769828
SMIM6	1E+08	6.289971631	3.92E-08	NC_000017.11	75644790	75648651
CST6	1474	6.389552074	1.78E-08	NC_000011.10	66011991	66013505
WNT2	7472	6.630922646	6.00E-08	NC_000007.14	117276631	117323289
DEFB4A	1673	6.746235489	0.037424564	NC_000008.11	7894565	7896716
PSG5	5673	6.973402433	3.30E-07	NC_000019.10	43166256	43186536
XAGE2	9502	7.001377845	2.06E-05	NC_000023.11	52322375	52384742
CCL18	6362	7.027657774	1.85E-16	NC_000017.11	36064272	36071481
SPRR2A	6700	7.09579701	0.001080139	NC_000001.11	153039725	153057563
PTPRN	5798	7.220755689	3.49E-08	NC_000002.12	219287537	219309605
SPRR3	6707	7.420995754	9.84E-06	NC_000001.11	153001662	153024640
GPR1	2825	7.425895845	5.44E-16	NC_000002.12	206175316	206218047
EPYC	1833	9.740016678	9.31E-09	NC_000012.12	90963679	91007916
CCL7	6354	9.75029787	1.52E-06	NC_000017.11	34270216	34272242

Table E2. GO biological processes (BP) items of the DEGs.

GO_P Term ID	GO_P Term Desc	GO_P Term Level1	GO_P Term Level2	Term Candidate Gene Num	Total Candidate Gene Num	Term Gene Num	Total Gene Num	Rich Ratio	P value	Q value
GO:0030030	cell projection organization	biological_process	cellular component organization or biogenesis	89	3366	195	24363	0.45641	3.87E-27	2.80E-23
GO:0007155	cell adhesion	biological_process	biological adhesion	212	3366	777	24363	0.272844	8.64E-24	3.13E-20
GO:0006954	inflammatory response	biological_process	response to stimulus	149	3366	532	24363	0.280075	3.76E-18	9.07E-15
GO:0002376	immune system process	biological_process	immune system process	145	3366	517	24363	0.280464	9.35E-18	1.69E-14
GO:0003341	cilium movement	biological_process	cellular process	33	3366	51	24363	0.647059	8.04E-17	1.16E-13
GO:0010469	regulation of signaling receptor activity	biological_process	cellular process	128	3366	449	24363	0.285078	1.97E-16	2.38E-13
GO:0030198	extracellular matrix organization	biological_process	cellular process	90	3366	275	24363	0.327273	7.44E-16	7.69E-13
GO:0007166	cell surface receptor signaling pathway	biological_process	regulation of biological process	107	3366	359	24363	0.29805	2.21E-15	1.87E-12
GO:0060271	cilium assembly	biological_process	cellular component organization or biogenesis	83	3366	248	24363	0.334677	2.32E-15	1.87E-12
GO:0006935	chemotaxis	biological_process	locomotion	69	3366	197	24363	0.350254	4.17E-14	3.02E-11
GO:0006811	ion transport	biological_process	localization	167	3366	690	24363	0.242029	9.03E-14	5.95E-11
GO:0007267	cell-cell signaling	biological_process	signaling	85	3366	287	24363	0.296167	2.39E-12	1.44E-09

GO:0030593	neutrophil chemotaxis	biological_process	immune system process	43	3366	105	24363	0.409524	6.88E-12	3.32E-09
GO:0043312	neutrophil degranulation	biological_process	immune system process	163	3366	702	24363	0.232194	6.72E-12	3.32E-09
GO:0055085	transmembrane transport	biological_process	localization	149	3366	625	24363	0.2384	6.82E-12	3.32E-09
GO:0007018	microtubule-based movement	biological_process	cellular process	43	3366	106	24363	0.40566	1.00E-11	4.55E-09
GO:0006955	immune response	biological_process	immune system process	141	3366	598	24363	0.235786	5.77E-11	2.46E-08
GO:0034220	ion transmembrane transport	biological_process	localization	79	3366	287	24363	0.275261	6.86E-10	2.76E-07
GO:0035735	intraciliary transport involved in cilium assembly	biological_process	localization	25	3366	50	24363	0.5	1.11E-09	4.23E-07
GO:0019221	cytokine-mediated signaling pathway	biological_process	biological regulation	97	3366	386	24363	0.251295	1.82E-09	6.59E-07
GO:0010951	negative regulation of endopeptidase activity	biological_process	metabolic process	48	3366	146	24363	0.328767	3.31E-09	1.14E-06
GO:0007165	signal transduction	biological_process	regulation of biological process	397	3366	2201	24363	0.180373	3.54E-09	1.17E-06
GO:0071805	potassium ion transmembrane transport	biological_process	localization	47	3366	143	24363	0.328671	4.85E-09	1.53E-06
GO:0036159	inner dynein arm assembly	biological_process	cellular process	14	3366	19	24363	0.736842	5.28E-09	1.59E-06

GO:0010466	negative regulation of peptidase activity	biological_process	metabolic process	42	3366	122	24363	0.344262	6.71E-09	1.94E-06
GO:0035082	axoneme assembly	biological_process	cellular process	15	3366	22	24363	0.681818	8.07E-09	2.25E-06
GO:0036158	outer dynein arm assembly	biological_process	cellular process	15	3366	23	24363	0.652174	2.02E-08	5.42E-06
GO:0044458	motile cilium assembly	biological_process	cellular process	16	3366	26	24363	0.615385	2.28E-08	5.89E-06
GO:0009612	response to mechanical stimulus	biological_process	response to stimulus	32	3366	85	24363	0.376471	3.68E-08	8.88E-06
GO:0042073	intraciliary transport	biological_process	cellular process	19	3366	36	24363	0.527778	3.57E-08	8.88E-06
GO:0070098	chemokine-mediated signaling pathway	biological_process	biological regulation	31	3366	82	24363	0.378049	5.34E-08	1.25E-05
GO:0055114	oxidation-reduction process	biological_process	metabolic process	159	3366	772	24363	0.205959	9.62E-08	2.18E-05
GO:0001503	ossification	biological_process	multicellular organismal process	39	3366	119	24363	0.327731	1.04E-07	2.29E-05
GO:0007268	chemical synaptic transmission	biological_process	signaling	74	3366	294	24363	0.251701	1.36E-07	2.91E-05
GO:0003351	epithelial cilium movement	biological_process	cellular process	13	3366	20	24363	0.65	1.95E-07	4.04E-05
GO:0007275	multicellular organism development	biological_process	developmental process	239	3366	1272	24363	0.187893	2.42E-07	4.74E-05
GO:0030574	collagen catabolic process	biological_process	metabolic process	20	3366	43	24363	0.465116	2.36E-07	4.74E-05
GO:0070286	axonemal dynein	biological_process	cellular process	10	3366	13	24363	0.769231	4.80E-07	9.15E-05

	complex assembly									
GO:0006814	sodium ion transport	biological_process	localization	41	3366	137	24363	0.29927	7.83E-07	1.45E-04
GO:0001525	angiogenesis	biological_process	developmental process	83	3366	359	24363	0.231198	1.16E-06	2.10E-04
GO:0071300	cellular response to retinoic acid	biological_process	response to stimulus	29	3366	84	24363	0.345238	1.30E-06	2.30E-04
GO:0030199	collagen fibril organization	biological_process	cellular process	25	3366	68	24363	0.367647	1.86E-06	3.20E-04
GO:0002548	monocyte chemotaxis	biological_process	locomotion	22	3366	56	24363	0.392857	2.11E-06	3.55E-04
GO:0019722	calcium-mediated signaling	biological_process	response to stimulus	33	3366	104	24363	0.317308	2.19E-06	3.60E-04
GO:0090023	positive regulation of neutrophil chemotaxis	biological_process	regulation of biological process	15	3366	30	24363	0.5	2.45E-06	3.94E-04
GO:0006813	potassium ion transport	biological_process	localization	42	3366	148	24363	0.283784	2.69E-06	4.24E-04
GO:0007399	nervous system development	biological_process	developmental process	132	3366	652	24363	0.202454	2.98E-06	4.59E-04
GO:0001501	skeletal system development	biological_process	developmental process	49	3366	185	24363	0.264865	3.68E-06	5.44E-04
GO:0060285	cilium-dependent cell motility	biological_process	locomotion	13	3366	24	24363	0.541667	3.65E-06	5.44E-04
GO:0019730	antimicrobial humoral response	biological_process	immune system process	23	3366	62	24363	0.370968	3.97E-06	5.76E-04
GO:0045087	innate immune response	biological_process	response to stimulus	135	3366	674	24363	0.200297	4.13E-06	5.86E-04
GO:0002544	chronic inflammatory	biological_process	response to stimulus	8	3366	10	24363	0.8	4.57E-06	6.24E-04

	response									
GO:0006898	receptor-mediated endocytosis	biological_process	localization	53	3366	207	24363	0.256039	4.50E-06	6.24E-04
GO:0034765	regulation of ion transmembrane transport	biological_process	regulation of biological process	47	3366	177	24363	0.265537	5.34E-06	7.16E-04
GO:0042493	response to drug	biological_process	response to stimulus	86	3366	394	24363	0.218274	8.58E-06	0.00113
GO:0006508	proteolysis	biological_process	metabolic process	140	3366	714	24363	0.196078	8.77E-06	0.001134
GO:0042554	superoxide anion generation	biological_process	metabolic process	10	3366	16	24363	0.625	9.01E-06	0.001145
GO:0007204	positive regulation of cytosolic calcium ion concentration	biological_process	cellular process	50	3366	196	24363	0.255102	9.21E-06	0.00115
GO:0007154	cell communication	biological_process	cellular process	20	3366	53	24363	0.377358	1.24E-05	0.001525
GO:0007368	determination of left/right symmetry	biological_process	developmental process	28	3366	89	24363	0.314607	1.50E-05	0.001808
GO:0070374	positive regulation of ERK1 and ERK2 cascade	biological_process	metabolic process	71	3366	315	24363	0.225397	1.66E-05	0.001969
GO:0007422	peripheral nervous system development	biological_process	developmental process	14	3366	31	24363	0.451613	2.34E-05	0.002691
GO:0019229	regulation of vasoconstriction	biological_process	regulation of biological process	14	3366	31	24363	0.451613	2.34E-05	0.002691
GO:0061844	antimicrobial humoral immune response mediated by	biological_process	immune system process	35	3366	125	24363	0.28	2.41E-05	0.002733

	antimicrobial peptide									
GO:0035235	ionotropic glutamate receptor signaling pathway	biological_process	regulation of biological process	12	3366	24	24363	0.5	2.54E-05	0.002827
GO:0045471	response to ethanol	biological_process	response to stimulus	40	3366	151	24363	0.264901	2.74E-05	0.002965
GO:0048247	lymphocyte chemotaxis	biological_process	immune system process	16	3366	39	24363	0.410256	2.71E-05	0.002965
GO:0007229	integrin-mediated signaling pathway	biological_process	regulation of biological process	39	3366	146	24363	0.267123	2.80E-05	0.002981
GO:0006629	lipid metabolic process	biological_process	metabolic process	113	3366	567	24363	0.199295	3.05E-05	0.003202
GO:0009611	response to wounding	biological_process	response to stimulus	32	3366	112	24363	0.285714	3.42E-05	0.003538
GO:0051965	positive regulation of synapse assembly	biological_process	developmental process	25	3366	79	24363	0.316456	3.77E-05	0.003846
GO:0050777	negative regulation of immune response	biological_process	negative regulation of biological process	9	3366	15	24363	0.6	4.12E-05	0.004146
GO:0006801	superoxide metabolic process	biological_process	metabolic process	12	3366	25	24363	0.48	4.27E-05	0.004232
GO:0007507	heart development	biological_process	developmental process	69	3366	313	24363	0.220447	4.58E-05	0.00448
GO:0033564	anterior/posterior axon guidance	biological_process	developmental process	5	3366	5	24363	1	5.02E-05	0.004663
GO:0046541	saliva secretion	biological_process	localization	5	3366	5	24363	1	5.02E-05	0.004663
GO:0060326	cell chemotaxis	biological_process	locomotion	31	3366	109	24363	0.284404	4.96E-05	0.004663
GO:1901318	negative regulation of flagellated sperm motility	biological_process	regulation of biological process	5	3366	5	24363	1	5.02E-05	0.004663

