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Research article

# Toe1 promotes proliferation and differentiation of neural progenitor cells

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A B S T R A C T

Toe1 (target of EGR1, member 1) is a 3′- exonuclease in the deadenylase family, essential for the maturation of small nuclear RNAs. Mutations in Toe1 are linked to pontocerebellar hypoplasia 7 (PCH7), a severe neurodegenerative syndrome affecting infants, characterized by progressive neurodegeneration, developmental delay, and genital abnormalities. The pathogenic mechanisms of PCH7 are unclear but are thought to involve abnormal neural stem cell (NSC) development during embryogenesis. This study investigates Toe1's role in NSC development using the C17.2 NSC line. Colony formation, EdU incorporation, and CFSE staining assays showed that Toe1 knockout inhibited C17.2 cell proliferation. Upon inducing differentiation, Toe1 knockout significantly reduced cell dendrites. Immunofluorescence, qPCR, and Western blot analyses indicated that Toe1 knockout suppressed the expression of neuronal marker βIII-tubulin and glial cell marker Gfap, thereby inhibiting C17.2 cell differentiation. Additionally, Toe1 knockout reduced the expression of Dll1 and Jag1, suggesting an inhibition of Notch signaling. High-throughput transcriptome sequencing revealed that Toe1 influenced calcium ion binding, ECM, and amino acid catabolism in undifferentiated C17.2 cells, and peptidase activity, chemotactic factors, ECM, and TNF signaling in differentiated cells. These findings underscore Toe1's critical regulatory role in NSC proliferation and differentiation, with significant implications for developing therapeutic targets for neurodegenerative diseases such as PCH7.

## 1. Introduction

Stem cells are a unique category of cells with self-renewal and multilineage differentiation abilities [1,2]. Stem cells can be categorized into embryonic and adult stem cells, based on their developmental stages. Adult stem cells are undifferentiated cells that exist in differentiated tissues, capable of self-renewal and differentiation into specialized cells that constitute of the respective tissue. Examples include neural stem cells (NSCs), hematopoietic stem cells, bone marrow mesenchymal stem cells, and epidermal stem cells. NSCs in this study belong to a class of cells that can self-renew and generate a large number of brain tissue cells. These cells have the capacity to differentiate into neurons, astrocytes, and oligodendrocytes [3,4]. The precise regulation of NSCs is essential during brain development, ensuring production of a specific number of neurons at distinct stages and maintaining normal brain development and function [5]. Dysregulation of NSC control can lead to various brain disorders including cerebellar hypoplasia, lissencephaly, and autism.

Pontocerebellar hypoplasia (PCH) is a rare congenital neurodegenerative disorder characterized by abnormal development of the cerebellum, particularly the pons [6]. In addition to impaired brain development, individuals with PCH often exhibit clinical features including microcephaly, delayed motor development, and mild to severe intellectual disabilities [7]. PCH has multiple subtypes with broad-ranging effects and thus far, 13 PCH subtypes have been identified based on their clinical features [6,8]. Among these, PCH7 is a

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subtype characterized by more severe symptoms, primarily affecting infants. In addition to poor brain development, PCH7 expression is also associated with respiratory abnormalities, muscle tone abnormalities, and gonadal dysfunction [9–11]. In 2017, Gleeson et al. identified the TOE1 gene mutations in 12 PCH7 families using genomic sequencing. Mutations A103T, F148Y, V173G, and E220K did not affect TOE1 mRNA levels; however, they significantly reduced TOE1 protein expression. By generating homozygous Toe1 knockout mice, they observed that the knockout mice died before embryonic day 11.5. Furthermore, zebrafish lacking Toe1 exhibited structural brain defects resembling the pathology in human PCH7 [12]. This highlights the crucial role of TOE1 in neurodevelopment. Given that defects in small nuclear RNA (snRNA) processing are common causes of early-onset neurodegenerative diseases [13], Gleeson et al. speculated that mutations in TOE1 leading to abnormal snRNA processing could represent a potential pathogenic factors for PCH7. However, whether TOE1 affects NSC development has not yet been reported. Recent sequencing of additional PCH7 patients has identified new TOE1 mutations [14–16], further demonstrating a close correlation between TOE1 and neurodevelopment.

The aim of the study was to investigate the impact of Toe1 on the development of NSC, by focusing on the C17.2 NSC line. Our research highlights the importance of Toe1 in the development of NSCs and provides novel potential targets and insights into the diagnosis and treatment of PCH7.

## 2. Materials and methods

### 2.1. The C17.2 cell line and culture conditions

The C17.2 cell line is derived from multipotent NSCs isolated from the neonatal mouse cerebellum and immortalized via v-myc transfection. The cell line was purchased C17.2 from FuHeng Cell Center, Shanghai, China (FH1164). C17.2 cells were cultured in Dulbecco's modified Eagle's medium (DMEM, SH30243.01, Hyclone) containing 10 % fetal bovine serum (10099141, Gibco), 5 % horse serum (SH30074.03, Hyclone), 2 mM L-glutamine (25030081, Life Technologies), and 1 % penicillin/streptomycin (15070063, Gibco). These cells were incubated in standard humidified incubators (37 °C and 5 % $CO_2$).

For differentiation studies, the C17.2 cells were seeded in a routine culture medium. Twenty-four hours after seeding, the medium was replaced with DMEM/F-12 medium (11330032, Thermo Fisher Scientific) supplemented with 1 mM L-glutamine, 1 % penicillin/streptomycin, modified N2 supplements (17502048, Thermo Fisher Scientific), 10 ng/mL NGF (1156-NG-100, R&D Systems), and 10 ng/mL BDNF (248-BDB-010, R&D Systems). The differentiation medium was changed every third day for the duration of differentiation.

### 2.2. Colony formation and 5-ethynyl-2′-deoxyuridine incorporation assays

C17.2 cells were seeded in 12-well plates at a density of 800 cells/well. The cells were subsequently cultured for 10 d, fixed with 4 % paraformaldehyde (DF0135, LEAGENE) for 30 min at room temperature (RT), and stained with 0.5 % crystal violet solution (G1065,

**Table 1**
The sequence of qPCR primers in the experiments.

| | |
|---|---|
| Gapdh-FP | AGGTCGGTGTGAACGGATTTG |
| Gapdh-RP | GGGGTCGTTGATGGCAACA |
| Gfap-FP | ACCAGCTTACGGCCAACAG |
| Gfap-RP | CCAGCGATTCAACCTTTCTCT |
| βIII-tubulin-FP | AGGCCCGACAACTTTATCT |
| βIII-tubulin-RP | CTCTTTCCGCACGACATCTA |
| Nestin-FP | AGAGTCAGATCGCTCAGATCC |
| Nestin -RP | GCAGAGTCCTGTATGTAGCCAC |
| Dll1-FP | GCAGGACCTTCTTTCGCGTAT |
| Dll1-RP | AAGGGGAATCGGATGGGGTT |
| Jagged1-FP | CCTCGGGTCAGTTTGAGCTG |
| Jagged1-RP | CCTTGAGGCACACTTTGAAGTA |
| Notch1-FP | GATGGCCTCAATGGGTACAAG |
| Notch1-RP | TCGTTGTTGTTGATGTCACAGT |
| Notch2-FP | ATGTGGACGAGTGTCTGTTGC |
| Notch2-RP | GGAAGCATAGGCACAGTCATC |
| Ucma-FP | GAATCTGATGCCTCCAATTTCCT |
| Ucma-RP | C TCGTTCCTTTGCTCCTCGTAATA |
| Cdkn1a-FP | CCTGGTGATGTCCGACCTG |
| Cdkn1a-RP | CCATGAGCGCATCGCAATC |
| Tnfsf18-FP | ATGGAGGAAATGCCTTTGAGAG |
| Tnfsf18-RP | GATGGCAGTTGGCTTGAGTGA |
| Cd74-FP | CCGCCTAGACAAGCTGACC |
| Cd74-RP | ACAGGTTTGGCAGATTTCGGA |
| Btn2a2-FP | TTGCCCGATAGCCTCCCTT |
| Btn2a2-RP | GGCAGTGTAGTGTGGTATTCTCT |
| Vnn1-FP | CTTTCCTCGCGGCTGTTTAC |
| Vnn1-RP | CCTCCAGGTATGGGTAGATCGT |

Solarbio) for 20 min. The plate was washed thrice with 1 × phosphate-buffered saline (PBS) and air-dried at RT. Colonies were imaged and counted.

To conduct the 5-ethynyl-2′-deoxyuridine (EdU) incorporation assay, cells were seeded in 96-well plates. The Click-iT EdU Lagging Kit (C10340, Invitrogen) was used to evaluate cell proliferation according to the manufacturer's instructions. DNA staining was performed using Hoechst 33342 solution.

### 2.3. Cell cycle analysis using flow cytometry

For cell cycle studies, collected cells were fixed with 75 % ethanol at 4 °C overnight, washed once with 1 × PBS, digested with 50 μg/mL RNase A (EN0531, Fermentas) at 37 °C for 10 min, and stained with propidium iodide. After staining, the cell cycle was analyzed using a BD Accuri C6 Plus flow cytometer. The data were analyzed using the FlowJo v10 software.

### 2.4. Reverse transcription and real-time quantitative PCR

RNA was extracted using TRIzol reagent (15596-018, Invitrogen), and cDNA was obtained via reverse transcription using an RT reagent Kit (T04897030001; Roche). qPCR was performed using the Universal SYBR Green Master Kit (04913850001; Roche) and conducted on Applied Biosystems StepOne™ Real-Time PCR Systems. The primer sequences are listed in Table 1.

### 2.5. Protein expression detected using Western blot (WB) analysis

Total protein was extracted using Beyotime RIPA buffer (P0013) supplemented with protease (Roche) and phosphatase inhibitor cocktails (Roche). Twenty micrograms of total protein were subjected to electrophoresis. Electrophoresis products were transferred onto polyvinylidene difluoride membranes (Millipore) using the wet transfer method. The membranes were blocked with 5 % skim milk for 1 h at RT and subsequently incubated with primary antibodies at 4° for overnight. The primary antibodies were washed with 1 × TBST and the membranes were incubated with the secondary antibody. Images were acquired using the Amersham Imager 680 system. The following antibodies were used: Gapdh (P30008M; Abmart); Nestin (MAB353; Merck millipore); βIII -Tubulin (TU-20) (4466S; CST); Gfap (MAB360; Merck millipore); goat anti-mouse IgG H&L (HRP) (ab6789; Abcam); goat anti-rabbit IgG H&L (HRP) (ab6721; Abcam). For immunofluorescence (IF), Nestin, βIII-tubulin, and GFAP were the same as WB, and the secondary antibodies of

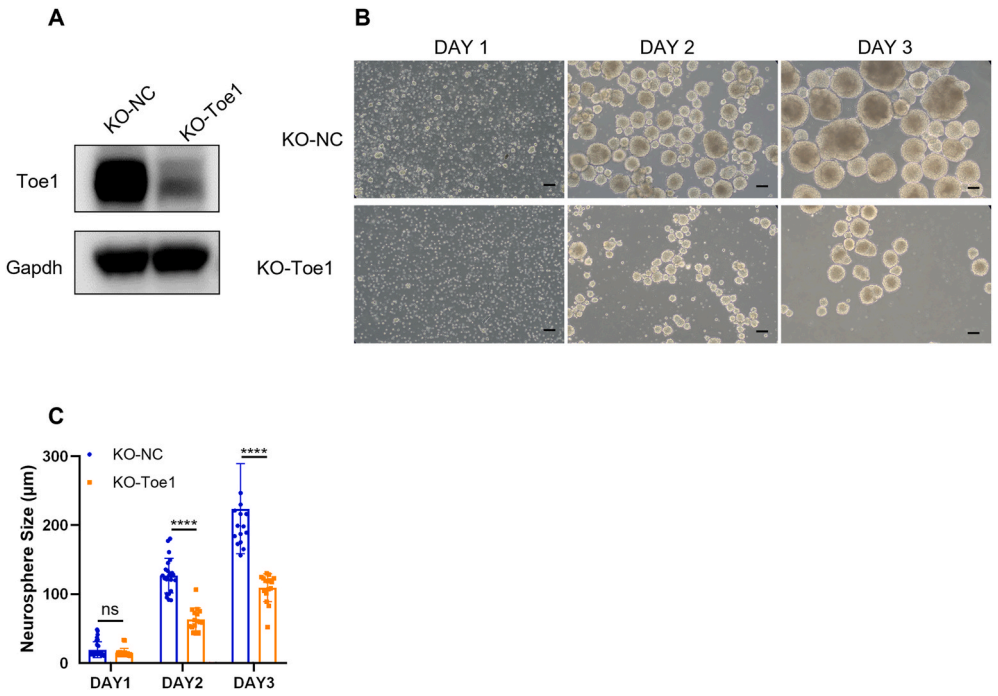



**Fig. 1.** Toe1 knockout inhibited the proliferation of neural stem cells
(A) Western blot analysis assessing the efficiency of Toe1 depletion.
(B) Microscopic bright-field images capturing the growth status of primary stem cells. These images, acquired at a scale of 100 μm, reveal alterations in cellular morphology and density attributable to Toe1 knockout.
(C) Quantitative analysis of the mean size of neurospheres using ImageJ software, indicating a significant reduction in the mean size of neurospheres upon Toe1 depletion (****$p < 0.0001$).

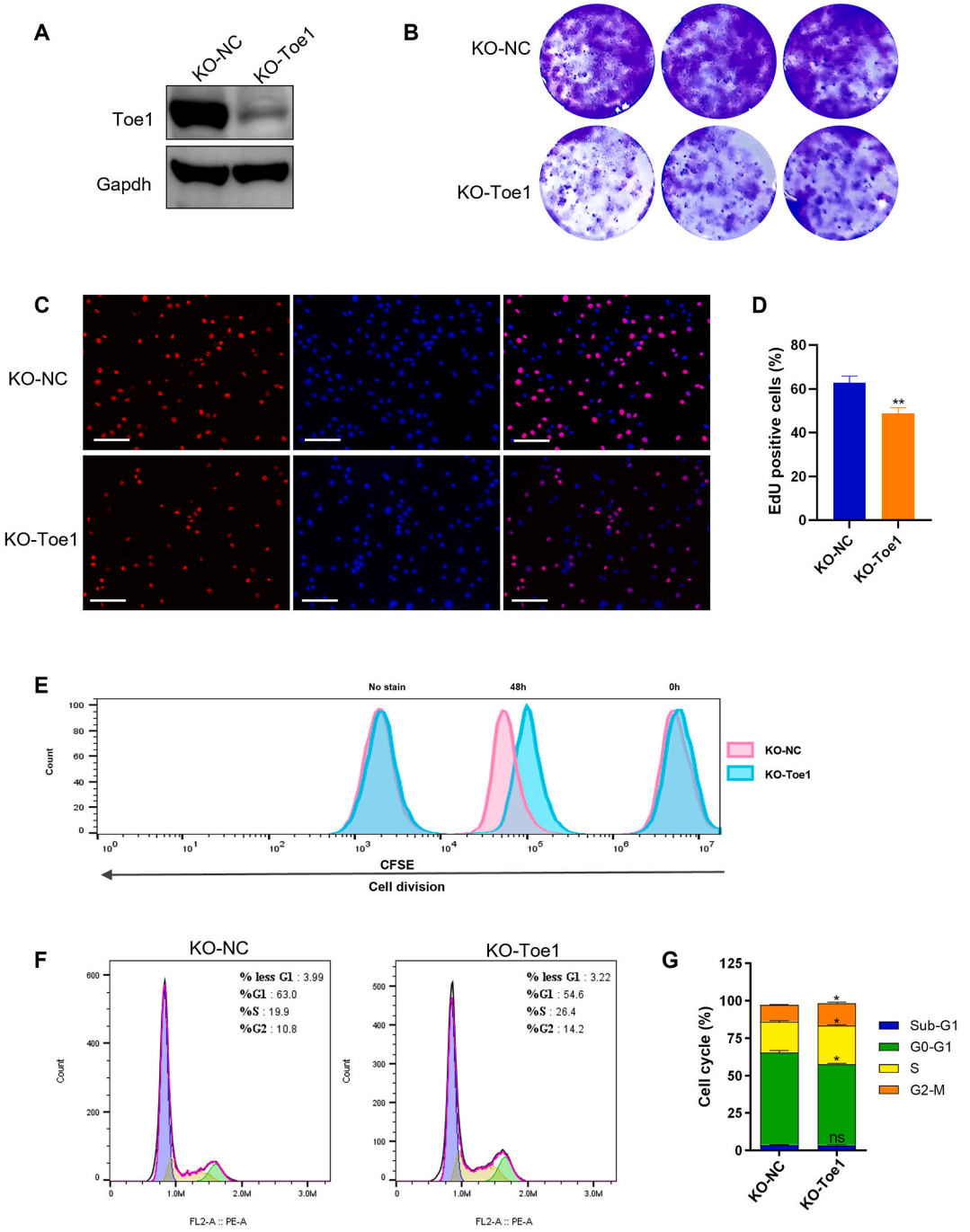



**Fig. 2.** Depletion of Toe1 Suppresses the Proliferation of C17.2 Cell Line
(A) Western blot analysis, quantitatively evaluating the efficacy of Toe1 depletion at the protein level.
(B) Images from the colony formation assay, offering a visual representation of the impact of Toe1 knockout on clonogenic potential.
(C) Fluorescence microscopy images capturing EdU-positive cells, indicative of active DNA synthesis. Scale bars indicate 60 μm.
(D) Statistical analysis of EdU-positive cells, $^{**}p < 0.01$.
(E) Flow cytometry detection of CFSE dye signal intensity, offering a quantitative assessment of cell proliferation kinetics.
(F) Flow cytometry analysis of the cell cycle, providing insights into alterations in cell cycle progression induced by Toe1 depletion.
(G) Statistical analysis of cell cycle phases, $^{*}p < 0.05$.

IF were Alexa Fluor 555-labeled donkey anti-mouse antibody (AB_2762848; Invitrogen) and Alexa Fluor 488-labeled donkey anti-mouse antibody (AB_2762823; Invitrogen).

### 2.6. RNA sequencing analysis

The total RNA from each group was extracted and sequenced on an Illumina HiSeq/MiSeq platform (Novogene Co., Ltd.) RNA-seq results were read in FASTA format following fastp data-quality evaluation and filtering. The DESeq2 R package (1.20.0) was used to analyze differentially expressed genes (DEGs) with a threshold of padj $<0.05$ and $|\log2(\text{foldchange})| > 1$. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis of DEGs were implemented using the clusterProfiler R package (3.8.1).

### 2.7. Statistical analyses

Data are represented as the mean ± SEM. Statistically significant differences between two groups were analyzed using a standard two-tailed Student's t-test in Prism (GraphPad software 8.0). Statistical significance was set at $p < 0.05$.

## 3. Results

### 3.1. Toe1 knockout inhibited the proliferation of neural stem cells

Primary NSCs were isolated from the brains of neonatal mice (within the first 3 d post-birth) and cultured *in vitro*. Subsequently, we designed single-guide RNA (sgRNA) targeting Toe1 or GFP (as a negative control) and introduced the sgRNA into primary cells via lentiviral infection. The sgRNA sequences were Toe1-sgRNA1 CTGTGTGAGATGTTCCCAGC, Toe1-sgRNA2 GTGCATTGAGGAACGTTACA, GFP-sgRNA1 GAGCTGGACGGCGACGTAAA, and GFP-sgRNA2, CAAGTTCAGCGTGTCCGGCG.

Western blotting verified that the knockout effect of the *Toe1* gene was good (Fig. 1-A), and we observed that, in comparison to the control group (KO-NC), NSCs with Toe1 knockout (KO-Toe1) exhibited slower growth, characterized by smaller and fewer neurospheres (Fig. 1-B/C). However, with prolonged culture time, the proliferation rates of both groups decreased, the cells gradually died, and the KO-Toe1 group showed a faster cell death rate than the control group.

Owing to the inability of primary cells to be cultured long-term *in vitro* (presumably due to the gradual loss of cell stemness during the culture process, leading to the inability of cells to continuously divide), subsequent experiments could not be conducted using primary cells. Isolating primary NSCs was cumbersome, posing challenges in maintaining consistent cell activity and stemness across each batch. Additionally, infecting of primary NSCs with the virus yields low efficiency, presenting challenges in achieving the desired knockout efficiency. Consequently, we adjusted our experimental approach and opted to use the mouse neural stem cell line C17.2 for further experiments.

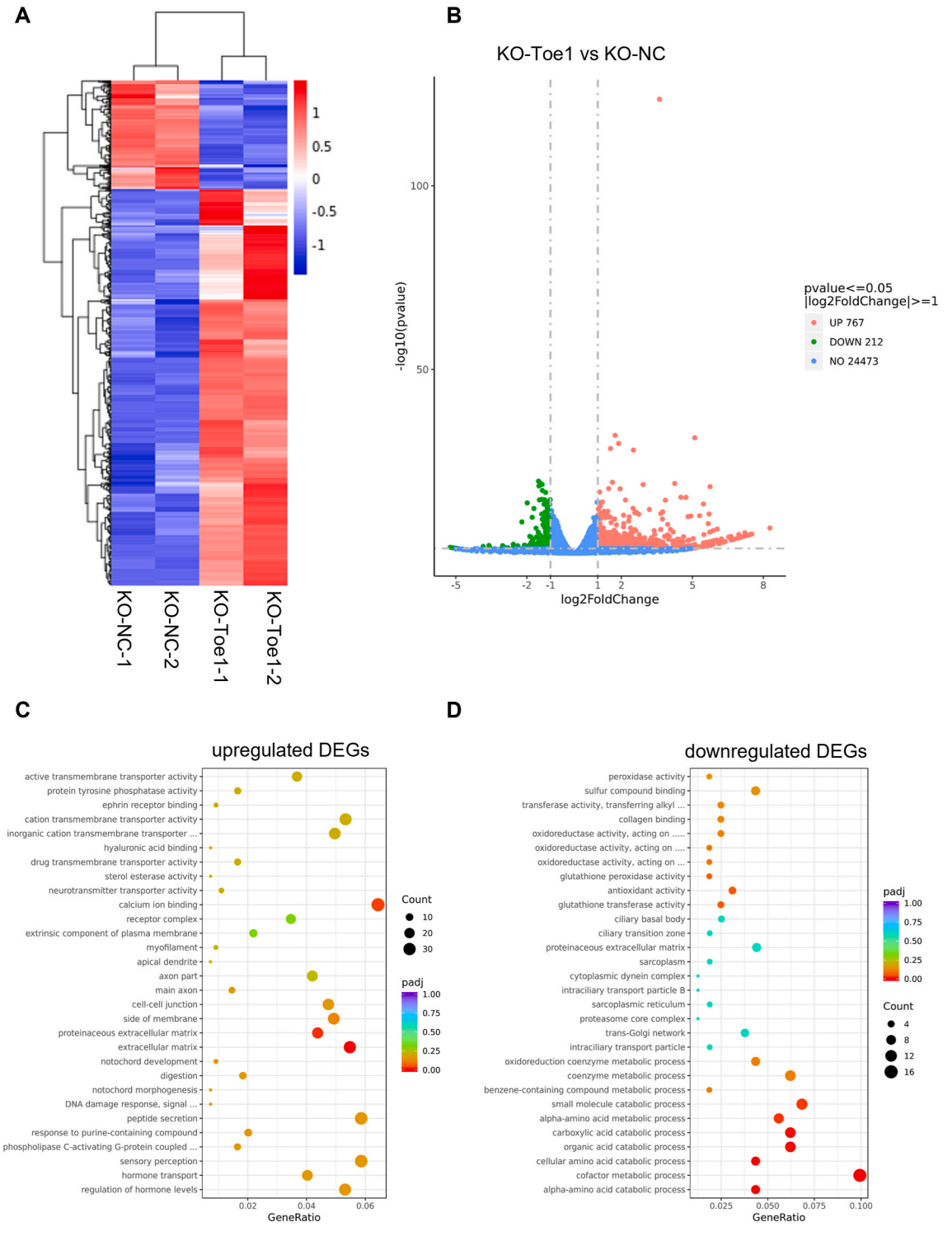
Similar to the previous step, we constructed a C17.2 knockout cell line via lentiviral transfection, and WB confirmed a successful gene knockout effect (Fig. 2-A). To explore the regulatory role of Toe1 in C17.2 cells, we performed a colony formation assay. The results revealed a reduced number of clones formed by Toe1 knockout cells compared to the that of the control group, with thinner clone shapes (Fig. 2-B). This indicated that Toe1 knockout resulted in slower proliferation of C17.2 cells, consistent with observations in primary stem cells. To further validate the phenotypic effects of Toe1 on C17.2 cell growth, EdU and CFSE experiments were conducted. Both experiments confirmed that Toe1 knockout inhibited the growth of NSCs (Fig. 2-C/D/E). Cell cycle analysis demonstrated that Toe1 knockout led to a decrease in the number of cells arrested in the G1 phase and an increase in the number of cells arrested in the S and G2-M phases (Fig. 2-F/G).

### 3.2. Transcriptome analysis of undifferentiated C17.2 cells

We extracted RNA from KO-NC and KO-Toe1 C17.2 cells for high-throughput transcriptome sequencing. A total of 979 DEGs were identified, of which 767 were upregulated and 212 were downregulated (Fig. 3-A/B). GO functional enrichment analysis was conducted to further understand the functions and features of DEGs.

GO results revealed that the most representative Molecular Function category among the upregulated DEGs is "calcium ion binding" (Fig. 3-C), involving 35 genes (Table 2). Calcium ions are common and widely present in living organisms. Calcium ion signaling is a crucial regulatory factor in cell growth and development. Calcium ion signaling can modulate cell proliferation, differentiation, and survival. Elevated intracellular calcium ion concentrations activate numerous calcium-binding proteins and calcium sensors, triggering a cascade of cell growth- and development-related signaling pathways and biological responses.

In the Cellular Component category, upregulated DEGs were predominantly involved in the "extracellular matrix" (Fig. 3-C). The ECM constitutes a three-dimensional network outside the cells, providing structural and biochemical support to the surrounding cells. The ECM is a critical environment for cell growth and development, with components such as collagen and fibronectin that significantly influence cell adhesion, proliferation, morphology, and migration. Growth factors and signaling molecules within the ECM also play a role in directing cell behavior. In our study, upregulated ECM genes (Table 2), including dermatopontin (*Dpt*), fibroblast growth factor receptor 2 (*Fgfr2*), interleukin 1 receptor-like 1 (*Il1rl1*), multimerin 2 (Mmrn2), and the serine (or cysteine) peptidase inhibitor clade E member 2 (*Serpine2*), were enriched in negative regulation of cell population proliferation (GO:0008285). Therefore, elevated expression of these genes may contribute to the observed deceleration in C17.2 cell proliferation.




*(caption on next page)*

**Fig. 3.** Transcriptome analysis of undifferentiated C17.2 cells
(A) Differential expression genes (DEGs) clustering heatmap, where the horizontal axis represents sample names, the vertical axis represents the normalized FPKM values of differentially expressed genes. The color scale ranges from red to blue, indicating higher and lower expression levels, respectively.
(B) Differential expression genes (DEGs) volcano plot, with log2FoldChange values on the horizontal axis and -log10(padj) values on the vertical axis. The blue dashed line represents the threshold line for differential gene selection criteria.
(C) Scatter plot of GO enrichment analysis for upregulated DEGs.
(D)Scatter plot of GO enrichment analysis for downregulated DEGs.

The biological processes associated with downregulated DEGs were primarily related to metabolism (Fig. 3-D), including small-molecule catabolic processes, alpha-amino acid metabolic processes, carboxylic acid catabolic processes, organic acid catabolic processes, cellular amino acid catabolic processes, cofactor metabolic processes, and alpha-amino acid catabolic processes. The potential associations between these metabolic pathways were investigated. Thus, we selected the top five significantly enriched metabolic processes as the primary nodes for constructing a Directed Acyclic Graph displaying the associated GO terms (Supplementary Fig. 1). The bottommost branch node in the graph corresponds to the alpha-amino acid catabolic process, suggesting that this metabolic pathway is most significantly influenced by Toe1.

Amino acid metabolic pathways include protein degradation and amino acid synthesis. During protein degradation, proteins undergo breakdown into amino acids, subsequently entering amino acid synthesis pathways. These amino acids can further synthesize proteins or can be metabolized into other metabolic products for cellular growth. Abnormal expression of genes related to amino acid degradation can disrupt normal amino acid metabolism, leading to downstream product synthesis and potentially impeding cell growth. Decreased expression of genes (Table 2), such as *Ddah2* [17], *Mcc2* [18], and *Tdo2* [19], can result in a decrease in cell proliferation.

### 3.3. Toe1 knockout inhibited the C17.2 cell differentiation

NSCs C17.2 possess the potential to differentiate into neuronal and glial cells. Therefore, we investigated the impact of Toe1 on the differentiation process of C17.2 cells. We induced differentiation of KO-NC and KO-Toe1 C17.2 cells using a differentiation medium. After 6 d of induction, we initially observed changes in cell morphology, where the majority of cells in the control group extended to one or more dendrites, whereas the KO-Toe1 group exhibited fewer cells with dendrites (Fig. 4-A/B). Morphological alterations provide preliminary evidence for the regulation of neural cell differentiation of Toe1. Next, we used Nestin (a marker of NSCs), βIII-tubulin (a marker of neurons), and Gfap (a marker of astrocytes) to determine the differentiation of C17.2 (Fig. 4-C). We also detected mRNA levels of these marker genes by qPCR. qPCR results showed that the expression levels of Nestin and βIII-tubulin were reduced in the KO-Toe1 group, whereas Gfap showed no significant change (Fig. 4-D). However, in WB experiments, the protein expression levels of Nestin, βIII-tubulin, and Gfap in the KO-Toe1 group were significantly lower than those in the control group (Fig. 4-E), aligning with the IF results. These findings suggested that the deletion of Toe1 inhibits the differentiation of NSCs C17.2.

The Notch signaling pathway is an evolutionarily conserved signaling cascade primarily composed of Notch receptors, Notch ligands, CSL/DNA-binding proteins, and downstream target genes [20]. Mammals have four Notch receptors (Notch1-4) and five transmembrane Notch ligands (Jag1, Jag2, Dll1, Dll3, and Dll4). Given the crucial role of the Notch signaling pathway in nervous system development [21], we aimed to investigate whether the deletion of Toe1 affects this pathway. qPCR results indicated that the deletion of Toe1 suppressed the expression of Notch ligands Dll1 and Jag1, while having no significant effect on the Notch receptors Notch1 and Notch2 (Fig. 4-F). These results suggest that Toe1 may regulate Notch pathway by regulating Notch ligand expression, thereby promoting the differentiation of NSCs.

### 3.4. Transcriptome analysis of differentiated C17.2 cells

To further elucidate the mechanisms by which Toe1 regulates the differentiation of NSCs, we performed RNA high-throughput sequencing on KO-NC and KO-Toe1 differentiated cells. A total of 1281 DEGs were obtained, of which 1035 were upregulated and 246 were downregulated genes (Fig. 5-A/B).

GO analysis revealed that the 1035 upregulated DEGs were primarily associated with 439 functional groups, including 359 biological processes (BP), 27 cellular components (CC), and 53 molecular functions (MF). The top 10 most statistically significant terms from each of the BP, CC, and MF subcategories were systematically selected for subsequent visualization.

In the BP category, the top 10 significantly enriched terms were delineated as follows (Fig. 5-C): regulation of endopeptidase activity (46 genes), regulation of peptidase activity (49 genes), defense response to other organisms (51 genes), response to interferon-gamma (25 genes), icosanoid metabolic process (18 genes), fatty acid derivative metabolic process (19 genes), response to interferon-beta (14 genes), cytokine-mediated signaling pathway (40 genes), negative regulation of endopeptidase activity (26 genes), and cell chemotaxis (32 genes), as depicted in Table 3.

Within the CC category, the top 10 significantly enriched terms were characterized as follows (Fig. 5-C): external side of the plasma membrane (37 genes), side of the membrane (50 genes), extracellular membrane-bounded organelle (8 genes), symbiont-containing vacuole (6 genes), plasma membrane protein complex (43 genes), proteinaceous extracellular matrix (34 genes), main axon (13 genes), plasma membrane receptor complex (20 genes), host cell cytoplasm (6 genes), and host cell cytoplasm part (6 genes), as illustrated in Table 3.