GO:0030041	actin filament polymerization	biological_process	cellular process	16	3366	41	24363	0.390244	5.63E-05	0.005164
GO:0032496	response to lipopolysaccharide	biological_process	response to stimulus	52	3366	220	24363	0.236364	5.81E-05	0.005232
GO:0044267	cellular protein metabolic process	biological_process	metabolic process	61	3366	270	24363	0.225926	5.85E-05	0.005232
GO:0007200	phospholipase C-activating G protein-coupled receptor signaling pathway	biological_process	regulation of biological process	23	3366	72	24363	0.319444	6.45E-05	0.005696
GO:0007052	mitotic spindle organization	biological_process	cellular process	18	3366	50	24363	0.36	6.93E-05	0.006048
GO:0007288	sperm axoneme assembly	biological_process	developmental process	9	3366	16	24363	0.5625	8.26E-05	0.007125
GO:0002430	complement receptor mediated signaling pathway	biological_process	regulation of biological process	8	3366	13	24363	0.615385	8.84E-05	0.007199
GO:0007626	locomotory behavior	biological_process	behavior	32	3366	117	24363	0.273504	8.66E-05	0.007199
GO:0008284	positive regulation of cell proliferation	biological_process	regulation of biological process	134	3366	710	24363	0.188732	8.70E-05	0.007199
GO:0035721	intraciliary retrograde transport	biological_process	localization	8	3366	13	24363	0.615385	8.84E-05	0.007199
GO:0060287	epithelial cilium movement involved in determination of	biological_process	developmental process	8	3366	13	24363	0.615385	8.84E-05	0.007199

	left/right asymmetry									
GO:0071356	cellular response to tumor necrosis factor	biological_process	response to stimulus	44	3366	180	24363	0.244444	9.13E-05	0.007346
GO:0010628	positive regulation of gene expression	biological_process	metabolic process	104	3366	527	24363	0.197343	9.24E-05	0.007352
GO:0007189	adenylate cyclase-activating G protein-coupled receptor signaling pathway	biological_process	regulation of biological process	33	3366	123	24363	0.268293	1.02E-04	0.008011
GO:0018108	peptidyl-tyrosine phosphorylation	biological_process	cellular process	45	3366	187	24363	0.240642	1.13E-04	0.008831
GO:0010575	positive regulation of vascular endothelial growth factor production	biological_process	regulation of biological process	15	3366	39	24363	0.384615	1.16E-04	0.008843
GO:0045840	positive regulation of mitotic nuclear division	biological_process	positive regulation of biological process	13	3366	31	24363	0.419355	1.17E-04	0.008843
GO:0060349	bone morphogenesis	biological_process	developmental process	15	3366	39	24363	0.384615	1.16E-04	0.008843
GO:0007215	glutamate receptor signaling pathway	biological_process	regulation of biological process	10	3366	20	24363	0.5	1.22E-04	0.008862
GO:0007411	axon guidance	biological_process	developmental process	57	3366	254	24363	0.224409	1.21E-04	0.008862
GO:0035556	intracellular signal transduction	biological_process	regulation of biological process	116	3366	604	24363	0.192053	1.22E-04	0.008862
GO:2000147	positive regulation of	biological_process	regulation of biological	10	3366	20	24363	0.5	1.22E-04	0.008862

	cell motility		process							
GO:0030282	bone mineralization	biological_process	developmental process	18	3366	52	24363	0.346154	1.24E-04	0.008928
GO:0007605	sensory perception of sound	biological_process	multicellular organismal process	45	3366	190	24363	0.236842	1.68E-04	0.011795
GO:0015721	bile acid and bile salt transport	biological_process	localization	12	3366	28	24363	0.428571	1.67E-04	0.011795
GO:0043576	regulation of respiratory gaseous exchange	biological_process	regulation of biological process	7	3366	11	24363	0.636364	1.89E-04	0.01291
GO:0048048	embryonic eye morphogenesis	biological_process	developmental process	7	3366	11	24363	0.636364	1.89E-04	0.01291
GO:0060054	positive regulation of epithelial cell proliferation involved in wound healing	biological_process	regulation of biological process	7	3366	11	24363	0.636364	1.89E-04	0.01291
GO:0030317	flagellated sperm motility	biological_process	localization	24	3366	82	24363	0.292683	2.09E-04	0.014144
GO:0001666	response to hypoxia	biological_process	response to stimulus	52	3366	231	24363	0.225108	2.17E-04	0.014528
GO:0042391	regulation of membrane potential	biological_process	biological regulation	33	3366	128	24363	0.257813	2.30E-04	0.015311
GO:0050806	positive regulation of synaptic transmission	biological_process	regulation of biological process	11	3366	25	24363	0.44	2.36E-04	0.015521
GO:0035987	endodermal cell differentiation	biological_process	developmental process	14	3366	37	24363	0.378378	2.39E-04	0.01561
GO:0051384	response to glucocorticoid	biological_process	response to stimulus	24	3366	83	24363	0.289157	2.56E-04	0.016549

GO:0050729	positive regulation of inflammatory response	biological_process	regulation of biological process	26	3366	93	24363	0.27957	2.62E-04	0.016803
GO:0035873	lactate transmembrane transport	biological_process	localization	5	3366	6	24363	0.833333	2.67E-04	0.016943
GO:0007613	memory	biological_process	multicellular organismal process	30	3366	114	24363	0.263158	2.96E-04	0.018661
GO:0048566	embryonic digestive tract development	biological_process	multicellular organismal process	10	3366	22	24363	0.454545	3.29E-04	0.020537
GO:0035589	G protein-coupled purinergic nucleotide receptor signaling pathway	biological_process	regulation of biological process	8	3366	15	24363	0.533333	3.41E-04	0.021139
GO:0001774	microglial cell activation	biological_process	immune system process	11	3366	26	24363	0.423077	3.58E-04	0.021426
GO:0016485	protein processing	biological_process	metabolic process	21	3366	70	24363	0.3	3.51E-04	0.021426
GO:0038094	Fc-gamma receptor signaling pathway	biological_process	immune system process	4	3366	4	24363	1	3.64E-04	0.021426
GO:0048245	eosinophil chemotaxis	biological_process	immune system process	11	3366	26	24363	0.423077	3.58E-04	0.021426
GO:1903539	protein localization to postsynaptic membrane	biological_process	localization	4	3366	4	24363	1	3.64E-04	0.021426
GO:1990834	response to odorant	biological_process	response to stimulus	4	3366	4	24363	1	3.64E-04	0.021426
GO:0006688	glycosphingolipid	biological_process	metabolic process	6	3366	9	24363	0.666667	3.99E-04	0.022606

	biosynthetic process									
GO:0006936	muscle contraction	biological_process	multicellular organismal process	37	3366	153	24363	0.24183	3.96E-04	0.022606
GO:0035356	cellular triglyceride homeostasis	biological_process	cellular process	6	3366	9	24363	0.666667	3.99E-04	0.022606
GO:0035988	chondrocyte proliferation	biological_process	cell proliferation	7	3366	12	24363	0.583333	3.99E-04	0.022606
GO:0097553	calcium ion transmembrane import into cytosol	biological_process	localization	6	3366	9	24363	0.666667	3.99E-04	0.022606
GO:0007218	neuropeptide signaling pathway	biological_process	regulation of biological process	30	3366	116	24363	0.258621	4.09E-04	0.022785
GO:0043392	negative regulation of DNA binding	biological_process	biological regulation	15	3366	43	24363	0.348837	4.07E-04	0.022785
GO:0001964	startle response	biological_process	response to stimulus	9	3366	19	24363	0.473684	4.51E-04	0.024546
GO:0034097	response to cytokine	biological_process	response to stimulus	22	3366	76	24363	0.289474	4.47E-04	0.024546
GO:0045730	respiratory burst	biological_process	metabolic process	9	3366	19	24363	0.473684	4.51E-04	0.024546
GO:0007162	negative regulation of cell adhesion	biological_process	regulation of biological process	18	3366	57	24363	0.315789	4.57E-04	0.024683
GO:0030154	cell differentiation	biological_process	developmental process	200	3366	1163	24363	0.171969	4.99E-04	0.026754
GO:0045987	positive regulation of smooth muscle contraction	biological_process	regulation of biological process	10	3366	23	24363	0.434783	5.10E-04	0.027169
GO:0045453	bone resorption	biological_process	multicellular organismal process	12	3366	31	24363	0.387097	5.19E-04	0.027418
GO:0007202	activation of	biological_process	biological regulation	15	3366	44	24363	0.340909	5.40E-04	0.028341

	phospholipase C activity									
GO:0042472	inner ear morphogenesis	biological_process	developmental process	24	3366	87	24363	0.275862	5.49E-04	0.028635
GO:0071625	vocalization behavior	biological_process	behavior	8	3366	16	24363	0.5	6.00E-04	0.03062
GO:0097242	amyloid-beta clearance	biological_process	multicellular organismal process	8	3366	16	24363	0.5	6.00E-04	0.03062
GO:0098742	cell-cell adhesion via plasma-membrane adhesion molecules	biological_process	biological adhesion	8	3366	16	24363	0.5	6.00E-04	0.03062
GO:0043547	positive regulation of GTPase activity	biological_process	biological regulation	80	3366	407	24363	0.19656	6.33E-04	0.032088
GO:0048661	positive regulation of smooth muscle cell proliferation	biological_process	cell proliferation	22	3366	78	24363	0.282051	6.61E-04	0.033268
GO:0071347	cellular response to interleukin-1	biological_process	response to stimulus	28	3366	109	24363	0.256881	7.03E-04	0.035117
GO:0042742	defense response to bacterium	biological_process	response to stimulus	49	3366	225	24363	0.217778	7.15E-04	0.035472
GO:1905515	non-motile cilium assembly	biological_process	cellular process	18	3366	59	24363	0.305085	7.25E-04	0.03573
GO:0001523	retinoid metabolic process	biological_process	metabolic process	20	3366	69	24363	0.289855	7.83E-04	0.038303
GO:0022617	extracellular matrix disassembly	biological_process	cellular process	23	3366	84	24363	0.27381	7.95E-04	0.038637
GO:0002283	neutrophil activation	biological_process	response to stimulus	5	3366	7	24363	0.714286	8.26E-04	0.038868