**Table 2**
GO categories significantly enriched for differentially expressed genes (DEGs) in undifferentiated C17.2 cells.

| upregulated DEGsupregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
| CC | GO:0031012 | extracellular matrix | 30/548 | 363/15676 | 1.21E-05 | 0.0047945679401624 | ENSMUSG00000019997/ENSMUSG00000031790/ENSMUSG00000072941/ENSMUSG00000025650/ENSMUSG00000026574/ENSMUSG00000022382/ENSMUSG00000060459/ENSMUSG00000026249/ENSMUSG00000031391/ENSMUSG00000055632/ENSMUSG00000030606/ENSMUSG00000020758/ENSMUSG00000022483/ENSMUSG00000041445/ENSMUSG00000026697/ENSMUSG00000048126/ENSMUSG00000004894/ENSMUSG00000026069/ENSMUSG00000033327/ENSMUSG00000043822/ENSMUSG00000064080/ENSMUSG00000041559/ENSMUSG00000035270/ENSMUSG00000005397/ENSMUSG00000038156/ENSMUSG00000044006/ENSMUSG00000029307/ENSMUSG00000030116/ENSMUSG00000025020/ENSMUSG00000030849 | Ctgf/Mmp15/Sod3/Col7a1/Dpt/Wnt7b/Kng2/Serpine2/L1cam/Hmcn2/Hapln3/Itgb4/Col2a1/Mmrn2/Myoc/Col6a3/Hapln2/Il1rl1/Tnxb/Adamtsl5/Fbln2/Fmod/Impg2/Nid1/Spon1/Cilp2/Dmp1/Mfap5/Slit1/Fgfr2 | 30 |
| CC | GO:0005578 | proteinaceous extracellular matrix | 24/548 | 292/15676 | 9.71E-05 | 0.0192247939442793 | ENSMUSG00000019997/ENSMUSG00000025650/ENSMUSG00000026574/ENSMUSG00000022382/ENSMUSG00000055632/ENSMUSG00000030606/ENSMUSG00000020758/ENSMUSG00000022483/ENSMUSG00000041445/ENSMUSG00000026697/ENSMUSG00000048126/ENSMUSG00000004894/ENSMUSG00000026069/ENSMUSG00000033327/ENSMUSG00000043822/ENSMUSG00000064080/ENSMUSG00000041559/ENSMUSG00000035270/ | Ctgf/Col7a1/Dpt/Wnt7b/Hmcn2/Hapln3/Itgb4/Col2a1/Mmrn2/Myoc/Col6a3/Hapln2/Il1rl1/Tnxb/Adamtsl5/Fbln2/Fmod/Impg2/Nid1/Spon1/Cilp2/Dmp1/Mfap5/Slit1 | 24 |

(*continued on next page*)

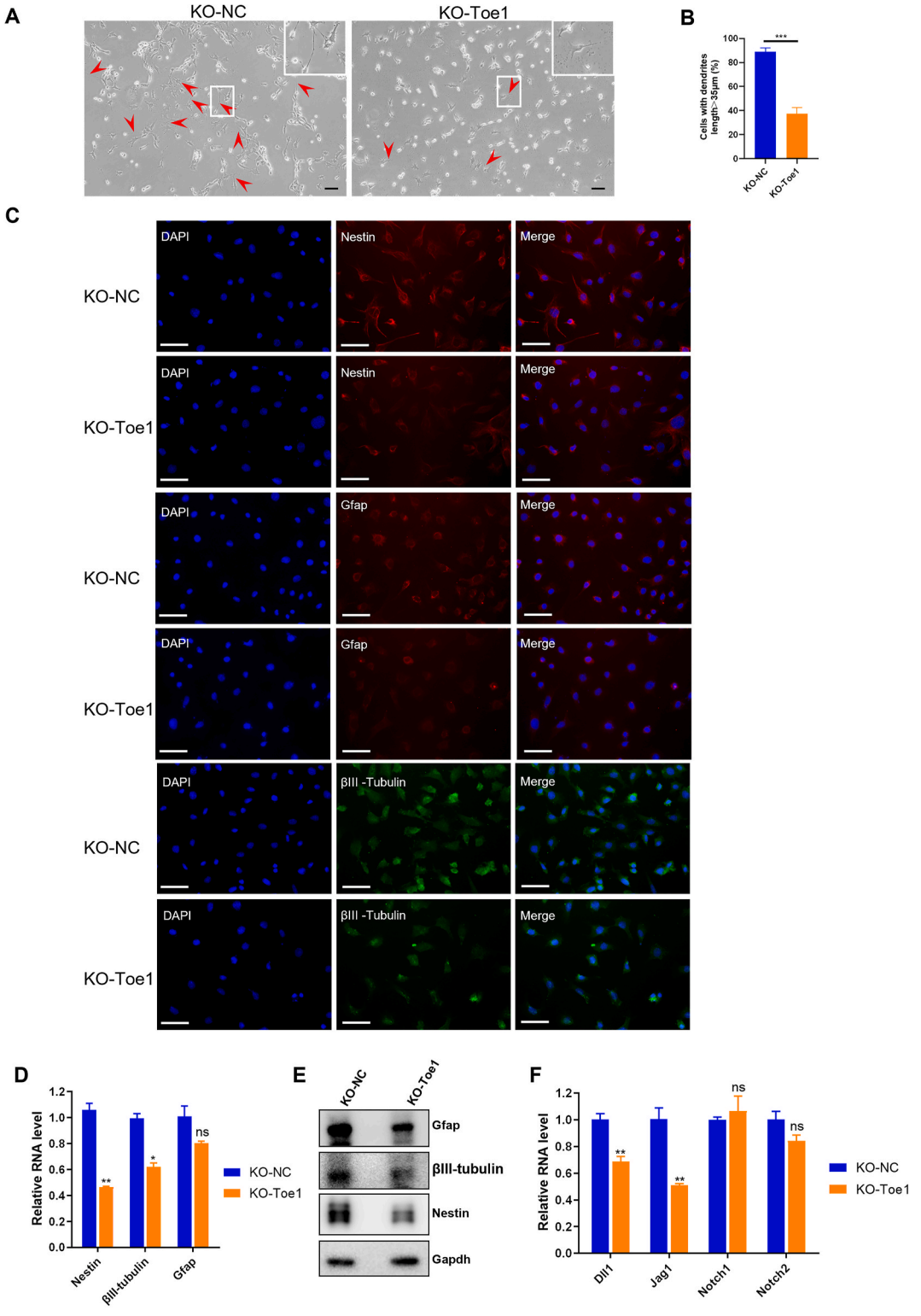
**Table 2** (*continued*)

| upregulated DEGsupregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
| MF | GO:0005509 | calcium ion binding | 35/544 | 483/15421 | 4.66E-05 | 0.0302625472019761 | ENSMUSG00000005397/ENSMUSG00000038156/ENSMUSG00000044006/ENSMUSG00000029307/ENSMUSG00000030116/ENSMUSG00000025020/ENSMUSG00000016995/ENSMUSG00000068923/ENSMUSG00000047428/ENSMUSG00000062591/ENSMUSG00000027171/ENSMUSG00000021950/ENSMUSG00000026414/ENSMUSG00000027861/ENSMUSG00000074264/ENSMUSG00000063767/ENSMUSG00000055632/ENSMUSG00000029055/ENSMUSG00000023000/ENSMUSG00000048895/ENSMUSG00000047216/ENSMUSG00000036862/ENSMUSG00000029608/ENSMUSG00000026175/ENSMUSG00000029544/ENSMUSG00000001021/ENSMUSG00000078144/ENSMUSG00000025473/ENSMUSG00000032776/ENSMUSG00000064080/ENSMUSG00000024430/ENSMUSG00000005397/ENSMUSG00000035860/ENSMUSG00000027435/ENSMUSG00000043789/ENSMUSG00000061723/ENSMUSG00000048827/ENSMUSG00000074486/ENSMUSG00000068452/ENSMUSG00000025020/ENSMUSG00000035183 | Matn4/Syt11/Dlk2/Tubb4a/Prrg4/Anxa8/Tnnt2/Casq2/Amy1/S100a7a/Hmcn2/Plch2/Dhh/Cdk5r1/Cdh19/Dchs1/Rph3a/Vil1/Cabp1/S100a3/Capns2/Adam8/Mctp2/Fbln2/Cabyr/Nid1/Cdhr3/Cd93/Vwce/Tnnt3/Pkd1l3/Bglap2/Duox2/Slit1/Slc24a5 | 35 |
| downregulated DEGs | | | | | | | | | |
| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
| BP | GO:1901606 | alpha-amino acid catabolic process | 7/161 | 66/15663 | 4.98E-06 | 0.00516906308729224 | ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000028011 | Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Tdo2 | 7 |

(*continued on next page*)

**Table 2** (*continued*)

| downregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
| BP | GO:0051186 | cofactor metabolic process | 16/161 | 414/15663 | 5.78E-06 | 0.00516906308729224 | ENSMUSG00000017390/ENSMUSG00000025150/ENSMUSG00000020150/ENSMUSG00000028070/ENSMUSG00000025911/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000001663/ENSMUSG00000004035/ENSMUSG00000040181/ENSMUSG00000062729/ENSMUSG00000029864/ENSMUSG00000026489/ENSMUSG00000029162/ENSMUSG00000028011/ENSMUSG00000004267 | Aldoc/Cbr2/Gamt/Naxe/Adhfe1/Gstz1/Mccc2/Gstt1/Gstm7/Fmo1/Ppox/Gstk1/Coq8a/Khk/Tdo2/Eno2 | 16 |
| BP | GO:0009063 | cellular amino acid catabolic process | 7/161 | 76/15663 | 1.28E-05 | 0.00764680373208239 | ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000028011 | Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Tdo2 | 7 |
| BP | GO:0016054 | organic acid catabolic process | 10/161 | 189/15663 | 2.59E-05 | 0.00925931069791845 | ENSMUSG00000036138/ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000031387/ENSMUSG00000021884/ENSMUSG00000028011 | Acaa1a/Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Renbp/Hacl1/Tdo2 | 10 |
| BP | GO:0046395 | carboxylic acid catabolic process | 10/161 | 189/15663 | 2.59E-05 | 0.00925931069791845 | ENSMUSG00000036138/ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000031387/ENSMUSG00000021884/ENSMUSG00000028011 | Acaa1a/Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Renbp/Hacl1/Tdo2 | 10 |
| BP | GO:1901605 | alpha-amino acid metabolic process | 9/161 | 173/15663 | 7.54E-05 | 0.0224649221494001 | ENSMUSG00000020150/ENSMUSG00000000958/ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000028011 | Gamt/Slc7a7/Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Tdo2 | 9 |
| BP | GO:0044282 | small molecule catabolic process | 11/161 | 266/15663 | 9.71E-05 | 0.0247915380253325 | ENSMUSG00000036138/ENSMUSG00000021238/ENSMUSG00000020840/ENSMUSG00000025911/ENSMUSG00000007039/ENSMUSG00000021033/ENSMUSG00000021646/ENSMUSG00000031387/ENSMUSG00000029162/ENSMUSG00000021884/ENSMUSG00000028011 | Acaa1a/Aldh6a1/Blmh/Adhfe1/Ddah2/Gstz1/Mccc2/Renbp/Khk/Hacl1/Tdo2 | 11 |




*(caption on next page)*

**Fig. 4.** Toe1 knockout inhibited the C17.2 cell differentiation
(A) Microscopic bright-field images capturing C17.2 cells after induction of differentiation. Enlarged images are presented in the upper right corner. Scale bars indicate 100 μm
(B) Quantitative analysis of cells with dendrites length >35 μm ***$p < 0.001$.
(C) Immunofluorescence staining of Nestin, Gfap and βIII-tubulin in differentiated C17.2 cells. Scale bars indicate 60 μm.
(D) qPCR analysis of mRNA levels for Nestin, βIII-tubulin, and Gfap, *$p < 0.05$, **$p < 0.01$.
(E) Western blot analysis of protein levels for Nestin, βIII-tubulin, and Gfap.
(F) qPCR analysis of the impact of Toe1 depletion on Notch pathway-related genes, **$p < 0.01$.

The MF category exhibited the top 10 significantly enriched terms as follows (Fig. 5-C): sterol esterase activity (9 genes), chemokine activity (11 genes), peptidase inhibitor activity (23 genes), chemokine receptor binding (12 genes), triglyceride lipase activity (9 genes), monooxygenase activity (16 genes), glycosaminoglycan binding (25 genes), endopeptidase inhibitor activity (22 genes), endopeptidase regulator activity (22 genes), and peptidase regulator activity (24 genes), as shown in Table 3.

Furthermore, a Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis was conducted on the upregulated DEGs. The findings disclosed four significantly enriched pathways: drug metabolism - other enzymes (15 genes), cytokine-cytokine receptor interaction (30 genes), Tumor Necrosis Factor (TNF) signaling pathway (17 genes), and retinol metabolism (nine genes) (Supplementary Figs. 2–A/B and Table 4).

IKKβ/NF-κB, a pro-inflammatory pathway downstream of the TNF, mediates high-fat diet-induced hypothalamic inflammation, and inflammatory changes can inhibit neurogenesis. Juxue Li et al. found that activation of IKKβ/NF-κB significantly reduces NSC survival and neurogenesis [22], whereas inhibition of IKKβ/NF-κB increases both cell survival and neurogenesis.

In KEGG analysis, seventeen genes exhibited associations with the Tumor Necrosis Factor (TNF) signaling pathway, while thirty genes demonstrated connections with cytokine-cytokine receptor interactions. Furthermore, previous GO analyses identified forty genes linked to the cytokine-mediated signaling pathway. Intriguingly, we discerned the presence of eight genes that concurrently participated in all three functional categories (Cxcl1/Cxcl10/Cx3cl1/Ccl2/Ccl20/Fas/Tnfrsf1b/Il15), as visually represented in Supplementary Figs. 2–C/D. Notably, in the schematic depiction of the TNF signaling pathway (Supplementary Fig. 3), these eight genes are distinctly highlighted in red.

In contrast to upregulated DEGs, the downregulated DEGs exhibited limited functional clustering composed of only nine terms. These include three CC and six MF categories (Fig. 5-D). The three CC terms were proteinaceous ECM (19 genes), ECM (20 genes), and ECM components (7 genes). The six MF terms included scavenger receptor activity (6 genes), extracellular matrix structural constituent (6 genes), cargo receptor activity (7 genes), Wnt protein binding (4 genes), collagen binding (5 genes), and scaffold protein binding (5 genes), as shown in Table 3. These findings suggested that in differentiated C17.2 cells, Toe1 influences downregulated DEGs primarily associated with the ECM.

### *3.5. qPCR validation of gene expression in differentiated C17.2 cells*

According to the results of transcriptome sequencing of differentiated cells, several genes potentially crucial in cell differentiation showing significant differential expression between the two groups were selected for qPCR verification (Fig. 6-A). These genes include: (1) *Ucma* (Ucma upper zone of growth plate and cartilage matrix associated), which encodes a chondrocyte-specific highly charged protein. Upon protein hydrolysis, this gene generates mature proteins secreted into the ECM. GO analysis revealed a strong association between *Ucma* and ECM-related functions. (2) *Cdkn1a* (cyclin-dependent kinase inhibitor 1A) encodes a potent cyclin-dependent kinase inhibitor, inhibiting the activity of CDK2/4. GO analysis indicated that this gene is associated with biological processes such as cell proliferation, leukocyte activation, reactive oxygen species metabolism, DNA damage response, and p53-mediated signal transduction. (3) *Tnfsf18* (tumor necrosis factor (ligand) superfamily, member 18) encodes a protein that belongs to the tumor necrosis factor ligand superfamily. GO analysis indicated that this gene was associated with biological processes such as cell-cell adhesion, monocyte chemotaxis, granulocyte migration, defense response regulation, lymphocyte proliferation regulation, lymphocyte activation regulation, and inflammation response regulation; (4) *Cd74* (CD74 antigen) encodes a protein that acts upstream or internally in various processes, including antigen processing, MHC class II presentation of exogenous peptide antigens, and regulation of T-cell differentiation. GO analysis indicated that this gene is associated with biological processes including class II MHC metabolism, fatty acid derivative metabolism, cytokine-mediated signaling pathways, cell chemotaxis, cell adhesion, granulocyte migration, defense response regulation, and lymphocyte proliferation regulation; (5) *Btn2a2* (butyrophilin, subfamily 2, member A2) encodes a protein that belongs to the butyrophilin protein subfamily A2, and is involved in the regulation of signal receptor binding activity. GO analysis indicated that this gene is associated with biological processes such as negative regulation of cell adhesion, lymphocyte proliferation, and cell activation. (6) *Vnn1* (vanin 1) encodes a protein predicted to be a component of the membrane, and participates in the regulation of theanine hydrolase activity. GO analysis indicated that this gene is associated with biological processes, such as cell-cell adhesion regulation, lymphocyte activation regulation, monocarboxylic acid metabolism, leukocyte differentiation, chronic inflammatory response, and cellular oxidative stress.

qPCR validation confirmed that the expression trends of these six genes were consistent with the sequencing results (Fig. 6-B), demonstrating the accuracy and reliability of the RNA-seq outcomes.

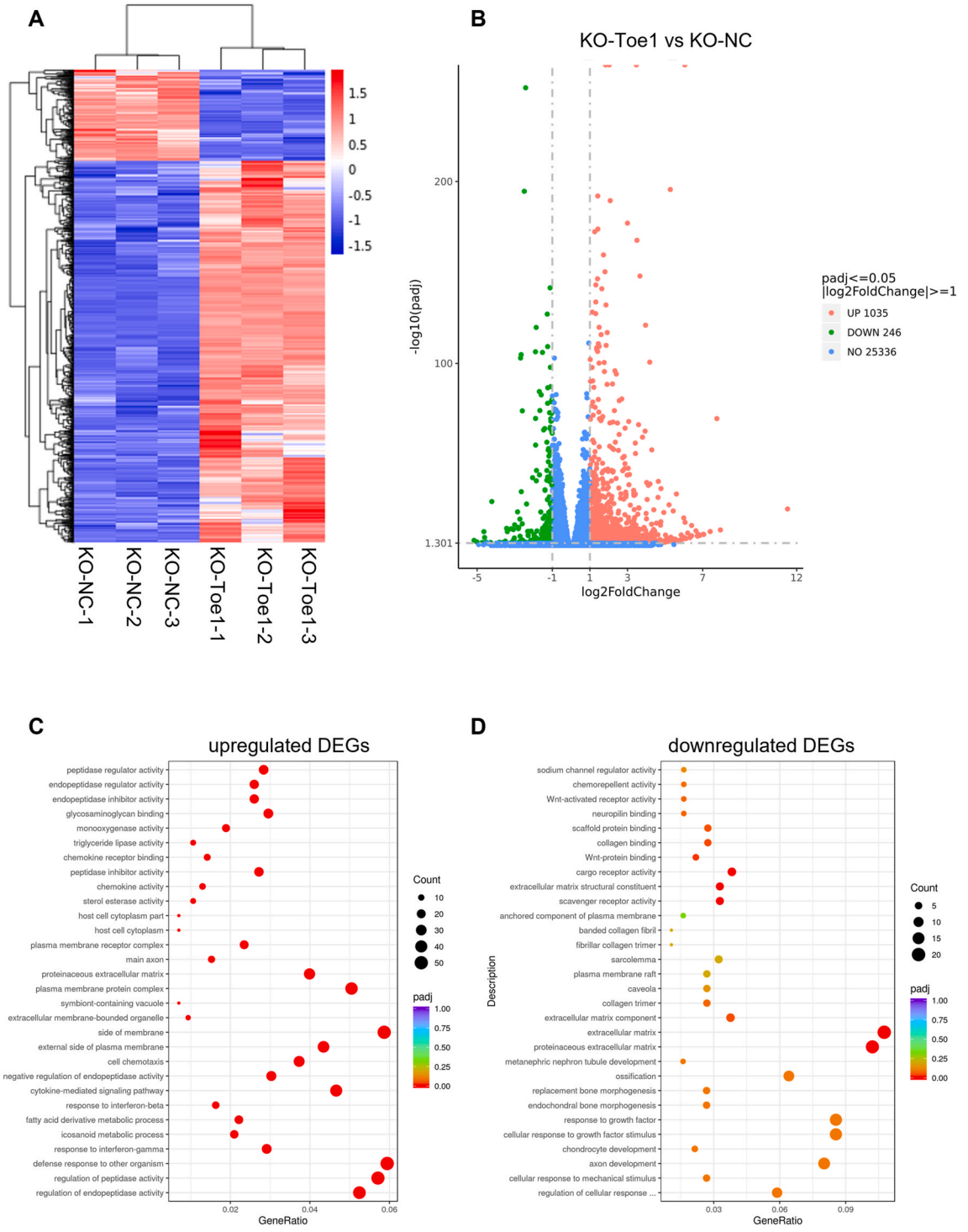



**Fig. 5.** Transcriptome analysis of differentiated C17.2 cells
(A) Hierarchical clustering heatmap of differentially expressed genes.
(B) Volcano plot of differentially expressed genes.
(C) Scatter plot of GO enrichment analysis for upregulated DEGs.
(D)Scatter plot of GO enrichment analysis for downregulated DEGs.

**Table 3**
GO categories significantly enriched for differentially expressed genes (DEGs) in differentiated C17.2 cells.