	involved in immune response									
GO:0003356	regulation of cilium beat frequency	biological_process	regulation of biological process	5	3366	7	24363	0.714286	8.26E-04	0.038868
GO:0006600	creatine metabolic process	biological_process	metabolic process	5	3366	7	24363	0.714286	8.26E-04	0.038868
GO:0021532	neural tube patterning	biological_process	developmental process	5	3366	7	24363	0.714286	8.26E-04	0.038868
GO:0045630	positive regulation of T-helper 2 cell differentiation	biological_process	developmental process	5	3366	7	24363	0.714286	8.26E-04	0.038868
GO:0003416	endochondral bone growth	biological_process	developmental process	6	3366	10	24363	0.6	8.82E-04	0.040673
GO:0009968	negative regulation of signal transduction	biological_process	regulation of biological process	30	3366	121	24363	0.247934	8.70E-04	0.040673
GO:0090238	positive regulation of arachidonic acid secretion	biological_process	regulation of biological process	6	3366	10	24363	0.6	8.82E-04	0.040673
GO:0031175	neuron projection development	biological_process	developmental process	40	3366	176	24363	0.227273	8.93E-04	0.040965
GO:0006816	calcium ion transport	biological_process	localization	38	3366	165	24363	0.230303	9.11E-04	0.041502
GO:0051897	positive regulation of protein kinase B signaling	biological_process	regulation of biological process	47	3366	216	24363	0.217593	9.23E-04	0.04181
GO:0042130	negative regulation of T cell proliferation	biological_process	negative regulation of biological process	20	3366	70	24363	0.285714	9.55E-04	0.042981
GO:0035725	sodium ion	biological_process	localization	21	3366	75	24363	0.28	9.63E-04	0.04304

	transmembrane transport									
GO:0002526	acute inflammatory response	biological_process	response to stimulus	8	3366	17	24363	0.470588	9.97E-04	0.04333
GO:0002687	positive regulation of leukocyte migration	biological_process	regulation of biological process	8	3366	17	24363	0.470588	9.97E-04	0.04333
GO:0008589	regulation of smoothed signaling pathway	biological_process	response to stimulus	12	3366	33	24363	0.363636	9.99E-04	0.04333
GO:0060134	prepulse inhibition	biological_process	regulation of biological process	8	3366	17	24363	0.470588	9.97E-04	0.04333
GO:0060294	cilium movement involved in cell motility	biological_process	locomotion	8	3366	17	24363	0.470588	9.97E-04	0.04333
GO:0014065	phosphatidylinositol 3-kinase signaling	biological_process	regulation of biological process	14	3366	42	24363	0.333333	0.001056	0.045253
GO:0051930	regulation of sensory perception of pain	biological_process	regulation of biological process	14	3366	42	24363	0.333333	0.001056	0.045253
GO:0006833	water transport	biological_process	localization	10	3366	25	24363	0.4	0.001121	0.047478
GO:0032331	negative regulation of chondrocyte differentiation	biological_process	developmental process	10	3366	25	24363	0.4	0.001121	0.047478
GO:0007611	learning or memory	biological_process	behavior	21	3366	76	24363	0.276316	0.001159	0.048831
GO:0006836	neurotransmitter transport	biological_process	localization	15	3366	47	24363	0.319149	0.001177	0.049288
GO:0014070	response to organic	biological_process	response to stimulus	34	3366	145	24363	0.234483	0.001186	0.049387

	cyclic compound									
GO:0060325	face morphogenesis	biological_process	developmental process	13	3366	38	24363	0.342105	0.001203	0.049791

Table E3. GO cellular component (CC) items of the DEGs.

GO_C Term ID	GO_C Term Desc	GO_C Term Level1	GO_C Term Level2	Term Candidate Gene Num	Total Candidate Gene Num	Term Gene Num	Total Gene Num	Rich Ratio	P value	Q value
GO:0005576	extracellular region	cellular_component	extracellular region	716	3524	2865	25187	0.249913	3.92E-63	3.94E-60
GO:0005615	extracellular space	cellular_component	extracellular region part	493	3524	1870	25187	0.263636	3.87E-49	1.94E-46
GO:0005929	cilium	cellular_component	organelle	176	3524	422	25187	0.417062	5.96E-45	1.99E-42
GO:0042995	cell projection	cellular_component	cell part	303	3524	988	25187	0.30668	2.75E-43	6.91E-41
GO:0016020	membrane	cellular_component	membrane	1694	3524	9539	25187	0.177587	1.33E-40	2.67E-38
GO:0005886	plasma membrane	cellular_component	cell	1200	3524	6315	25187	0.190024	3.02E-38	5.06E-36
GO:0016021	integral component of membrane	cellular_component	membrane part	1294	3524	7102	25187	0.182202	1.14E-32	1.63E-30
GO:0031012	extracellular matrix	cellular_component	extracellular region	134	3524	343	25187	0.390671	5.76E-31	7.22E-29
GO:0005856	cytoskeleton	cellular_component	organelle	361	3524	1446	25187	0.249654	1.86E-30	1.86E-28
GO:0005887	integral component of plasma membrane	cellular_component	membrane part	422	3524	1778	25187	0.237345	1.82E-30	1.86E-28
GO:0062023	collagen-containing extracellular matrix	cellular_component	extracellular region part	142	3524	414	25187	0.342995	5.99E-26	5.47E-24
GO:0031514	motile cilium	cellular_component	organelle	79	3524	182	25187	0.434066	3.55E-22	2.97E-20
GO:0005930	axoneme	cellular_component	organelle	62	3524	131	25187	0.473282	4.70E-20	3.63E-18
GO:0005581	collagen trimer	cellular_component	protein-containing complex	52	3524	104	25187	0.5	2.27E-18	1.63E-16
GO:0009986	cell surface	cellular_component	cell	204	3524	900	25187	0.226667	6.08E-13	4.07E-11

GO:0031225	anchored component of membrane	cellular_component	membrane	59	3524	165	25187	0.357576	1.79E-12	1.13E-10
GO:0030054	cell junction	cellular_component	cell junction	216	3524	1016	25187	0.212598	7.84E-11	4.63E-09
GO:0097542	ciliary tip	cellular_component	organelle	28	3524	56	25187	0.5	1.51E-10	8.44E-09
GO:0030286	dynein complex	cellular_component	organelle	24	3524	45	25187	0.533333	5.55E-10	2.93E-08
GO:0043235	receptor complex	cellular_component	protein-containing complex	71	3524	246	25187	0.288618	9.27E-10	4.66E-08
GO:0005874	microtubule	cellular_component	organelle	116	3524	483	25187	0.240166	1.97E-09	9.42E-08
GO:0009897	external side of plasma membrane	cellular_component	membrane	92	3524	362	25187	0.254144	4.92E-09	2.24E-07
GO:0036126	sperm flagellum	cellular_component	organelle	26	3524	56	25187	0.464286	5.17E-09	2.26E-07
GO:0060076	excitatory synapse	cellular_component	synapse	20	3524	37	25187	0.540541	1.13E-08	4.64E-07
GO:0070821	tertiary granule membrane	cellular_component	organelle	36	3524	97	25187	0.371134	1.16E-08	4.64E-07
GO:0005788	endoplasmic reticulum lumen	cellular_component	membrane-enclosed lumen	92	3524	379	25187	0.242744	5.26E-08	2.03E-06
GO:0045202	synapse	cellular_component	synapse	153	3524	723	25187	0.211618	6.42E-08	2.39E-06
GO:0030667	secretory granule membrane	cellular_component	organelle	45	3524	144	25187	0.3125	8.31E-08	2.98E-06
GO:0030992	intraciliary transport particle B	cellular_component	protein-containing complex	17	3524	31	25187	0.548387	1.08E-07	3.74E-06
GO:0005604	basement membrane	cellular_component	extracellular region part	39	3524	121	25187	0.322314	2.40E-07	8.04E-06
GO:0043025	neuronal cell body	cellular_component	cell	119	3524	548	25187	0.217153	4.64E-07	1.50E-05
GO:0016324	apical plasma	cellular_component	membrane part	96	3524	430	25187	0.223256	1.66E-06	5.04E-05

	membrane									
GO:0030141	secretory granule	cellular_component	organelle	37	3524	120	25187	0.308333	1.63E-06	5.04E-05
GO:0035579	specific granule membrane	cellular_component	organelle	35	3524	115	25187	0.304348	4.27E-06	1.21E-04
GO:0036038	MKS complex	cellular_component	organelle	10	3524	15	25187	0.666667	4.34E-06	1.21E-04
GO:0043005	neuron projection	cellular_component	cell	106	3524	496	25187	0.21371	4.12E-06	1.21E-04
GO:0030424	axon	cellular_component	cell part	100	3524	466	25187	0.214592	6.34E-06	1.72E-04
GO:0099061	integral component of postsynaptic density membrane	cellular_component	membrane	22	3524	61	25187	0.360656	1.33E-05	3.52E-04
GO:0032391	photoreceptor connecting cilium	cellular_component	organelle	19	3524	51	25187	0.372549	3.02E-05	7.77E-04
GO:0005737	cytoplasm	cellular_component	cell part	1286	3524	8450	25187	0.152189	3.90E-05	9.80E-04
GO:0036064	ciliary basal body	cellular_component	organelle	54	3524	228	25187	0.236842	5.65E-05	0.001384
GO:0045211	postsynaptic membrane	cellular_component	membrane	71	3524	323	25187	0.219814	5.95E-05	0.001423
GO:0043020	NADPH oxidase complex	cellular_component	membrane	8	3524	13	25187	0.615385	9.70E-05	0.002265
GO:1903561	extracellular vesicle	cellular_component	organelle	22	3524	70	25187	0.314286	1.46E-04	0.00333
GO:0031234	extrinsic component of cytoplasmic side of plasma membrane	cellular_component	membrane	25	3524	85	25187	0.294118	1.75E-04	0.003905
GO:0097546	ciliary base	cellular_component	organelle	16	3524	45	25187	0.355556	2.38E-04	0.005186
GO:0035580	specific granule lumen	cellular_component	organelle	24	3524	82	25187	0.292683	2.54E-04	0.00542

GO:0097729	9+2 motile cilium	cellular_component	organelle	5	3524	6	25187	0.833333	2.84E-04	0.005931
GO:0005858	axonemal dynein complex	cellular_component	organelle	9	3524	18	25187	0.5	2.98E-04	0.006107
GO:0005922	connexin complex	cellular_component	cell junction	10	3524	22	25187	0.454545	3.65E-04	0.007052
GO:0016529	sarcoplasmic reticulum	cellular_component	cell part	22	3524	74	25187	0.297297	3.54E-04	0.007052
GO:0097228	sperm principal piece	cellular_component	organelle	10	3524	22	25187	0.454545	3.65E-04	0.007052
GO:0031262	Ndc80 complex	cellular_component	organelle	4	3524	4	25187	1	3.83E-04	0.007249
GO:0017146	NMDA selective glutamate receptor complex	cellular_component	membrane	7	3524	12	25187	0.583333	4.32E-04	0.007892
GO:0036157	outer dynein arm	cellular_component	organelle	6	3524	9	25187	0.666667	4.29E-04	0.007892
GO:0005813	centrosome	cellular_component	organelle	121	3524	649	25187	0.186441	5.11E-04	0.009169
GO:0005871	kinesin complex	cellular_component	organelle	22	3524	78	25187	0.282051	7.86E-04	0.013614
GO:0101003	ficolin-1-rich granule membrane	cellular_component	organelle	22	3524	78	25187	0.282051	7.86E-04	0.013614
GO:0072686	mitotic spindle	cellular_component	organelle	28	3524	109	25187	0.256881	8.59E-04	0.014623
GO:0005879	axonemal microtubule	cellular_component	organelle	5	3524	7	25187	0.714286	8.77E-04	0.01468
GO:0008076	voltage-gated potassium channel complex	cellular_component	membrane	26	3524	99	25187	0.262626	9.08E-04	0.014946
GO:0043229	intracellular organelle	cellular_component	organelle	6	3524	10	25187	0.6	9.45E-04	0.015053
GO:0044309	neuron spine	cellular_component	cell part	6	3524	10	25187	0.6	9.45E-04	0.015053