upregulated DEGs

| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
|---|---|---|---|---|---|---|---|---|---|
| BP | GO:0052548 | regulation of endopeptidase activity | 45/858 | 286/15881 | 8.74E-11 | 2.13E-07 | ENSMUSG00000023030/ENSMUSG00000000753/ENSMUSG00000024778/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000017737/ENSMUSG00000028039/ENSMUSG00000035873/ENSMUSG00000033538/ENSMUSG00000078945/ENSMUSG00000042842/ENSMUSG00000096472/ENSMUSG00000019997/ENSMUSG00000028128/ENSMUSG00000025507/ENSMUSG00000019823/ENSMUSG00000028599/ENSMUSG00000022510/ENSMUSG00000096727/ENSMUSG00000041481/ENSMUSG00000046223/ENSMUSG00000078942/ENSMUSG00000031387/ENSMUSG00000027985/ENSMUSG00000079017/ENSMUSG00000021403/ENSMUSG00000024338/ENSMUSG00000079014/ENSMUSG00000025889/ENSMUSG00000020340/ENSMUSG00000060459/ENSMUSG00000026315/ENSMUSG00000026249/ENSMUSG00000037860/ENSMUSG00000027834/ENSMUSG00000000120/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000071203/ENSMUSG00000051029/ENSMUSG00000019278/ENSMUSG00000028864/ENSMUSG00000004231/ENSMUSG00000025888/ENSMUSG00000079012 | Slc11a2/Serpinf1/Fas/Xdh/Cdkn2a/Mmp9/Efna3/Pawr/Casp4/Naip2/Serpinb6b/Cdkn2d/Ctgf/F3/Pidd1/Mical1/Tnfrsf1b/Trp63/Psmb9/Serpina3g/Plaur/Naip6/Renbp/Lef1/Ifi27l2a/Serpinb9b/Psmb8/Serpina3i/Snca/Cyfip2/Kng2/Serpinb8/Serpine2/Aim2/Serpini1/Ngfr/Adora2a/P2rx1/Naip5/Serpinb1b/Dpep1/Hgf/Pax2/Casp1/Serpina3m | 45 |
| BP | GO:0052547 | regulation of peptidase activity | 49/858 | 329/15881 | 9.29E-11 | 2.13E-07 | ENSMUSG00000017002/ENSMUSG00000023030/ENSMUSG00000000753/ENSMUSG00000024778/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000017737/ENSMUSG00000028039/ENSMUSG00000035873/ENSMUSG00000033538/ENSMUSG00000078945/ENSMUSG00000042842/ENSMUSG00000096472/ENSMUSG00000027082/ENSMUSG00000019997/ENSMUSG00000028128/ENSMUSG00000025507/ENSMUSG00000019823/ENSMUSG00000028599/ENSMUSG00000022510/ENSMUSG00000096727/ENSMUSG00000041481/ENSMUSG00000046223/ENSMUSG00000078942/ENSMUSG00000031387/ENSMUSG00000027985/ENSMUSG00000032359/ENSMUSG00000079017/ENSMUSG00000021403/ENSMUSG00000024338/ENSMUSG00000079014/ENSMUSG00000025889/ENSMUSG00000020340/ENSMUSG00000060459/ENSMUSG00000078949/ENSMUSG00000026315/ENSMUSG00000026249/ENSMUSG00000037860/ENSMUSG00000027834/ENSMUSG00000000120/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000071203/ENSMUSG00000051029/ENSMUSG00000019278/ENSMUSG00000028864/ENSMUSG00000004231/ENSMUSG00000025888/ENSMUSG00000079012 | Slpi/Slc11a2/Serpinf1/Fas/Xdh/Cdkn2a/Mmp9/Efna3/Pawr/Casp4/Naip2/Serpinb6b/Cdkn2d/Tfpi/Ctgf/F3/Pidd1/Mical1/Tnfrsf1b/Trp63/Psmb9/Serpina3g/Plaur/Naip6/Renbp/Lef1/Ctsh/Ifi27l2a/Serpinb9b/Psmb8/Serpina3i/Snca/Cyfip2/Kng2/R3hdml/Serpinb8/Serpine2/Aim2/Serpini1/Ngfr/Adora2a/P2rx1/Naip5/Serpinb1b/Dpep1/Hgf/Pax2/Casp1/Serpina3m | 49 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0098542 | defense response to other organism | 51/858 | 363/15881 | 3.25E-10 | 4.96E-07 | ENSMUSG00000029380/ENSMUSG00000017002/ENSMUSG00000061232/ENSMUSG00000046718/ENSMUSG00000016024/ENSMUSG00000030921/ENSMUSG00000042677/ENSMUSG00000035208/ENSMUSG00000066800/ENSMUSG00000020826/ENSMUSG00000078945/ENSMUSG00000069516/ENSMUSG00000027995/ENSMUSG00000021457/ENSMUSG00000040253/ENSMUSG00000053175/ENSMUSG00000079363/ENSMUSG00000029373/ENSMUSG00000001166/ENSMUSG00000078942/ENSMUSG00000055994/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000035692/ENSMUSG00000026177/ENSMUSG00000028268/ENSMUSG00000017830/ENSMUSG00000032690/ENSMUSG00000020641/ENSMUSG00000000386/ENSMUSG00000002944/ENSMUSG00000104713/ENSMUSG00000059108/ENSMUSG00000029605/ENSMUSG00000029371/ENSMUSG00000034459/ENSMUSG00000032661/ENSMUSG00000037860/ENSMUSG00000034855/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000041515/ENSMUSG00000071203/ENSMUSG00000079164/ENSMUSG00000075370/ENSMUSG00000079339/ENSMUSG00000053318/ENSMUSG00000062157/ENSMUSG00000021948/ENSMUSG00000034266/ENSMUSG00000067773 | Cxcl1/Slpi/H2-K1/Bst2/Lbp/Trim30a/Zc3h12a/Slfn8/Rnasel/Nos2/Naip2/Lyz2/Tlr2/Syk/Gbp7/Bcl3/Gbp4/Pf4/Oas1c/Naip6/Nod2/Gbp9/Iigp1/Isg15/Slc11a1/Gbp3/Dhx58/Oas2/Rsad2/Mx1/Cd36/Gbp6/Ifitm6/Oas1b/Cxcl5/Ifit1/Oas3/Aim2/Cxcl10/Il12rb1/Il15/Irf8/Naip5/Tlr5/Igll1/Ifit1bl1/Slamf8/Ifnlr1/Prkcd/Batf/Defb41 | 51 |
| BP | GO:0034341 | response to interferon-gamma | 25/858 | 110/15881 | 6.60E-10 | 7.56E-07 | ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000046718/ENSMUSG00000035373/ENSMUSG00000074151/ENSMUSG00000037580/ENSMUSG00000020826/ENSMUSG00000026166/ENSMUSG00000040253/ENSMUSG00000019122/ENSMUSG00000079363/ENSMUSG00000029298/ENSMUSG00000034438/ENSMUSG00000026177/ENSMUSG00000025889/ENSMUSG00000028268/ENSMUSG00000031504/ENSMUSG00000035186/ENSMUSG00000104713/ENSMUSG00000059108/ENSMUSG00000000791/ENSMUSG00000041515/ENSMUSG00000031780/ENSMUSG00000078922/ENSMUSG00000025888 | Ccl2/Cx3cl1/Bst2/Ccl7/Nlrc5/Gch1/Nos2/Ccl20/Gbp7/Ccl9/Gbp4/Gbp9/Gbp8/Slc11a1/Snca/Gbp3/Rab20/Ubd/Gbp6/Ifitm6/Il12rb1/Irf8/Ccl17/Tgtp1/Casp1 | 25 |
| BP | GO:0006690 | icosanoid metabolic process | 18/858 | 69/15881 | 1.63E-08 | 1.50E-05 | ENSMUSG00000024610/ENSMUSG00000047250/ENSMUSG00000006344/ENSMUSG00000050737/ENSMUSG00000027995/ENSMUSG00000021457/ENSMUSG00000026688/ENSMUSG00000025002/ENSMUSG00000033715/ENSMUSG00000003484/ENSMUSG00000074604/ENSMUSG00000017969/ENSMUSG00000041193/ENSMUSG00000052974/ENSMUSG00000020892/ENSMUSG00000060063/ENSMUSG00000025955/ENSMUSG00000025197 | Cd74/Ptgs1/Ggt5/Ptges/Tlr2/Syk/Mgst3/Cyp2c55/Akr1c14/Cyp4f18/Mgst2/Ptgis/Pla2g5/Cyp2f2/Aloxe3/Alox5ap/Akr1cl/Cyp2c23 | 18 |
| BP | GO:1901568 | fatty acid derivative metabolic process | 19/858 | 84/15881 | 8.03E-08 | 5.49E-05 | ENSMUSG00000024610/ENSMUSG00000047250/ENSMUSG00000006344/ENSMUSG00000050737/ | Cd74/Ptgs1/Ggt5/Ptges/Tlr2/Syk/Mgst3/Cyp2c55/ | 19 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000026688/ENSMUSG00000025002/ ENSMUSG00000033715/ENSMUSG00000003484/ ENSMUSG00000074604/ENSMUSG00000017969/ ENSMUSG00000041193/ENSMUSG00000052974/ ENSMUSG00000020892/ENSMUSG00000060063/ ENSMUSG00000025955/ENSMUSG00000007908/ ENSMUSG00000025197 | Akr1c14/Cyp4f18/Mgst2/ Ptgis/Pla2g5/Cyp2f2/ Aloxe3/Alox5ap/Akr1cl/ Hmgcll1/Cyp2c23 | |
| BP | GO:0035456 | response to interferon-beta | 14/858 | 47/ 15881 | 1.04E-07 | 5.49E-05 | ENSMUSG00000046718/ENSMUSG00000069893/ ENSMUSG00000054072/ENSMUSG00000028268/ ENSMUSG00000048852/ENSMUSG00000104713/ ENSMUSG00000059108/ENSMUSG00000034459/ ENSMUSG00000037860/ENSMUSG00000068606/ ENSMUSG00000054203/ENSMUSG00000078922/ ENSMUSG00000058163/ENSMUSG00000078921 | Bst2/9930111J21Rik1/ Iigp1/Gbp3/Gm12185/ Gbp6/Ifitm6/Ifit1/Aim2/ Gm4841/Ifi205/Tgtp1/ Gm5431/Tgtp2 | 14 |
| BP | GO:0019221 | cytokine-mediated signaling pathway | 40/858 | 299/ 15881 | 1.05E-07 | 5.49E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000024778/ENSMUSG00000035373/ ENSMUSG00000028965/ENSMUSG00000074151/ ENSMUSG00000033538/ENSMUSG00000022514/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000028599/ENSMUSG00000021457/ ENSMUSG00000012889/ENSMUSG00000019122/ ENSMUSG00000026068/ENSMUSG00000029373/ ENSMUSG00000066755/ENSMUSG00000005057/ ENSMUSG00000054072/ENSMUSG00000008318/ ENSMUSG00000055003/ENSMUSG00000074272/ ENSMUSG00000068227/ENSMUSG00000032690/ ENSMUSG00000059108/ENSMUSG00000029371/ ENSMUSG00000025494/ENSMUSG00000037860/ ENSMUSG00000034855/ENSMUSG00000031712/ ENSMUSG00000000120/ENSMUSG00000040329/ ENSMUSG00000062157/ENSMUSG00000028602/ ENSMUSG00000051379/ENSMUSG00000031780/ ENSMUSG00000025888/ENSMUSG00000004266 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Fas/Ccl7/Tnfrsf9/Nlrc5/ Casp4/Il1rap/F3/Ccl20/ Tnfrsf1b/Syk/Podnl1/Ccl9/ Il18rap/Pf4/Tnfsf18/ Sh2b2/Iigp1/Relt/Lrtm2/ Ceacam1/Il2rb/Oas2/ Ifitm6/Cxcl5/Sigirr/Aim2/ Cxcl10/Il15/Ngfr/Il7/ Ifnlr1/Tnfrsf8/Flrt3/Ccl17/ Casp1/Ptpn6 | 40 |
| BP | GO:0010951 | negative regulation of endopeptidase activity | 26/858 | 150/ 15881 | 1.19E-07 | 5.49E-05 | ENSMUSG00000000753/ENSMUSG00000017737/ ENSMUSG00000078945/ENSMUSG00000042842/ ENSMUSG00000096472/ENSMUSG00000019823/ ENSMUSG00000028599/ENSMUSG00000041481/ ENSMUSG00000046223/ENSMUSG00000078942/ ENSMUSG00000031387/ENSMUSG00000027985/ ENSMUSG00000021403/ENSMUSG00000079014/ ENSMUSG00000025889/ENSMUSG00000060459/ ENSMUSG00000026315/ENSMUSG00000026249/ ENSMUSG00000027834/ENSMUSG00000020178/ ENSMUSG00000071203/ENSMUSG00000051029/ ENSMUSG00000019278/ENSMUSG00000028864/ ENSMUSG00000004231/ENSMUSG00000079012 | Serpinf1/Mmp9/Naip2/ Serpinb6b/Cdkn2d/Mical1/ Tnfrsf1b/Serpina3g/Plaur/ Naip6/Renbp/Lef1/ Serpinb9b/Serpina3i/Snca/ Kng2/Serpinb8/Serpine2/ Serpini1/Adora2a/Naip5/ Serpinb1b/Dpep1/Hgf/ Pax2/Serpina3m | 26 |
| BP | GO:0060326 | cell chemotaxis | 32/858 | 212/ 15881 | 1.26E-07 | 5.49E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ | 32 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000023913/ENSMUSG00000039621/ ENSMUSG00000022676/ENSMUSG00000026166/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000027985/ ENSMUSG00000066755/ENSMUSG00000031520/ ENSMUSG00000040026/ENSMUSG00000074715/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000002489/ENSMUSG00000037362/ ENSMUSG00000074115/ENSMUSG00000053318/ ENSMUSG00000028864/ENSMUSG00000031780/ ENSMUSG00000021948/ENSMUSG00000030707 | Pla2g7/Prex1/Snai2/Ccl20/ Syk/Ccl9/Fgf1/Pf4/Nod2/ Lef1/Tnfsf18/Vegfc/Saa3/ Ccl28/Cxcl5/Cxcl10/ Tiam1/Nov/Saa1/Slamf8/ Hgf/Ccl17/Prkcd/Coro1a | |
| BP | GO:0007162 | negative regulation of cell adhesion | 34/858 | 234/ 15881 | 1.32E-07 | 5.49E-05 | ENSMUSG00000024610/ENSMUSG00000027750/ ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000054855/ENSMUSG00000053965/ ENSMUSG00000019850/ENSMUSG00000022676/ ENSMUSG00000048826/ENSMUSG00000027985/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000076441/ ENSMUSG00000032020/ENSMUSG00000039981/ ENSMUSG00000074715/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000030004/ ENSMUSG00000026249/ENSMUSG00000051262/ ENSMUSG00000020178/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000079494/ ENSMUSG00000021948/ENSMUSG00000028519/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000068748/ENSMUSG00000034652 | Cd74/Postn/Gpnmb/ Cdkn2a/Lgals3/Pawr/ Rnd1/Pde5a/Tnfaip3/ Snai2/Dact2/Lef1/Cd80/ Tnfsf18/Btn2a2/Ass1/ Ubash3b/Zc3h12d/Ccl28/ Ceacam1/Lrrc32/Nat8/ Serpine2/Nat8f3/Adora2a/ Btn1a1/Btla/Nat8f5/Prkcd/ Dab1/Lpxn/Ptpn6/Ptprz1/ Cd300a | 34 |
| BP | GO:1990266 | neutrophil migration | 18/858 | 80/ 15881 | 1.92E-07 | 7.03E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000039621/ ENSMUSG00000026166/ENSMUSG00000021457/ ENSMUSG00000019122/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000029371/ ENSMUSG00000053318/ENSMUSG00000031780 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ Pawr/Prex1/Ccl20/Syk/ Ccl9/Pf4/Nod2/Cxcl5/ Slamf8/Ccl17 | 18 |
| BP | GO:0010466 | negative regulation of peptidase activity | 29/858 | 185/ 15881 | 2.15E-07 | 7.03E-05 | ENSMUSG00000017002/ENSMUSG00000000753/ ENSMUSG00000017737/ENSMUSG00000078945/ ENSMUSG00000042842/ENSMUSG00000096472/ ENSMUSG00000027082/ENSMUSG00000019823/ ENSMUSG00000028599/ENSMUSG00000041481/ ENSMUSG00000046223/ENSMUSG00000078942/ ENSMUSG00000031387/ENSMUSG00000027985/ ENSMUSG00000021403/ENSMUSG00000079014/ ENSMUSG00000025889/ENSMUSG00000060459/ ENSMUSG00000078949/ENSMUSG00000026315/ | Slpi/Serpinf1/Mmp9/ Naip2/Serpinb6b/Cdkn2d/ Tfpi/Mical1/Tnfrsf1b/ Serpina3g/Plaur/Naip6/ Renbp/Lef1/Serpinb9b/ Serpina3i/Snca/Kng2/ R3hdml/Serpinb8/ Serpine2/Serpini1/ Adora2a/Naip5/Serpinb1b/ | 29 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000026249/ENSMUSG00000027834/ ENSMUSG00000020178/ENSMUSG00000071203/ ENSMUSG00000051029/ENSMUSG00000019278/ ENSMUSG00000028864/ENSMUSG00000004231/ ENSMUSG00000079012 | Dpep1/Hgf/Pax2/ Serpina3m | |
| BP | GO:0050878 | regulation of body fluid levels | 35/858 | 250/ 15881 | 2.18E-07 | 7.03E-05 | ENSMUSG00000024164/ENSMUSG00000031778/ ENSMUSG00000024066/ENSMUSG00000042429/ ENSMUSG00000057123/ENSMUSG00000032860/ ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000028128/ENSMUSG00000021457/ ENSMUSG00000022510/ENSMUSG00000032839/ ENSMUSG00000006435/ENSMUSG00000022512/ ENSMUSG00000029373/ENSMUSG00000082361/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000032690/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000041245/ENSMUSG00000020892/ ENSMUSG00000027611/ENSMUSG00000026249/ ENSMUSG00000068323/ENSMUSG00000020178/ ENSMUSG00000063415/ENSMUSG00000020787/ ENSMUSG00000006488/ENSMUSG00000050578/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000044338 | C3/Cx3cl1/Xdh/Adora1/ Gja5/P2ry2/Plau/Tfpi/F3/ Syk/Trp63/Trpc1/Neurl1a/ Cldn1/Pf4/Btc/Ubash3b/ Ceacam1/Oas2/Cd36/ Kng2/Selp/Wnk3/Aloxe3/ Procr/Serpine2/Slc4a5/ Adora2a/Cyp26b1/P2rx1/ Prl7a1/Mmp13/Prkcd/ Ptpn6/Aplnr | 35 |
| BP | GO:2000116 | regulation of cysteine-type endopeptidase activity | 31/858 | 207/ 15881 | 2.37E-07 | 7.03E-05 | ENSMUSG00000023030/ENSMUSG00000024778/ ENSMUSG00000024066/ENSMUSG00000044303/ ENSMUSG00000017737/ENSMUSG00000035873/ ENSMUSG00000033538/ENSMUSG00000078945/ ENSMUSG00000096472/ENSMUSG00000019997/ ENSMUSG00000028128/ENSMUSG00000025507/ ENSMUSG00000019823/ENSMUSG00000028599/ ENSMUSG00000022510/ENSMUSG00000096727/ ENSMUSG00000046223/ENSMUSG00000078942/ ENSMUSG00000027985/ENSMUSG00000079017/ ENSMUSG00000025889/ENSMUSG00000020340/ ENSMUSG00000037860/ENSMUSG00000000120/ ENSMUSG00000020178/ENSMUSG00000020787/ ENSMUSG00000071203/ENSMUSG00000019278/ ENSMUSG00000028864/ENSMUSG00000004231/ ENSMUSG00000025888 | Slc11a2/Fas/Xdh/Cdkn2a/ Mmp9/Pawr/Casp4/Naip2/ Cdkn2d/Ctgf/F3/Pidd1/ Mical1/Tnfrsf1b/Trp63/ Psmb9/Plaur/Naip6/Lef1/ Ifi27l2a/Snca/Cyfip2/ Aim2/Ngfr/Adora2a/ P2rx1/Naip5/Dpep1/Hgf/ Pax2/Casp1 | 31 |
| BP | GO:0022408 | negative regulation of cell-cell adhesion | 25/858 | 146/ 15881 | 2.65E-07 | 7.03E-05 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000044303/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000019850/ENSMUSG00000022676/ ENSMUSG00000027985/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000076441/ENSMUSG00000032020/ ENSMUSG00000039981/ENSMUSG00000074715/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000026249/ENSMUSG00000020178/ ENSMUSG00000000706/ENSMUSG00000052013/ | Cd74/Gpnmb/Cdkn2a/ Lgals3/Pawr/Pde5a/ Tnfaip3/Snai2/Lef1/Cd80/ Tnfsf18/Btn2a2/Ass1/ Ubash3b/Zc3h12d/Ccl28/ Ceacam1/Lrrc32/Serpine2/ Adora2a/Btn1a1/Btla/ Prkcd/Ptpn6/Cd300a | 25 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034652 | | |
| BP | GO:0042742 | defense response to bacterium | 27/858 | 167/ 15881 | 2.97E-07 | 7.03E-05 | ENSMUSG00000017002/ENSMUSG00000061232/ ENSMUSG00000016024/ENSMUSG00000020826/ ENSMUSG00000078945/ENSMUSG00000069516/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000040253/ENSMUSG00000053175/ ENSMUSG00000078942/ENSMUSG00000055994/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000035692/ENSMUSG00000026177/ ENSMUSG00000028268/ENSMUSG00000002944/ ENSMUSG00000104713/ENSMUSG00000029371/ ENSMUSG00000041515/ENSMUSG00000071203/ ENSMUSG00000079164/ENSMUSG00000075370/ ENSMUSG00000053318/ENSMUSG00000021948/ ENSMUSG00000067773 | Slpi/H2-K1/Lbp/Nos2/ Naip2/Lyz2/Tlr2/Syk/ Gbp7/Bcl3/Naip6/Nod2/ Gbp9/Iigp1/Isg15/Slc11a1/ Gbp3/Cd36/Gbp6/Cxcl5/ Irf8/Naip5/Tlr5/Igll1/ Slamf8/Prkcd/Defb41 | 27 |
| BP | GO:0002548 | monocyte chemotaxis | 12/858 | 37/ 15881 | 3.03E-07 | 7.03E-05 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000050335/ ENSMUSG00000023913/ENSMUSG00000026166/ ENSMUSG00000019122/ENSMUSG00000066755/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000053318/ENSMUSG00000031780 | Ccl2/Cx3cl1/Ccl7/Lgals3/ Pla2g7/Ccl20/Ccl9/ Tnfsf18/Cxcl10/Nov/ Slamf8/Ccl17 | 12 |
| BP | GO:0035458 | cellular response to interferon-beta | 12/858 | 37/ 15881 | 3.03E-07 | 7.03E-05 | ENSMUSG00000069893/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000048852/ ENSMUSG00000104713/ENSMUSG00000034459/ ENSMUSG00000037860/ENSMUSG00000068606/ ENSMUSG00000054203/ENSMUSG00000078922/ ENSMUSG00000058163/ENSMUSG00000078921 | 9930111J21Rik1/Iigp1/ Gbp3/Gm12185/Gbp6/ Ifit1/Aim2/Gm4841/ Ifi205/Tgtp1/Gm5431/ Tgtp2 | 12 |
| BP | GO:0030593 | neutrophil chemotaxis | 16/858 | 66/ 15881 | 3.07E-07 | 7.03E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000039621/ENSMUSG00000026166/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000029371/ENSMUSG00000031780 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ Prex1/Ccl20/Syk/Ccl9/Pf4/ Nod2/Cxcl5/Ccl17 | 16 |
| BP | GO:0006691 | leukotriene metabolic process | 8/858 | 15/ 15881 | 3.22E-07 | 7.03E-05 | ENSMUSG00000006344/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000026688/ ENSMUSG00000003484/ENSMUSG00000074604/ ENSMUSG00000041193/ENSMUSG00000060063 | Ggt5/Tlr2/Syk/Mgst3/ Cyp4f18/Mgst2/Pla2g5/ Alox5ap | 8 |
| BP | GO:0097530 | granulocyte migration | 20/858 | 102/ 15881 | 4.44E-07 | 8.93E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000039621/ ENSMUSG00000026166/ENSMUSG00000021457/ ENSMUSG00000019122/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000066755/ ENSMUSG00000029371/ENSMUSG00000053318/ ENSMUSG00000031780/ENSMUSG00000034652 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ Pawr/Prex1/Ccl20/Syk/ Ccl9/Pf4/Nod2/Tnfsf18/ Cxcl5/Slamf8/Ccl17/ Cd300a | 20 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0097529 | myeloid leukocyte migration | 24/858 | 140/15881 | 4.48E-07 | 8.93E-05 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000016024/ENSMUSG00000035373/ENSMUSG00000029082/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000023913/ENSMUSG00000039621/ENSMUSG00000026166/ENSMUSG00000021457/ENSMUSG00000019122/ENSMUSG00000029373/ENSMUSG00000055994/ENSMUSG00000066755/ENSMUSG00000031520/ENSMUSG00000029371/ENSMUSG00000034855/ENSMUSG00000037362/ENSMUSG00000053318/ENSMUSG00000031780/ENSMUSG00000034652 | Cd74/Cxcl1/Ccl2/Cx3cl1/Lbp/Ccl7/Bst1/Lgals3/Pawr/Pla2g7/Prex1/Ccl20/Syk/Ccl9/Pf4/Nod2/Tnfsf18/Vegfc/Cxcl5/Cxcl10/Nov/Slamf8/Ccl17/Cd300a | 24 |
| BP | GO:0031347 | regulation of defense response | 52/858 | 469/15881 | 6.51E-07 | 0.000124324454186619 | ENSMUSG00000024164/ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000016024/ENSMUSG00000000753/ENSMUSG00000030921/ENSMUSG00000042677/ENSMUSG00000029082/ENSMUSG00000074151/ENSMUSG00000003541/ENSMUSG00000042429/ENSMUSG00000033538/ENSMUSG00000053965/ENSMUSG00000020826/ENSMUSG00000019850/ENSMUSG00000062300/ENSMUSG00000079685/ENSMUSG00000027995/ENSMUSG00000028599/ENSMUSG00000034023/ENSMUSG00000053475/ENSMUSG00000019122/ENSMUSG00000079363/ENSMUSG00000026068/ENSMUSG00000055994/ENSMUSG00000066755/ENSMUSG00000025889/ENSMUSG00000017969/ENSMUSG00000041193/ENSMUSG00000017830/ENSMUSG00000074272/ENSMUSG00000020641/ENSMUSG00000002944/ENSMUSG00000029371/ENSMUSG00000037860/ENSMUSG00000030468/ENSMUSG00000000791/ENSMUSG00000037362/ENSMUSG00000031712/ENSMUSG00000060063/ENSMUSG00000020178/ENSMUSG00000030107/ENSMUSG00000044258/ENSMUSG00000079164/ENSMUSG00000021322/ENSMUSG00000053318/ENSMUSG00000062157/ENSMUSG00000059588/ENSMUSG00000028864/ENSMUSG00000025888/ENSMUSG00000034652/ENSMUSG00000025279 | C3/Cd74/Cxcl1/Lbp/Serpinf1/Trim30a/Zc3h12a/Bst1/Nlrc5/Ier3/Adora1/Casp4/Pde5a/Nos2/Tnfaip3/Nectin2/Ulbp1/Tlr2/Tnfrsf1b/Fancd2/Tnfaip6/Ccl9/Gbp4/Il18rap/Nod2/Tnfsf18/Snca/Ptgis/Pla2g5/Dhx58/Ceacam1/Rsad2/Cd36/Cxcl5/Aim2/Siglecg/Il12rb1/Nov/Il15/Alox5ap/Adora2a/Usp18/Ctla2a/Tlr5/Aoah/Slamf8/Ifnlr1/Calcrl/Hgf/Casp1/Cd300a/Dnase1l3 | 52 |
| BP | GO:0001562 | response to protozoan | 11/858 | 33/15881 | 6.94E-07 | 0.000127320561383514 | ENSMUSG00000003541/ENSMUSG00000040253/ENSMUSG00000053175/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000026177/ENSMUSG00000028268/ENSMUSG00000104713/ENSMUSG00000041515/ENSMUSG00000034266 | Ier3/Gbp7/Bcl3/Pf4/Gbp9/Iigp1/Slc11a1/Gbp3/Gbp6/Irf8/Batf | 11 |
| BP | GO:0006935 | chemotaxis | 50/858 | 446/15881 | 7.70E-07 | 0.000135903313202798 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000016024/ENSMUSG00000022995/ENSMUSG00000096188/ENSMUSG00000022636/ENSMUSG00000035373/ENSMUSG00000029082/ENSMUSG00000050335/ENSMUSG00000028039/ | Cd74/Cxcl1/Ccl2/Cx3cl1/Lbp/Enah/Cmtm4/Alcam/Ccl7/Bst1/Lgals3/Efna3/Pla2g7/Prex1/Nrg1/Sema4g/Snai2/Ccl20/Syk/Ccl9/Fgf1/Pf4/Nod2/Etv1/ | 50 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000023913/ENSMUSG00000039621/ ENSMUSG00000062991/ENSMUSG00000025207/ ENSMUSG00000022676/ENSMUSG00000026166/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000004151/ ENSMUSG00000027985/ENSMUSG00000066755/ ENSMUSG00000056486/ENSMUSG00000031520/ ENSMUSG00000040026/ENSMUSG00000074715/ ENSMUSG00000020340/ENSMUSG00000017724/ ENSMUSG00000029371/ENSMUSG00000026442/ ENSMUSG00000052516/ENSMUSG00000025427/ ENSMUSG00000034855/ENSMUSG00000002489/ ENSMUSG00000037362/ENSMUSG00000000120/ ENSMUSG00000074115/ENSMUSG00000053318/ ENSMUSG00000028602/ENSMUSG00000028864/ ENSMUSG00000051379/ENSMUSG00000031780/ ENSMUSG00000043953/ENSMUSG00000021948/ ENSMUSG00000048251/ENSMUSG00000030707 | Lef1/Tnfsf18/Chn1/Vegfc/ Saa3/Ccl28/Cyfip2/Etv4/ Cxcl5/Nfasc/Robo2/ Rnf165/Cxcl10/Tiam1/ Nov/Ngfr/Saa1/Slamf8/ Tnfrsf8/Hgf/Flrt3/Ccl17/ Ccrl2/Prkcd/Bcl11b/Coro1a | |
| BP | GO:0042330 | taxis | 50/858 | 448/ 15881 | 8.80E-07 | 0.000149504937037632 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000022995/ ENSMUSG00000096188/ENSMUSG00000022636/ ENSMUSG00000035373/ENSMUSG00000029082/ ENSMUSG00000050335/ENSMUSG00000028039/ ENSMUSG00000023913/ENSMUSG00000039621/ ENSMUSG00000062991/ENSMUSG00000025207/ ENSMUSG00000022676/ENSMUSG00000026166/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000004151/ ENSMUSG00000027985/ENSMUSG00000066755/ ENSMUSG00000056486/ENSMUSG00000031520/ ENSMUSG00000040026/ENSMUSG00000074715/ ENSMUSG00000020340/ENSMUSG00000017724/ ENSMUSG00000029371/ENSMUSG00000026442/ ENSMUSG00000052516/ENSMUSG00000025427/ ENSMUSG00000034855/ENSMUSG00000002489/ ENSMUSG00000037362/ENSMUSG00000000120/ ENSMUSG00000074115/ENSMUSG00000053318/ ENSMUSG00000028602/ENSMUSG00000028864/ ENSMUSG00000051379/ENSMUSG00000031780/ ENSMUSG00000043953/ENSMUSG00000021948/ ENSMUSG00000048251/ENSMUSG00000030707 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Enah/Cmtm4/Alcam/ Ccl7/Bst1/Lgals3/Efna3/ Pla2g7/Prex1/Nrg1/ Sema4g/Snai2/Ccl20/Syk/ Ccl9/Fgf1/Pf4/Nod2/Etv1/ Lef1/Tnfsf18/Chn1/Vegfc/ Saa3/Ccl28/Cyfip2/Etv4/ Cxcl5/Nfasc/Robo2/ Rnf165/Cxcl10/Tiam1/ Nov/Ngfr/Saa1/Slamf8/ Tnfrsf8/Hgf/Flrt3/Ccl17/ Ccrl2/Prkcd/Bcl11b/Coro1a | 50 |
| BP | GO:0071346 | cellular response to interferon-gamma | 18/858 | 89/ 15881 | 1.03E-06 | 0.000169109125338634 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000074151/ ENSMUSG00000020826/ENSMUSG00000026166/ ENSMUSG00000040253/ENSMUSG00000019122/ ENSMUSG00000079363/ENSMUSG00000029298/ ENSMUSG00000034438/ENSMUSG00000028268/ | Ccl2/Cx3cl1/Ccl7/Nlrc5/ Nos2/Ccl20/Gbp7/Ccl9/ Gbp4/Gbp9/Gbp8/Gbp3/ Rab20/Gbp6/Il12rb1/Irf8/ Ccl17/Casp1 | 18 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000031504/ENSMUSG00000104713/ENSMUSG00000000791/ENSMUSG00000041515/ENSMUSG00000031780/ENSMUSG00000025888 | | |
| BP | GO:0006942 | regulation of striated muscle contraction | 15/858 | 64/15881 | 1.14E-06 | 0.000173364212662983 | ENSMUSG00000042677/ENSMUSG00000006457/ENSMUSG00000042429/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000019997/ENSMUSG00000050541/ENSMUSG00000061603/ENSMUSG00000024065/ENSMUSG00000041695/ENSMUSG00000036570/ENSMUSG00000027470/ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Actn3/Adora1/Pde5a/Gja5/Atp1b1/Ctgf/Adra1b/Akap6/Ehd3/Kcnj2/Fxyd1/Mylk2/Tnni3/Hrc | 15 |
| BP | GO:1903038 | negative regulation of leukocyte cell-cell adhesion | 19/858 | 99/15881 | 1.21E-06 | 0.000173364212662983 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000044303/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000076441/ENSMUSG00000039981/ENSMUSG00000074715/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000020178/ENSMUSG00000000706/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000034652 | Cd74/Gpnmb/Cdkn2a/Lgals3/Pawr/Pde5a/Cd80/Tnfsf18/Btn2a2/Ass1/Zc3h12d/Ccl28/Ceacam1/Lrrc32/Adora2a/Btn1a1/Btla/Ptpn6/Cd300a | 19 |
| BP | GO:0022407 | regulation of cell-cell adhesion | 38/858 | 304/15881 | 1.23E-06 | 0.000173364212662983 | ENSMUSG00000024610/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000029816/ENSMUSG00000044303/ENSMUSG00000037440/ENSMUSG00000000732/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000019850/ENSMUSG00000022676/ENSMUSG00000021457/ENSMUSG00000027985/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000076441/ENSMUSG00000032020/ENSMUSG00000039981/ENSMUSG00000041351/ENSMUSG00000074715/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000026249/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000020178/ENSMUSG00000040329/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000021948/ENSMUSG00000004266/ENSMUSG00000020325/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Ccl2/Cx3cl1/Gpnmb/Cdkn2a/Vnn1/Icosl/Lgals3/Pawr/Pde5a/Tnfaip3/Snai2/Syk/Lef1/Cd80/Tnfsf18/Btn2a2/Ass1/Ubash3b/Zc3h12d/Rap1gap/Ccl28/Ceacam1/Lrrc32/Serpine2/Il12rb1/Il15/Adora2a/Il7/Btn1a1/Igfbp2/Btla/Prkcd/Ptpn6/Fstl3/Cd300a/Coro1a/Zap70 | 38 |