GO:0031982	vesicle	cellular_component	organelle	48	3524	220	25187	0.218182	0.001017	0.015954
GO:0042629	mast cell granule	cellular_component	organelle	11	3524	29	25187	0.37931	0.001198	0.018506
GO:0045121	membrane raft	cellular_component	membrane	64	3524	317	25187	0.201893	0.001438	0.02187
GO:0016323	basolateral plasma membrane	cellular_component	cell part	58	3524	282	25187	0.205674	0.001493	0.022373
GO:0000776	kinetochore	cellular_component	organelle	35	3524	151	25187	0.231788	0.001571	0.023196
GO:0032010	phagolysosome	cellular_component	organelle	4	3524	5	25187	0.8	0.001699	0.024726
GO:0005814	centriole	cellular_component	organelle	46	3524	214	25187	0.214953	0.001756	0.02519
GO:0098688	parallel fiber to Purkinje cell synapse	cellular_component	synapse	9	3524	22	25187	0.409091	0.001799	0.02544
GO:0005861	troponin complex	cellular_component	organelle	5	3524	8	25187	0.625	0.002069	0.028456
GO:0098978	glutamatergic synapse	cellular_component	synapse	92	3524	492	25187	0.186992	0.002043	0.028456
GO:0042734	presynaptic membrane	cellular_component	membrane	25	3524	100	25187	0.25	0.002368	0.032132
GO:0030425	dendrite	cellular_component	cell part	106	3524	582	25187	0.182131	0.002407	0.032227
GO:0001669	acrosomal vesicle	cellular_component	organelle	27	3524	111	25187	0.243243	0.00248	0.03281

									4	
GO:0000777	condensed chromosome kinetochore	cellular_component	organelle	30	3524	128	25187	0.234375	0.002728	0.033924
GO:0001536	radial spoke stalk	cellular_component	organelle	3	3524	3	25187	1	0.002737	0.033924
GO:0005589	collagen type VI trimer	cellular_component	protein-containing complex	3	3524	3	25187	1	0.002737	0.033924
GO:0005594	collagen type IX trimer	cellular_component	protein-containing complex	3	3524	3	25187	1	0.002737	0.033924
GO:0097545	axonemal outer doublet	cellular_component	organelle	3	3524	3	25187	1	0.002737	0.033924
GO:0005815	microtubule organizing center	cellular_component	organelle	92	3524	497	25187	0.185111	0.002773	0.033946
GO:0005881	cytoplasmic microtubule	cellular_component	organelle	18	3524	65	25187	0.276923	0.002837	0.03432
GO:0031410	cytoplasmic vesicle	cellular_component	organelle	136	3524	776	25187	0.175258	0.002925	0.034717
GO:0046658	anchored component of plasma membrane	cellular_component	membrane	13	3524	41	25187	0.317073	0.002939	0.034717
GO:0051233	spindle midzone	cellular_component	organelle	12	3524	37	25187	0.324324	0.003414	0.039853
GO:0042383	sarcolemma	cellular_component	membrane	33	3524	147	25187	0.22449	0.003605	0.041604
GO:0043197	dendritic spine	cellular_component	cell part	40	3524	188	25187	0.212766	0.00404	0.046182

									8	
GO:0030991	intraciliary transport particle A	cellular_component	protein-containing complex	5	3524	9	25187	0.555556	0.004119	0.04647
GO:0071944	cell periphery	cellular_component	cell part	22	3524	88	25187	0.25	0.004185	0.046683
GO:0000942	condensed nuclear chromosome outer kinetochore	cellular_component	membrane-enclosed lumen	4	3524	6	25187	0.666667	0.004531	0.049989

Table E4. GO molecular function (MF) items of the DEGs.

GO_F Term ID	GO_F Term Desc	GO_F Term Level1	GO_F Term Level2	Term Candidate Gene Num	Total Candidate Gene Num	Term Gene Num	Total Gene Num	Rich Ratio	P value	Q value
GO:0005515	protein binding	molecular_function	binding	1680	3343	9446	24468	0.177853	3.05E-49	6.70E-46
GO:0005509	calcium ion binding	molecular_function	binding	243	3343	946	24468	0.256871	7.54E-24	8.29E-21
GO:0005201	extracellular matrix structural constituent	molecular_function	structural molecule activity	62	3343	174	24468	0.356322	2.02E-13	1.48E-10
GO:0008201	heparin binding	molecular_function	binding	69	3343	226	24468	0.30531	3.67E-11	2.02E-08
GO:0003774	motor activity	molecular_function	catalytic activity	46	3343	132	24468	0.348485	5.75E-10	1.86E-07
GO:0030020	extracellular matrix structural constituent conferring tensile strength	molecular_function	structural molecule activity	22	3343	39	24468	0.564103	4.35E-10	1.86E-07
GO:0030246	carbohydrate binding	molecular_function	binding	76	3343	274	24468	0.277372	5.91E-10	1.86E-07
GO:0016491	oxidoreductase activity	molecular_function	catalytic activity	140	3343	620	24468	0.225806	7.17E-10	1.97E-07
GO:0005125	cytokine activity	molecular_function	binding	71	3343	255	24468	0.278431	1.79E-09	4.38E-07
GO:0003777	microtubule motor	molecular_function	catalytic activity	37	3343	101	24468	0.366337	5.71E-09	1.26E-06

7	activity									
GO:000488 8	transmembrane signaling receptor activity	molecular_function	molecular transducer activity	92	3343	376	24468	0.244681	1.11E-08	2.22E-06
GO:003041 4	peptidase inhibitor activity	molecular_function	molecular function regulator	41	3343	121	24468	0.338843	1.23E-08	2.26E-06
GO:003802 3	signaling receptor activity	molecular_function	molecular transducer activity	84	3343	341	24468	0.246334	3.43E-08	5.81E-06
GO:000857 4	ATP-dependent microtubule motor activity, plus-end-directed	molecular_function	catalytic activity	17	3343	31	24468	0.548387	7.57E-08	1.19E-05
GO:000425 2	serine-type endopeptidase activity	molecular_function	catalytic activity	70	3343	275	24468	0.254545	1.20E-07	1.76E-05
GO:000497 0	ionotropic glutamate receptor activity	molecular_function	molecular transducer activity	12	3343	18	24468	0.666667	3.45E-07	4.75E-05
GO:000823 6	serine-type peptidase activity	molecular_function	catalytic activity	49	3343	174	24468	0.281609	3.81E-07	4.94E-05
GO:004550 3	dynein light chain binding	molecular_function	binding	17	3343	35	24468	0.485714	7.50E-07	9.17E-05
GO:000510 2	signaling receptor binding	molecular_function	binding	122	3343	586	24468	0.208191	9.46E-07	1.10E-04
GO:000521 6	ion channel activity	molecular_function	transporter activity	53	3343	201	24468	0.263682	1.24E-06	1.37E-04
GO:000489 6	cytokine receptor activity	molecular_function	molecular transducer activity	19	3343	44	24468	0.431818	1.62E-06	1.70E-04

GO:0005244	voltage-gated ion channel activity	molecular_function	transporter activity	45	3343	163	24468	0.276074	2.02E-06	2.02E-04
GO:0005518	collagen binding	molecular_function	binding	29	3343	87	24468	0.333333	2.34E-06	2.24E-04
GO:0008233	peptidase activity	molecular_function	catalytic activity	113	3343	544	24468	0.207721	2.63E-06	2.41E-04
GO:0003674	molecular_function	molecular_function	molecular_function	151	3343	777	24468	0.194337	3.53E-06	3.11E-04
GO:0005044	scavenger receptor activity	molecular_function	cargo receptor activity	23	3343	63	24468	0.365079	4.50E-06	3.81E-04
GO:0008289	lipid binding	molecular_function	binding	76	3343	341	24468	0.222874	8.73E-06	7.12E-04
GO:0015293	symporter activity	molecular_function	transporter activity	36	3343	127	24468	0.283465	1.08E-05	8.48E-04
GO:0008009	chemokine activity	molecular_function	binding	22	3343	62	24468	0.354839	1.22E-05	9.29E-04
GO:0048020	CCR chemokine receptor binding	molecular_function	binding	15	3343	34	24468	0.441176	1.48E-05	0.001085
GO:0005178	integrin binding	molecular_function	binding	47	3343	186	24468	0.252688	1.64E-05	0.001155
GO:0008083	growth factor activity	molecular_function	molecular function regulator	52	3343	213	24468	0.244131	1.69E-05	0.001155
GO:0030021	extracellular matrix structural constituent conferring compression	molecular_function	structural molecule activity	10	3343	17	24468	0.588235	1.73E-05	0.001155

	resistance									
GO:005084 0	extracellular matrix binding	molecular_function	binding	16	3343	39	24468	0.410256	2.35E-05	0.001522
GO:000486 7	serine-type endopeptidase inhibitor activity	molecular_function	molecular function regulator	34	3343	122	24468	0.278689	2.76E-05	0.001737
GO:000801 7	microtubule binding	molecular_function	binding	75	3343	347	24468	0.216138	3.04E-05	0.001856
GO:001986 4	IgG binding	molecular_function	binding	9	3343	15	24468	0.6	3.76E-05	0.002179
GO:004550 4	dynein heavy chain binding	molecular_function	binding	9	3343	15	24468	0.6	3.76E-05	0.002179
GO:001995 5	cytokine binding	molecular_function	binding	18	3343	49	24468	0.367347	4.38E-05	0.002471
GO:000526 7	potassium channel activity	molecular_function	transporter activity	26	3343	86	24468	0.302326	5.27E-05	0.002899
GO:000553 9	glycosaminoglycan binding	molecular_function	binding	13	3343	30	24468	0.433333	6.92E-05	0.003715
GO:001617 5	superoxide-generating NADPH oxidase activity	molecular_function	catalytic activity	7	3343	10	24468	0.7	7.25E-05	0.0038
GO:001512 5	bile acid transmembrane transporter activity	molecular_function	transporter activity	8	3343	13	24468	0.615385	8.15E-05	0.004172
GO:000823 7	metallopeptidase activity	molecular_function	catalytic activity	44	3343	182	24468	0.241758	9.25E-05	0.004627