| BP | GO:0006936 | muscle contraction | 31/858 | 223/15881 | 1.24E-06 | 0.000173364212662983 | ENSMUSG00000042677/ENSMUSG00000006457/ENSMUSG00000047250/ENSMUSG00000035873/ENSMUSG00000042429/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000022144/ENSMUSG00000019997/ENSMUSG00000040907/ENSMUSG00000050541/ENSMUSG00000026251/ENSMUSG00000026253/ENSMUSG00000061603/ENSMUSG00000021070/ENSMUSG00000028834/ENSMUSG00000055632/ENSMUSG00000042451/ENSMUSG00000064329/ | Zc3h12a/Actn3/Ptgs1/Pawr/Adora1/Pde5a/Gja5/Atp1b1/Gdnf/Ctgf/Atp1a3/Adra1b/Chrnd/Chrng/Akap6/Bdkrb2/Trim63/Hmcn2/Mybph/Scn1a/Ehd3/P2rx1/Tnni1/Kcnj2/Calcrl/P2rx3/Fxyd1/Mylk2/Tnni3/Hrc/Tacr2 | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000024065/ENSMUSG00000020787/ ENSMUSG00000026418/ENSMUSG00000041695/ ENSMUSG00000059588/ENSMUSG00000027071/ ENSMUSG00000036570/ENSMUSG00000027470/ ENSMUSG00000035458/ENSMUSG00000038239/ ENSMUSG00000020081 | | |
| BP | GO:0003013 circulatory system process | 43/858 | 365/ 15881 | 1.25E-06 | 0.000173364212662983 | ENSMUSG00000031778/ENSMUSG00000059895/ ENSMUSG00000027750/ENSMUSG00000042677/ ENSMUSG00000026463/ENSMUSG00000038235/ ENSMUSG00000028024/ENSMUSG00000003541/ ENSMUSG00000047250/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000020826/ ENSMUSG00000032860/ENSMUSG00000026576/ ENSMUSG00000029084/ENSMUSG00000019997/ ENSMUSG00000024039/ENSMUSG00000040907/ ENSMUSG00000050541/ENSMUSG00000003484/ ENSMUSG00000061603/ENSMUSG00000031520/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000024481/ENSMUSG00000021070/ ENSMUSG00000041046/ENSMUSG00000064329/ ENSMUSG00000068323/ENSMUSG00000024065/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000035296/ ENSMUSG00000026418/ENSMUSG00000041695/ ENSMUSG00000036570/ENSMUSG00000031489/ ENSMUSG00000035458/ENSMUSG00000038239/ ENSMUSG00000020081 | Cx3cl1/Ptp4a3/Postn/ Zc3h12a/Atp2b4/F11r/ Enpep/Ier3/Ptgs1/Adora1/ Gch1/Pde5a/Gja5/Nos2/ P2ry2/Atp1b1/Cd38/Ctgf/ Cbs/Atp1a3/Adra1b/ Cyp4f18/Akap6/Vegfc/ Ceacam1/Cd36/Lvrn/ Bdkrb2/Ramp3/Scn1a/ Slc4a5/Ehd3/Nos3/ Adora2a/P2rx1/Sgcg/ Tnni1/Kcnj2/Fxyd1/Adrb3/ Tnni3/Hrc/Tacr2 | 43 |
| BP | GO:0009617 response to bacterium | 47/858 | 416/ 15881 | 1.33E-06 | 0.00017943813373397 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000017002/ENSMUSG00000061232/ ENSMUSG00000016024/ENSMUSG00000024778/ ENSMUSG00000042677/ENSMUSG00000028965/ ENSMUSG00000037580/ENSMUSG00000020826/ ENSMUSG00000078945/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000069516/ ENSMUSG00000027995/ENSMUSG00000028599/ ENSMUSG00000021457/ENSMUSG00000040253/ ENSMUSG00000053175/ENSMUSG00000029373/ ENSMUSG00000078942/ENSMUSG00000055994/ ENSMUSG00000029298/ENSMUSG00000075122/ ENSMUSG00000054072/ENSMUSG00000035692/ ENSMUSG00000008318/ENSMUSG00000026177/ ENSMUSG00000025889/ENSMUSG00000028268/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000104713/ENSMUSG00000070034/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000028978/ENSMUSG00000000120/ ENSMUSG00000041515/ENSMUSG00000071203/ ENSMUSG00000079164/ENSMUSG00000075370/ ENSMUSG00000053318/ENSMUSG00000028602/ | Cxcl1/Ccl2/Slpi/H2-K1/ Lbp/Fas/Zc3h12a/Tnfrsf9/ Gch1/Nos2/Naip2/Tnfaip3/ Trib1/Lyz2/Tlr2/Tnfrsf1b/ Syk/Gbp7/Bcl3/Pf4/Naip6/ Nod2/Gbp9/Cd80/Iigp1/ Isg15/Relt/Slc11a1/Snca/ Gbp3/Abca1/Cd36/Gbp6/ Sp110/Cxcl5/Cxcl10/Nos3/ Ngfr/Irf8/Naip5/Tlr5/Igll1/ Slamf8/Tnfrsf8/Prkcd/ Casp1/Defb41 | 47 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000021948/ENSMUSG00000025888/ ENSMUSG00000067773 | | |
| BP | GO:0050670 | regulation of lymphocyte proliferation | 27/858 | 182/ 15881 | 1.69E-06 | 0.00022198362143384 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000023067/ENSMUSG00000044303/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000029084/ ENSMUSG00000021457/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000040329/ ENSMUSG00000000706/ENSMUSG00000039323/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Cd74/Gpnmb/Cdkn1a/ Cdkn2a/Icosl/Bst1/Lgals3/ Pawr/Pde5a/Cd38/Syk/ Cd80/Tnfsf18/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Il12rb1/Il15/Il7/Btn1a1/ Igfbp2/Btla/Ptpn6/Cd300a/ Coro1a/Zap70 | 27 |
| BP | GO:0006937 | regulation of muscle contraction | 21/858 | 121/ 15881 | 1.89E-06 | 0.000240633636531606 | ENSMUSG00000042677/ENSMUSG00000006457/ ENSMUSG00000047250/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000026576/ ENSMUSG00000019997/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000024065/ ENSMUSG00000020787/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000059588/ ENSMUSG00000036570/ENSMUSG00000027470/ ENSMUSG00000035458/ENSMUSG00000038239/ ENSMUSG00000020081 | Zc3h12a/Actn3/Ptgs1/ Pawr/Adora1/Pde5a/Gja5/ Atp1b1/Ctgf/Adra1b/ Akap6/Ehd3/P2rx1/Tnni1/ Kcnj2/Calcrl/Fxyd1/Mylk2/ Tnni3/Hrc/Tacr2 | 21 |
| BP | GO:0032944 | regulation of mononuclear cell proliferation | 27/858 | 184/ 15881 | 2.10E-06 | 0.000260386556786972 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000023067/ENSMUSG00000044303/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000029084/ ENSMUSG00000021457/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000040329/ ENSMUSG00000000706/ENSMUSG00000039323/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Cd74/Gpnmb/Cdkn1a/ Cdkn2a/Icosl/Bst1/Lgals3/ Pawr/Pde5a/Cd38/Syk/ Cd80/Tnfsf18/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Il12rb1/Il15/Il7/Btn1a1/ Igfbp2/Btla/Ptpn6/Cd300a/ Coro1a/Zap70 | 27 |
| BP | GO:0042832 | defense response to protozoan | 10/858 | 30/ 15881 | 2.25E-06 | 0.000269734057898988 | ENSMUSG00000040253/ENSMUSG00000053175/ ENSMUSG00000029373/ENSMUSG00000029298/ ENSMUSG00000054072/ENSMUSG00000026177/ ENSMUSG00000028268/ENSMUSG00000104713/ ENSMUSG00000041515/ENSMUSG00000034266 | Gbp7/Bcl3/Pf4/Gbp9/ Iigp1/Slc11a1/Gbp3/Gbp6/ Irf8/Batf | 10 |
| BP | GO:0008015 | blood circulation | 42/858 | 361/ 15881 | 2.29E-06 | 0.000269734057898988 | ENSMUSG00000031778/ENSMUSG00000059895/ ENSMUSG00000027750/ENSMUSG00000042677/ ENSMUSG00000026463/ENSMUSG00000038235/ ENSMUSG00000028024/ENSMUSG00000003541/ | Cx3cl1/Ptp4a3/Postn/ Zc3h12a/Atp2b4/F11r/ Enpep/Ier3/Ptgs1/Adora1/ Gch1/Pde5a/Gja5/Nos2/ | 42 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000047250/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000020826/ ENSMUSG00000032860/ENSMUSG00000026576/ ENSMUSG00000029084/ENSMUSG00000019997/ ENSMUSG00000024039/ENSMUSG00000040907/ ENSMUSG00000050541/ENSMUSG00000003484/ ENSMUSG00000061603/ENSMUSG00000031520/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000024481/ENSMUSG00000021070/ ENSMUSG00000064329/ENSMUSG00000068323/ ENSMUSG00000024065/ENSMUSG00000028978/ ENSMUSG00000020178/ENSMUSG00000020787/ ENSMUSG00000035296/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000036570/ ENSMUSG00000031489/ENSMUSG00000035458/ ENSMUSG00000038239/ENSMUSG00000020081 | P2ry2/Atp1b1/Cd38/Ctgf/ Cbs/Atp1a3/Adra1b/ Cyp4f18/Akap6/Vegfc/ Ceacam1/Cd36/Lvrn/ Bdkrb2/Scn1a/Slc4a5/ Ehd3/Nos3/Adora2a/ P2rx1/Sgcg/Tnni1/Kcnj2/ Fxyd1/Adrb3/Tnni3/Hrc/ Tacr2 | |
| BP | GO:0050865 | regulation of cell activation | 48/858 | 439/ 15881 | 2.60E-06 | 0.000298397855416916 | ENSMUSG00000024610/ENSMUSG00000035385/ ENSMUSG00000029816/ENSMUSG00000016024/ ENSMUSG00000023067/ENSMUSG00000024778/ ENSMUSG00000044303/ENSMUSG00000037440/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000019850/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000019997/ENSMUSG00000079685/ ENSMUSG00000034023/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000025889/ENSMUSG00000041193/ ENSMUSG00000032020/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000026580/ENSMUSG00000026249/ ENSMUSG00000031548/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000020178/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000044258/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000075370/ ENSMUSG00000052013/ENSMUSG00000021948/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/Lbp/ Cdkn1a/Fas/Cdkn2a/Vnn1/ Icosl/Bst1/Lgals3/Pawr/ Pde5a/Tnfaip3/Cd38/ Nectin2/Ctgf/Ulbp1/ Fancd2/Syk/Nod2/Cd80/ Tnfsf18/Btn2a2/Snca/ Pla2g5/Ubash3b/Zc3h12d/ Ceacam1/Lrrc32/Selp/ Serpine2/Sfrp1/Il12rb1/ Il15/Adora2a/Il7/ Cyp26b1/Ctla2a/Btn1a1/ Igfbp2/Igll1/Btla/Prkcd/ Ptpn6/Cd300a/Coro1a/ Zap70 | 48 |
| BP | GO:0071621 | granulocyte chemotaxis | 17/858 | 86/ 15881 | 2.86E-06 | 0.000314568211123084 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000039621/ENSMUSG00000026166/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000066755/ENSMUSG00000029371/ ENSMUSG00000031780 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ Prex1/Ccl20/Syk/Ccl9/Pf4/ Nod2/Tnfsf18/Cxcl5/Ccl17 | 17 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0070663 | regulation of leukocyte proliferation | 27/858 | 187/15881 | 2.88E-06 | 0.000314568211123084 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000023067/ENSMUSG00000044303/ENSMUSG00000000732/ENSMUSG00000029082/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000029084/ENSMUSG00000021457/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000040329/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Gpnmb/Cdkn1a/Cdkn2a/Icosl/Bst1/Lgals3/Pawr/Pde5a/Cd38/Syk/Cd80/Tnfsf18/Btn2a2/Zc3h12d/Ceacam1/Lrrc32/Il12rb1/Il15/Il7/Btn1a1/Igfbp2/Btla/Ptpn6/Cd300a/Coro1a/Zap70 | 27 |
| BP | GO:0042110 | T cell activation | 43/858 | 378/15881 | 3.14E-06 | 0.000332999720706009 | ENSMUSG00000024610/ENSMUSG00000035385/ENSMUSG00000029816/ENSMUSG00000024778/ENSMUSG00000029570/ENSMUSG00000023927/ENSMUSG00000044303/ENSMUSG00000037440/ENSMUSG00000000732/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000039621/ENSMUSG00000034023/ENSMUSG00000021457/ENSMUSG00000053175/ENSMUSG00000027985/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000026177/ENSMUSG00000049109/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000020641/ENSMUSG00000090958/ENSMUSG00000036587/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000020178/ENSMUSG00000040329/ENSMUSG00000063415/ENSMUSG00000044258/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000048251/ENSMUSG00000004266/ENSMUSG00000021998/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000034266/ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/Fas/Lfng/Satb1/Cdkn2a/Vnn1/Icosl/Lgals3/Pawr/Pde5a/Prex1/Fancd2/Syk/Bcl3/Lef1/Cd80/Tnfsf18/Btn2a2/Slc11a1/Themis/Zc3h12d/Ceacam1/Rsad2/Lrrc32/Fut7/Il12rb1/Il15/Adora2a/Il7/Cyp26b1/Ctla2a/Btn1a1/Igfbp2/Btla/Bcl11b/Ptpn6/Lcp1/Cd300a/Coro1a/Batf/Zap70 | 43 |
| BP | GO:0043281 | regulation of cysteine-type endopeptidase activity involved in apoptotic process | 27/858 | 188/15881 | 3.19E-06 | 0.000332999720706009 | ENSMUSG00000023030/ENSMUSG00000024778/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000017737/ENSMUSG00000033538/ENSMUSG00000078945/ENSMUSG00000096472/ENSMUSG00000019997/ENSMUSG00000028128/ENSMUSG00000025507/ENSMUSG00000019823/ENSMUSG00000028599/ENSMUSG00000022510/ENSMUSG00000046223/ENSMUSG00000078942/ENSMUSG00000027985/ENSMUSG00000079017/ENSMUSG00000025889/ENSMUSG00000000120/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000071203/ENSMUSG00000019278/ENSMUSG00000028864/ENSMUSG00000004231/ENSMUSG00000025888 | Slc11a2/Fas/Xdh/Cdkn2a/Mmp9/Casp4/Naip2/Cdkn2d/Ctgf/F3/Pidd1/Mical1/Tnfrsf1b/Trp63/Plaur/Naip6/Lef1/Ifi27l2a/Snca/Ngfr/Adora2a/P2rx1/Naip5/Dpep1/Hgf/Pax2/Casp1 | 27 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0002685 | regulation of leukocyte migration | 24/858 | 156/15881 | 3.31E-06 | 0.000337249425959055 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000016024/ENSMUSG00000029082/ENSMUSG00000017737/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000042429/ENSMUSG00000023913/ENSMUSG00000026166/ENSMUSG00000027995/ENSMUSG00000029373/ENSMUSG00000055994/ENSMUSG00000066755/ENSMUSG00000031520/ENSMUSG00000074715/ENSMUSG00000026580/ENSMUSG00000029371/ENSMUSG00000034855/ENSMUSG00000037362/ENSMUSG00000053318/ENSMUSG00000034652 | Cd74/Cxcl1/Ccl2/Cx3cl1/Lbp/Bst1/Mmp9/Lgals3/Pawr/Adora1/Pla2g7/Ccl20/Tlr2/Pf4/Nod2/Tnfsf18/Vegfc/Ccl28/Selp/Cxcl5/Cxcl10/Nov/Slamf8/Cd300a | 24 |
| BP | GO:0055117 | regulation of cardiac muscle contraction | 13/858 | 53/15881 | 3.42E-06 | 0.000341319570521802 | ENSMUSG00000042677/ENSMUSG00000042429/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000019997/ENSMUSG00000050541/ENSMUSG00000061603/ENSMUSG00000024065/ENSMUSG00000041695/ENSMUSG00000036570/ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Adora1/Pde5a/Gja5/Atp1b1/Ctgf/Adra1b/Akap6/Ehd3/Kcnj2/Fxyd1/Tnni3/Hrc | 13 |
| BP | GO:0050727 | regulation of inflammatory response | 33/858 | 258/15881 | 3.71E-06 | 0.000361653508798864 | ENSMUSG00000024164/ENSMUSG00000016024/ENSMUSG00000000753/ENSMUSG00000042677/ENSMUSG00000029082/ENSMUSG00000003541/ENSMUSG00000042429/ENSMUSG00000033538/ENSMUSG00000053965/ENSMUSG00000020826/ENSMUSG00000019850/ENSMUSG00000027995/ENSMUSG00000028599/ENSMUSG00000034023/ENSMUSG00000053475/ENSMUSG00000019122/ENSMUSG00000055994/ENSMUSG00000066755/ENSMUSG00000025889/ENSMUSG00000017969/ENSMUSG00000041193/ENSMUSG00000030468/ENSMUSG00000037362/ENSMUSG00000060063/ENSMUSG00000020178/ENSMUSG00000030107/ENSMUSG00000044258/ENSMUSG00000021322/ENSMUSG00000053318/ENSMUSG00000059588/ENSMUSG00000028864/ENSMUSG00000025888/ENSMUSG00000025279 | C3/Lbp/Serpinf1/Zc3h12a/Bst1/Ier3/Adora1/Casp4/Pde5a/Nos2/Tnfaip3/Tlr2/Tnfrsf1b/Fancd2/Tnfaip6/Ccl9/Nod2/Tnfsf18/Snca/Ptgis/Pla2g5/Siglecg/Nov/Alox5ap/Adora2a/Usp18/Ctla2a/Aoah/Slamf8/Calcrl/Hgf/Casp1/Dnase1l3 | 33 |
| BP | GO:0019370 | leukotriene biosynthetic process | 6/858 | 10/15881 | 4.26E-06 | 0.000406611537396964 | ENSMUSG00000006344/ENSMUSG00000021457/ENSMUSG00000026688/ENSMUSG00000074604/ENSMUSG00000041193/ENSMUSG00000060063 | Ggt5/Syk/Mgst3/Mgst2/Pla2g5/Alox5ap | 6 |
| BP | GO:0006941 | striated muscle contraction | 21/858 | 128/15881 | 4.78E-06 | 0.000447693376838909 | ENSMUSG00000042677/ENSMUSG00000006457/ENSMUSG00000042429/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000019997/ENSMUSG00000040907/ENSMUSG00000050541/ENSMUSG00000026251/ENSMUSG00000026253/ENSMUSG00000061603/ENSMUSG00000042451/ENSMUSG00000064329/ENSMUSG00000024065/ENSMUSG00000026418/ENSMUSG00000041695/ENSMUSG00000036570/ENSMUSG00000027470/ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Actn3/Adora1/Pde5a/Gja5/Atp1b1/Ctgf/Atp1a3/Adra1b/Chrnd/Chrng/Akap6/Mybph/Scn1a/Ehd3/Tnni1/Kcnj2/Fxyd1/Mylk2/Tnni3/Hrc | 21 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0046651 | lymphocyte proliferation | 31/858 | 238/15881 | 4.98E-06 | 0.00045658805184466 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000023067/ENSMUSG00000023927/ENSMUSG00000044303/ENSMUSG00000000732/ENSMUSG00000029082/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000029084/ENSMUSG00000021457/ENSMUSG00000027985/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000026177/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000040329/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000021948/ENSMUSG00000004266/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Gpnmb/Cdkn1a/Satb1/Cdkn2a/Icosl/Bst1/Lgals3/Pawr/Pde5a/Cd38/Syk/Lef1/Cd80/Tnfsf18/Btn2a2/Slc11a1/Zc3h12d/Ceacam1/Lrrc32/Il12rb1/Il15/Il7/Btn1a1/Igfbp2/Btla/Prkcd/Ptpn6/Cd300a/Coro1a/Zap70 | 31 |
| BP | GO:0051249 | regulation of lymphocyte activation | 39/858 | 335/15881 | 5.17E-06 | 0.000464882194057896 | ENSMUSG00000024610/ENSMUSG00000035385/ENSMUSG00000029816/ENSMUSG00000023067/ENSMUSG00000024778/ENSMUSG00000044303/ENSMUSG00000037440/ENSMUSG00000000732/ENSMUSG00000029082/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000019850/ENSMUSG00000029084/ENSMUSG00000079685/ENSMUSG00000034023/ENSMUSG00000021457/ENSMUSG00000055994/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000031548/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000020178/ENSMUSG00000040329/ENSMUSG00000063415/ENSMUSG00000044258/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000075370/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/Cdkn1a/Fas/Cdkn2a/Vnn1/Icosl/Bst1/Lgals3/Pawr/Pde5a/Tnfaip3/Cd38/Ulbp1/Fancd2/Syk/Nod2/Cd80/Tnfsf18/Btn2a2/Zc3h12d/Ceacam1/Lrrc32/Sfrp1/Il12rb1/Il15/Adora2a/Il7/Cyp26b1/Ctla2a/Btn1a1/Igfbp2/Igll1/Btla/Ptpn6/Cd300a/Coro1a/Zap70 | 39 |
| BP | GO:0051250 | negative regulation of lymphocyte activation | 20/858 | 119/15881 | 5.49E-06 | 0.000484555701703014 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000024778/ENSMUSG00000044303/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000019850/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000031548/ENSMUSG00000020178/ENSMUSG00000000706/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000034652 | Cd74/Gpnmb/Fas/Cdkn2a/Lgals3/Pawr/Pde5a/Tnfaip3/Cd80/Tnfsf18/Btn2a2/Zc3h12d/Ceacam1/Lrrc32/Sfrp1/Adora2a/Btn1a1/Btla/Ptpn6/Cd300a | 20 |
| BP | GO:0032943 | mononuclear cell proliferation | 31/858 | 240/15881 | 5.92E-06 | 0.00051253118978055 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000023067/ENSMUSG00000023927/ENSMUSG00000044303/ENSMUSG00000000732/ENSMUSG00000029082/ENSMUSG00000050335/ | Cd74/Gpnmb/Cdkn1a/Satb1/Cdkn2a/Icosl/Bst1/Lgals3/Pawr/Pde5a/Cd38/Syk/Lef1/Cd80/Tnfsf18/ | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000027985/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000026177/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000052013/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Btn2a2/Slc11a1/Zc3h12d/ Ceacam1/Lrrc32/Il12rb1/ Il15/Il7/Btn1a1/Igfbp2/ Btla/Prkcd/Ptpn6/Cd300a/ Coro1a/Zap70 | |
| BP | GO:0050868 | negative regulation of T cell activation | 17/858 | 91/ 15881 | 6.40E-06 | 0.000543617089267539 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000044303/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000020178/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652 | Cd74/Gpnmb/Cdkn2a/ Lgals3/Pawr/Pde5a/Cd80/ Tnfsf18/Btn2a2/Zc3h12d/ Ceacam1/Lrrc32/Adora2a/ Btn1a1/Btla/Ptpn6/Cd300a | 17 |
| BP | GO:0045071 | negative regulation of viral genome replication | 12/858 | 48/ 15881 | 6.57E-06 | 0.000547761946633226 | ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000001166/ENSMUSG00000035692/ ENSMUSG00000074272/ENSMUSG00000032690/ ENSMUSG00000020641/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000032661 | Slpi/Bst2/Zc3h12a/Rnasel/ Oas1c/Isg15/Ceacam1/ Oas2/Rsad2/Ifitm6/Oas1b/ Oas3 | 12 |
| BP | GO:1903037 | regulation of leukocyte cell-cell adhesion | 29/858 | 219/ 15881 | 7.22E-06 | 0.000591013280582534 | ENSMUSG00000024610/ENSMUSG00000035385/ ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000037440/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000076441/ ENSMUSG00000039981/ENSMUSG00000074715/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000020178/ENSMUSG00000040329/ ENSMUSG00000000706/ENSMUSG00000039323/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/ Cdkn2a/Vnn1/Icosl/Lgals3/ Pawr/Pde5a/Syk/Cd80/ Tnfsf18/Btn2a2/Ass1/ Zc3h12d/Ccl28/Ceacam1/ Lrrc32/Il12rb1/Il15/ Adora2a/Il7/Btn1a1/ Igfbp2/Btla/Ptpn6/Cd300a/ Coro1a/Zap70 | 29 |
| BP | GO:0046456 | icosanoid biosynthetic process | 10/858 | 34/ 15881 | 8.05E-06 | 0.000647325607203432 | ENSMUSG00000024610/ENSMUSG00000047250/ ENSMUSG00000006344/ENSMUSG00000050737/ ENSMUSG00000021457/ENSMUSG00000026688/ ENSMUSG00000074604/ENSMUSG00000017969/ ENSMUSG00000041193/ENSMUSG00000060063 | Cd74/Ptgs1/Ggt5/Ptges/ Syk/Mgst3/Mgst2/Ptgis/ Pla2g5/Alox5ap | 10 |
| BP | GO:0003012 | muscle system process | 36/858 | 305/ 15881 | 8.70E-06 | 0.000688133234172638 | ENSMUSG00000026185/ENSMUSG00000042677/ ENSMUSG00000026463/ENSMUSG00000006457/ ENSMUSG00000047250/ENSMUSG00000035873/ | Igfbp5/Zc3h12a/Atp2b4/ Actn3/Ptgs1/Pawr/Sorbs2/ Adora1/Pde5a/Gja5/ | 36 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000031626/ENSMUSG00000042429/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000022144/ ENSMUSG00000019997/ENSMUSG00000040907/ ENSMUSG00000050541/ENSMUSG00000026251/ ENSMUSG00000026253/ENSMUSG00000061603/ ENSMUSG00000021070/ENSMUSG00000028834/ ENSMUSG00000055632/ENSMUSG00000042451/ ENSMUSG00000064329/ENSMUSG00000024065/ ENSMUSG00000002489/ENSMUSG00000028978/ ENSMUSG00000020787/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000059588/ ENSMUSG00000027071/ENSMUSG00000036570/ ENSMUSG00000027470/ENSMUSG00000035458/ ENSMUSG00000038239/ENSMUSG00000020081 | Atp1b1/Gdnf/Ctgf/Atp1a3/ Adra1b/Chrnd/Chrng/ Akap6/Bdkrb2/Trim63/ Hmcn2/Mybph/Scn1a/ Ehd3/Tiam1/Nos3/P2rx1/ Tnni1/Kcnj2/Calcrl/P2rx3/ Fxyd1/Mylk2/Tnni3/Hrc/ Tacr2 | |
| BP | GO:0030595 | leukocyte chemotaxis | 23/858 | 155/ 15881 | 9.75E-06 | 0.000750098118624512 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000035373/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000023913/ENSMUSG00000039621/ ENSMUSG00000026166/ENSMUSG00000021457/ ENSMUSG00000019122/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000053318/ENSMUSG00000031780/ ENSMUSG00000030707 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Ccl7/Bst1/Lgals3/ Pla2g7/Prex1/Ccl20/Syk/ Ccl9/Pf4/Nod2/Tnfsf18/ Vegfc/Cxcl5/Cxcl10/Nov/ Slamf8/Ccl17/Coro1a | 23 |
| BP | GO:1901570 | fatty acid derivative biosynthetic process | 11/858 | 42/ 15881 | 9.81E-06 | 0.000750098118624512 | ENSMUSG00000024610/ENSMUSG00000047250/ ENSMUSG00000006344/ENSMUSG00000050737/ ENSMUSG00000021457/ENSMUSG00000026688/ ENSMUSG00000074604/ENSMUSG00000017969/ ENSMUSG00000041193/ENSMUSG00000060063/ ENSMUSG00000007908 | Cd74/Ptgs1/Ggt5/Ptges/ Syk/Mgst3/Mgst2/Ptgis/ Pla2g5/Alox5ap/Hmgcll1 | 11 |
| BP | GO:0070661 | leukocyte proliferation | 31/858 | 247/ 15881 | 1.07E-05 | 0.000802908155121352 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000023067/ENSMUSG00000023927/ ENSMUSG00000044303/ENSMUSG00000000732/ ENSMUSG00000029082/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000027985/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000053216/ ENSMUSG00000026177/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000052013/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Cd74/Gpnmb/Cdkn1a/ Satb1/Cdkn2a/Icosl/Bst1/ Lgals3/Pawr/Pde5a/Cd38/ Syk/Lef1/Cd80/Tnfsf18/ Btn2a2/Slc11a1/Zc3h12d/ Ceacam1/Lrrc32/Il12rb1/ Il15/Il7/Btn1a1/Igfbp2/ Btla/Prkcd/Ptpn6/Cd300a/ Coro1a/Zap70 | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0050866 | negative regulation of cell activation | 23/858 | 157/15881 | 1.21E-05 | 0.000894677453366934 | ENSMUSG00000024610/ENSMUSG00000029816/ENSMUSG00000024778/ENSMUSG00000044303/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000019850/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000032020/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000026249/ENSMUSG00000031548/ENSMUSG00000020178/ENSMUSG00000000706/ENSMUSG00000052013/ENSMUSG00000021948/ENSMUSG00000004266/ENSMUSG00000034652 | Cd74/Gpnmb/Fas/Cdkn2a/Lgals3/Pawr/Pde5a/Tnfaip3/Cd80/Tnfsf18/Btn2a2/Ubash3b/Zc3h12d/Ceacam1/Lrrc32/Serpine2/Sfrp1/Adora2a/Btn1a1/Btla/Prkcd/Ptpn6/Cd300a | 23 |
| BP | GO:0050863 | regulation of T cell activation | 30/858 | 237/15881 | 1.25E-05 | 0.000905445009573326 | ENSMUSG00000024610/ENSMUSG00000035385/ENSMUSG00000029816/ENSMUSG00000044303/ENSMUSG00000037440/ENSMUSG00000000732/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000034023/ENSMUSG00000021457/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000020178/ENSMUSG00000040329/ENSMUSG00000063415/ENSMUSG00000044258/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000034652/ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/Cdkn2a/Vnn1/Icosl/Lgals3/Pawr/Pde5a/Fancd2/Syk/Cd80/Tnfsf18/Btn2a2/Zc3h12d/Ceacam1/Lrrc32/Il12rb1/Il15/Adora2a/Il7/Cyp26b1/Ctla2a/Btn1a1/Igfbp2/Btla/Ptpn6/Cd300a/Coro1a/Zap70 | 30 |
| BP | GO:0042129 | regulation of T cell proliferation | 21/858 | 136/15881 | 1.26E-05 | 0.000905445009573326 | ENSMUSG00000029816/ENSMUSG00000044303/ENSMUSG00000000732/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000053965/ENSMUSG00000021457/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000053216/ENSMUSG00000039981/ENSMUSG00000074272/ENSMUSG00000090958/ENSMUSG00000000791/ENSMUSG00000031712/ENSMUSG00000000706/ENSMUSG00000039323/ENSMUSG00000052013/ENSMUSG00000004266/ENSMUSG00000030707/ENSMUSG00000026117 | Gpnmb/Cdkn2a/Icosl/Lgals3/Pawr/Pde5a/Syk/Cd80/Tnfsf18/Btn2a2/Zc3h12d/Ceacam1/Lrrc32/Il12rb1/Il15/Btn1a1/Igfbp2/Btla/Ptpn6/Coro1a/Zap70 | 21 |
| BP | GO:0070098 | chemokine-mediated signaling pathway | 10/858 | 36/15881 | 1.41E-05 | 0.000997089774295324 | ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000035373/ENSMUSG00000026166/ENSMUSG00000019122/ENSMUSG00000029373/ENSMUSG00000029371/ENSMUSG00000034855/ENSMUSG00000031780 | Cxcl1/Ccl2/Cx3cl1/Ccl7/Ccl20/Ccl9/Pf4/Cxcl5/Cxcl10/Ccl17 | 10 |
| BP | GO:0050900 | leukocyte migration | 31/858 | 252/15881 | 1.60E-05 | 0.00111112566403895 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000016024/ENSMUSG00000035373/ENSMUSG00000029082/ENSMUSG00000017737/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000042429/ENSMUSG00000023913/ENSMUSG00000039621/ENSMUSG00000026166/ | Cd74/Cxcl1/Ccl2/Cx3cl1/Lbp/Ccl7/Bst1/Mmp9/Lgals3/Pawr/Adora1/Pla2g7/Prex1/Ccl20/Tlr2/Syk/Ccl9/Pf4/Nod2/Tnfsf18/Vegfc/Ccl28/Selp/Cxcl5/Fut7/Cxcl10/Nov/ | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000019122/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000074715/ ENSMUSG00000026580/ENSMUSG00000029371/ ENSMUSG00000036587/ENSMUSG00000034855/ ENSMUSG00000037362/ENSMUSG00000053318/ ENSMUSG00000031780/ENSMUSG00000034652/ ENSMUSG00000030707 | Slamf8/Ccl17/Cd300a/ Coro1a | |