GO:0002020	protease binding	molecular_function	binding	36	3343	141	24468	0.255319	1.21E-04	0.00592
GO:0004222	metalloendopeptidase activity	molecular_function	catalytic activity	37	3343	148	24468	0.25	1.56E-04	0.007482
GO:0008329	signaling pattern recognition receptor activity	molecular_function	molecular transducer activity	7	3343	11	24468	0.636364	1.76E-04	0.008231
GO:0045505	dynein intermediate chain binding	molecular_function	binding	15	3343	41	24468	0.365854	1.97E-04	0.009044
GO:0005042	netrin receptor activity	molecular_function	molecular transducer activity	5	3343	6	24468	0.833333	2.53E-04	0.011116
GO:0043394	proteoglycan binding	molecular_function	binding	9	3343	18	24468	0.5	2.48E-04	0.011116
GO:0005319	lipid transporter activity	molecular_function	transporter activity	14	3343	38	24468	0.368421	2.94E-04	0.012693
GO:0017147	Wnt-protein binding	molecular_function	binding	16	3343	47	24468	0.340426	3.19E-04	0.013244
GO:0045028	G protein-coupled purinergic nucleotide receptor activity	molecular_function	molecular transducer activity	8	3343	15	24468	0.533333	3.16E-04	0.013244
GO:0004522	ribonuclease A activity	molecular_function	catalytic activity	4	3343	4	24468	1	3.48E-04	0.014181
GO:0016174	NAD(P)H oxidase activity	molecular_function	catalytic activity	6	3343	9	24468	0.666667	3.75E-04	0.015016
GO:0005249	voltage-gated potassium channel	molecular_function	transporter activity	21	3343	73	24468	0.287671	5.63E-04	0.021516

	activity									
GO:000819 1	metalloendopeptidase inhibitor activity	molecular_function	molecular function regulator	8	3343	16	24468	0.5	5.56E-04	0.021516
GO:001670 5	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	molecular_function	catalytic activity	22	3343	78	24468	0.282051	5.67E-04	0.021516
GO:000526 1	cation channel activity	molecular_function	transporter activity	13	3343	36	24468	0.361111	6.02E-04	0.022449
GO:004830 6	calcium-dependent protein binding	molecular_function	binding	24	3343	89	24468	0.269663	6.68E-04	0.024497
GO:001995 6	chemokine binding	molecular_function	binding	10	3343	24	24468	0.416667	7.01E-04	0.025232
GO:004840 7	platelet-derived growth factor binding	molecular_function	binding	7	3343	13	24468	0.538462	7.11E-04	0.025232
GO:001512 9	lactate transmembrane transporter activity	molecular_function	transporter activity	5	3343	7	24468	0.714286	7.84E-04	0.027379
GO:000381 0	protein-glutamine gamma-glutamyltransferase activity	molecular_function	catalytic activity	6	3343	10	24468	0.6	8.29E-04	0.027777
GO:000551 6	calmodulin binding	molecular_function	binding	56	3343	270	24468	0.207407	8.33E-04	0.027777
GO:000804	axon guidance	molecular_function	molecular	6	3343	10	24468	0.6	8.29E-04	0.027777

6	receptor activity		transducer activity							
GO:0001540	amyloid-beta binding	molecular_function	binding	26	3343	101	24468	0.257426	8.76E-04	0.028768
GO:0005031	tumor necrosis factor-activated receptor activity	molecular_function	molecular transducer activity	8	3343	17	24468	0.470588	9.24E-04	0.029483
GO:0015269	calcium-activated potassium channel activity	molecular_function	transporter activity	8	3343	17	24468	0.470588	9.24E-04	0.029483
GO:0008569	ATP-dependent microtubule motor activity, minus-end-directed	molecular_function	catalytic activity	10	3343	25	24468	0.4	0.001026	0.031807
GO:0042813	Wnt-activated receptor activity	molecular_function	molecular transducer activity	10	3343	25	24468	0.4	0.001026	0.031807
GO:0005272	sodium channel activity	molecular_function	transporter activity	12	3343	34	24468	0.352941	0.001224	0.037414
GO:0005520	insulin-like growth factor binding	molecular_function	binding	11	3343	30	24468	0.366667	0.001358	0.040932
GO:0001968	fibronectin binding	molecular_function	binding	13	3343	39	24468	0.333333	0.001423	0.041757
GO:0005496	steroid binding	molecular_function	binding	13	3343	39	24468	0.333333	0.001423	0.041757
GO:0004656	procollagen-proline 4-dioxygenase activity	molecular_function	catalytic activity	4	3343	5	24468	0.8	0.00155	0.042108

GO:0005007	fibroblast growth factor-activated receptor activity	molecular_function	molecular transducer activity	4	3343	5	24468	0.8	0.00155	0.042108
GO:0005008	Ras guanyl-nucleotide exchange factor activity	molecular_function	binding	35	3343	154	24468	0.227273	0.001487	0.042108
GO:0016787	hydrolase activity	molecular_function	catalytic activity	268	3343	1659	24468	0.161543	0.001513	0.042108
GO:0031005	filamin binding	molecular_function	binding	8	3343	18	24468	0.444444	0.001465	0.042108
GO:0031727	CCR2 chemokine receptor binding	molecular_function	binding	4	3343	5	24468	0.8	0.00155	0.042108
GO:0004972	NMDA glutamate receptor activity	molecular_function	molecular transducer activity	5	3343	8	24468	0.625	0.001854	0.049078
GO:0030550	acetylcholine receptor inhibitor activity	molecular_function	molecular function regulator	5	3343	8	24468	0.625	0.001854	0.049078
GO:0046934	phosphatidylinositol-4,5-bisphosphate 3-kinase activity	molecular_function	catalytic activity	23	3343	90	24468	0.255556	0.001873	0.049078

Table E5. KEGG pathways of the DEGs.

KEGG Pathway Term ID	KEGG Pathway Term Desc	KEGG Pathway Term Level1	KEGG Pathway Term Level2	Term Candidate Gene Num	Total Candidate Gene Num	Term Gene Num	Total Gene Num	Rich Ratio	P value	Q value
4060	Cytokine-cytokine receptor interaction	Environmental Information Processing	Signaling molecules and interaction	115	2147	371	15870	0.309973	1.02E-18	3.73E-16
4080	Neuroactive ligand-receptor interaction	Environmental Information Processing	Signaling molecules and interaction	90	2147	338	15870	0.266272	8.30E-11	1.51E-08
4974	Protein digestion and absorption	Organismal Systems	Digestive system	40	2147	105	15870	0.380952	2.50E-10	3.03E-08
4970	Salivary secretion	Organismal Systems	Digestive system	39	2147	110	15870	0.354545	4.68E-09	4.26E-07
4024	cAMP signaling pathway	Environmental Information Processing	Signal transduction	61	2147	255	15870	0.239216	4.53E-06	3.30E-04
4380	Osteoclast differentiation	Organismal Systems	Development	52	2147	210	15870	0.247619	7.95E-06	4.32E-04
4724	Glutamatergic synapse	Organismal Systems	Nervous system	38	2147	137	15870	0.277372	8.30E-06	4.32E-04
4512	ECM-receptor interaction	Environmental Information Processing	Signaling molecules and interaction	35	2147	126	15870	0.277778	1.79E-05	8.17E-04
4062	Chemokine signaling	Organismal Systems	Immune system	58	2147	252	15870	0.230159	2.62E-05	0.001059

	pathway									
4972	Pancreatic secretion	Organismal Systems	Digestive system	31	2147	111	15870	0.279279	4.72E-05	0.00167
5146	Amoebiasis	Human Diseases	Infectious diseases: Parasitic	36	2147	137	15870	0.262774	5.05E-05	0.00167
590	Arachidonic acid metabolism	Metabolism	Lipid metabolism	24	2147	82	15870	0.292683	1.49E-04	0.004396
4610	Complement and coagulation cascades	Organismal Systems	Immune system	31	2147	118	15870	0.262712	1.64E-04	0.004396
4750	Inflammatory mediator regulation of TRP channels	Organismal Systems	Sensory system	31	2147	119	15870	0.260504	1.93E-04	0.004396
4976	Bile secretion	Organismal Systems	Digestive system	24	2147	83	15870	0.289157	1.83E-04	0.004396
5200	Pathways in cancer	Human Diseases	Cancers: Overview	133	2147	733	15870	0.181446	1.91E-04	0.004396
260	Glycine, serine and threonine metabolism	Metabolism	Amino acid metabolism	17	2147	51	15870	0.333333	2.45E-04	0.005252
5033	Nicotine addiction	Human Diseases	Substance dependence	15	2147	43	15870	0.348837	3.21E-04	0.006489
4657	IL-17 signaling pathway	Organismal Systems	Immune system	32	2147	129	15870	0.248062	4.00E-04	0.007667

5144	Malaria	Human Diseases	Infectious diseases: Parasitic	20	2147	68	15870	0.294118	4.79E-04	0.008726
5219	Bladder cancer	Human Diseases	Cancers: Specific types	17	2147	56	15870	0.303571	8.37E-04	0.014511
4933	AGE-RAGE signaling pathway in diabetic complications	Human Diseases	Endocrine and metabolic diseases	31	2147	131	15870	0.236641	0.001139	0.018847
591	Linoleic acid metabolism	Metabolism	Lipid metabolism	12	2147	35	15870	0.342857	0.001491	0.022863
4020	Calcium signaling pathway	Environmental Information Processing	Signal transduction	52	2147	256	15870	0.203125	0.00157	0.022863
4670	Leukocyte transendothelial migration	Organismal Systems	Immune system	35	2147	156	15870	0.224359	0.001556	0.022863
4978	Mineral absorption	Organismal Systems	Digestive system	18	2147	66	15870	0.272727	0.002325	0.032546
4911	Insulin secretion	Organismal Systems	Endocrine system	25	2147	104	15870	0.240385	0.00261	0.035185
5418	Fluid shear stress and atherosclerosis	Human Diseases	Cardiovascular diseases	41	2147	198	15870	0.207071	0.003241	0.042133
5231	Choline	Human Diseases	Cancers:	30	2147	135	15870	0.222222	0.003758	0.047169

	metabolism in cancer		Overview							
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Table E6. The GSEA parameters details.

database_name:	msigdb_c5_bp
database_version:	MSigDB database v6.2
control_group_name:	Con
treat_group_name:	ACP
control_group_sample:	tpm_Con1, tpm_Con2, tpm_Con3, tpm_Con4, tpm_Con5, tpm_Con6
treat_group_sample:	tpm_ACP1, tpm_ACP2, tpm_ACP3, tpm_ACP4, tpm_ACP5, tpm_ACP6
gene_num:	18914
gsea_metric:	Signal2Noise
gsea_permute:	gene_set
gsea_nperm:	1000
gsea_set_min:	15
gsea_set_max:	500
gsea_order:	descending
gsea_version:	gsea-3.0

Table E7.The GSEA items.