| BP | GO:0002694 | regulation of leukocyte activation | 43/858 | 404/ 15881 | 1.68E-05 | 0.00113843736732177 | ENSMUSG00000024610/ENSMUSG00000035385/ ENSMUSG00000029816/ENSMUSG00000016024/ ENSMUSG00000023067/ENSMUSG00000024778/ ENSMUSG00000044303/ENSMUSG00000037440/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000019850/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000034023/ ENSMUSG00000021457/ENSMUSG00000055994/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000025889/ ENSMUSG00000041193/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000031548/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000020178/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000044258/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000075370/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/Lbp/ Cdkn1a/Fas/Cdkn2a/Vnn1/ Icosl/Bst1/Lgals3/Pawr/ Pde5a/Tnfaip3/Cd38/ Nectin2/Ulbp1/Fancd2/ Syk/Nod2/Cd80/Tnfsf18/ Btn2a2/Snca/Pla2g5/ Zc3h12d/Ceacam1/Lrrc32/ Sfrp1/Il12rb1/Il15/ Adora2a/Il7/Cyp26b1/ Ctla2a/Btn1a1/Igfbp2/ Igll1/Btla/Ptpn6/Cd300a/ Coro1a/Zap70 | 43 |
| BP | GO:0032787 | monocarboxylic acid metabolic process | 47/858 | 457/ 15881 | 1.69E-05 | 0.00113843736732177 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000060600/ENSMUSG00000053279/ ENSMUSG00000037440/ENSMUSG00000006457/ ENSMUSG00000021196/ENSMUSG00000003541/ ENSMUSG00000047250/ENSMUSG00000006344/ ENSMUSG00000027332/ENSMUSG00000019577/ ENSMUSG00000056973/ENSMUSG00000020333/ ENSMUSG00000050737/ENSMUSG00000042010/ ENSMUSG00000020010/ENSMUSG00000023963/ ENSMUSG00000028497/ENSMUSG00000019806/ ENSMUSG00000029167/ENSMUSG00000025002/ ENSMUSG00000033327/ENSMUSG00000033715/ ENSMUSG00000027068/ENSMUSG00000003484/ ENSMUSG00000021947/ENSMUSG00000025889/ ENSMUSG00000017969/ENSMUSG00000031725/ ENSMUSG00000055782/ENSMUSG00000002944/ ENSMUSG00000052974/ENSMUSG00000020892/ ENSMUSG00000032262/ENSMUSG00000027412/ ENSMUSG00000026435/ENSMUSG00000090145/ | C3/Cd74/Eno3/Aldh1a1/ Vnn1/Actn3/Pfkp/Ier3/ Ptgs1/Ggt5/Ivd/Pdk4/ Ces1d/Acsl6/Ptges/Acacb/ Vnn3/Cyp39a1/Hacd4/ Aig1/Ppargc1a/Cyp2c55/ Tnxb/Akr1c14/Dhrs9/ Cyp4f18/Cryl1/Snca/Ptgis/ Ces1f/Abcd2/Cd36/ Cyp2f2/Aloxe3/Elovl4/ Lpin3/Slc45a3/Ugt1a6b/ Cyp4f40/Alox5ap/Bco2/ Cyp26b1/Akr1cl/Acaa1b/ Abhd3/Ugt1a6a/Cyp2c23 | 47 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000090700/ENSMUSG00000060063/ ENSMUSG00000032066/ENSMUSG00000063415/ ENSMUSG00000025955/ENSMUSG00000010651/ ENSMUSG00000002475/ENSMUSG00000054545/ ENSMUSG00000025197 | | |
| BP | GO:0050851 | antigen receptor-mediated signaling pathway | 19/858 | 118/ 15881 | 1.77E-05 | 0.0011733303986913 | ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000021457/ENSMUSG00000005057/ ENSMUSG00000053216/ENSMUSG00000049109/ ENSMUSG00000000706/ENSMUSG00000075370/ ENSMUSG00000109713/ENSMUSG00000021108/ ENSMUSG00000002699/ENSMUSG00000024696/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000026117 | Zc3h12a/Icosl/Lgals3/ Pawr/Cd38/Nectin2/Syk/ Sh2b2/Btn2a2/Themis/ Btn1a1/Igll1/Pvrig/Prkch/ Lcp2/Lpxn/Ptpn6/Cd300a/ Zap70 | 19 |
| BP | GO:0007159 | leukocyte cell-cell adhesion | 30/858 | 243/ 15881 | 2.03E-05 | 0.0013331880123945 | ENSMUSG00000024610/ENSMUSG00000035385/ ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000037440/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000076441/ ENSMUSG00000039981/ENSMUSG00000074715/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000026580/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000020178/ ENSMUSG00000040329/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000052013/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Ccl2/Gpnmb/ Cdkn2a/Vnn1/Icosl/Lgals3/ Pawr/Pde5a/Syk/Cd80/ Tnfsf18/Btn2a2/Ass1/ Zc3h12d/Ccl28/Ceacam1/ Lrrc32/Selp/Il12rb1/Il15/ Adora2a/Il7/Btn1a1/ Igfbp2/Btla/Ptpn6/Cd300a/ Coro1a/Zap70 | 30 |
| BP | GO:0043900 | regulation of multi-organism process | 38/858 | 343/ 15881 | 2.12E-05 | 0.00137015496136892 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000053965/ ENSMUSG00000066800/ENSMUSG00000020826/ ENSMUSG00000032860/ENSMUSG00000019850/ ENSMUSG00000021822/ENSMUSG00000032501/ ENSMUSG00000030220/ENSMUSG00000062300/ ENSMUSG00000027995/ENSMUSG00000079363/ ENSMUSG00000001166/ENSMUSG00000055994/ ENSMUSG00000027985/ENSMUSG00000035692/ ENSMUSG00000017830/ENSMUSG00000074272/ ENSMUSG00000032690/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000029371/ ENSMUSG00000079173/ENSMUSG00000032661/ ENSMUSG00000037860/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000041515/ ENSMUSG00000000266/ENSMUSG00000062157 | Cd74/Cxcl1/Slpi/Bst2/Lbp/ Trim30a/Zc3h12a/Pde5a/ Rnasel/Nos2/P2ry2/ Tnfaip3/Plau/Trib1/ Arhgdib/Nectin2/Tlr2/ Gbp4/Oas1c/Nod2/Lef1/ Isg15/Dhx58/Ceacam1/ Oas2/Rsad2/Cd36/Ifitm6/ Oas1b/Cxcl5/Zan/Oas3/ Aim2/Il12rb1/Il15/Irf8/ Mid2/Ifnlr1 | 38 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0044057 | regulation of system process | 42/858 | 395/15881 | 2.15E-05 | 0.00137015496136892 | ENSMUSG00000031778/ENSMUSG00000032561/ ENSMUSG00000026185/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000026463/ ENSMUSG00000006457/ENSMUSG00000047250/ ENSMUSG00000035873/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000062991/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000050541/ENSMUSG00000061603/ ENSMUSG00000028834/ENSMUSG00000041245/ ENSMUSG00000027674/ENSMUSG00000024065/ ENSMUSG00000037362/ENSMUSG00000028978/ ENSMUSG00000000120/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000049044/ ENSMUSG00000026418/ENSMUSG00000041695/ ENSMUSG00000028602/ENSMUSG00000059588/ ENSMUSG00000027071/ENSMUSG00000028864/ ENSMUSG00000050578/ENSMUSG00000036570/ ENSMUSG00000027470/ENSMUSG00000035458/ ENSMUSG00000038239/ENSMUSG00000020081 | Cx3cl1/Acpp/Igfbp5/ Zc3h12a/Dab2/Atp2b4/ Actn3/Ptgs1/Pawr/Adora1/ Gch1/Pde5a/Gja5/Nrg1/ Atp1b1/Cd38/Lif/Ctgf/ Adra1b/Akap6/Trim63/ Wnk3/Pex5l/Ehd3/Nov/ Nos3/Ngfr/Adora2a/P2rx1/ Rapgef4/Tnni1/Kcnj2/ Tnfrsf8/Calcrl/P2rx3/Hgf/ Mmp13/Fxyd1/Mylk2/ Tnni3/Hrc/Tacr2 | 42 |
| BP | GO:0043901 | negative regulation of multi-organism process | 22/858 | 152/15881 | 2.26E-05 | 0.00141679455304625 | ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000066800/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000030220/ ENSMUSG00000027995/ENSMUSG00000001166/ ENSMUSG00000055994/ENSMUSG00000035692/ ENSMUSG00000017830/ENSMUSG00000074272/ ENSMUSG00000032690/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000032661/ ENSMUSG00000041515/ENSMUSG00000000266 | Slpi/Bst2/Lbp/Zc3h12a/ Rnasel/Tnfaip3/Trib1/ Arhgdib/Tlr2/Oas1c/Nod2/ Isg15/Dhx58/Ceacam1/ Oas2/Rsad2/Cd36/Ifitm6/ Oas1b/Oas3/Irf8/Mid2 | 22 |
| BP | GO:0042136 | neurotransmitter biosynthetic process | 15/858 | 81/15881 | 2.47E-05 | 0.00153312538579441 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000006764/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000002944/ ENSMUSG00000006235/ENSMUSG00000040046/ ENSMUSG00000028978/ENSMUSG00000079164/ ENSMUSG00000007034 | Zc3h12a/Atp2b4/Tph2/ Gch1/Nos2/Ulbp1/Tlr2/ Ptgis/Ass1/Cd36/Epor/ Tph1/Nos3/Tlr5/Slc44a4 | 15 |
| BP | GO:0055065 | metal ion homeostasis | 49/858 | 492/15881 | 2.62E-05 | 0.00160205833694635 | ENSMUSG00000012428/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000003617/ ENSMUSG00000023030/ENSMUSG00000066152/ ENSMUSG00000022032/ENSMUSG00000026463/ ENSMUSG00000035873/ENSMUSG00000021831/ ENSMUSG00000042429/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000040907/ENSMUSG00000032839/ ENSMUSG00000050541/ENSMUSG00000035694/ ENSMUSG00000044026/ENSMUSG00000038403/ | Steap4/Cxcl1/Ccl2/Cp/ Slc11a2/Slc31a2/Scara5/ Atp2b4/Pawr/Ero1l/ Adora1/P2ry2/Atp1b1/ Cd38/Atp1a3/Trpc1/ Adra1b/Caps2/Slc35g1/ Hfe2/Tmtc2/Cacna1i/ Mcub/Slc11a1/Akap6/ Snca/Atp1b2/Ubash3b/ Lcn2/Ccl28/Rhd/Cd36/ | 49 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000036019/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000026177/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000032020/ ENSMUSG00000026822/ENSMUSG00000074715/ ENSMUSG00000028825/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000021070/ ENSMUSG00000063354/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000034855/ ENSMUSG00000020178/ENSMUSG00000029716/ ENSMUSG00000030523/ENSMUSG00000004266/ ENSMUSG00000036570/ENSMUSG00000035458/ ENSMUSG00000030707/ENSMUSG00000044338/ ENSMUSG00000038239/ENSMUSG00000021337/ ENSMUSG00000043051 | Kng2/Bdkrb2/Slc39a4/ Ramp3/Epor/Cxcl10/ Adora2a/Tfr2/Trpm1/ Ptpn6/Fxyd1/Tnni3/ Coro1a/Aplnr/Hrc/Scgn/ Disc1 | |
| BP | GO:0002768 | immune response-regulating cell surface receptor signaling pathway | 21/858 | 143/ 15881 | 2.76E-05 | 0.00166064117495872 | ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000005057/ENSMUSG00000053216/ ENSMUSG00000049109/ENSMUSG00000000706/ ENSMUSG00000075370/ENSMUSG00000052013/ ENSMUSG00000109713/ENSMUSG00000021108/ ENSMUSG00000002699/ENSMUSG00000024696/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000026117 | Zc3h12a/Icosl/Lgals3/ Pawr/Cd38/Nectin2/Tlr2/ Syk/Sh2b2/Btn2a2/ Themis/Btn1a1/Igll1/Btla/ Pvrig/Prkch/Lcp2/Lpxn/ Ptpn6/Cd300a/Zap70 | 21 |
| BP | GO:0002764 | immune response-regulating signaling pathway | 30/858 | 247/ 15881 | 2.79E-05 | 0.00166064117495872 | ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000019850/ENSMUSG00000029084/ ENSMUSG00000062300/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000055994/ ENSMUSG00000032359/ENSMUSG00000005057/ ENSMUSG00000053216/ENSMUSG00000049109/ ENSMUSG00000017830/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000000706/ ENSMUSG00000079164/ENSMUSG00000075370/ ENSMUSG00000052013/ENSMUSG00000109713/ ENSMUSG00000021108/ENSMUSG00000002699/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000026117 | Lbp/Trim30a/Zc3h12a/ Icosl/Lgals3/Pawr/Tnfaip3/ Cd38/Nectin2/Tlr2/Syk/ Nod2/Ctsh/Sh2b2/Btn2a2/ Themis/Dhx58/Rsad2/ Cd36/Btn1a1/Tlr5/Igll1/ Btla/Pvrig/Prkch/Lcp2/ Lpxn/Ptpn6/Cd300a/Zap70 | 30 |
| BP | GO:0032102 | negative regulation of response to external stimulus | 31/858 | 260/ 15881 | 2.97E-05 | 0.00174327104677398 | ENSMUSG00000000753/ENSMUSG00000042677/ ENSMUSG00000003541/ENSMUSG00000042429/ ENSMUSG00000019850/ENSMUSG00000025207/ ENSMUSG00000021822/ENSMUSG00000032501/ ENSMUSG00000027082/ENSMUSG00000022676/ ENSMUSG00000028599/ENSMUSG00000053475/ ENSMUSG00000055994/ENSMUSG00000115388/ ENSMUSG00000017969/ENSMUSG00000041193/ ENSMUSG00000032020/ENSMUSG00000017830/ | Serpinf1/Zc3h12a/Ier3/ Adora1/Tnfaip3/Sema4g/ Plau/Trib1/Tfpi/Snai2/ Tnfrsf1b/Tnfaip6/Nod2/ Eppk1/Ptgis/Pla2g5/ Ubash3b/Dhx58/Ceacam1/ Kng2/Serpine2/Robo2/ Siglecg/Nov/Adora2a/ | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000074272/ENSMUSG00000060459/ ENSMUSG00000026249/ENSMUSG00000052516/ ENSMUSG00000030468/ENSMUSG00000037362/ ENSMUSG00000020178/ENSMUSG00000044258/ ENSMUSG00000021322/ENSMUSG00000053318/ ENSMUSG00000059588/ENSMUSG00000028864/ ENSMUSG00000021948 | Ctla2a/Aoah/Slamf8/ Calcrl/Hgf/Prkcd | |
| BP | GO:0090257 | regulation of muscle system process | 25/858 | 189/ 15881 | 3.09E-05 | 0.00179395859923885 | ENSMUSG00000026185/ENSMUSG00000042677/ ENSMUSG00000026463/ENSMUSG00000006457/ ENSMUSG00000047250/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000026576/ ENSMUSG00000019997/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000028834/ ENSMUSG00000024065/ENSMUSG00000028978/ ENSMUSG00000020787/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000059588/ ENSMUSG00000036570/ENSMUSG00000027470/ ENSMUSG00000035458/ENSMUSG00000038239/ ENSMUSG00000020081 | Igfbp5/Zc3h12a/Atp2b4/ Actn3/Ptgs1/Pawr/Adora1/ Pde5a/Gja5/Atp1b1/Ctgf/ Adra1b/Akap6/Trim63/ Ehd3/Nos3/P2rx1/Tnni1/ Kcnj2/Calcrl/Fxyd1/Mylk2/ Tnni3/Hrc/Tacr2 | 25 |
| BP | GO:0060048 | cardiac muscle contraction | 16/858 | 93/ 15881 | 3.48E-05 | 0.00199330800472934 | ENSMUSG00000042677/ENSMUSG00000042429/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000040907/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000064329/ ENSMUSG00000024065/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Adora1/Pde5a/ Gja5/Atp1b1/Ctgf/Atp1a3/ Adra1b/Akap6/Scn1a/ Ehd3/Tnni1/Kcnj2/Fxyd1/ Tnni3/Hrc | 16 |
| BP | GO:0042098 | T cell proliferation | 23/858 | 168/ 15881 | 3.67E-05 | 0.00205844052277085 | ENSMUSG00000029816/ENSMUSG00000023927/ ENSMUSG00000044303/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000026177/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000000706/ ENSMUSG00000039323/ENSMUSG00000052013/ ENSMUSG00000004266/ENSMUSG00000030707/ ENSMUSG00000026117 | Gpnmb/Satb1/Cdkn2a/ Icosl/Lgals3/Pawr/Pde5a/ Syk/Cd80/Tnfsf18/Btn2a2/ Slc11a1/Zc3h12d/ Ceacam1/Lrrc32/Il12rb1/ Il15/Btn1a1/Igfbp2/Btla/ Ptpn6/Coro1a/Zap70 | 23 |
| BP | GO:0030003 | cellular cation homeostasis | 48/858 | 485/ 15881 | 3.71E-05 | 0.00205844052277085 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000003617/ENSMUSG00000023030/ ENSMUSG00000066152/ENSMUSG00000022032/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000040907/ENSMUSG00000032839/ ENSMUSG00000050541/ENSMUSG00000044026/ ENSMUSG00000038403/ENSMUSG00000060961/ ENSMUSG00000022416/ENSMUSG00000027994/ | Cxcl1/Ccl2/Cp/Slc11a2/ Slc31a2/Scara5/Atp2b4/ Pawr/Ero1l/P2ry2/Atp1b1/ Cd38/Atp1a3/Trpc1/ Adra1b/Slc35g1/Hfe2/ Slc4a4/Cacna1i/Mcub/ Slc11a1/Akap6/Snca/ Atp1b2/Ubash3b/Rab20/ Ccl28/Cd36/Kng2/Slc4a8/ Bdkrb2/Slc39a4/Ramp3/ | 48 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000026177/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000041329/ ENSMUSG00000032020/ENSMUSG00000031504/ ENSMUSG00000074715/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000023032/ ENSMUSG00000021070/ENSMUSG00000063354/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000068323/ENSMUSG00000034855/ ENSMUSG00000029716/ENSMUSG00000038600/ ENSMUSG00000030523/ENSMUSG00000053318/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Epor/Slc4a5/Cxcl10/Tfr2/ Atp6v0a4/Trpm1/Slamf8/ Ptpn6/Fxyd1/Tnni3/ Coro1a/Aplnr/Hrc/Scgn/ Disc1 | |
| BP | GO:0050858 | negative regulation of antigen receptor-mediated signaling pathway | 7/858 | 19/ 15881 | 3.73E-05 | 0.00205844052277085 | ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053216/ENSMUSG00000109713/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652 | Lgals3/Pawr/Btn2a2/Pvrig/ Lpxn/Ptpn6/Cd300a | 7 |
| BP | GO:0042130 | negative regulation of T cell proliferation | 12/858 | 57/ 15881 | 4.26E-05 | 0.00229737713698819 | ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000075122/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000004266 | Gpnmb/Cdkn2a/Pawr/ Pde5a/Cd80/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Btn1a1/Btla/Ptpn6 | 12 |
| BP | GO:0071674 | mononuclear cell migration | 12/858 | 57/ 15881 | 4.26E-05 | 0.00229737713698819 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000050335/ ENSMUSG00000023913/ENSMUSG00000026166/ ENSMUSG00000019122/ENSMUSG00000066755/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000053318/ENSMUSG00000031780 | Ccl2/Cx3cl1/Ccl7/Lgals3/ Pla2g7/Ccl20/Ccl9/ Tnfsf18/Cxcl10/Nov/ Slamf8/Ccl17 | 12 |
| BP | GO:0045861 | negative regulation of proteolysis | 32/858 | 278/ 15881 | 4.46E-05 | 0.00237804532103481 | ENSMUSG00000017002/ENSMUSG00000000753/ ENSMUSG00000044303/ENSMUSG00000017737/ ENSMUSG00000078945/ENSMUSG00000042842/ ENSMUSG00000096472/ENSMUSG00000027082/ ENSMUSG00000019823/ENSMUSG00000028599/ ENSMUSG00000041481/ENSMUSG00000046223/ ENSMUSG00000078942/ENSMUSG00000031387/ ENSMUSG00000027985/ENSMUSG00000021403/ ENSMUSG00000079014/ENSMUSG00000025889/ ENSMUSG00000060459/ENSMUSG00000078949/ ENSMUSG00000026315/ENSMUSG00000026249/ ENSMUSG00000027834/ENSMUSG00000020178/ ENSMUSG00000044258/ENSMUSG00000071203/ ENSMUSG00000051029/ENSMUSG00000019278/ ENSMUSG00000028864/ENSMUSG00000004231/ ENSMUSG00000079012/ENSMUSG00000060579 | Slpi/Serpinf1/Cdkn2a/ Mmp9/Naip2/Serpinb6b/ Cdkn2d/Tfpi/Mical1/ Tnfrsf1b/Serpina3g/Plaur/ Naip6/Renbp/Lef1/ Serpinb9b/Serpina3i/Snca/ Kng2/R3hdml/Serpinb8/ Serpine2/Serpini1/ Adora2a/Ctla2a/Naip5/ Serpinb1b/Dpep1/Hgf/ Pax2/Serpina3m/Fhit | 32 |
| BP | GO:0002429 | immune response-activating cell surface receptor signaling pathway | 20/858 | 137/ 15881 | 4.63E-05 | 0.0024417914537119 | ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000027995/ENSMUSG00000021457/ | Zc3h12a/Icosl/Lgals3/ Pawr/Cd38/Nectin2/Tlr2/ Syk/Sh2b2/Btn2a2/ Themis/Btn1a1/Igll1/ | 20 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000005057/ENSMUSG00000053216/ ENSMUSG00000049109/ENSMUSG00000000706/ ENSMUSG00000075370/ENSMUSG00000109713/ ENSMUSG00000021108/ENSMUSG00000002699/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000026117 | Pvrig/Prkch/Lcp2/Lpxn/ Ptpn6/Cd300a/Zap70 | |
| BP | GO:0050728 | negative regulation of inflammatory response | 18/858 | 116/ 15881 | 4.84E-05 | 0.00252352323242011 | ENSMUSG00000000753/ENSMUSG00000042677/ ENSMUSG00000003541/ENSMUSG00000042429/ ENSMUSG00000019850/ENSMUSG00000028599/ ENSMUSG00000053475/ENSMUSG00000055994/ ENSMUSG00000017969/ENSMUSG00000041193/ ENSMUSG00000030468/ENSMUSG00000037362/ ENSMUSG00000020178/ENSMUSG00000044258/ ENSMUSG00000021322/ENSMUSG00000053318/ ENSMUSG00000059588/ENSMUSG00000028864 | Serpinf1/Zc3h12a/Ier3/ Adora1/Tnfaip3/Tnfrsf1b/ Tnfaip6/Nod2/Ptgis/ Pla2g5/Siglecg/Nov/ Adora2a/Ctla2a/Aoah/ Slamf8/Calcrl/Hgf | 18 |
| BP | GO:0072593 | reactive oxygen species metabolic process | 28/858 | 230/ 15881 | 4.90E-05 | 0.00252377207245588 | ENSMUSG00000029380/ENSMUSG00000023067/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000024066/ENSMUSG00000026463/ ENSMUSG00000003541/ENSMUSG00000037580/ ENSMUSG00000039621/ENSMUSG00000020826/ ENSMUSG00000019577/ENSMUSG00000021822/ ENSMUSG00000019997/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000024039/ENSMUSG00000025889/ ENSMUSG00000017969/ENSMUSG00000076441/ ENSMUSG00000002944/ENSMUSG00000006235/ ENSMUSG00000028978/ENSMUSG00000032066/ ENSMUSG00000000120/ENSMUSG00000079164/ ENSMUSG00000004231/ENSMUSG00000021948 | Cxcl1/Cdkn1a/Trim30a/ Zc3h12a/Xdh/Atp2b4/Ier3/ Gch1/Prex1/Nos2/Pdk4/ Plau/Ctgf/Ulbp1/Tlr2/Syk/ Cbs/Snca/Ptgis/Ass1/Cd36/ Epor/Nos3/Bco2/Ngfr/ Tlr5/Pax2/Prkcd | 28 |
| BP | GO:0016042 | lipid catabolic process | 29/858 | 244/ 15881 | 5.62E-05 | 0.0028641673164529 | ENSMUSG00000031877/ENSMUSG00000016194/ ENSMUSG00000031886/ENSMUSG00000057074/ ENSMUSG00000042429/ENSMUSG00000023913/ ENSMUSG00000027332/ENSMUSG00000056973/ ENSMUSG00000042010/ENSMUSG00000023963/ ENSMUSG00000002847/ENSMUSG00000019806/ ENSMUSG00000071047/ENSMUSG00000003484/ ENSMUSG00000074604/ENSMUSG00000041193/ ENSMUSG00000062826/ENSMUSG00000031725/ ENSMUSG00000055782/ENSMUSG00000061825/ ENSMUSG00000027412/ENSMUSG00000030825/ ENSMUSG00000032066/ENSMUSG00000063415/ ENSMUSG00000010651/ENSMUSG00000050097/ ENSMUSG00000036834/ENSMUSG00000002475/ ENSMUSG00000021948 | Ces2g/Hsd11b1/Ces2e/ Ces1g/Adora1/Pla2g7/Ivd/ Ces1d/Acacb/Cyp39a1/ Pla1a/Aig1/Ces1a/ Cyp4f18/Mgst2/Pla2g5/ Ces2f/Ces1f/Abcd2/Ces2c/ Lpin3/Hsd17b14/Bco2/ Cyp26b1/Acaa1b/Ces2b/ Plch1/Abhd3/Prkcd | 29 |
| BP | GO:0006631 | fatty acid metabolic process | 34/858 | 307/ 15881 | 5.73E-05 | 0.00288850487619805 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000047250/ENSMUSG00000006344/ ENSMUSG00000027332/ENSMUSG00000019577/ ENSMUSG00000056973/ENSMUSG00000020333/ ENSMUSG00000050737/ENSMUSG00000042010/ ENSMUSG00000028497/ENSMUSG00000019806/ | C3/Cd74/Ptgs1/Ggt5/Ivd/ Pdk4/Ces1d/Acsl6/Ptges/ Acacb/Hacd4/Aig1/ Ppargc1a/Cyp2c55/Tnxb/ Akr1c14/Cyp4f18/Cryl1/ Snca/Ptgis/Ces1f/Abcd2/ | 34 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000029167/ENSMUSG00000025002/ ENSMUSG00000033327/ENSMUSG00000033715/ ENSMUSG00000003484/ENSMUSG00000021947/ ENSMUSG00000025889/ENSMUSG00000017969/ ENSMUSG00000031725/ENSMUSG00000055782/ ENSMUSG00000002944/ENSMUSG00000052974/ ENSMUSG00000020892/ENSMUSG00000032262/ ENSMUSG00000027412/ENSMUSG00000026435/ ENSMUSG00000090700/ENSMUSG00000060063/ ENSMUSG00000025955/ENSMUSG00000010651/ ENSMUSG00000002475/ENSMUSG00000025197 | Cd36/Cyp2f2/Aloxe3/ Elovl4/Lpin3/Slc45a3/ Cyp4f40/Alox5ap/Akr1cl/ Acaa1b/Abhd3/Cyp2c23 | |
| BP | GO:0032945 | negative regulation of mononuclear cell proliferation | 13/858 | 68/ 15881 | 6.02E-05 | 0.00296571992427505 | ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000075122/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652 | Gpnmb/Cdkn2a/Pawr/ Pde5a/Cd80/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Btn1a1/Btla/Ptpn6/Cd300a | 13 |
| BP | GO:0050672 | negative regulation of lymphocyte proliferation | 13/858 | 68/ 15881 | 6.02E-05 | 0.00296571992427505 | ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000075122/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652 | Gpnmb/Cdkn2a/Pawr/ Pde5a/Cd80/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Btn1a1/Btla/Ptpn6/Cd300a | 13 |
| BP | GO:0002683 | negative regulation of immune system process | 39/858 | 373/ 15881 | 6.08E-05 | 0.00296571992427505 | ENSMUSG00000023367/ENSMUSG00000024610/ ENSMUSG00000029810/ENSMUSG00000029816/ ENSMUSG00000030921/ENSMUSG00000024778/ ENSMUSG00000044303/ENSMUSG00000074151/ ENSMUSG00000050335/ENSMUSG00000049577/ ENSMUSG00000035873/ENSMUSG00000042429/ ENSMUSG00000053965/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000007805/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000032020/ ENSMUSG00000017830/ENSMUSG00000039981/ ENSMUSG00000074715/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000031548/ ENSMUSG00000037362/ENSMUSG00000020178/ ENSMUSG00000000706/ENSMUSG00000052013/ ENSMUSG00000109713/ENSMUSG00000053318/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000020325/ENSMUSG00000034652/ ENSMUSG00000070524 | Tmem176a/Cd74/ Tmem176b/Gpnmb/ Trim30a/Fas/Cdkn2a/ Nlrc5/Lgals3/Zfpm1/Pawr/ Adora1/Pde5a/Tnfaip3/ Trib1/Twist2/Pf4/Nod2/ Cd80/Tnfsf18/Btn2a2/ Ubash3b/Dhx58/Zc3h12d/ Ccl28/Ceacam1/Lrrc32/ Sfrp1/Nov/Adora2a/ Btn1a1/Btla/Pvrig/Slamf8/ Lpxn/Ptpn6/Fstl3/Cd300a/ Fcrlb | 39 |
| BP | GO:0002695 | negative regulation of leukocyte activation | 20/858 | 140/ 15881 | 6.34E-05 | 0.0030265076324846 | ENSMUSG00000024610/ENSMUSG00000029816/ ENSMUSG00000024778/ENSMUSG00000044303/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053965/ENSMUSG00000019850/ ENSMUSG00000075122/ENSMUSG00000066755/ | Cd74/Gpnmb/Fas/Cdkn2a/ Lgals3/Pawr/Pde5a/ Tnfaip3/Cd80/Tnfsf18/ Btn2a2/Zc3h12d/Ceacam1/ | 20 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000053216/ENSMUSG00000039981/ ENSMUSG00000074272/ENSMUSG00000090958/ ENSMUSG00000031548/ENSMUSG00000020178/ ENSMUSG00000000706/ENSMUSG00000052013/ ENSMUSG00000004266/ENSMUSG00000034652 | Lrrc32/Sfrp1/Adora2a/ Btn1a1/Btla/Ptpn6/Cd300a | |
| BP | GO:0008217 | regulation of blood pressure | 20/858 | 140/ 15881 | 6.34E-05 | 0.0030265076324846 | ENSMUSG00000027750/ENSMUSG00000038235/ ENSMUSG00000028024/ENSMUSG00000003541/ ENSMUSG00000047250/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000057123/ ENSMUSG00000020826/ENSMUSG00000050541/ ENSMUSG00000003484/ENSMUSG00000031520/ ENSMUSG00000002944/ENSMUSG00000024481/ ENSMUSG00000021070/ENSMUSG00000068323/ ENSMUSG00000028978/ENSMUSG00000020787/ ENSMUSG00000031489/ENSMUSG00000035458 | Postn/F11r/Enpep/Ier3/ Ptgs1/Adora1/Gch1/Gja5/ Nos2/Adra1b/Cyp4f18/ Vegfc/Cd36/Lvrn/Bdkrb2/ Slc4a5/Nos3/P2rx1/Adrb3/ Tnni3 | 20 |
| BP | GO:0006873 | cellular ion homeostasis | 48/858 | 496/ 15881 | 6.50E-05 | 0.0030732742201079 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000003617/ENSMUSG00000023030/ ENSMUSG00000066152/ENSMUSG00000022032/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000040907/ENSMUSG00000032839/ ENSMUSG00000050541/ENSMUSG00000044026/ ENSMUSG00000038403/ENSMUSG00000060961/ ENSMUSG00000022416/ENSMUSG00000027994/ ENSMUSG00000026177/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000041329/ ENSMUSG00000032020/ENSMUSG00000031504/ ENSMUSG00000074715/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000023032/ ENSMUSG00000021070/ENSMUSG00000063354/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000068323/ENSMUSG00000034855/ ENSMUSG00000029716/ENSMUSG00000038600/ ENSMUSG00000030523/ENSMUSG00000053318/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Cp/Slc11a2/ Slc31a2/Scara5/Atp2b4/ Pawr/Ero1l/P2ry2/Atp1b1/ Cd38/Atp1a3/Trpc1/ Adra1b/Slc35g1/Hfe2/ Slc4a4/Cacna1i/Mcub/ Slc11a1/Akap6/Snca/ Atp1b2/Ubash3b/Rab20/ Ccl28/Cd36/Kng2/Slc4a8/ Bdkrb2/Slc39a4/Ramp3/ Epor/Slc4a5/Cxcl10/Tfr2/ Atp6v0a4/Trpm1/Slamf8/ Ptpn6/Fxyd1/Tnni3/ Coro1a/Aplnr/Hrc/Scgn/ Disc1 | 48 |
| BP | GO:0070664 | negative regulation of leukocyte proliferation | 13/858 | 69/ 15881 | 7.06E-05 | 0.00330221028539629 | ENSMUSG00000029816/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000053965/ ENSMUSG00000075122/ENSMUSG00000053216/ ENSMUSG00000039981/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000000706/ ENSMUSG00000052013/ENSMUSG00000004266/ ENSMUSG00000034652 | Gpnmb/Cdkn2a/Pawr/ Pde5a/Cd80/Btn2a2/ Zc3h12d/Ceacam1/Lrrc32/ Btn1a1/Btla/Ptpn6/Cd300a | 13 |
| BP | GO:2000377 | regulation of reactive oxygen species metabolic process | 22/858 | 164/ 15881 | 7.34E-05 | 0.00340034638495104 | ENSMUSG00000029380/ENSMUSG00000023067/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000024066/ENSMUSG00000026463/ ENSMUSG00000003541/ENSMUSG00000037580/ | Cxcl1/Cdkn1a/Trim30a/ Zc3h12a/Xdh/Atp2b4/Ier3/ Gch1/Plau/Ulbp1/Tlr2/ Syk/Snca/Ptgis/Ass1/Cd36/ | 22 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000021822/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000025889/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000002944/ ENSMUSG00000006235/ENSMUSG00000032066/ ENSMUSG00000000120/ENSMUSG00000079164/ ENSMUSG00000004231/ENSMUSG00000021948 | Epor/Bco2/Ngfr/Tlr5/ Pax2/Prkcd | |
| BP | GO:0002250 | adaptive immune response | 32/858 | 286/ 15881 | 7.72E-05 | 0.00354054418441462 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000073411/ENSMUSG00000061232/ ENSMUSG00000024778/ENSMUSG00000022636/ ENSMUSG00000000732/ENSMUSG00000019850/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000021457/ENSMUSG00000053175/ ENSMUSG00000026068/ENSMUSG00000041481/ ENSMUSG00000055994/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000066755/ ENSMUSG00000026177/ENSMUSG00000049109/ ENSMUSG00000020641/ENSMUSG00000079343/ ENSMUSG00000030468/ENSMUSG00000000791/ ENSMUSG00000033107/ENSMUSG00000075370/ ENSMUSG00000052013/ENSMUSG00000041439/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034266/ENSMUSG00000026117 | C3/Cd74/H2-D1/H2-K1/ Fas/Alcam/Icosl/Tnfaip3/ Nectin2/Ulbp1/Syk/Bcl3/ Il18rap/Serpina3g/Nod2/ Lef1/Ctsh/Tnfsf18/ Slc11a1/Themis/Rsad2/ C1s2/Siglecg/Il12rb1/ Rnf125/Igll1/Btla/Mfsd6/ Prkcd/Ptpn6/Batf/Zap70 | 32 |
| BP | GO:0051272 | positive regulation of cellular component movement | 46/858 | 473/ 15881 | 8.18E-05 | 0.00370646980177729 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000027750/ENSMUSG00000029816/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000037685/ ENSMUSG00000035873/ENSMUSG00000023913/ ENSMUSG00000039621/ENSMUSG00000032860/ ENSMUSG00000025207/ENSMUSG00000021822/ ENSMUSG00000022676/ENSMUSG00000029851/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000053475/ ENSMUSG00000036585/ENSMUSG00000048779/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000046761/ ENSMUSG00000026580/ENSMUSG00000055632/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000002489/ENSMUSG00000038756/ ENSMUSG00000028978/ENSMUSG00000049044/ ENSMUSG00000050315/ENSMUSG00000028864/ ENSMUSG00000030170/ENSMUSG00000068748/ ENSMUSG00000030707/ENSMUSG00000020081 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Postn/Gpnmb/Lbp/ Zc3h12a/Dab2/Mmp9/ Lgals3/Atp8a1/Pawr/ Pla2g7/Prex1/P2ry2/ Sema4g/Plau/Snai2/Tcaf2/ F3/Ccl20/Tlr2/Tnfaip6/ Fgf1/P2ry6/Pf4/Lef1/Ctsh/ Tnfsf18/Vegfc/Fam83h/ Selp/Hmcn2/Cxcl5/Cxcl10/ Tiam1/Ttll6/Nos3/ Rapgef4/Synpo2/Hgf/ Wnt5b/Ptprz1/Coro1a/ Tacr2 | 46 |
| BP | GO:1903901 | negative regulation of viral life cycle | 13/858 | 70/ 15881 | 8.24E-05 | 0.00370646980177729 | ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000001166/ENSMUSG00000035692/ ENSMUSG00000074272/ENSMUSG00000032690/ | Slpi/Bst2/Zc3h12a/Rnasel/ Oas1c/Isg15/Ceacam1/ Oas2/Rsad2/Ifitm6/Oas1b/ Oas3/Mid2 | 13 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| | | | | | | | ENSMUSG00000020641/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000032661/ ENSMUSG00000000266 | | |
| BP | GO:0030335 | positive regulation of cell migration | 44/858 | 446/ 15881 | 8.36E-05 | 0.00372069810958262 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000027750/ENSMUSG00000029816/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000037685/ ENSMUSG00000035873/ENSMUSG00000023913/ ENSMUSG00000039621/ENSMUSG00000032860/ ENSMUSG00000025207/ENSMUSG00000021822/ ENSMUSG00000022676/ENSMUSG00000029851/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000053475/ ENSMUSG00000036585/ENSMUSG00000048779/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000046761/ ENSMUSG00000026580/ENSMUSG00000055632/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000002489/ENSMUSG00000028978/ ENSMUSG00000049044/ENSMUSG00000050315/ ENSMUSG00000028864/ENSMUSG00000030170/ ENSMUSG00000068748/ENSMUSG00000030707 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Postn/Gpnmb/Lbp/ Zc3h12a/Dab2/Mmp9/ Lgals3/Atp8a1/Pawr/ Pla2g7/Prex1/P2ry2/ Sema4g/Plau/Snai2/Tcaf2/ F3/Ccl20/Tlr2/Tnfaip6/ Fgf1/P2ry6/Pf4/Lef1/Ctsh/ Tnfsf18/Vegfc/Fam83h/ Selp/Hmcn2/Cxcl5/Cxcl10/ Tiam1/Nos3/Rapgef4/ Synpo2/Hgf/Wnt5b/ Ptprz1/Coro1a | 44 |
| BP | GO:2000147 | positive regulation of cell motility | 45/858 | 460/ 15881 | 8.49E-05 | 0.00374401953504159 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000027750/ENSMUSG00000029816/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000037685/ ENSMUSG00000035873/ENSMUSG00000023913/ ENSMUSG00000039621/ENSMUSG00000032860/ ENSMUSG00000025207/ENSMUSG00000021822/ ENSMUSG00000022676/ENSMUSG00000029851/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000053475/ ENSMUSG00000036585/ENSMUSG00000048779/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000046761/ ENSMUSG00000026580/ENSMUSG00000055632/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000002489/ENSMUSG00000028978/ ENSMUSG00000049044/ENSMUSG00000050315/ ENSMUSG00000028864/ENSMUSG00000030170/ ENSMUSG00000068748/ENSMUSG00000030707/ ENSMUSG00000020081 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Postn/Gpnmb/Lbp/ Zc3h12a/Dab2/Mmp9/ Lgals3/Atp8a1/Pawr/ Pla2g7/Prex1/P2ry2/ Sema4g/Plau/Snai2/Tcaf2/ F3/Ccl20/Tlr2/Tnfaip6/ Fgf1/P2ry6/Pf4/Lef1/Ctsh/ Tnfsf18/Vegfc/Fam83h/ Selp/Hmcn2/Cxcl5/Cxcl10/ Tiam1/Nos3/Rapgef4/ Synpo2/Hgf/Wnt5b/ Ptprz1/Coro1a/Tacr2 | 45 |
| BP | GO:0043154 | negative regulation of cysteine-type | 14/858 | 80/ 15881 | 8.74E-05 | 0.00381916224731035 | ENSMUSG00000017737/ENSMUSG00000078945/ ENSMUSG00000096472/ENSMUSG00000019823/ | Mmp9/Naip2/Cdkn2d/ Mical1/Tnfrsf1b/Plaur/ | 14 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | endopeptidase activity involved in apoptotic process | | | | | ENSMUSG00000028599/ENSMUSG00000046223/ ENSMUSG00000078942/ENSMUSG00000027985/ ENSMUSG00000025889/ENSMUSG00000020178/ ENSMUSG00000071203/ENSMUSG00000019278/ ENSMUSG00000028864/ENSMUSG00000004231 | Naip6/Lef1/Snca/Adora2a/ Naip5/Dpep1/Hgf/Pax2 | |
| BP | GO:0002688 | regulation of leukocyte chemotaxis | 15/858 | 90/ 15881 | 8.84E-05 | 0.00382446422924776 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000029082/ ENSMUSG00000023913/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000053318 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Bst1/Pla2g7/Pf4/ Nod2/Tnfsf18/Vegfc/ Cxcl5/Cxcl10/Nov/Slamf8 | 15 |
| BP | GO:0006875 | cellular metal ion homeostasis | 42/858 | 421/ 15881 | 9.39E-05 | 0.00402631155299779 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000003617/ENSMUSG00000023030/ ENSMUSG00000066152/ENSMUSG00000022032/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000040907/ENSMUSG00000032839/ ENSMUSG00000050541/ENSMUSG00000044026/ ENSMUSG00000038403/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000026177/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000032020/ ENSMUSG00000074715/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000021070/ ENSMUSG00000063354/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000034855/ ENSMUSG00000029716/ENSMUSG00000030523/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Cp/Slc11a2/ Slc31a2/Scara5/Atp2b4/ Pawr/Ero1l/P2ry2/Atp1b1/ Cd38/Atp1a3/Trpc1/ Adra1b/Slc35g1/Hfe2/ Cacna1i/Mcub/Slc11a1/ Akap6/Snca/Atp1b2/ Ubash3b/Ccl28/Cd36/ Kng2/Bdkrb2/Slc39a4/ Ramp3/Epor/Cxcl10/Tfr2/ Trpm1/Ptpn6/Fxyd1/ Tnni3/Coro1a/Aplnr/Hrc/ Scgn/Disc1 | 42 |
| BP | GO:1905954 | positive regulation of lipid localization | 13/858 | 71/ 15881 | 9.60E-05 | 0.00406232590811864 | ENSMUSG00000024164/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000037685/ ENSMUSG00000032860/ENSMUSG00000020333/ ENSMUSG00000042010/ENSMUSG00000003484/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000024030/ENSMUSG00000025044/ ENSMUSG00000021948 | C3/Zc3h12a/Dab2/Atp8a1/ P2ry2/Acsl6/Acacb/ Cyp4f18/Abca1/Cd36/ Abcg1/Msr1/Prkcd | 13 |
| BP | GO:0002757 | immune response-activating signal transduction | 28/858 | 239/ 15881 | 9.66E-05 | 0.00406232590811864 | ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000019850/ENSMUSG00000029084/ ENSMUSG00000062300/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000055994/ ENSMUSG00000005057/ENSMUSG00000053216/ ENSMUSG00000049109/ENSMUSG00000017830/ ENSMUSG00000020641/ENSMUSG00000002944/ | Lbp/Trim30a/Zc3h12a/ Icosl/Lgals3/Pawr/Tnfaip3/ Cd38/Nectin2/Tlr2/Syk/ Nod2/Sh2b2/Btn2a2/ Themis/Dhx58/Rsad2/ Cd36/Btn1a1/Tlr5/Igll1/ Pvrig/Prkch/Lcp2/Lpxn/ Ptpn6/Cd300a/Zap70 | 28 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000000706/ENSMUSG00000079164/ ENSMUSG00000075370/ENSMUSG00000109713/ ENSMUSG00000021108/ENSMUSG00000002699/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000026117 | | |
| BP | GO:0034612 | response to tumor necrosis factor | 21/858 | 156/ 15881 | 0.000100951848736192 | 0.00420877434821977 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000024778/ENSMUSG00000042677/ ENSMUSG00000035373/ENSMUSG00000028965/ ENSMUSG00000033538/ENSMUSG00000037580/ ENSMUSG00000026166/ENSMUSG00000028599/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000066755/ENSMUSG00000008318/ ENSMUSG00000035186/ENSMUSG00000037860/ ENSMUSG00000031548/ENSMUSG00000000120/ ENSMUSG00000028602/ENSMUSG00000031780/ ENSMUSG00000025888 | Ccl2/Cx3cl1/Fas/Zc3h12a/ Ccl7/Tnfrsf9/Casp4/Gch1/ Ccl20/Tnfrsf1b/Syk/Ccl9/ Tnfsf18/Relt/Ubd/Aim2/ Sfrp1/Ngfr/Tnfrsf8/Ccl17/ Casp1 | 21 |
| BP | GO:0043903 | regulation of symbiosis, encompassing mutualism through parasitism | 24/858 | 192/ 15881 | 0.000109655268381809 | 0.00453044198917997 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000062300/ENSMUSG00000027995/ ENSMUSG00000001166/ENSMUSG00000055994/ ENSMUSG00000027985/ENSMUSG00000035692/ ENSMUSG00000074272/ENSMUSG00000032690/ ENSMUSG00000020641/ENSMUSG00000002944/ ENSMUSG00000059108/ENSMUSG00000029605/ ENSMUSG00000029371/ENSMUSG00000032661/ ENSMUSG00000041515/ENSMUSG00000000266 | Cd74/Cxcl1/Slpi/Bst2/Lbp/ Trim30a/Zc3h12a/Rnasel/ Nectin2/Tlr2/Oas1c/Nod2/ Lef1/Isg15/Ceacam1/Oas2/ Rsad2/Cd36/Ifitm6/Oas1b/ Cxcl5/Oas3/Irf8/Mid2 | 24 |
| BP | GO:0071622 | regulation of granulocyte chemotaxis | 10/858 | 45/ 15881 | 0.000113960125000942 | 0.00466626011834212 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000029082/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000066755/ENSMUSG00000029371 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Bst1/Pf4/Nod2/ Tnfsf18/Cxcl5 | 10 |
| BP | GO:0072511 | divalent inorganic cation transport | 38/858 | 371/ 15881 | 0.000116128420110225 | 0.00471296402323445 | ENSMUSG00000023030/ENSMUSG00000020432/ ENSMUSG00000026463/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000021831/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000032839/ENSMUSG00000044026/ ENSMUSG00000022416/ENSMUSG00000027994/ ENSMUSG00000050777/ENSMUSG00000057897/ ENSMUSG00000026177/ENSMUSG00000034353/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000041245/ ENSMUSG00000028214/ENSMUSG00000063354/ ENSMUSG00000028255/ENSMUSG00000041046/ ENSMUSG00000053395/ENSMUSG00000034855/ ENSMUSG00000024065/ENSMUSG00000028978/ ENSMUSG00000020178/ENSMUSG00000020787/ ENSMUSG00000037418/ENSMUSG00000041695/ ENSMUSG00000030523/ENSMUSG00000059588/ | Slc11a2/Tcn2/Atp2b4/ Lgals3/Pawr/Ero1l/ Atp1b1/Ctgf/Trpc1/ Slc35g1/Cacna1i/Mcub/ Tmem37/Camk2b/Slc11a1/ Ramp1/Akap6/Snca/ Ubash3b/Wnk3/Gem/ Slc39a4/Clca1/Ramp3/ Cacng8/Cxcl10/Ehd3/ Nos3/Adora2a/P2rx1/ Best1/Kcnj2/Trpm1/Calcrl/ Ptpn6/Coro1a/Aplnr/Hrc | 38 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000004266/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239 | | |
| BP | GO:1902622 | regulation of neutrophil migration | 9/858 | 37/ 15881 | 0.000118882427709863 | 0.00478241064453887 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000016024/ENSMUSG00000029082/ ENSMUSG00000035873/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000029371/ ENSMUSG00000053318 | Cd74/Cxcl1/Lbp/Bst1/ Pawr/Pf4/Nod2/Cxcl5/ Slamf8 | 9 |
| BP | GO:0070269 | pyroptosis | 6/858 | 16/ 15881 | 0.000122567148312901 | 0.00488776471446055 | ENSMUSG00000033538/ENSMUSG00000078945/ ENSMUSG00000078942/ENSMUSG00000037860/ ENSMUSG00000071203/ENSMUSG00000025888 | Casp4/Naip2/Naip6/Aim2/ Naip5/Casp1 | 6 |
| BP | GO:0002687 | positive regulation of leukocyte migration | 17/858 | 114/ 15881 | 0.000129025830779554 | 0.00510096948237099 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000023913/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000029373/ ENSMUSG00000066755/ENSMUSG00000031520/ ENSMUSG00000026580/ENSMUSG00000029371/ ENSMUSG00000034855 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Mmp9/Lgals3/Pawr/ Pla2g7/Ccl20/Tlr2/Pf4/ Tnfsf18/Vegfc/Selp/Cxcl5/ Cxcl10 | 17 |
| BP | GO:0002521 | leukocyte differentiation | 42/858 | 429/ 15881 | 0.000142537425242417 | 0.00558697976206603 | ENSMUSG00000023367/ENSMUSG00000024610/ ENSMUSG00000029810/ENSMUSG00000024778/ ENSMUSG00000029570/ENSMUSG00000023927/ ENSMUSG00000044303/ENSMUSG00000037440/ ENSMUSG00000049577/ENSMUSG00000038387/ ENSMUSG00000039621/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000034394/ ENSMUSG00000027995/ENSMUSG00000034023/ ENSMUSG00000021457/ENSMUSG00000053175/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000027858/ENSMUSG00000066755/ ENSMUSG00000018169/ENSMUSG00000035158/ ENSMUSG00000053216/ENSMUSG00000049109/ ENSMUSG00000032020/ENSMUSG00000035186/ ENSMUSG00000074272/ENSMUSG00000020641/ ENSMUSG00000032750/ENSMUSG00000036587/ ENSMUSG00000031548/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000044258/ENSMUSG00000048251/ ENSMUSG00000004266/ENSMUSG00000020325/ ENSMUSG00000034266/ENSMUSG00000026117 | Tmem176a/Cd74/ Tmem176b/Fas/Lfng/ Satb1/Cdkn2a/Vnn1/ Zfpm1/Rras/Prex1/ Tnfaip3/Trib1/Lif/Tlr2/ Fancd2/Syk/Bcl3/Pf4/Lef1/ Tspan2/Tnfsf18/Mfng/ Mitf/Btn2a2/Themis/ Ubash3b/Ubd/Ceacam1/ Rsad2/Gab3/Fut7/Sfrp1/ Il15/Il7/Cyp26b1/Ctla2a/ Bcl11b/Ptpn6/Fstl3/Batf/ Zap70 | 42 |
| BP | GO:0002253 | activation of immune response | 31/858 | 283/ 15881 | 0.00014664053773129 | 0.00569909750877709 | ENSMUSG00000024164/ENSMUSG00000016024/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000000732/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000019850/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000005057/ ENSMUSG00000053216/ENSMUSG00000049109/ ENSMUSG00000017830/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000079343/ | C3/Lbp/Trim30a/Zc3h12a/ Icosl/Lgals3/Pawr/Tnfaip3/ Cd38/Nectin2/Tlr2/Syk/ Nod2/Sh2b2/Btn2a2/ Themis/Dhx58/Rsad2/ Cd36/C1s2/Aim2/Btn1a1/ Tlr5/Igll1/Pvrig/Prkch/ Lcp2/Lpxn/Ptpn6/Cd300a/ Zap70 | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000037860/ENSMUSG00000000706/ ENSMUSG00000079164/ENSMUSG00000075370/ ENSMUSG00000109713/ENSMUSG00000021108/ ENSMUSG00000002699/ENSMUSG00000024696/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000026117 | | |
| BP | GO:1902105 | regulation of leukocyte differentiation | 26/858 | 221/ 15881 | 0.000158055893150143 | 0.00607074786034588 | ENSMUSG00000023367/ENSMUSG00000024610/ ENSMUSG00000029810/ENSMUSG00000024778/ ENSMUSG00000044303/ENSMUSG00000037440/ ENSMUSG00000049577/ENSMUSG00000032501/ ENSMUSG00000034394/ENSMUSG00000034023/ ENSMUSG00000021457/ENSMUSG00000029373/ ENSMUSG00000027985/ENSMUSG00000066755/ ENSMUSG00000035158/ENSMUSG00000053216/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000031548/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000044258/ENSMUSG00000004266/ ENSMUSG00000020325/ENSMUSG00000026117 | Tmem176a/Cd74/ Tmem176b/Fas/Cdkn2a/ Vnn1/Zfpm1/Trib1/Lif/ Fancd2/Syk/Pf4/Lef1/ Tnfsf18/Mitf/Btn2a2/ Ubash3b/Ceacam1/Sfrp1/ Il15/Il7/Cyp26b1/Ctla2a/ Ptpn6/Fstl3/Zap70 | 26 |
| BP | GO:0003015 | heart process | 21/858 | 161/ 15881 | 0.000158850794426844 | 0.00607074786034588 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000040907/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000041046/ ENSMUSG00000064329/ENSMUSG00000024065/ ENSMUSG00000028978/ENSMUSG00000035296/ ENSMUSG00000026418/ENSMUSG00000041695/ ENSMUSG00000036570/ENSMUSG00000035458/ ENSMUSG00000038239 | Zc3h12a/Atp2b4/Adora1/ Gch1/Pde5a/Gja5/Atp1b1/ Ctgf/Atp1a3/Adra1b/ Akap6/Ramp3/Scn1a/ Ehd3/Nos3/Sgcg/Tnni1/ Kcnj2/Fxyd1/Tnni3/Hrc | 21 |
| BP | GO:0032496 | response to lipopolysaccharide | 28/858 | 248/ 15881 | 0.000182068558890856 | 0.00690054885184683 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000017002/ENSMUSG00000016024/ ENSMUSG00000024778/ENSMUSG00000042677/ ENSMUSG00000028965/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000028599/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000075122/ENSMUSG00000008318/ ENSMUSG00000026177/ENSMUSG00000025889/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000104713/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000028978/ ENSMUSG00000000120/ENSMUSG00000041515/ ENSMUSG00000028602/ENSMUSG00000025888 | Cxcl1/Ccl2/Slpi/Lbp/Fas/ Zc3h12a/Tnfrsf9/Gch1/ Nos2/Tnfaip3/Trib1/ Tnfrsf1b/Pf4/Nod2/Cd80/ Relt/Slc11a1/Snca/Abca1/ Cd36/Gbp6/Cxcl5/Cxcl10/ Nos3/Ngfr/Irf8/Tnfrsf8/ Casp1 | 28 |
| BP | GO:0071356 | cellular response to tumor necrosis factor | 19/858 | 140/ 15881 | 0.000190997312605754 | 0.00717962029188513 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000024778/ENSMUSG00000042677/ ENSMUSG00000035373/ENSMUSG00000028965/ ENSMUSG00000033538/ENSMUSG00000026166/ ENSMUSG00000028599/ENSMUSG00000021457/ ENSMUSG00000019122/ENSMUSG00000066755/ | Ccl2/Cx3cl1/Fas/Zc3h12a/ Ccl7/Tnfrsf9/Casp4/Ccl20/ Tnfrsf1b/Syk/Ccl9/Tnfsf18/ Relt/Aim2/Sfrp1/Ngfr/ Tnfrsf8/Ccl17/Casp1 | 19 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000008318/ENSMUSG00000037860/ ENSMUSG00000031548/ENSMUSG00000000120/ ENSMUSG00000028602/ENSMUSG00000031780/ ENSMUSG00000025888 | | |
| BP | GO:0007271 | synaptic transmission, cholinergic | 7/858 | 24/ 15881 | 0.000201785211911171 | 0.00752347139694821 | ENSMUSG00000026251/ENSMUSG00000057897/ ENSMUSG00000026253/ENSMUSG00000002104/ ENSMUSG00000000120/ENSMUSG00000020178/ ENSMUSG00000020081 | Chrnd/Camk2b/Chrng/ Rapsn/Ngfr/Adora2a/Tacr2 | 7 |
| BP | GO:0070838 | divalent metal ion transport | 37/858 | 368/ 15881 | 0.000206448244838139 | 0.00763525524861053 | ENSMUSG00000023030/ENSMUSG00000026463/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000026576/ ENSMUSG00000019997/ENSMUSG00000032839/ ENSMUSG00000044026/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000050777/ ENSMUSG00000057897/ENSMUSG00000026177/ ENSMUSG00000034353/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000032020/ ENSMUSG00000041245/ENSMUSG00000028214/ ENSMUSG00000063354/ENSMUSG00000028255/ ENSMUSG00000041046/ENSMUSG00000053395/ ENSMUSG00000034855/ENSMUSG00000024065/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000037418/ ENSMUSG00000041695/ENSMUSG00000030523/ ENSMUSG00000059588/ENSMUSG00000004266/ ENSMUSG00000030707/ENSMUSG00000044338/ ENSMUSG00000038239 | Slc11a2/Atp2b4/Lgals3/ Pawr/Ero1l/Atp1b1/Ctgf/ Trpc1/Slc35g1/Cacna1i/ Mcub/Tmem37/Camk2b/ Slc11a1/Ramp1/Akap6/ Snca/Ubash3b/Wnk3/Gem/ Slc39a4/Clca1/Ramp3/ Cacng8/Cxcl10/Ehd3/ Nos3/Adora2a/P2rx1/ Best1/Kcnj2/Trpm1/Calcrl/ Ptpn6/Coro1a/Aplnr/Hrc | 37 |
| BP | GO:0048771 | tissue remodeling | 20/858 | 154/ 15881 | 0.000239306428798747 | 0.00873571316526715 | ENSMUSG00000029816/ENSMUSG00000026185/ ENSMUSG00000044303/ENSMUSG00000017737/ ENSMUSG00000057123/ENSMUSG00000019577/ ENSMUSG00000029084/ENSMUSG00000024743/ ENSMUSG00000034394/ENSMUSG00000021457/ ENSMUSG00000024039/ENSMUSG00000050541/ ENSMUSG00000003051/ENSMUSG00000035158/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000031548/ENSMUSG00000040046/ ENSMUSG00000028978/ENSMUSG00000040329 | Gpnmb/Igfbp5/Cdkn2a/ Mmp9/Gja5/Pdk4/Cd38/ Syt7/Lif/Syk/Cbs/Adra1b/ Elf3/Mitf/Ubash3b/ Ceacam1/Sfrp1/Tph1/ Nos3/Il7 | 20 |
| BP | GO:0045776 | negative regulation of blood pressure | 10/858 | 49/ 15881 | 0.00024131476200782 | 0.00873571316526715 | ENSMUSG00000003541/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000057123/ ENSMUSG00000020826/ENSMUSG00000031520/ ENSMUSG00000002944/ENSMUSG00000021070/ ENSMUSG00000028978/ENSMUSG00000031489 | Ier3/Adora1/Gch1/Gja5/ Nos2/Vegfc/Cd36/Bdkrb2/ Nos3/Adrb3 | 10 |
| BP | GO:0002697 | regulation of immune effector process | 31/858 | 291/ 15881 | 0.000241917918008925 | 0.00873571316526715 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000050335/ENSMUSG00000019850/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000079363/ENSMUSG00000026068/ | C3/Cd74/Cxcl1/H2-D1/ Ccl2/H2-K1/Lbp/Zc3h12a/ Lgals3/Tnfaip3/Nectin2/ Ulbp1/Tlr2/Syk/Gbp4/ Il18rap/Nod2/Tnfsf18/ Dhx58/Ceacam1/Rsad2/ Cd36/Cxcl5/Aim2/Il12rb1/ | 31 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000055994/ENSMUSG00000066755/ ENSMUSG00000017830/ENSMUSG00000074272/ ENSMUSG00000020641/ENSMUSG00000002944/ ENSMUSG00000029371/ENSMUSG00000037860/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000053318/ENSMUSG00000062157/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000025279 | Il15/Slamf8/Ifnlr1/Ptpn6/ Cd300a/Dnase1l3 | |
| BP | GO:2000117 | negative regulation of cysteine-type endopeptidase activity | 14/858 | 88/ 15881 | 0.000249819990082415 | 0.00879334040478286 | ENSMUSG00000017737/ENSMUSG00000078945/ ENSMUSG00000096472/ENSMUSG00000019823/ ENSMUSG00000028599/ENSMUSG00000046223/ ENSMUSG00000078942/ENSMUSG00000027985/ ENSMUSG00000025889/ENSMUSG00000020178/ ENSMUSG00000071203/ENSMUSG00000019278/ ENSMUSG00000028864/ENSMUSG00000004231 | Mmp9/Naip2/Cdkn2d/ Mical1/Tnfrsf1b/Plaur/ Naip6/Lef1/Snca/Adora2a/ Naip5/Dpep1/Hgf/Pax2 | 14 |
| BP | GO:0051346 | negative regulation of hydrolase activity | 33/858 | 318/ 15881 | 0.000251672221386859 | 0.00879334040478286 | ENSMUSG00000017002/ENSMUSG00000000753/ ENSMUSG00000017737/ENSMUSG00000038235/ ENSMUSG00000078945/ENSMUSG00000019852/ ENSMUSG00000042842/ENSMUSG00000096472/ ENSMUSG00000027082/ENSMUSG00000019823/ ENSMUSG00000028599/ENSMUSG00000041481/ ENSMUSG00000046223/ENSMUSG00000078942/ ENSMUSG00000031387/ENSMUSG00000027985/ ENSMUSG00000021403/ENSMUSG00000079014/ ENSMUSG00000025889/ENSMUSG00000060459/ ENSMUSG00000078949/ENSMUSG00000026315/ ENSMUSG00000026249/ENSMUSG00000027834/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000071203/ENSMUSG00000051029/ ENSMUSG00000019278/ENSMUSG00000028864/ ENSMUSG00000004231/ENSMUSG00000079012/ ENSMUSG00000035458 | Slpi/Serpinf1/Mmp9/F11r/ Naip2/Arfgef3/Serpinb6b/ Cdkn2d/Tfpi/Mical1/ Tnfrsf1b/Serpina3g/Plaur/ Naip6/Renbp/Lef1/ Serpinb9b/Serpina3i/Snca/ Kng2/R3hdml/Serpinb8/ Serpine2/Serpini1/Nos3/ Adora2a/Naip5/Serpinb1b/ Dpep1/Hgf/Pax2/ Serpina3m/Tnni3 | 33 |
| BP | GO:0032612 | interleukin-1 production | 12/858 | 68/ 15881 | 0.000253862078810326 | 0.00879334040478286 | ENSMUSG00000042677/ENSMUSG00000033538/ ENSMUSG00000019850/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000055994/ ENSMUSG00000015243/ENSMUSG00000074272/ ENSMUSG00000002944/ENSMUSG00000037860/ ENSMUSG00000071203/ENSMUSG00000025888 | Zc3h12a/Casp4/Tnfaip3/ Ccl20/Tlr2/Nod2/Abca1/ Ceacam1/Cd36/Aim2/ Naip5/Casp1 | 12 |
| BP | GO:0001909 | leukocyte mediated cytotoxicity | 13/858 | 78/ 15881 | 0.000256961692737955 | 0.00879334040478286 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000026068/ENSMUSG00000032359/ ENSMUSG00000074272/ENSMUSG00000029371/ ENSMUSG00000004266/ENSMUSG00000030707/ ENSMUSG00000025279 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nectin2/Ulbp1/Il18rap/ Ctsh/Ceacam1/Cxcl5/ Ptpn6/Coro1a/Dnase1l3 | 13 |
| BP | GO:0002237 | response to molecule of bacterial origin | 29/858 | 266/ 15881 | 0.000256970018461393 | 0.00879334040478286 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000017002/ENSMUSG00000016024/ ENSMUSG00000024778/ENSMUSG00000042677/ ENSMUSG00000028965/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000019850/ | Cxcl1/Ccl2/Slpi/Lbp/Fas/ Zc3h12a/Tnfrsf9/Gch1/ Nos2/Tnfaip3/Trib1/Tlr2/ Tnfrsf1b/Pf4/Nod2/Cd80/ Relt/Slc11a1/Snca/Abca1/ | 29 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000032501/ENSMUSG00000027995/ ENSMUSG00000028599/ENSMUSG00000029373/ ENSMUSG00000055994/ENSMUSG00000075122/ ENSMUSG00000008318/ENSMUSG00000026177/ ENSMUSG00000025889/ENSMUSG00000015243/ ENSMUSG00000002944/ENSMUSG00000104713/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000028978/ENSMUSG00000000120/ ENSMUSG00000041515/ENSMUSG00000028602/ ENSMUSG00000025888 | Cd36/Gbp6/Cxcl5/Cxcl10/ Nos3/Ngfr/Irf8/Tnfrsf8/ Casp1 | |
| BP | GO:0042113 | B cell activation | 24/858 | 203/ 15881 | 0.000258771964595043 | 0.00879334040478286 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000024778/ENSMUSG00000029570/ ENSMUSG00000044303/ENSMUSG00000061132/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000035873/ENSMUSG00000019850/ ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000053175/ENSMUSG00000055994/ ENSMUSG00000027985/ENSMUSG00000018169/ ENSMUSG00000031548/ENSMUSG00000040329/ ENSMUSG00000075370/ENSMUSG00000052013/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000034266 | Cd74/Cdkn1a/Fas/Lfng/ Cdkn2a/Blnk/Icosl/Bst1/ Pawr/Tnfaip3/Cd38/Syk/ Bcl3/Nod2/Lef1/Mfng/ Sfrp1/Il7/Igll1/Btla/Prkcd/ Ptpn6/Cd300a/Batf | 24 |
| BP | GO:0090025 | regulation of monocyte chemotaxis | 6/858 | 18/ 15881 | 0.00025885323912902 | 0.00879334040478286 | ENSMUSG00000035385/ENSMUSG00000023913/ ENSMUSG00000066755/ENSMUSG00000034855/ ENSMUSG00000037362/ENSMUSG00000053318 | Ccl2/Pla2g7/Tnfsf18/ Cxcl10/Nov/Slamf8 | 6 |