NAME	MSigDB C5(GO) biological processes Term Desc	Original size	Size (after restricting to dataset)	ES	NES	NOM p-val	FDR q-val	RANK AT MAX	LEADING EDGE
GO_CILIUM_ORGANIZATION	A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of a cilium, a specialized eukaryotic organelle that consists of a filiform extrusion of the cell surface. Each cilium is bounded by an extrusion of the cytoplasmic membrane, and contains a regular longitudinal array of microtubules, anchored basally in a centriole.	188	187	0.586377	2.25303	0	0	6094	tags=79%, list=32%, signal=115%
GO_CILIUM_MORPHOGENESIS	A process that is carried out at the cellular level and in which the structure of a cilium is organized.	207	205	0.582078	2.245388	0	0	6094	tags=77%, list=32%, signal=112%
GO_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_EXOGENOUS_PEPTIDE_ANTIGEN_VIA_MHC_CLASS_I	The process in which an antigen-presenting cell expresses a peptide antigen of exogenous origin on its cell surface in association with an MHC class I protein complex. The peptide antigen is typically, but not always, processed from a whole protein. Class I here refers to classical class I molecules.	66	65	0.609771	2.146041	0	3.14E-04	4810	tags=68%, list=25%, signal=90%
GO_CILIUM_MOVEMENT	The directed, self-propelled movement of a cilium.	36	36	0.654985	2.12425	0	2.36E-04	6210	tags=92%, list=33%,

									signal=136%
GO_AXONEME_ASSEMBLY	The assembly and organization of an axoneme, the bundle of microtubules and associated proteins that forms the core of cilia (also called flagella) in eukaryotic cells and is responsible for their movements.	44	44	0.626592	2.088422	0	0.0011 32	6210	tags=89%, list=33%, signal=132%
GO_ANAPHASE_PROMOTING_COMPLEX_DEPENDENT_CATABOLIC_PROCESS	The chemical reactions and pathways resulting in the breakdown of a protein or peptide by hydrolysis of its peptide bonds, initiated by the covalent attachment of ubiquitin, with ubiquitin-protein ligation catalyzed by the anaphase-promoting complex, and mediated by the proteasome.	77	77	0.575709	2.077858	0	0.0012 59	6568	tags=81%, list=35%, signal=123%
GO_REGULATION_OF_MAST_CELL_ACTIVATION_INVOLVED_IN_IMMUNE_RESPONSE	Any process that modulates the frequency, rate, or extent of mast cell activation as part of an immune response.	31	31	0.650732	2.062907	0	0.0013 48	1965	tags=48%, list=10%, signal=54%
GO_AXONEMAL_DYNEIN_COMPLEX_ASSEMBLY	The aggregation, arrangement and bonding together of a set of components to form an axonemal dynein complex, a dynein complex found in eukaryotic cilia and flagella, in which the motor domain heads interact with adjacent microtubules to generate a sliding force which is converted to a bending motion.	22	22	0.690713	2.055208	0	0.0012 98	2923	tags=77%, list=15%, signal=91%

GO_CELL_PROJECTION_ASSEMBLY	Formation of a prolongation or process extending from a cell, e.g. a flagellum or axon.	264	263	0.518195	2.022424	0	0.002937	6299	tags=68%, list=33%, signal=101%
GO_POSITIVE_REGULATION_OF_LIGASE_ACTIVITY	Any process that activates or increases the frequency, rate or extent of ligase activity, the catalysis of the ligation of two substances with concomitant breaking of a diphosphate linkage, usually in a nucleoside triphosphate.	110	107	0.545195	2.021428	0	0.002643	6568	tags=71%, list=35%, signal=108%
GO_REGULATION_OF_CELLULAR_AMINO_ACID_METABOLIC_PROCESS	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways involving amino acids.	66	65	0.571721	2.016051	0	0.002489	5267	tags=69%, list=28%, signal=96%
GO_REGULATION_OF_LIGASE_ACTIVITY	Any process that modulates the frequency, rate or extent of ligase activity, the catalysis of the ligation of two substances with concomitant breaking of a diphosphate linkage, usually in a nucleoside triphosphate. Ligase is the systematic name for any enzyme of EC class 6.	130	127	0.529771	2.008704	0	0.002675	6568	tags=69%, list=35%, signal=104%
GO_POSITIVE_REGULATION_OF_MYELOID_LEUKOCYTE_MEDIATED_IMMUNITY	Any process that activates or increases the frequency, rate, or extent of myeloid leukocyte mediated immunity.	18	18	0.700831	1.978983	0	0.003921	1743	tags=50%, list=9%, signal=55%
GO_CELLULAR_COMPONENT_ASSEMBLY	The cellular component assembly that is part of the initial shaping of the component during its	246	243	0.507105	1.977165	0	0.003775	6257	tags=66%, list=33%,

SSEMBLY_INVO LVED_IN_MORP HOGENESIS	developmental progression.								signal=98%
GO_INNATE_IM MUNE_RESPONS E_ACTIVATING_ CELL_SURFACE _RECEPTOR_SIG NALING_PATHW AY	Any series of molecular signals leading to activation of the innate immune response generated as a consequence of binding to a cell surface receptor.	106	106	0.531578	1.976808	0	0.0035 24	5097	tags=61%, list=27%, signal=83%
GO_G_PROTEIN_ COUPLED_PURI NERGIC_RECEPTOR_SIGNALING_ PATHWAY	The series of molecular signals generated as a consequence of a receptor binding to an extracellular purine or purine derivative and transmitting the signal to a heterotrimeric G-protein complex to initiate a change in cell activity.	20	20	0.670494	1.971055	0	0.0037 16	1398	tags=45%, list=7%, signal=49%
GO_MICROTUBU LE_BUNDLE_FO RMATION	A process that results in a parallel arrangement of microtubules.	69	69	0.556537	1.9708	0	0.0034 98	6210	tags=75%, list=33%, signal=112%
GO_REGULATIO N_OF_CELLULA R_AMINE_META BOLIC_PROCESS	Any process that modulates the frequency, rate or extent of the chemical reactions and pathways by which individual cells transform amines.	88	86	0.543528	1.957915	0	0.0044 58	5267	tags=59%, list=28%, signal=82%
GO_PROTEIN_TR ANSPORT_ALON G_MICROTUBUL	The directed movement of a protein along a microtubule, mediated by motor proteins.	27	27	0.624676	1.935863	0	0.0058 13	4485	tags=74%, list=24%, signal=97%

E									
GO_TUMOR_NECROSIS_FACTOR_MEDIATED_SIGNALING_PATHWAY	A series of molecular signals initiated by the binding of a tumor necrosis factor to a receptor on the surface of a cell, and ending with regulation of a downstream cellular process, e.g. transcription.	118	118	0.51698	1.927795	0	0.006466	4810	tags=58%, list=25%, signal=77%
GO_EPITHELIAL_CILIUM_MOVEMENT	The directed, self-propelled movement of a cilium of an epithelial cell. This movement is usually coordinated between many epithelial cells, and serves to move fluid.	18	18	0.675649	1.921556	0	0.006741	3249	tags=67%, list=17%, signal=80%
GO_CENTROMERE_COMPLEX_ASSEMBLY	The aggregation, arrangement and bonding together of proteins and centromeric DNA molecules to form a centromeric protein-DNA complex. Includes the formation of the chromatin structures which form a platform for the kinetochore, and assembly of the kinetochore onto this specialized chromatin. In fission yeast and higher eukaryotes this process also includes the formation of heterochromatin at the outer repeat (pericentric) regions of the centromere.	48	47	0.565253	1.914224	0	0.007808	3457	tags=49%, list=18%, signal=60%
GO_ACTIVATION_OF_INNATE_IMMUNE_RESPONSE	Any process that initiates an innate immune response. Innate immune responses are defense responses mediated by germline encoded components that directly recognize components of potential pathogens. Examples of this process include activation of the hypersensitive response	204	204	0.496959	1.913388	0	0.007591	4810	tags=55%, list=25%, signal=73%

	of <i>Arabidopsis thaliana</i> and activation of any NOD or TLR signaling pathway in vertebrate species.								
GO_DNA_REPLICATION_INITIATION	The process in which DNA-dependent DNA replication is started; this involves the separation of a stretch of the DNA double helix, the recruitment of DNA polymerases and the initiation of polymerase action.	29	29	0.613686	1.912026	0	0.007354	4447	tags=66%, list=24%, signal=86%
GO_POSITIVE_REGULATION_OF_LEUKOCYTE_DEGRANULATION	Any process that activates or increases the frequency, rate or extent of leukocyte degranulation.	18	18	0.678421	1.909903	0	0.00721	1743	tags=44%, list=9%, signal=49%
GO_DNA_REPLICATION_INDEPENDENT_NUCLEOSOME_ORGANIZATION	The formation or destruction of chromatin structures, occurring outside the context of DNA replication.	53	52	0.553377	1.898449	0	0.008567	3434	tags=48%, list=18%, signal=59%
GO_HISTONE_EXCHANGE	The replacement, within chromatin, of resident histones or histone subunits with alternative, sometimes variant, histones or subunits.	53	50	0.556231	1.8943	0	0.00888	3588	tags=50%, list=19%, signal=62%
GO_ARP2_3_COMPLEX_MEDIATED_ACTIN_NUCLEATION	The actin nucleation process in which actin monomers combine to form a new branch on the side of an existing actin filament; mediated by the Arp2/3 protein complex and its interaction with other proteins.	17	16	0.676048	1.886944	0	0.00981	2061	tags=56%, list=11%, signal=63%
GO_FC_RECEPT	A series of molecular signals initiated by the	184	184	0.48933	1.880329	0	0.0105	5370	tags=57%,

OR_SIGNALING_PATHWAY	binding of the Fc portion of an immunoglobulin to an Fc receptor on the surface of a signal-receiving cell, and ending with regulation of a downstream cellular process, e.g. transcription. The Fc portion of an immunoglobulin is its C-terminal constant region.						46		list=28%, signal=79%
GO_NIK_NF_KAPPA_B_PATHWAY	The process in which a signal is passed on to downstream components within the cell through the NIK-dependent processing and activation of NF-KappaB. Begins with activation of the NF-KappaB-inducing kinase (NIK), which in turn phosphorylates and activates IkkappaB kinase alpha (IKKalpha). IKKalpha phosphorylates the NF-Kappa B2 protein (p100) leading to p100 processing and release of an active NF-KappaB (p52).	83	83	0.522677	1.880146	0	0.010257	5721	tags=65%, list=30%, signal=93%
GO_REGULATION_OF_MAST_CELL_ACTIVATION	Any process that modulates the frequency, rate, or extent of mast cell activation.	39	39	0.57207	1.856464	0	0.014127	1965	tags=41%, list=10%, signal=46%
GO_FC_EPSILON_RECEPTOR_SIGNALING_PATHWAY	A series of molecular signals initiated by the binding of the Fc portion of immunoglobulin E (IgE) to an Fc-epsilon receptor on the surface of a signal-receiving cell, and ending with regulation of a downstream cellular process, e.g. transcription. The Fc portion of an immunoglobulin is its C-terminal constant region.	124	124	0.494486	1.850292	0	0.014984	5671	tags=60%, list=30%, signal=86%