| BP | GO:0098581 | detection of external biotic stimulus | 6/858 | 18/ 15881 | 0.00025885323912902 | 0.00879334040478286 | ENSMUSG00000016024/ENSMUSG00000078945/ ENSMUSG00000027995/ENSMUSG00000078942/ ENSMUSG00000055994/ENSMUSG00000071203 | Lbp/Naip2/Tlr2/Naip6/ Nod2/Naip5 | 6 |
| BP | GO:0044406 | adhesion of symbiont to host | 5/858 | 12/ 15881 | 0.000261985176601372 | 0.00882472904169313 | ENSMUSG00000062300/ENSMUSG00000040253/ ENSMUSG00000029298/ENSMUSG00000028268/ ENSMUSG00000104713 | Nectin2/Gbp7/Gbp9/Gbp3/ Gbp6 | 5 |
| BP | GO:0001906 | cell killing | 15/858 | 99/ 15881 | 0.000264424934497735 | 0.00882472904169313 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000020826/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000026068/ ENSMUSG00000029373/ENSMUSG00000032359/ ENSMUSG00000074272/ENSMUSG00000029371/ ENSMUSG00000004266/ENSMUSG00000030707/ ENSMUSG00000025279 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nos2/Nectin2/Ulbp1/ Il18rap/Pf4/Ctsh/Ceacam1/ Cxcl5/Ptpn6/Coro1a/ Dnase1l3 | 15 |
| BP | GO:0031348 | negative regulation of defense response | 21/858 | 167/ 15881 | 0.000265550067107207 | 0.00882472904169313 | ENSMUSG00000000753/ENSMUSG00000042677/ ENSMUSG00000074151/ENSMUSG00000003541/ ENSMUSG00000042429/ENSMUSG00000019850/ ENSMUSG00000028599/ENSMUSG00000053475/ ENSMUSG00000055994/ENSMUSG00000017969/ ENSMUSG00000041193/ENSMUSG00000017830/ ENSMUSG00000074272/ENSMUSG00000030468/ ENSMUSG00000037362/ENSMUSG00000020178/ ENSMUSG00000044258/ENSMUSG00000021322/ ENSMUSG00000053318/ENSMUSG00000059588/ ENSMUSG00000028864 | Serpinf1/Zc3h12a/Nlrc5/ Ier3/Adora1/Tnfaip3/ Tnfrsf1b/Tnfaip6/Nod2/ Ptgis/Pla2g5/Dhx58/ Ceacam1/Siglecg/Nov/ Adora2a/Ctla2a/Aoah/ Slamf8/Calcrl/Hgf | 21 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0006820 | anion transport | 41/858 | 428/15881 | 0.000270048169616867 | 0.00890964680476945 | ENSMUSG00000023947/ENSMUSG00000037685/ENSMUSG00000029334/ENSMUSG00000042429/ENSMUSG00000005089/ENSMUSG00000020826/ENSMUSG00000032860/ENSMUSG00000020333/ENSMUSG00000054720/ENSMUSG00000029851/ENSMUSG00000021457/ENSMUSG00000003341/ENSMUSG00000046808/ENSMUSG00000037762/ENSMUSG00000048779/ENSMUSG00000060961/ENSMUSG00000026177/ENSMUSG00000003484/ENSMUSG00000025889/ENSMUSG00000041193/ENSMUSG00000015243/ENSMUSG00000027070/ENSMUSG00000002944/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000021070/ENSMUSG00000070280/ENSMUSG00000028255/ENSMUSG00000068323/ENSMUSG00000020600/ENSMUSG00000020178/ENSMUSG00000054753/ENSMUSG00000025557/ENSMUSG00000037418/ENSMUSG00000038963/ENSMUSG00000028020/ENSMUSG00000024030/ENSMUSG00000007034/ENSMUSG00000025938/ENSMUSG00000021948/ENSMUSG00000036570 | Nfkbie/Atp8a1/Prkg2/Adora1/Slc1a2/Nos2/P2ry2/Acsl6/Lrrc8c/Tcaf2/Syk/Atp8b3/Atp10d/Slc16a9/P2ry6/Slc4a4/Slc11a1/Cyp4f18/Snca/Pla2g5/Abca1/Lrp2/Cd36/Slc17a7/Slc4a8/Bdkrb2/Slc22a14/Clca1/Slc4a5/Slc7a15/Adora2a/AU018091/Slc15a1/Best1/Slco4a1/Glrb/Abcg1/Slc44a4/Slco5a1/Prkcd/Fxyd1 | 41 |
| BP | GO:0019228 | neuronal action potential | 8/858 | 33/15881 | 0.000291339609061732 | 0.00954345319397931 | ENSMUSG00000035873/ENSMUSG00000057182/ENSMUSG00000022416/ENSMUSG00000075318/ENSMUSG00000064329/ENSMUSG00000020787/ENSMUSG00000049044/ENSMUSG00000027071 | Pawr/Scn3a/Cacna1i/Scn2a/Scn1a/P2rx1/Rapgef4/P2rx3 | 8 |
| BP | GO:0015711 | organic anion transport | 33/858 | 321/15881 | 0.000298849721664433 | 0.00963241536880744 | ENSMUSG00000023947/ENSMUSG00000037685/ENSMUSG00000042429/ENSMUSG00000005089/ENSMUSG00000020826/ENSMUSG00000032860/ENSMUSG00000020333/ENSMUSG00000021457/ENSMUSG00000003341/ENSMUSG00000046808/ENSMUSG00000037762/ENSMUSG00000060961/ENSMUSG00000026177/ENSMUSG00000003484/ENSMUSG00000025889/ENSMUSG00000041193/ENSMUSG00000015243/ENSMUSG00000027070/ENSMUSG00000002944/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000021070/ENSMUSG00000070280/ENSMUSG00000068323/ENSMUSG00000020600/ENSMUSG00000020178/ENSMUSG00000054753/ENSMUSG00000025557/ENSMUSG00000038963/ENSMUSG00000024030/ENSMUSG00000007034/ENSMUSG00000025938/ENSMUSG00000021948 | Nfkbie/Atp8a1/Adora1/Slc1a2/Nos2/P2ry2/Acsl6/Syk/Atp8b3/Atp10d/Slc16a9/Slc4a4/Slc11a1/Cyp4f18/Snca/Pla2g5/Abca1/Lrp2/Cd36/Slc17a7/Slc4a8/Bdkrb2/Slc22a14/Slc4a5/Slc7a15/Adora2a/AU018091/Slc15a1/Slco4a1/Abcg1/Slc44a4/Slco5a1/Prkcd | 33 |
| BP | GO:0046631 | alpha-beta T cell activation | 16/858 | 111/15881 | 0.000300356606572059 | 0.00963241536880744 | ENSMUSG00000023927/ENSMUSG00000021457/ENSMUSG00000053175/ENSMUSG00000027985/ENSMUSG00000075122/ENSMUSG00000066755/ENSMUSG00000074272/ENSMUSG00000020641/ENSMUSG00000036587/ENSMUSG00000031712/ENSMUSG00000020178/ENSMUSG00000052013/ENSMUSG00000048251/ENSMUSG00000034652/ENSMUSG00000034266/ENSMUSG00000026117 | Satb1/Syk/Bcl3/Lef1/Cd80/Tnfsf18/Ceacam1/Rsad2/Fut7/Il15/Adora2a/Btla/Bcl11b/Cd300a/Batf/Zap70 | 16 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0050864 | regulation of B cell activation | 16/858 | 111/15881 | 0.000300356606572059 | 0.00963241536880744 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000024778/ENSMUSG00000044303/ ENSMUSG00000029082/ENSMUSG00000035873/ ENSMUSG00000019850/ENSMUSG00000029084/ ENSMUSG00000021457/ENSMUSG00000055994/ ENSMUSG00000031548/ENSMUSG00000040329/ ENSMUSG00000075370/ENSMUSG00000052013/ ENSMUSG00000004266/ENSMUSG00000034652 | Cd74/Cdkn1a/Fas/Cdkn2a/ Bst1/Pawr/Tnfaip3/Cd38/ Syk/Nod2/Sfrp1/Il7/Igll1/ Btla/Ptpn6/Cd300a | 16 |
| BP | GO:0019932 | second-messenger-mediated signaling | 28/858 | 256/15881 | 0.000309101693061903 | 0.009776140444013 | ENSMUSG00000026463/ENSMUSG00000006457/ ENSMUSG00000029082/ENSMUSG00000062991/ ENSMUSG00000020826/ENSMUSG00000026576/ ENSMUSG00000026166/ENSMUSG00000021457/ ENSMUSG00000050541/ENSMUSG00000029373/ ENSMUSG00000034353/ENSMUSG00000061603/ ENSMUSG00000015243/ENSMUSG00000074272/ ENSMUSG00000002944/ENSMUSG00000026580/ ENSMUSG00000027674/ENSMUSG00000041046/ ENSMUSG00000034855/ENSMUSG00000028978/ ENSMUSG00000020178/ENSMUSG00000049044/ ENSMUSG00000059588/ENSMUSG00000031489/ ENSMUSG00000035458/ENSMUSG00000044338/ ENSMUSG00000038239/ENSMUSG00000026117 | Atp2b4/Actn3/Bst1/Nrg1/ Nos2/Atp1b1/Ccl20/Syk/ Adra1b/Pf4/Ramp1/ Akap6/Abca1/Ceacam1/ Cd36/Selp/Pex5l/Ramp3/ Cxcl10/Nos3/Adora2a/ Rapgef4/Calcrl/Adrb3/ Tnni3/Aplnr/Hrc/Zap70 | 28 |
| BP | GO:0045765 | regulation of angiogenesis | 28/858 | 256/15881 | 0.000309101693061903 | 0.009776140444013 | ENSMUSG00000024164/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000000753/ ENSMUSG00000042677/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000028039/ ENSMUSG00000038387/ENSMUSG00000034394/ ENSMUSG00000028128/ENSMUSG00000029669/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000032359/ENSMUSG00000056758/ ENSMUSG00000018983/ENSMUSG00000064246/ ENSMUSG00000031520/ENSMUSG00000017969/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000034855/ENSMUSG00000028978/ ENSMUSG00000000120/ENSMUSG00000021256/ ENSMUSG00000028864/ENSMUSG00000044338 | C3/Ccl2/Cx3cl1/Serpinf1/ Zc3h12a/Mmp9/Lgals3/ Efna3/Rras/Lif/F3/ Tspan12/Fgf1/Pf4/Ctsh/ Hmga2/E2f2/Chil1/Vegfc/ Ptgis/Ceacam1/Cd36/ Cxcl10/Nos3/Ngfr/Vash1/ Hgf/Aplnr | 28 |
| BP | GO:0051051 | negative regulation of transport | 40/858 | 418/15881 | 0.00032624342721905 | 0.0102476188851134 | ENSMUSG00000024610/ENSMUSG00000031778/ ENSMUSG00000046718/ENSMUSG00000042677/ ENSMUSG00000028965/ENSMUSG00000017737/ ENSMUSG00000020806/ENSMUSG00000050335/ ENSMUSG00000003541/ENSMUSG00000047250/ ENSMUSG00000035873/ENSMUSG00000029334/ ENSMUSG00000042429/ENSMUSG00000034394/ ENSMUSG00000021596/ENSMUSG00000029851/ ENSMUSG00000027995/ENSMUSG00000079363/ ENSMUSG00000005057/ENSMUSG00000004347/ ENSMUSG00000024873/ENSMUSG00000053216/ ENSMUSG00000003484/ENSMUSG00000025889/ ENSMUSG00000027457/ENSMUSG00000020641/ ENSMUSG00000090958/ENSMUSG00000041245/ | Cd74/Cx3cl1/Bst2/ Zc3h12a/Tnfrsf9/Mmp9/ Rhbdf2/Lgals3/Ier3/Ptgs1/ Pawr/Prkg2/Adora1/Lif/ Mctp1/Tcaf2/Tlr2/Gbp4/ Sh2b2/Pde1c/Cnih2/ Btn2a2/Cyp4f18/Snca/ Snph/Rsad2/Lrrc32/Wnk3/ Gem/Serpine2/Sfrp1/Nov/ Nos3/Slc15a1/Btn1a1/ Ostn/Cd300a/Coro1a/Hrc/ Tacr2 | 40 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000028214/ENSMUSG00000026249/ ENSMUSG00000031548/ENSMUSG00000037362/ ENSMUSG00000028978/ENSMUSG00000025557/ ENSMUSG00000000706/ENSMUSG00000052276/ ENSMUSG00000034652/ENSMUSG00000030707/ ENSMUSG00000038239/ENSMUSG00000020081 | | |
| BP | GO:0045058 | T cell selection | 9/858 | 42/ 15881 | 0.000334254632359693 | 0.0104278349932078 | ENSMUSG00000024610/ENSMUSG00000024778/ ENSMUSG00000021457/ENSMUSG00000066755/ ENSMUSG00000049109/ENSMUSG00000031712/ ENSMUSG00000048251/ENSMUSG00000034266/ ENSMUSG00000026117 | Cd74/Fas/Syk/Tnfsf18/ Themis/Il15/Bcl11b/Batf/ Zap70 | 9 |
| BP | GO:0060047 | heart contraction | 20/858 | 158/ 15881 | 0.000337441777285922 | 0.0104293930991892 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000040907/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000064329/ ENSMUSG00000024065/ENSMUSG00000028978/ ENSMUSG00000035296/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Atp2b4/Adora1/ Gch1/Pde5a/Gja5/Atp1b1/ Ctgf/Atp1a3/Adra1b/ Akap6/Scn1a/Ehd3/Nos3/ Sgcg/Tnni1/Kcnj2/Fxyd1/ Tnni3/Hrc | 20 |
| BP | GO:0040017 | positive regulation of locomotion | 45/858 | 489/ 15881 | 0.000338852937588135 | 0.0104293930991892 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000027750/ENSMUSG00000029816/ ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000037685/ ENSMUSG00000035873/ENSMUSG00000023913/ ENSMUSG00000039621/ENSMUSG00000032860/ ENSMUSG00000025207/ENSMUSG00000021822/ ENSMUSG00000022676/ENSMUSG00000029851/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000053475/ ENSMUSG00000036585/ENSMUSG00000048779/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000046761/ ENSMUSG00000026580/ENSMUSG00000055632/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000002489/ENSMUSG00000028978/ ENSMUSG00000049044/ENSMUSG00000050315/ ENSMUSG00000028864/ENSMUSG00000030170/ ENSMUSG00000068748/ENSMUSG00000030707/ ENSMUSG00000020081 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Postn/Gpnmb/Lbp/ Zc3h12a/Dab2/Mmp9/ Lgals3/Atp8a1/Pawr/ Pla2g7/Prex1/P2ry2/ Sema4g/Plau/Snai2/Tcaf2/ F3/Ccl20/Tlr2/Tnfaip6/ Fgf1/P2ry6/Pf4/Lef1/Ctsh/ Tnfsf18/Vegfc/Fam83h/ Selp/Hmcn2/Cxcl5/Cxcl10/ Tiam1/Nos3/Rapgef4/ Synpo2/Hgf/Wnt5b/ Ptprz1/Coro1a/Tacr2 | 45 |
| BP | GO:0090075 | relaxation of muscle | 7/858 | 26/ 15881 | 0.000348844793164584 | 0.0106653481430185 | ENSMUSG00000006457/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000053965/ ENSMUSG00000026576/ENSMUSG00000061603/ ENSMUSG00000041695 | Actn3/Pawr/Adora1/ Pde5a/Atp1b1/Akap6/ Kcnj2 | 7 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| BP | GO:0010743 | regulation of macrophage derived foam cell differentiation | 6/858 | 19/15881 | 0.000361129436712539 | 0.0108845657965879 | ENSMUSG00000018800/ENSMUSG00000029373/ENSMUSG00000002944/ENSMUSG00000021108/ENSMUSG00000024030/ENSMUSG00000025044 | Abca5/Pf4/Cd36/Prkch/Abcg1/Msr1 | 6 |
| BP | GO:0072677 | eosinophil migration | 6/858 | 19/15881 | 0.000361129436712539 | 0.0108845657965879 | ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000035373/ENSMUSG00000050335/ENSMUSG00000019122/ENSMUSG00000034652 | Ccl2/Cx3cl1/Ccl7/Lgals3/Ccl9/Cd300a | 6 |
| BP | GO:0050702 | interleukin-1 beta secretion | 8/858 | 34/15881 | 0.000363135317679448 | 0.0108845657965879 | ENSMUSG00000042677/ENSMUSG00000033538/ENSMUSG00000027995/ENSMUSG00000055994/ENSMUSG00000015243/ENSMUSG00000002944/ENSMUSG00000037860/ENSMUSG00000025888 | Zc3h12a/Casp4/Tlr2/Nod2/Abca1/Cd36/Aim2/Casp1 | 8 |
| BP | GO:0042133 | neurotransmitter metabolic process | 16/858 | 113/15881 | 0.000369131254286211 | 0.0109924411178998 | ENSMUSG00000042677/ENSMUSG00000026463/ENSMUSG00000006764/ENSMUSG00000037580/ENSMUSG00000020826/ENSMUSG00000079685/ENSMUSG00000027995/ENSMUSG00000017969/ENSMUSG00000076441/ENSMUSG00000002944/ENSMUSG00000006235/ENSMUSG00000040046/ENSMUSG00000028978/ENSMUSG00000079164/ENSMUSG00000007034/ENSMUSG00000043943 | Zc3h12a/Atp2b4/Tph2/Gch1/Nos2/Ulbp1/Tlr2/Ptgis/Ass1/Cd36/Epor/Tph1/Nos3/Tlr5/Slc44a4/Naalad2 | 16 |
| BP | GO:0033559 | unsaturated fatty acid metabolic process | 11/858 | 61/15881 | 0.000374774185133528 | 0.0110884800840152 | ENSMUSG00000024610/ENSMUSG00000047250/ENSMUSG00000050737/ENSMUSG00000025002/ENSMUSG00000033715/ENSMUSG00000003484/ENSMUSG00000017969/ENSMUSG00000052974/ENSMUSG00000020892/ENSMUSG00000025955/ENSMUSG00000025197 | Cd74/Ptgs1/Ptges/Cyp2c55/Akr1c14/Cyp4f18/Ptgis/Cyp2f2/Aloxe3/Akr1cl/Cyp2c23 | 11 |
| BP | GO:0016045 | detection of bacterium | 5/858 | 13/15881 | 0.000406841158871168 | 0.0118839079909757 | ENSMUSG00000078945/ENSMUSG00000027995/ENSMUSG00000078942/ENSMUSG00000055994/ENSMUSG00000071203 | Naip2/Tlr2/Naip6/Nod2/Naip5 | 5 |
| BP | GO:0098543 | detection of other organism | 5/858 | 13/15881 | 0.000406841158871168 | 0.0118839079909757 | ENSMUSG00000078945/ENSMUSG00000027995/ENSMUSG00000078942/ENSMUSG00000055994/ENSMUSG00000071203 | Naip2/Tlr2/Naip6/Nod2/Naip5 | 5 |
| BP | GO:0006816 | calcium ion transport | 33/858 | 327/15881 | 0.000417435079780642 | 0.0121161852903419 | ENSMUSG00000026463/ENSMUSG00000050335/ENSMUSG00000035873/ENSMUSG00000021831/ENSMUSG00000026576/ENSMUSG00000019997/ENSMUSG00000032839/ENSMUSG00000044026/ENSMUSG00000022416/ENSMUSG00000027994/ENSMUSG00000050777/ENSMUSG00000057897/ENSMUSG00000034353/ENSMUSG00000061603/ENSMUSG00000025889/ENSMUSG00000032020/ENSMUSG00000041245/ENSMUSG00000028214/ENSMUSG00000028255/ENSMUSG00000041046/ENSMUSG00000053395/ENSMUSG00000034855/ENSMUSG00000024065/ENSMUSG00000028978/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000037418/ENSMUSG00000030523/ENSMUSG00000059588/ENSMUSG00000004266/ENSMUSG00000030707/ENSMUSG00000044338/ENSMUSG00000038239 | Atp2b4/Lgals3/Pawr/Ero1l/Atp1b1/Ctgf/Trpc1/Slc35g1/Cacna1i/Mcub/Tmem37/Camk2b/Ramp1/Akap6/Snca/Ubash3b/Wnk3/Gem/Clca1/Ramp3/Cacng8/Cxcl10/Ehd3/Nos3/Adora2a/P2rx1/Best1/Trpm1/Calcrl/Ptpn6/Coro1a/Aplnr/Hrc | 33 |
| BP | GO:0050778 | positive regulation of immune response | 40/858 | 424/15881 | 0.000435087229367824 | 0.0125491197099424 | ENSMUSG00000024164/ENSMUSG00000024610/ENSMUSG00000073411/ENSMUSG00000061232/ENSMUSG00000016024/ENSMUSG00000030921/ | C3/Cd74/H2-D1/H2-K1/Lbp/Trim30a/Zc3h12a/Icosl/Nlrc5/Lgals3/Pawr/ | 40 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000074151/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000019850/ ENSMUSG00000029084/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000026068/ ENSMUSG00000055994/ENSMUSG00000005057/ ENSMUSG00000053216/ENSMUSG00000026177/ ENSMUSG00000049109/ENSMUSG00000017830/ ENSMUSG00000020641/ENSMUSG00000002944/ ENSMUSG00000079343/ENSMUSG00000037860/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000000706/ENSMUSG00000079164/ ENSMUSG00000075370/ENSMUSG00000109713/ ENSMUSG00000021108/ENSMUSG00000002699/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652/ENSMUSG00000026117 | Tnfaip3/Cd38/Nectin2/ Ulbp1/Tlr2/Syk/Il18rap/ Nod2/Sh2b2/Btn2a2/ Slc11a1/Themis/Dhx58/ Rsad2/Cd36/C1s2/Aim2/ Il12rb1/Il15/Btn1a1/Tlr5/ Igll1/Pvrig/Prkch/Lcp2/ Lpxn/Ptpn6/Cd300a/Zap70 | |
| BP | GO:1901099 | negative regulation of signal transduction in absence of ligand | 7/858 | 27/ 15881 | 0.000449180833664319 | 0.0127571229529175 | ENSMUSG00000031778/ENSMUSG00000022144/ ENSMUSG00000022676/ENSMUSG00000029373/ ENSMUSG00000025915/ENSMUSG00000040329/ ENSMUSG00000022483 | Cx3cl1/Gdnf/Snai2/Pf4/ Sgk3/Il7/Col2a1 | 7 |
| BP | GO:2001240 | negative regulation of extrinsic apoptotic signaling pathway in absence of ligand | 7/858 | 27/ 15881 | 0.000449180833664319 | 0.0127571229529175 | ENSMUSG00000031778/ENSMUSG00000022144/ ENSMUSG00000022676/ENSMUSG00000029373/ ENSMUSG00000025915/ENSMUSG00000040329/ ENSMUSG00000022483 | Cx3cl1/Gdnf/Snai2/Pf4/ Sgk3/Il7/Col2a1 | 7 |
| BP | GO:0070372 | regulation of ERK1 and ERK2 cascade | 28/858 | 262/ 15881 | 0.000450644116522597 | 0.0127571229529175 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000029816/ENSMUSG00000022150/ ENSMUSG00000035373/ENSMUSG00000038387/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000026166/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000055994/ENSMUSG00000042662/ ENSMUSG00000025665/ENSMUSG00000053216/ ENSMUSG00000064246/ENSMUSG00000041193/ ENSMUSG00000002944/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000002489/ ENSMUSG00000039661/ENSMUSG00000031780/ ENSMUSG00000024427/ENSMUSG00000004266 | C3/Cd74/Ccl2/Cx3cl1/ Gpnmb/Dab2/Ccl7/Rras/ Lif/Ctgf/Ccl20/Tlr2/Syk/ Ccl9/Nod2/Dusp15/ Rps6ka6/Btn2a2/Chil1/ Pla2g5/Cd36/Ramp3/Epor/ Tiam1/Dusp26/Ccl17/ Spry4/Ptpn6 | 28 |
| BP | GO:0050854 | regulation of antigen receptor-mediated signaling pathway | 9/858 | 44/ 15881 | 0.000482356583472322 | 0.0135710876797796 | ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000062300/ENSMUSG00000053216/ ENSMUSG00000109713/ENSMUSG00000021108/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652 | Lgals3/Pawr/Nectin2/ Btn2a2/Pvrig/Prkch/Lpxn/ Ptpn6/Cd300a | 9 |
| BP | GO:0009595 | detection of biotic stimulus | 6/858 | 20/ 15881 | 0.000492477261652845 | 0.0137713458654875 | ENSMUSG00000016024/ENSMUSG00000078945/ ENSMUSG00000027995/ENSMUSG00000078942/ ENSMUSG00000055994/ENSMUSG00000071203 | Lbp/Naip2/Tlr2/Naip6/ Nod2/Naip5 | 6 |
| BP | GO:0010952 | positive regulation of peptidase activity | 18/858 | 139/ 15881 | 0.000498314227573973 | 0.01382058704367 | ENSMUSG00000023030/ENSMUSG00000024778/ ENSMUSG00000024066/ENSMUSG00000044303/ ENSMUSG00000028039/ENSMUSG00000035873/ | Slc11a2/Fas/Xdh/Cdkn2a/ Efna3/Pawr/Casp4/Ctgf/ F3/Pidd1/Ctsh/Ifi27l2a/ | 18 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| | | | | | | | ENSMUSG00000033538/ENSMUSG00000019997/ ENSMUSG00000028128/ENSMUSG00000025507/ ENSMUSG00000032359/ENSMUSG00000079017/ ENSMUSG00000025889/ENSMUSG00000020340/ ENSMUSG00000037860/ENSMUSG00000000120/ ENSMUSG00000020787/ENSMUSG00000025888 | Snca/Cyfip2/Aim2/Ngfr/ P2rx1/Casp1 | |
| BP | GO:0006809 | nitric oxide biosynthetic process | 11/858 | 63/ 15881 | 0.000500265470834981 | 0.01382058704367 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000020826/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000002944/ ENSMUSG00000006235/ENSMUSG00000028978/ ENSMUSG00000079164 | Zc3h12a/Atp2b4/Nos2/ Ulbp1/Tlr2/Ptgis/Ass1/ Cd36/Epor/Nos3/Tlr5 | 11 |
| BP | GO:0051607 | defense response to virus | 22/858 | 188/ 15881 | 0.000529484283797058 | 0.01443947870858 | ENSMUSG00000046718/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000035208/ ENSMUSG00000066800/ENSMUSG00000079363/ ENSMUSG00000001166/ENSMUSG00000035692/ ENSMUSG00000017830/ENSMUSG00000032690/ ENSMUSG00000020641/ENSMUSG00000000386/ ENSMUSG00000059108/ENSMUSG00000029605/ ENSMUSG00000034459/ENSMUSG00000032661/ ENSMUSG00000037860/ENSMUSG00000034855/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000079339/ENSMUSG00000062157 | Bst2/Trim30a/Zc3h12a/ Slfn8/Rnasel/Gbp4/Oas1c/ Isg15/Dhx58/Oas2/Rsad2/ Mx1/Ifitm6/Oas1b/Ifit1/ Oas3/Aim2/Cxcl10/ Il12rb1/Il15/Ifit1bl1/Ifnlr1 | 22 |
| BP | GO:0070371 | ERK1 and ERK2 cascade | 29/858 | 278/ 15881 | 0.000535251660202259 | 0.01443947870858 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000029816/ENSMUSG00000022150/ ENSMUSG00000035373/ENSMUSG00000038387/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000026166/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000055994/ENSMUSG00000032359/ ENSMUSG00000042662/ENSMUSG00000025665/ ENSMUSG00000053216/ENSMUSG00000064246/ ENSMUSG00000041193/ENSMUSG00000002944/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000002489/ENSMUSG00000039661/ ENSMUSG00000031780/ENSMUSG00000024427/ ENSMUSG00000004266 | C3/Cd74/Ccl2/Cx3cl1/ Gpnmb/Dab2/Ccl7/Rras/ Lif/Ctgf/Ccl20/Tlr2/Syk/ Ccl9/Nod2/Ctsh/Dusp15/ Rps6ka6/Btn2a2/Chil1/ Pla2g5/Cd36/Ramp3/Epor/ Tiam1/Dusp26/Ccl17/ Spry4/Ptpn6 | 29 |
| BP | GO:1901342 | regulation of vasculature development | 29/858 | 278/ 15881 | 0.000535251660202259 | 0.01443947870858 | ENSMUSG00000024164/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000000753/ ENSMUSG00000042677/ENSMUSG00000024066/ ENSMUSG00000017737/ENSMUSG00000050335/ ENSMUSG00000028039/ENSMUSG00000038387/ ENSMUSG00000034394/ENSMUSG00000028128/ ENSMUSG00000029669/ENSMUSG00000036585/ ENSMUSG00000029373/ENSMUSG00000032359/ ENSMUSG00000056758/ENSMUSG00000018983/ ENSMUSG00000064246/ENSMUSG00000031520/ ENSMUSG00000017969/ENSMUSG00000074272/ ENSMUSG00000002944/ENSMUSG00000034855/ | C3/Ccl2/Cx3cl1/Serpinf1/ Zc3h12a/Xdh/Mmp9/ Lgals3/Efna3/Rras/Lif/F3/ Tspan12/Fgf1/Pf4/Ctsh/ Hmga2/E2f2/Chil1/Vegfc/ Ptgis/Ceacam1/Cd36/ Cxcl10/Nos3/Ngfr/Vash1/ Hgf/Aplnr | 29 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000028978/ENSMUSG00000000120/ ENSMUSG00000021256/ENSMUSG00000028864/ ENSMUSG00000044338 | | |
| BP | GO:0048525 | negative regulation of viral process | 13/858 | 84/ 15881 | 0.000541100646624817 | 0.01443947870858 | ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000001166/ENSMUSG00000035692/ ENSMUSG00000074272/ENSMUSG00000032690/ ENSMUSG00000020641/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000032661/ ENSMUSG00000000266 | Slpi/Bst2/Zc3h12a/Rnasel/ Oas1c/Isg15/Ceacam1/ Oas2/Rsad2/Ifitm6/Oas1b/ Oas3/Mid2 | 13 |
| BP | GO:0002443 | leukocyte mediated immunity | 27/858 | 252/ 15881 | 0.000543307325915146 | 0.01443947870858 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000061232/ENSMUSG00000024778/ ENSMUSG00000000732/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000053175/ ENSMUSG00000026068/ENSMUSG00000055994/ ENSMUSG00000032359/ENSMUSG00000026177/ ENSMUSG00000074272/ENSMUSG00000020641/ ENSMUSG00000079343/ENSMUSG00000029371/ ENSMUSG00000075370/ENSMUSG00000021948/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000030707/ENSMUSG00000034266/ ENSMUSG00000025279 | C3/Cd74/Cxcl1/H2-D1/H2-K1/Fas/Icosl/Nectin2/ Ulbp1/Tlr2/Syk/Bcl3/ Il18rap/Nod2/Ctsh/ Slc11a1/Ceacam1/Rsad2/ C1s2/Cxcl5/Igll1/Prkcd/ Ptpn6/Cd300a/Coro1a/ Batf/Dnase1l3 | 27 |
| BP | GO:0051480 | regulation of cytosolic calcium ion concentration | 27/858 | 252/ 15881 | 0.000543307325915146 | 0.01443947870858 | ENSMUSG00000029380/ENSMUSG00000026463/ ENSMUSG00000035873/ENSMUSG00000021831/ ENSMUSG00000032860/ENSMUSG00000029084/ ENSMUSG00000032839/ENSMUSG00000050541/ ENSMUSG00000044026/ENSMUSG00000022416/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000074715/ ENSMUSG00000002944/ENSMUSG00000060459/ ENSMUSG00000021070/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000034855/ ENSMUSG00000030523/ENSMUSG00000004266/ ENSMUSG00000036570/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337 | Cxcl1/Atp2b4/Pawr/Ero1l/ P2ry2/Cd38/Trpc1/ Adra1b/Slc35g1/Cacna1i/ Akap6/Snca/Ubash3b/ Ccl28/Cd36/Kng2/Bdkrb2/ Ramp3/Epor/Cxcl10/ Trpm1/Ptpn6/Fxyd1/ Coro1a/Aplnr/Hrc/Scgn | 27 |
| BP | GO:0032611 | interleukin-1 beta production | 10/858 | 54/ 15881 | 0.000550363262307986 | 0.01443947870858 | ENSMUSG00000042677/ENSMUSG00000033538/ ENSMUSG00000019850/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000015243/ ENSMUSG00000002944/ENSMUSG00000037860/ ENSMUSG00000071203/ENSMUSG00000025888 | Zc3h12a/Casp4/Tnfaip3/ Tlr2/Nod2/Abca1/Cd36/ Aim2/Naip5/Casp1 | 10 |
| BP | GO:0006909 | phagocytosis | 19/858 | 152/ 15881 | 0.000551004965983757 | 0.01443947870858 | ENSMUSG00000024164/ENSMUSG00000035385/ ENSMUSG00000016024/ENSMUSG00000024743/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000071715/ENSMUSG00000055994/ ENSMUSG00000026177/ENSMUSG00000015243/ ENSMUSG00000031504/ENSMUSG00000041351/ ENSMUSG00000002944/ENSMUSG00000032174/ | C3/Ccl2/Lbp/Syt7/Tlr2/ Syk/Ncf4/Nod2/Slc11a1/ Abca1/Rab20/Rap1gap/ Cd36/Icam5/Irf8/Igll1/ Msr1/Cd300a/Coro1a | 19 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000041515/ENSMUSG00000075370/ ENSMUSG00000025044/ENSMUSG00000034652/ ENSMUSG00000030707 | | |
| BP | GO:0015893 | drug transport | 19/858 | 152/ 15881 | 0.000551004965983757 | 0.01443947870858 | ENSMUSG00000020432/ENSMUSG00000055368/ ENSMUSG00000023947/ENSMUSG00000005089/ ENSMUSG00000024743/ENSMUSG00000022144/ ENSMUSG00000027995/ENSMUSG00000022512/ ENSMUSG00000032373/ENSMUSG00000028970/ ENSMUSG00000026177/ENSMUSG00000025889/ ENSMUSG00000027070/ENSMUSG00000070570/ ENSMUSG00000020178/ENSMUSG00000054753/ ENSMUSG00000022899/ENSMUSG00000007034/ ENSMUSG00000020081 | Tcn2/Slc6a2/Nfkbie/ Slc1a2/Syt7/Gdnf/Tlr2/ Cldn1/Car12/Abcb1b/ Slc11a1/Snca/Lrp2/ Slc17a7/Adora2a/ AU018091/Slc15a2/ Slc44a4/Tacr2 | 19 |
| BP | GO:0090022 | regulation of neutrophil chemotaxis | 7/858 | 28/ 15881 | 0.000571259755077194 | 0.0147755938908119 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000016024/ENSMUSG00000029082/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000029371 | Cd74/Cxcl1/Lbp/Bst1/Pf4/ Nod2/Cxcl5 | 7 |
| BP | GO:0072507 | divalent inorganic cation homeostasis | 36/858 | 374/ 15881 | 0.000571379056596305 | 0.0147755938908119 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000032839/ENSMUSG00000050541/ ENSMUSG00000035694/ENSMUSG00000044026/ ENSMUSG00000036019/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000026177/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000074715/ ENSMUSG00000002944/ENSMUSG00000060459/ ENSMUSG00000021070/ENSMUSG00000063354/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000030523/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Atp2b4/Pawr/ Ero1l/P2ry2/Atp1b1/Cd38/ Trpc1/Adra1b/Caps2/ Slc35g1/Tmtc2/Cacna1i/ Mcub/Slc11a1/Akap6/ Snca/Ubash3b/Ccl28/ Cd36/Kng2/Bdkrb2/ Slc39a4/Ramp3/Epor/ Cxcl10/Trpm1/Ptpn6/ Fxyd1/Tnni3/Coro1a/ Aplnr/Hrc/Scgn/Disc1 | 36 |