GO_POSTREPLICATION_REPAIR	The conversion of DNA-damage induced single-stranded gaps into large molecular weight DNA after replication. Includes pathways that remove replication-blocking lesions in conjunction with DNA replication.	54	53	0.540637	1.845695	0	0.01579	6026	tags=68%, list=32%, signal=99%
GO_ACTIVATION_OF_IMMUNE_RESPONSE	Any process that initiates an immune response.	395	393	0.462227	1.832675	0	0.018657	5116	tags=51%, list=27%, signal=69%
GO_REGULATION_OF_ACTIVATED_T_CELL_PROLIFERATION	Any process that modulates the frequency, rate or extent of activated T cell proliferation.	40	40	0.555731	1.830281	0	0.018475	4489	tags=55%, list=24%, signal=72%
GO_NEGATIVE_REGULATION_OF_CYTOKINE_PRODUCTION_INVOLVED_IN_IMMUNE_RESPONSE	Any process that stops, prevents, or reduces the frequency, rate, or extent of cytokine production contributing to an immune response.	22	20	0.62373	1.830009	0.002191	0.01804	4807	tags=70%, list=25%, signal=94%
GO_PHAGOCYTOSIS_ENGULFMENT	The internalization of bacteria, immune complexes and other particulate matter or of an apoptotic cell by phagocytosis, including the membrane and cytoskeletal processes required, which involves one of three mechanisms: zippering of pseudopods around a target via repeated receptor-ligand interactions, sinking of the target directly into plasma membrane of the	19	19	0.638586	1.829346	0.001115	0.017808	3576	tags=47%, list=19%, signal=58%

	phagocytosing cell, or induced uptake via an enhanced membrane ruffling of the phagocytosing cell similar to macropinocytosis.								
GO_MICROTUBULE_BASED_MOVEMENT	A microtubule-based process that is mediated by motor proteins and results in the movement of organelles, other microtubules, or other particles along microtubules.	204	204	0.47551	1.828026	0	0.017612	6351	tags=63%, list=34%, signal=94%
GO_FC_GAMMA_RECEPTOR_SIGNALING_PATHWAY	A series of molecular signals initiated by the binding of the Fc portion of immunoglobulin G (IgG) to an Fc-gamma receptor on the surface of a signal-receiving cell, and ending with regulation of a downstream cellular process, e.g. transcription. The Fc portion of an immunoglobulin is its C-terminal constant region.	74	74	0.512512	1.826751	0	0.0175	4574	tags=53%, list=24%, signal=69%
GO_MEMBRANE_INVAGINATION	The infolding of a membrane, resulting in formation of a vesicle.	29	29	0.586291	1.824261	0.001074	0.018054	2809	tags=41%, list=15%, signal=49%
GO_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	Any series of molecular signals generated as a consequence of binding to a toll-like receptor. Toll-like receptors directly bind pattern motifs from a variety of microbial sources to initiate innate immune response.	85	85	0.501569	1.822334	0	0.018029	4808	tags=54%, list=25%, signal=72%
GO_REGULATION_OF_LEUKOCYTE_DEGRANULATION	Any process that modulates the frequency, rate, or extent of leukocyte degranulation.	41	41	0.550714	1.814765	0	0.019578	1965	tags=41%, list=10%, signal=46%

GO_IMMUNE_RESPONSE_REGULATING_CELL_SURFACE_RECEPTOR_SIGNALING_PATHWAY	A series of molecular signals initiated by the binding of an extracellular ligand to a receptor on the surface of the target cell capable of activating, perpetuating, or inhibiting an immune response.	291	291	0.458731	1.809802	0	0.020659	5370	tags=52%, list=28%, signal=71%
GO_NEGATIVE_REGULATION_OF_INTERLEUKIN_10_PRODUCTION	Any process that stops, prevents, or reduces the frequency, rate, or extent of interleukin-10 production.	16	16	0.648554	1.808228	0.001121	0.020554	3642	tags=63%, list=19%, signal=77%
GO_POSITIVE_REGULATION_OF_ALPHA_BETA_T_CELL_ACTIVATION	Any process that activates or increases the frequency, rate or extent of alpha-beta T cell activation.	51	51	0.532566	1.806057	0.001035	0.020749	4731	tags=59%, list=25%, signal=78%
GO_NEGATIVE_REGULATION_OF_CD4_POSITIVE_ALPHA_BETA_T_CELL_ACTIVATION	Any process that stops, prevents or reduces the frequency, rate or extent of CD4-positive, alpha-beta T cell activation.	15	15	0.660857	1.803119	0.001129	0.021139	4083	tags=73%, list=22%, signal=93%
GO_REGULATION_OF_T_HELPER_1_TYPE_IMMUNE_RESPONSE	Any process that modulates the frequency, rate, or extent of a T-helper 1 type immune response.	22	22	0.604663	1.80104	0.001076	0.021352	4743	tags=73%, list=25%, signal=97%

GO_ACTIN_NUCLEATION	The initial step in the formation of an actin filament, in which actin monomers combine to form a new filament. Nucleation is slow relative to the subsequent addition of more monomers to extend the filament.	23	22	0.606668	1.793109	0.0011 1	0.0236 6	2061	tags=45%, list=11%, signal=51%
GO_SISTER_CHROMATID_SEGREGATION	The cell cycle process in which sister chromatids are organized and then physically separated and apportioned to two or more sets.	176	176	0.467314	1.791245	0	0.0238 32	5978	tags=59%, list=32%, signal=86%
GO_NEGATIVE_REGULATION_OF_ALPHA_BETA_T_CELL_ACTIVATION	Any process that stops, prevents, or reduces the frequency, rate or extent of alpha-beta T cell activation.	23	23	0.593821	1.787918	0	0.0246 4	4510	tags=65%, list=24%, signal=86%
GO_REGULATION_OF_PROTEIN_UBIQUITINATION_INVOLVED_IN_UBIQUITIN_DEPENDENT_PROTEIN_CATABOLIC_PROCESS	Any process that modulates the frequency, rate or extent of protein ubiquitination involved in ubiquitin-dependent protein catabolic process.	103	103	0.484081	1.78679	0	0.0244 34	6847	tags=68%, list=36%, signal=106%
GO_POSITIVE_REGULATION_OF_ALPHA_BETA_T_CELL_DIFFERENTIATION	Any process that activates or increases the frequency, rate or extent of alpha-beta T cell differentiation.	37	37	0.544316	1.786124	0	0.0243 45	4731	tags=59%, list=25%, signal=79%

GO_ORGANELLE_ASSEMBLY	The aggregation, arrangement and bonding together of a set of components to form an organelle. An organelle is an organized structure of distinctive morphology and function. Includes the nucleus, mitochondria, plastids, vacuoles, vesicles, ribosomes and the cytoskeleton. Excludes the plasma membrane.	494	485	0.44703	1.784689	0	0.024652	6210	tags=56%, list=33%, signal=81%
GO_REGULATION_OF_DEFENSE_RESPONSE_TO_VIRUS_BY_VIRUS	Any viral process that modulates the frequency, rate, or extent of the antiviral response of the host cell or organism.	29	29	0.566741	1.783904	0.002114	0.024458	5834	tags=69%, list=31%, signal=100%
GO_NEURON_APOPTOTIC_PROCESS	Any apoptotic process in a neuron, the basic cellular unit of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system.	34	34	0.549446	1.781323	0.002101	0.025112	3946	tags=53%, list=21%, signal=67%
GO_REGULATION_OF_B_CELL_RECEPTOR_SIGNALING_PATHWAY	Any process that modulates the frequency, rate or extent of signaling pathways initiated by the cross-linking of an antigen receptor on a B cell.	15	15	0.658617	1.780691	0	0.024798	6139	tags=93%, list=32%, signal=138%
GO_POSITIVE_REGULATION_OF_INNATE_IMMUNE_RESPONSE	Any process that activates or increases the frequency, rate or extent of the innate immune response, the organism's first line of defense against infection.	246	245	0.457053	1.779914	0	0.024661	5121	tags=52%, list=27%, signal=71%

GO_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDE_ANTIGEN	The process in which an antigen-presenting cell expresses peptide antigen in association with an MHC protein complex on its cell surface, including proteolysis and transport steps for the peptide antigen both prior to and following assembly with the MHC protein complex. The peptide antigen is typically, but not always, processed from an endogenous or exogenous protein.	177	176	0.465463	1.775874	0	0.025376	5178	tags=54%, list=27%, signal=74%
GO_RECOMBINATIONAL_REPAIR	A DNA repair process that involves the exchange, reciprocal or nonreciprocal, of genetic material between the broken DNA molecule and a homologous region of DNA.	80	80	0.490868	1.77303	0	0.026227	7858	tags=75%, list=42%, signal=128%
GO_REGULATION_OF_INTERLEUKIN_10_PRODUCTION	Any process that modulates the frequency, rate, or extent of interleukin-10 production.	46	46	0.533125	1.772059	0.001042	0.026073	3747	tags=50%, list=20%, signal=62%
GO_POSITIVE_REGULATION_OF_T_CELL_PROLIFERATION	Any process that activates or increases the rate or extent of T cell proliferation.	95	94	0.480326	1.768804	0	0.026836	4554	tags=48%, list=24%, signal=63%
GO_REGULATION_OF_TELOMERASE_RNA_LOCALIZATION_TO_CAJAL_BODY	Any process that modulates the frequency, rate or extent of telomerase RNA localization to Cajal body.	15	15	0.6564	1.767992	0.001151	0.026632	4385	tags=73%, list=23%, signal=95%

GO_NEGATIVE_REGULATION_OF_PROTEIN_MODIFICATION_BY_SMALL_PROTEIN_CONJUGATION_OR_REMOVAL	Any process that stops, prevents or reduces the frequency, rate or extent of protein modification by small protein conjugation or removal.	139	137	0.46668	1.764314	0	0.027843	6583	tags=63%, list=35%, signal=96%
GO_POSITIVE_REGULATION_OF_CD4_POSITIVE_ALPHA_BETA_T_CELL_ACTIVATION	Any process that activates or increases the frequency, rate or extent of CD4-positive, alpha-beta T cell activation.	27	27	0.580162	1.762056	0	0.028308	4731	tags=67%, list=25%, signal=89%
GO_ANTIGEN_PROCESSING_AND_PRESENTATION	The process in which an antigen-presenting cell expresses antigen (peptide or lipid) on its cell surface in association with an MHC protein complex.	213	212	0.453509	1.761124	0	0.028264	5207	tags=52%, list=28%, signal=71%
GO_DEOXYRIBONUCLEOSIDE_TRIPHOSPHATE_METABOLIC_PROCESS	The chemical reactions and pathways involving a deoxyribonucleoside triphosphate, a compound consisting of a nucleobase linked to a deoxyribose sugar esterified with triphosphate on the sugar.	18	18	0.62885	1.756679	0.002193	0.029495	5286	tags=72%, list=28%, signal=100%
GO_REGULATION_OF_TRANSCRIPTION_INVOLVED_IN_G1_S_TRANSITION	Any process that regulates transcription such that the target genes are involved in the transition between G1 and S phase of the mitotic cell cycle.	26	26	0.56919	1.754687	0.004329	0.029801	3333	tags=58%, list=18%, signal=70%

D_IN_G1_S_TRANSITION_OF_MITOTIC_CELL_CYCLE									
GO_REGULATION_OF_ESTABLISHMENT_OF_PLANAR_POLARITY	Any process that modulates the rate, frequency or extent of the establishment of planar polarity, the coordinated organization of groups of cells in a tissue, such that they all orient to similar coordinates.	110	110	0.473765	1.754052	0	0.029655	5155	tags=52%, list=27%, signal=71%
GO_MOTILE_CILIUM_ASSEMBLY	The assembly of a motile cilium, a cilium that contains a regular longitudinal array of axonemal microtubules. In vertebrates, motile cilia are usually formed around a 9 + 2 microtubule core structure. Motile cilia are often found in tissues where propagation of fluid is necessary for proper organ development or function.	15	15	0.642745	1.752973	0.001129	0.029677	6094	tags=87%, list=32%, signal=128%
GO_T_CELL_RECEPTOR_SIGNALING_PATHWAY	A series of molecular signals initiated by the cross-linking of an antigen receptor on a T cell.	143	143	0.462659	1.742559	0	0.033852	5671	tags=57%, list=30%, signal=81%
GO_REGULATION_OF_T_CELL_PROLIFERATION	Any process that modulates the frequency, rate or extent of T cell proliferation.	147	145	0.456889	1.740508	0	0.034398	4554	tags=47%, list=24%, signal=61%
GO_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDES	The process in which an antigen-presenting cell expresses a peptide antigen on its cell surface in association with an MHC class I protein complex. Class I here refers to classical class I molecules.	91	90	0.479693	1.736753	0	0.036032	4810	tags=52%, list=25%, signal=70%

ANTIGEN_VIA_MHC_CLASS_I									
GO_CHROMOSOME_LOCALIZATION	Any process in which a chromosome is transported to, or maintained in, a specific location.	61	60	0.499352	1.736538	0	0.035642	6253	tags=63%, list=33%, signal=94%
GO_NEGATIVE_REGULATION_OF_LEUKOCYTE_MEDIATED_IMMUNITY	Any process that stops, prevents, or reduces the frequency, rate, or extent of leukocyte mediated immunity.	47	46	0.516146	1.735269	0.001037	0.035709	4868	tags=57%, list=26%, signal=76%
GO_NEGATIVE_REGULATION_OF_INTERLEUKIN_12_PRODUCTION	Any process that stops, prevents, or reduces the frequency, rate, or extent of interleukin-12 production.	15	15	0.642571	1.734778	0.002235	0.035548	3315	tags=67%, list=18%, signal=81%
GO_REGULATION_OF_T_HELPER_CELL_DIFFERENTIATION	Any process that modulates the frequency, rate or extent of T-helper cell differentiation.	26	26	0.572129	1.734592	0.002144	0.035142	4731	tags=62%, list=25%, signal=82%
GO_ANTIGEN_RECEPTOR_MEDIATED_SIGNALING_PATHWAY	A series of molecular signals initiated by the cross-linking of an antigen receptor on a B or T cell.	173	173	0.454074	1.73221	0	0.035912	5671	tags=56%, list=30%, signal=79%
GO_REGULATION_OF_INTERFERON_GAMMA_PRODUCTION	Any process that modulates the frequency, rate, or extent of interferon-gamma production. Interferon-gamma is also known as type II	97	97	0.463377	1.731026	0	0.036189	7304	tags=67%, list=39%, signal=109%

ODUCTION	interferon.								
GO_TRANSLESION_SYNTHESIS	The replication of damaged DNA by synthesis across a lesion in the template strand; a specialized DNA polymerase or replication complex inserts a defined nucleotide across from the lesion which allows DNA synthesis to continue beyond the lesion. This process can be mutagenic depending on the damaged nucleotide and the inserted nucleotide.	41	41	0.519214	1.731018	0.0010 41	0.0357 31	6026	tags=66%, list=32%, signal=96%
GO_REGULATION_OF_INFLAMMATORY_RESPONSE_TO_ANTIGENIC_STIMULUS	Any process that modulates the frequency, rate, or extent of an inflammatory response to an antigenic stimulus.	19	19	0.609447	1.729963	0	0.0360 17	3280	tags=47%, list=17%, signal=57%
GO_REGULATION_OF_INTERLEUKIN_17_PRODUCTION	Any process that modulates the frequency, rate, or extent of production of any member of the interleukin-17 family of cytokines.	22	22	0.584916	1.729932	0	0.0355 96	3747	tags=55%, list=20%, signal=68%
GO_PROTEIN_REFOLDING	The process carried out by a cell that restores the biological activity of an unfolded or misfolded protein, using helper proteins such as chaperones.	20	20	0.590099	1.729342	0	0.0353 8	5114	tags=60%, list=27%, signal=82%
GO_MICROTUBULE_CYTOSKELETON_ORGANIZATION	A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of cytoskeletal structures comprising microtubules and their associated proteins.	348	345	0.437395	1.727244	0	0.0358 75	6267	tags=58%, list=33%, signal=85%

GO_CILIUM_OR_FLAGELLUM_DEPENDENT_CELL_MOTILITY	Cell motility due to movement of eukaryotic cilia or bacterial-type flagella or archaeal-type flagella.	15	15	0.640362	1.726164	0.001129	0.035976	6094	tags=87%, list=32%, signal=128%
GO_POSITIVE_REGULATION_OF_MAST_CELL_ACTIVATION	Any process that activates or increases the frequency, rate, or extent of mast cell activation.	16	16	0.619549	1.724413	0.003359	0.036507	1743	tags=38%, list=9%, signal=41%
GO_SISTER_CHROMATID_COHESION	The cell cycle process in which the sister chromatids of a replicated chromosome are associated with each other.	111	111	0.467519	1.723912	0	0.036291	5804	tags=58%, list=31%, signal=83%
GO_METAPHASE_PLATE_CONGRESSION	The alignment of chromosomes at the metaphase plate (spindle equator), a plane halfway between the poles of the spindle.	42	42	0.520735	1.723309	0	0.036091	6246	tags=71%, list=33%, signal=106%
GO_REGULATION_OF_ALPHA_BETA_T_CELL_DIFFERENTIATION	Any process that modulates the frequency, rate or extent of alpha-beta T cell differentiation.	46	46	0.502913	1.7229	0.001034	0.035896	4731	tags=54%, list=25%, signal=72%
GO_POSITIVE_REGULATION_OF_T_HELPER_CELL_DIFFERENTIATION	Any process that activates or increases the frequency, rate or extent of T-helper cell differentiation.	18	18	0.608733	1.717242	0.001104	0.038133	4731	tags=67%, list=25%, signal=89%
GO_REGULATION_OF_ALPHA_BETA_T_CELL_ACTIVATION	Any process that modulates the frequency, rate or extent of alpha-beta T cell activation.	68	68	0.485921	1.713339	0	0.039838	4731	tags=53%, list=25%, signal=70%

TIVATION									
GO_PURINERGIC_RECEPTOR_SIGNALING_PATHWAY	The series of molecular signals generated as a consequence of a receptor binding to an extracellular purine or purine derivative to initiate a change in cell activity.	28	28	0.549702	1.711892	0.003191	0.040188	1467	tags=36%, list=8%, signal=39%
GO_PROTEIN_COMPLEX_LOCALIZATION	A localization process that acts on a protein complex; the complex is transported to, or maintained in, a specific location.	53	53	0.498167	1.705101	0	0.043721	5795	tags=60%, list=31%, signal=87%
GO_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION	Any process that modulates the frequency, rate or extent of cell cycle phase transition.	321	319	0.430704	1.704027	0	0.04386	6614	tags=58%, list=35%, signal=88%
GO_MITOTIC_SISTER_CHROMATID_SEGREGATION	The cell cycle process in which replicated homologous chromosomes are organized and then physically separated and apportioned to two sets during the mitotic cell cycle. Each replicated chromosome, composed of two sister chromatids, aligns at the cell equator, paired with its homologous partner. One homolog of each morphologic type goes into each of the resulting chromosome sets.	91	91	0.464764	1.701399	0	0.045009	6614	tags=65%, list=35%, signal=99%
GO_NUCLEAR_CHROMOSOME_SEGREGATION	The process in which genetic material, in the form of nuclear chromosomes, is organized into specific structures and then physically separated and apportioned to two or more sets. Nuclear chromosome segregation begins with the	228	226	0.434248	1.692999	0	0.049793	6696	tags=57%, list=35%, signal=87%

	condensation of chromosomes, includes chromosome separation, and ends when chromosomes have completed movement to the spindle poles.								
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Table E8. Primer Sequences of inflammatory factors for qRT-PCR Validation.

Genes	RNA-seq Analysis		qRT-PCR Validation			
	log ₂ (Fold Change)	adj. <i>P</i> Value	Forward Primer (5' to 3')	Reverse Primer (5' to 3')	Fold Change	<i>P</i> Value
CCL7	9.750	1.52E-06	TTGCTCAGCCAGTTGGGATT	GACAGTGGCTACTGGTGGTC	98.53	<0.001
CCL18	7.028	1.85E-16	TGCTGCCTCGTCTATACCTC	CCGGCCTCTCTTGGTTAGG	191.9	<0.001
CCL20	4.338	0.00148	GCTCCTGGCTGCTTTGATGT	GCATTGATGTCACAGCCTTCA	3.742	<0.05
CXCL6	4.225	3.72E-08	TGCGTTGCACTTGTTTACGC	CTTCCCGTTCTTCAGGGAGG	16.22	<0.001
CXCL8	2.574	0.00806	ACTGAGAGTGATTGAGAGTGGAC	AACCCTCTGCACCCAGTTTTTC	5.076	<0.05
IFNG	-1.644	0.0139	TCGGTAACTGACTTGAATGTCCA	TCGCTTCCCTGTTTTAGCTGC	-3.321	<0.01
IL13RA2	-3.113	1.02E-06	ACCTGGCATAGGTGTACTTCT	CCAAATAGGGAAATCTGCATCC	-9.760	<0.001
				T		
IL17REL	4.570	0.0257	CAGGAGACGCAGTGTCAGAG	TGGGCACTTGCACCAGAATC	9.366	<0.01
GAPDH	0.864	0.139	ACAGTTGCCATGTAGACC	TTTTTGGTTGAGCACAGG	-	-

For RNA-seq Analysis, Fold change cutoff: 2.0; > 2.0 as upregulated and < - 2.0 as downregulated; adj. *P* < 0.05 was considered statistically significant. For qRT-PCR Validation, *P* < 0.05 was considered statistically significant.

Table E9. Primer Sequences, Fold change, and adj. *P* Value of the DEGs for qRT-PCR Validation.

Genes	RNA-seq Analysis		qRT-PCR Validation			
	log ₂ (Fold Change)	adj. <i>P</i> Value	Forward Primer (5' to 3')	Reverse Primer (5' to 3')	Fold Change	<i>P</i> Value
FOXJ1	2.808	6.00 E-05	GTGAAGCCTCCCTACTC	AATTCTGCCAGGTGGG	2.196	0.028
CP110	1.725	9.11E-07	CTTAGTAGACAAGGAACCCC	CCGCTTCTTTGGATTTTC	0.7653	0.568
DNAI1	3.206	9.10E-06	TCAGTGGGAGATCTATGATG	ACTCCATAGATGTCAGCTTC	2.200	0.011
DNALI1	2.421	2.49E-07	GGAGCAGTTAGACTTAAAGC	ACTCATCAAAACACTGTGAG	0.533	0.718
DNAH5	2.740	0.003	ACTGATGCAACTAATGAAGC	AGTGTAGGAATAGCATCCATC	0.822	0.675
DNAH9	2.884	5.53E-04	AGCAGGCCTCTAATTATCTC	CTCTTTGAAGTAAGTGTGGAG	3.725	0.044
RSPH1	3.095	2.45E-06	GGAAAGAGGAGAAGAGGAAG	AATTCAGTGATTTGGGTAGC	2.534	0.001
RSPH9	3.582	7.96E-07	GAATATGAACACACTGAGCTG	CTTGATCTGGACCACTATTTTC	6.9310	0.005
RSPH4A	2.920	5.44E-06	TTTGACACCAATCTCTGAAG	TTGTGGAATGAGATTTGAGG	4.372	0.015
GAPDH	0.864	0.139	ACAGTTGCCATGTAGACC	TTTTTGTTGAGCACAGG	-	-

For RNA-seq Analysis, Fold change cutoff: 2.0; > 2.0 as upregulated and < - 2.0 as downregulated; adj. *P* < 0.05 was considered statistically significant. For qRT-PCR Validation, *P* < 0.05 was considered statistically significant.