| BP | GO:0009615 | response to virus | 25/858 | 227/ 15881 | 0.000573496666499021 | 0.0147755938908119 | ENSMUSG00000046718/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000035208/ ENSMUSG00000066800/ENSMUSG00000053175/ ENSMUSG00000079363/ENSMUSG00000001166/ ENSMUSG00000079017/ENSMUSG00000035692/ ENSMUSG00000026822/ENSMUSG00000017830/ ENSMUSG00000032690/ENSMUSG00000020641/ ENSMUSG00000000386/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000034459/ ENSMUSG00000032661/ENSMUSG00000037860/ ENSMUSG00000034855/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000079339/ ENSMUSG00000062157 | Bst2/Trim30a/Zc3h12a/ Slfn8/Rnasel/Bcl3/Gbp4/ Oas1c/Ifi27l2a/Isg15/Lcn2/ Dhx58/Oas2/Rsad2/Mx1/ Ifitm6/Oas1b/Ifit1/Oas3/ Aim2/Cxcl10/Il12rb1/Il15/ Ifit1bl1/Ifnlr1 | 25 |
| BP | GO:0051606 | detection of stimulus | 21/858 | 177/ 15881 | 0.000584942167711563 | 0.0149461184621132 | ENSMUSG00000016024/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000078945/ | Lbp/Pawr/Adora1/Naip2/ Reep6/Tlr2/Naip6/Nod2/ | 21 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000035504/ENSMUSG00000027995/ ENSMUSG00000078942/ENSMUSG00000055994/ ENSMUSG00000030313/ENSMUSG00000062168/ ENSMUSG00000035916/ENSMUSG00000026249/ ENSMUSG00000042774/ENSMUSG00000064329/ ENSMUSG00000000120/ENSMUSG00000071203/ ENSMUSG00000037418/ENSMUSG00000045381/ ENSMUSG00000062873/ENSMUSG00000046493/ ENSMUSG00000061972 | Dennd5b/Ppef1/Ptprq/ Serpine2/Olfr1353/Scn1a/ Ngfr/Naip5/Best1/Olfr433/ Olfr1355/Olfr1352/Olfr99 | |
| BP | GO:0055074 | calcium ion homeostasis | 34/858 | 347/ 15881 | 0.000586633520100386 | 0.0149461184621132 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000032839/ENSMUSG00000050541/ ENSMUSG00000035694/ENSMUSG00000044026/ ENSMUSG00000036019/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000032020/ ENSMUSG00000074715/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000021070/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000030523/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Atp2b4/Pawr/ Ero1l/P2ry2/Atp1b1/Cd38/ Trpc1/Adra1b/Caps2/ Slc35g1/Tmtc2/Cacna1i/ Mcub/Akap6/Snca/ Ubash3b/Ccl28/Cd36/ Kng2/Bdkrb2/Ramp3/ Epor/Cxcl10/Trpm1/ Ptpn6/Fxyd1/Tnni3/ Coro1a/Aplnr/Hrc/Scgn/ Disc1 | 34 |
| BP | GO:0003018 | vascular process in circulatory system | 19/858 | 153/ 15881 | 0.000598067518127224 | 0.0151532466195108 | ENSMUSG00000031778/ENSMUSG00000059895/ ENSMUSG00000047250/ENSMUSG00000042429/ ENSMUSG00000037580/ENSMUSG00000053965/ ENSMUSG00000057123/ENSMUSG00000020826/ ENSMUSG00000032860/ENSMUSG00000029084/ ENSMUSG00000024039/ENSMUSG00000050541/ ENSMUSG00000074272/ENSMUSG00000021070/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000031489/ ENSMUSG00000020081 | Cx3cl1/Ptp4a3/Ptgs1/ Adora1/Gch1/Pde5a/Gja5/ Nos2/P2ry2/Cd38/Cbs/ Adra1b/Ceacam1/Bdkrb2/ Nos3/Adora2a/P2rx1/ Adrb3/Tacr2 | 19 |
| BP | GO:2001056 | positive regulation of cysteine-type endopeptidase activity | 16/858 | 118/ 15881 | 0.000603054882769216 | 0.0151571025816052 | ENSMUSG00000023030/ENSMUSG00000024778/ ENSMUSG00000024066/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000033538/ ENSMUSG00000019997/ENSMUSG00000028128/ ENSMUSG00000025507/ENSMUSG00000079017/ ENSMUSG00000025889/ENSMUSG00000020340/ ENSMUSG00000037860/ENSMUSG00000000120/ ENSMUSG00000020787/ENSMUSG00000025888 | Slc11a2/Fas/Xdh/Cdkn2a/ Pawr/Casp4/Ctgf/F3/ Pidd1/Ifi27l2a/Snca/ Cyfip2/Aim2/Ngfr/P2rx1/ Casp1 | 16 |
| BP | GO:0044130 | negative regulation of growth of symbiont in host | 5/858 | 14/ 15881 | 0.000604829867517171 | 0.0151571025816052 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0007596 | blood coagulation | 17/858 | 130/ 15881 | 0.000630619880035597 | 0.0157175150534959 | ENSMUSG00000024164/ENSMUSG00000031778/ ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000028128/ENSMUSG00000021457/ | C3/Cx3cl1/Plau/Tfpi/F3/ Syk/Pf4/Ubash3b/ Ceacam1/Cd36/Kng2/Selp/ | 17 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| | | | | | | ENSMUSG00000029373/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000027611/ENSMUSG00000026249/ ENSMUSG00000020787/ENSMUSG00000021948/ ENSMUSG00000004266 | Procr/Serpine2/P2rx1/ Prkcd/Ptpn6 | |
| BP | GO:0044419 | interspecies interaction between organisms | 33/858 | 335/ 15881 | 0.000639610983265425 | 0.0157953347131211 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000017002/ ENSMUSG00000046718/ENSMUSG00000016024/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000017737/ENSMUSG00000066800/ ENSMUSG00000020826/ENSMUSG00000062300/ ENSMUSG00000027995/ENSMUSG00000040253/ ENSMUSG00000029373/ENSMUSG00000001166/ ENSMUSG00000055994/ENSMUSG00000027985/ ENSMUSG00000029298/ENSMUSG00000035692/ ENSMUSG00000028268/ENSMUSG00000074272/ ENSMUSG00000032690/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000104713/ ENSMUSG00000059108/ENSMUSG00000029605/ ENSMUSG00000029371/ENSMUSG00000032661/ ENSMUSG00000006235/ENSMUSG00000041515/ ENSMUSG00000000266 | Cd74/Cxcl1/Ccl2/Slpi/ Bst2/Lbp/Trim30a/ Zc3h12a/Mmp9/Rnasel/ Nos2/Nectin2/Tlr2/Gbp7/ Pf4/Oas1c/Nod2/Lef1/ Gbp9/Isg15/Gbp3/ Ceacam1/Oas2/Rsad2/ Cd36/Gbp6/Ifitm6/Oas1b/ Cxcl5/Oas3/Epor/Irf8/ Mid2 | 33 |
| BP | GO:0001910 | regulation of leukocyte mediated cytotoxicity | 10/858 | 55/ 15881 | 0.000640630670876695 | 0.0157953347131211 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000026068/ENSMUSG00000074272/ ENSMUSG00000029371/ENSMUSG00000025279 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nectin2/Ulbp1/Il18rap/ Ceacam1/Cxcl5/Dnase1l3 | 10 |
| BP | GO:0001818 | negative regulation of cytokine production | 23/858 | 204/ 15881 | 0.000676907739947814 | 0.01660052885241 | ENSMUSG00000031778/ENSMUSG00000029816/ ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000028965/ ENSMUSG00000049577/ENSMUSG00000019850/ ENSMUSG00000027995/ENSMUSG00000053175/ ENSMUSG00000079363/ENSMUSG00000007805/ ENSMUSG00000055994/ENSMUSG00000027985/ ENSMUSG00000053216/ENSMUSG00000026177/ ENSMUSG00000017830/ENSMUSG00000074272/ ENSMUSG00000090958/ENSMUSG00000025494/ ENSMUSG00000031438/ENSMUSG00000000706/ ENSMUSG00000028864 | Cx3cl1/Gpnmb/Lbp/ Trim30a/Zc3h12a/Tnfrsf9/ Zfpm1/Tnfaip3/Tlr2/Bcl3/ Gbp4/Twist2/Nod2/Lef1/ Btn2a2/Slc11a1/Dhx58/ Ceacam1/Lrrc32/Sigirr/ Rnf128/Btn1a1/Hgf | 23 |
| BP | GO:0045785 | positive regulation of cell adhesion | 32/858 | 324/ 15881 | 0.0007341327752338 | 0.0179081537618203 | ENSMUSG00000024610/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000031785/ ENSMUSG00000022150/ENSMUSG00000037440/ ENSMUSG00000000732/ENSMUSG00000035873/ ENSMUSG00000039621/ENSMUSG00000021457/ ENSMUSG00000029307/ENSMUSG00000027985/ ENSMUSG00000075122/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000031520/ ENSMUSG00000041351/ENSMUSG00000074715/ ENSMUSG00000074272/ENSMUSG00000002944/ | Cd74/Ccl2/Cx3cl1/Adgrg1/ Dab2/Vnn1/Icosl/Pawr/ Prex1/Syk/Dmp1/Lef1/ Cd80/Tnfsf18/Btn2a2/ Vegfc/Rap1gap/Ccl28/ Ceacam1/Cd36/Selp/ Abi3bp/Il12rb1/Il15/Il7/ Dusp26/Igfbp2/Ptpn6/ Fstl3/Coro1a/Zap70/Disc1 | 32 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000026580/ENSMUSG00000035258/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000039661/ ENSMUSG00000039323/ENSMUSG00000004266/ ENSMUSG00000020325/ENSMUSG00000030707/ ENSMUSG00000026117/ENSMUSG00000043051 | | |
| BP | GO:0007599 | hemostasis | 17/858 | 132/ 15881 | 0.00075207878783594 | 0.0179855496941041 | ENSMUSG00000024164/ENSMUSG00000031778/ ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000028128/ENSMUSG00000021457/ ENSMUSG00000029373/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000027611/ENSMUSG00000026249/ ENSMUSG00000020787/ENSMUSG00000021948/ ENSMUSG00000004266 | C3/Cx3cl1/Plau/Tfpi/F3/ Syk/Pf4/Ubash3b/ Ceacam1/Cd36/Kng2/Selp/ Procr/Serpine2/P2rx1/ Prkcd/Ptpn6 | 17 |
| BP | GO:0010950 | positive regulation of endopeptidase activity | 17/858 | 132/ 15881 | 0.00075207878783594 | 0.0179855496941041 | ENSMUSG00000023030/ENSMUSG00000024778/ ENSMUSG00000024066/ENSMUSG00000044303/ ENSMUSG00000028039/ENSMUSG00000035873/ ENSMUSG00000033538/ENSMUSG00000019997/ ENSMUSG00000028128/ENSMUSG00000025507/ ENSMUSG00000079017/ENSMUSG00000025889/ ENSMUSG00000020340/ENSMUSG00000037860/ ENSMUSG00000000120/ENSMUSG00000020787/ ENSMUSG00000025888 | Slc11a2/Fas/Xdh/Cdkn2a/ Efna3/Pawr/Casp4/Ctgf/ F3/Pidd1/Ifi27l2a/Snca/ Cyfip2/Aim2/Ngfr/P2rx1/ Casp1 | 17 |
| BP | GO:0015844 | monoamine transport | 11/858 | 66/ 15881 | 0.00075299292221282 | 0.0179855496941041 | ENSMUSG00000055368/ENSMUSG00000050335/ ENSMUSG00000047250/ENSMUSG00000024743/ ENSMUSG00000022144/ENSMUSG00000021457/ ENSMUSG00000025889/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000054423/ ENSMUSG00000034652 | Slc6a2/Lgals3/Ptgs1/Syt7/ Gdnf/Syk/Snca/Adora2a/ P2rx1/Cadps/Cd300a | 11 |
| BP | GO:0046209 | nitric oxide metabolic process | 11/858 | 66/ 15881 | 0.00075299292221282 | 0.0179855496941041 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000020826/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000002944/ ENSMUSG00000006235/ENSMUSG00000028978/ ENSMUSG00000079164 | Zc3h12a/Atp2b4/Nos2/ Ulbp1/Tlr2/Ptgis/Ass1/ Cd36/Epor/Nos3/Tlr5 | 11 |
| BP | GO:0046394 | carboxylic acid biosynthetic process | 30/858 | 298/ 15881 | 0.00077931721660527 | 0.0185178691987138 | ENSMUSG00000024610/ENSMUSG00000060600/ ENSMUSG00000053279/ENSMUSG00000026463/ ENSMUSG00000006457/ENSMUSG00000021196/ ENSMUSG00000003541/ENSMUSG00000047250/ ENSMUSG00000037580/ENSMUSG00000006344/ ENSMUSG00000019577/ENSMUSG00000050737/ ENSMUSG00000042010/ENSMUSG00000023963/ ENSMUSG00000021457/ENSMUSG00000026688/ ENSMUSG00000024039/ENSMUSG00000028497/ ENSMUSG00000029167/ENSMUSG00000027068/ ENSMUSG00000074604/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000041193/ ENSMUSG00000020892/ENSMUSG00000032262/ | Cd74/Eno3/Aldh1a1/ Atp2b4/Actn3/Pfkp/Ier3/ Ptgs1/Gch1/Ggt5/Pdk4/ Ptges/Acacb/Cyp39a1/Syk/ Mgst3/Cbs/Hacd4/ Ppargc1a/Dhrs9/Mgst2/ Ptgis/Ass1/Pla2g5/Aloxe3/ Elovl4/Slc45a3/Gm5424/ Alox5ap/Abhd3 | 30 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000026435/ENSMUSG00000046687/ ENSMUSG00000060063/ENSMUSG00000002475 | | |
| BP | GO:0043410 | positive regulation of MAPK cascade | 39/858 | 423/ 15881 | 0.000794890589252611 | 0.0187405349921828 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000029816/ENSMUSG00000024778/ ENSMUSG00000042677/ENSMUSG00000022150/ ENSMUSG00000024066/ENSMUSG00000035373/ ENSMUSG00000042429/ENSMUSG00000053965/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000020901/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000028599/ ENSMUSG00000021457/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000050541/ ENSMUSG00000055994/ENSMUSG00000042662/ ENSMUSG00000024013/ENSMUSG00000064246/ ENSMUSG00000041193/ENSMUSG00000074272/ ENSMUSG00000002944/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000002489/ ENSMUSG00000020312/ENSMUSG00000000120/ ENSMUSG00000060548/ENSMUSG00000028864/ ENSMUSG00000031780/ENSMUSG00000021948/ ENSMUSG00000031489 | C3/Cd74/Ccl2/Cx3cl1/ Gpnmb/Fas/Zc3h12a/ Dab2/Xdh/Ccl7/Adora1/ Pde5a/Lif/Ctgf/Pik3r5/ Ccl20/Tlr2/Tnfrsf1b/Syk/ Ccl9/Fgf1/Adra1b/Nod2/ Dusp15/Fgd2/Chil1/ Pla2g5/Ceacam1/Cd36/ Ramp3/Epor/Tiam1/Shc2/ Ngfr/Tnfrsf19/Hgf/Ccl17/ Prkcd/Adrb3 | 39 |
| BP | GO:0002831 | regulation of response to biotic stimulus | 16/858 | 121/ 15881 | 0.000796860951477464 | 0.0187405349921828 | ENSMUSG00000029380/ENSMUSG00000042677/ ENSMUSG00000019850/ENSMUSG00000032501/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000079363/ ENSMUSG00000055994/ENSMUSG00000017830/ ENSMUSG00000074272/ENSMUSG00000029371/ ENSMUSG00000037860/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000062157 | Cxcl1/Zc3h12a/Tnfaip3/ Trib1/Nectin2/Ulbp1/Tlr2/ Gbp4/Nod2/Dhx58/ Ceacam1/Cxcl5/Aim2/ Il12rb1/Il15/Ifnlr1 | 16 |
| BP | GO:0071675 | regulation of mononuclear cell migration | 8/858 | 38/ 15881 | 0.000807592760747748 | 0.018896022453006 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000050335/ENSMUSG00000023913/ ENSMUSG00000066755/ENSMUSG00000034855/ ENSMUSG00000037362/ENSMUSG00000053318 | Ccl2/Cx3cl1/Lgals3/ Pla2g7/Tnfsf18/Cxcl10/ Nov/Slamf8 | 8 |
| BP | GO:0050817 | coagulation | 17/858 | 133/ 15881 | 0.000819959118850693 | 0.0190586968613609 | ENSMUSG00000024164/ENSMUSG00000031778/ ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000028128/ENSMUSG00000021457/ ENSMUSG00000029373/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000027611/ENSMUSG00000026249/ ENSMUSG00000020787/ENSMUSG00000021948/ ENSMUSG00000004266 | C3/Cx3cl1/Plau/Tfpi/F3/ Syk/Pf4/Ubash3b/ Ceacam1/Cd36/Kng2/Selp/ Procr/Serpine2/P2rx1/ Prkcd/Ptpn6 | 17 |
| BP | GO:0016053 | organic acid biosynthetic process | 30/858 | 299/ 15881 | 0.000822856951275501 | 0.0190586968613609 | ENSMUSG00000024610/ENSMUSG00000060600/ ENSMUSG00000053279/ENSMUSG00000026463/ ENSMUSG00000006457/ENSMUSG00000021196/ ENSMUSG00000003541/ENSMUSG00000047250/ ENSMUSG00000037580/ENSMUSG00000006344/ ENSMUSG00000019577/ENSMUSG00000050737/ ENSMUSG00000042010/ENSMUSG00000023963/ | Cd74/Eno3/Aldh1a1/ Atp2b4/Actn3/Pfkp/Ier3/ Ptgs1/Gch1/Ggt5/Pdk4/ Ptges/Acacb/Cyp39a1/Syk/ Mgst3/Cbs/Hacd4/ Ppargc1a/Dhrs9/Mgst2/ Ptgis/Ass1/Pla2g5/Aloxe3/ | 30 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000021457/ENSMUSG00000026688/ ENSMUSG00000024039/ENSMUSG00000028497/ ENSMUSG00000029167/ENSMUSG00000027068/ ENSMUSG00000074604/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000041193/ ENSMUSG00000020892/ENSMUSG00000032262/ ENSMUSG00000026435/ENSMUSG00000046687/ ENSMUSG00000060063/ENSMUSG00000002475 | Elovl4/Slc45a3/Gm5424/ Alox5ap/Abhd3 | |
| BP | GO:0002460 | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 23/858 | 207/ 15881 | 0.000828651915640465 | 0.0190953375232548 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000073411/ENSMUSG00000061232/ ENSMUSG00000024778/ENSMUSG00000000732/ ENSMUSG00000019850/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000053175/ ENSMUSG00000026068/ENSMUSG00000055994/ ENSMUSG00000027985/ENSMUSG00000032359/ ENSMUSG00000066755/ENSMUSG00000026177/ ENSMUSG00000020641/ENSMUSG00000079343/ ENSMUSG00000000791/ENSMUSG00000075370/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000034266 | C3/Cd74/H2-D1/H2-K1/ Fas/Icosl/Tnfaip3/Nectin2/ Ulbp1/Bcl3/Il18rap/Nod2/ Lef1/Ctsh/Tnfsf18/ Slc11a1/Rsad2/C1s2/ Il12rb1/Igll1/Prkcd/Ptpn6/ Batf | 23 |
| BP | GO:0072503 | cellular divalent inorganic cation homeostasis | 34/858 | 354/ 15881 | 0.000834557744598251 | 0.0190953375232548 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000032839/ENSMUSG00000050541/ ENSMUSG00000044026/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000026177/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000074715/ ENSMUSG00000002944/ENSMUSG00000060459/ ENSMUSG00000021070/ENSMUSG00000063354/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000030523/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Atp2b4/Pawr/ Ero1l/P2ry2/Atp1b1/Cd38/ Trpc1/Adra1b/Slc35g1/ Cacna1i/Mcub/Slc11a1/ Akap6/Snca/Ubash3b/ Ccl28/Cd36/Kng2/Bdkrb2/ Slc39a4/Ramp3/Epor/ Cxcl10/Trpm1/Ptpn6/ Fxyd1/Tnni3/Coro1a/ Aplnr/Hrc/Scgn/Disc1 | 34 |
| BP | GO:0006766 | vitamin metabolic process | 10/858 | 57/ 15881 | 0.00085795936568356 | 0.0190953375232548 | ENSMUSG00000032561/ENSMUSG00000037440/ ENSMUSG00000022676/ENSMUSG00000020010/ ENSMUSG00000025545/ENSMUSG00000003484/ ENSMUSG00000027070/ENSMUSG00000090700/ ENSMUSG00000063415/ENSMUSG00000025069 | Acpp/Vnn1/Snai2/Vnn3/ Clybl/Cyp4f18/Lrp2/ Cyp4f40/Cyp26b1/Gsto2 | 10 |
| BP | GO:0001525 | angiogenesis | 40/858 | 439/ 15881 | 0.000860648906622334 | 0.0190953375232548 | ENSMUSG00000024164/ENSMUSG00000038146/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000000753/ENSMUSG00000042677/ ENSMUSG00000031785/ENSMUSG00000017737/ ENSMUSG00000050335/ENSMUSG00000028039/ ENSMUSG00000028024/ENSMUSG00000038387/ ENSMUSG00000021822/ENSMUSG00000034394/ ENSMUSG00000019997/ENSMUSG00000028128/ | C3/Notch3/Ccl2/Cx3cl1/ Serpinf1/Zc3h12a/Adgrg1/ Mmp9/Lgals3/Efna3/ Enpep/Rras/Plau/Lif/Ctgf/ F3/Syk/Tspan12/Fgf1/ Egfl7/Pf4/Lef1/Ctsh/ Hmga2/E2f2/Chil1/ Ramp1/Vegfc/Ptgis/ | 40 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000021457/ENSMUSG00000029669/ ENSMUSG00000036585/ENSMUSG00000026921/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000032359/ENSMUSG00000056758/ ENSMUSG00000018983/ENSMUSG00000064246/ ENSMUSG00000034353/ENSMUSG00000031520/ ENSMUSG00000017969/ENSMUSG00000074272/ ENSMUSG00000002944/ENSMUSG00000041046/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000028978/ENSMUSG00000000120/ ENSMUSG00000021256/ENSMUSG00000059588/ ENSMUSG00000028864/ENSMUSG00000044338 | Ceacam1/Cd36/Ramp3/ Cxcl10/Nov/Nos3/Ngfr/ Vash1/Calcrl/Hgf/Aplnr | |
| BP | GO:0042119 | neutrophil activation | 6/858 | 22/ 15881 | 0.000864026997747057 | 0.0190953375232548 | ENSMUSG00000021457/ENSMUSG00000026068/ ENSMUSG00000029371/ENSMUSG00000021948/ ENSMUSG00000034652/ENSMUSG00000025279 | Syk/Il18rap/Cxcl5/Prkcd/ Cd300a/Dnase1l3 | 6 |
| BP | GO:0006837 | serotonin transport | 5/858 | 15/ 15881 | 0.000867112810748753 | 0.0190953375232548 | ENSMUSG00000050335/ENSMUSG00000021457/ ENSMUSG00000025889/ENSMUSG00000020787/ ENSMUSG00000034652 | Lgals3/Syk/Snca/P2rx1/ Cd300a | 5 |
| BP | GO:0042448 | progesterone metabolic process | 5/858 | 15/ 15881 | 0.000867112810748753 | 0.0190953375232548 | ENSMUSG00000029167/ENSMUSG00000033715/ ENSMUSG00000027068/ENSMUSG00000025955/ ENSMUSG00000054932 | Ppargc1a/Akr1c14/Dhrs9/ Akr1cl/Afp | 5 |
| BP | GO:0044126 | regulation of growth of symbiont in host | 5/858 | 15/ 15881 | 0.000867112810748753 | 0.0190953375232548 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0044146 | negative regulation of growth of symbiont involved in interaction with host | 5/858 | 15/ 15881 | 0.000867112810748753 | 0.0190953375232548 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0048245 | eosinophil chemotaxis | 5/858 | 15/ 15881 | 0.000867112810748753 | 0.0190953375232548 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000050335/ ENSMUSG00000019122 | Ccl2/Cx3cl1/Ccl7/Lgals3/ Ccl9 | 5 |
| BP | GO:1903522 | regulation of blood circulation | 20/858 | 170/ 15881 | 0.000870241068983918 | 0.0190953375232548 | ENSMUSG00000031778/ENSMUSG00000042677/ ENSMUSG00000026463/ENSMUSG00000047250/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000019997/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000024065/ ENSMUSG00000028978/ENSMUSG00000020787/ ENSMUSG00000041695/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000038239 | Cx3cl1/Zc3h12a/Atp2b4/ Ptgs1/Adora1/Gch1/ Pde5a/Gja5/Atp1b1/Cd38/ Ctgf/Adra1b/Akap6/Ehd3/ Nos3/P2rx1/Kcnj2/Fxyd1/ Tnni3/Hrc | 20 |
| BP | GO:0071827 | plasma lipoprotein particle organization | 7/858 | 30/ 15881 | 0.000893728924968136 | 0.0195173373804946 | ENSMUSG00000018800/ENSMUSG00000057074/ ENSMUSG00000023913/ENSMUSG00000056973/ ENSMUSG00000041193/ENSMUSG00000015243/ ENSMUSG00000024030 | Abca5/Ces1g/Pla2g7/ Ces1d/Pla2g5/Abca1/ Abcg1 | 7 |
| BP | GO:0002791 | regulation of peptide secretion | 37/858 | 398/ 15881 | 0.000921525026239421 | 0.020028975214853 | ENSMUSG00000024610/ENSMUSG00000031778/ ENSMUSG00000027750/ENSMUSG00000042677/ ENSMUSG00000028965/ENSMUSG00000020806/ ENSMUSG00000042429/ENSMUSG00000033538/ ENSMUSG00000022514/ENSMUSG00000057123/ | Cd74/Cx3cl1/Postn/ Zc3h12a/Tnfrsf9/Rhbdf2/ Adora1/Casp4/Il1rap/Gja5/ Nos2/Cd38/Syt7/Lif/Tlr2/ Syk/Nod2/Pde1c/Hmga2/ | 37 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000020826/ENSMUSG00000029084/ ENSMUSG00000024743/ENSMUSG00000034394/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000004347/ ENSMUSG00000056758/ENSMUSG00000053216/ ENSMUSG00000031520/ENSMUSG00000074272/ ENSMUSG00000020641/ENSMUSG00000002944/ ENSMUSG00000090958/ENSMUSG00000027674/ ENSMUSG00000037860/ENSMUSG00000031548/ ENSMUSG00000002489/ENSMUSG00000037362/ ENSMUSG00000020178/ENSMUSG00000049044/ ENSMUSG00000000706/ENSMUSG00000079164/ ENSMUSG00000029716/ENSMUSG00000050578/ ENSMUSG00000025888 | Btn2a2/Vegfc/Ceacam1/ Rsad2/Cd36/Lrrc32/Pex5l/ Aim2/Sfrp1/Tiam1/Nov/ Adora2a/Rapgef4/Btn1a1/ Tlr5/Tfr2/Mmp13/Casp1 | |
| BP | GO:0030217 | T cell differentiation | 23/858 | 209/ 15881 | 0.000945460086560352 | 0.0203257037707111 | ENSMUSG00000024610/ENSMUSG00000024778/ ENSMUSG00000029570/ENSMUSG00000023927/ ENSMUSG00000044303/ENSMUSG00000037440/ ENSMUSG00000039621/ENSMUSG00000034023/ ENSMUSG00000021457/ENSMUSG00000053175/ ENSMUSG00000027985/ENSMUSG00000066755/ ENSMUSG00000053216/ENSMUSG00000049109/ ENSMUSG00000020641/ENSMUSG00000036587/ ENSMUSG00000031712/ENSMUSG00000040329/ ENSMUSG00000063415/ENSMUSG00000044258/ ENSMUSG00000048251/ENSMUSG00000034266/ ENSMUSG00000026117 | Cd74/Fas/Lfng/Satb1/ Cdkn2a/Vnn1/Prex1/ Fancd2/Syk/Bcl3/Lef1/ Tnfsf18/Btn2a2/Themis/ Rsad2/Fut7/Il15/Il7/ Cyp26b1/Ctla2a/Bcl11b/ Batf/Zap70 | 23 |
| BP | GO:0044070 | regulation of anion transport | 13/858 | 89/ 15881 | 0.000948473747695634 | 0.0203257037707111 | ENSMUSG00000037685/ENSMUSG00000029334/ ENSMUSG00000042429/ENSMUSG00000032860/ ENSMUSG00000020333/ENSMUSG00000029851/ ENSMUSG00000021457/ENSMUSG00000003484/ ENSMUSG00000025889/ENSMUSG00000020178/ ENSMUSG00000025557/ENSMUSG00000021948/ ENSMUSG00000036570 | Atp8a1/Prkg2/Adora1/ P2ry2/Acsl6/Tcaf2/Syk/ Cyp4f18/Snca/Adora2a/ Slc15a1/Prkcd/Fxyd1 | 13 |
| BP | GO:0050852 | T cell receptor signaling pathway | 13/858 | 89/ 15881 | 0.000948473747695634 | 0.0203257037707111 | ENSMUSG00000042677/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000062300/ENSMUSG00000053216/ ENSMUSG00000049109/ENSMUSG00000000706/ ENSMUSG00000109713/ENSMUSG00000002699/ ENSMUSG00000004266/ENSMUSG00000034652/ ENSMUSG00000026117 | Zc3h12a/Icosl/Lgals3/ Pawr/Nectin2/Btn2a2/ Themis/Btn1a1/Pvrig/ Lcp2/Ptpn6/Cd300a/Zap70 | 13 |
| BP | GO:0050701 | interleukin-1 secretion | 8/858 | 39/ 15881 | 0.000968583783366871 | 0.0205902738885799 | ENSMUSG00000042677/ENSMUSG00000033538/ ENSMUSG00000027995/ENSMUSG00000055994/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000037860/ENSMUSG00000025888 | Zc3h12a/Casp4/Tlr2/ Nod2/Abca1/Cd36/Aim2/ Casp1 | 8 |
| BP | GO:0031341 | regulation of cell killing | 11/858 | 68/ 15881 | 0.000974289017405545 | 0.0205902738885799 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000020826/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000026068/ ENSMUSG00000074272/ENSMUSG00000029371/ ENSMUSG00000025279 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nos2/Nectin2/Ulbp1/ Il18rap/Ceacam1/Cxcl5/ Dnase1l3 | 11 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| BP | GO:0050818 | regulation of coagulation | 11/858 | 68/15881 | 0.000974289017405545 | 0.0205902738885799 | ENSMUSG00000021822/ENSMUSG00000027082/ENSMUSG00000021457/ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000002944/ENSMUSG00000060459/ENSMUSG00000026580/ENSMUSG00000027611/ENSMUSG00000026249/ENSMUSG00000021948 | Plau/Tfpi/Syk/Ubash3b/Ceacam1/Cd36/Kng2/Selp/Procr/Serpine2/Prkcd | 11 |
| BP | GO:0032652 | regulation of interleukin-1 production | 10/858 | 58/15881 | 0.000987409633426868 | 0.0207718375178698 | ENSMUSG00000042677/ENSMUSG00000033538/ENSMUSG00000019850/ENSMUSG00000026166/ENSMUSG00000027995/ENSMUSG00000055994/ENSMUSG00000074272/ENSMUSG00000037860/ENSMUSG00000071203/ENSMUSG00000025888 | Zc3h12a/Casp4/Tnfaip3/Ccl20/Tlr2/Nod2/Ceacam1/Aim2/Naip5/Casp1 | 10 |
| BP | GO:0044403 | symbiont process | 31/858 | 317/15881 | 0.00103735755028291 | 0.0217229302538695 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000017002/ENSMUSG00000046718/ENSMUSG00000016024/ENSMUSG00000030921/ENSMUSG00000042677/ENSMUSG00000017737/ENSMUSG00000066800/ENSMUSG00000062300/ENSMUSG00000027995/ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000001166/ENSMUSG00000055994/ENSMUSG00000027985/ENSMUSG00000029298/ENSMUSG00000035692/ENSMUSG00000028268/ENSMUSG00000074272/ENSMUSG00000032690/ENSMUSG00000020641/ENSMUSG00000002944/ENSMUSG00000104713/ENSMUSG00000059108/ENSMUSG00000029605/ENSMUSG00000029371/ENSMUSG00000032661/ENSMUSG00000006235/ENSMUSG00000041515/ENSMUSG00000000266 | Cd74/Cxcl1/Slpi/Bst2/Lbp/Trim30a/Zc3h12a/Mmp9/Rnasel/Nectin2/Tlr2/Gbp7/Pf4/Oas1c/Nod2/Lef1/Gbp9/Isg15/Gbp3/Ceacam1/Oas2/Rsad2/Cd36/Gbp6/Ifitm6/Oas1b/Cxcl5/Oas3/Epor/Irf8/Mid2 | 31 |
| BP | GO:0050869 | negative regulation of B cell activation | 7/858 | 31/15881 | 0.00110125116707285 | 0.0226956242244217 | ENSMUSG00000024778/ENSMUSG00000044303/ENSMUSG00000035873/ENSMUSG00000019850/ENSMUSG00000031548/ENSMUSG00000052013/ENSMUSG00000034652 | Fas/Cdkn2a/Pawr/Tnfaip3/Sfrp1/Btla/Cd300a | 7 |
| BP | GO:0006919 | activation of cysteine-type endopeptidase activity involved in apoptotic process | 11/858 | 69/15881 | 0.00110360318404842 | 0.0226956242244217 | ENSMUSG00000023030/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000033538/ENSMUSG00000028128/ENSMUSG00000025507/ENSMUSG00000079017/ENSMUSG00000025889/ENSMUSG00000000120/ENSMUSG00000020787/ENSMUSG00000025888 | Slc11a2/Xdh/Cdkn2a/Casp4/F3/Pidd1/Ifi27l2a/Snca/Ngfr/P2rx1/Casp1 | 11 |
| BP | GO:0030799 | regulation of cyclic nucleotide metabolic process | 11/858 | 69/15881 | 0.00110360318404842 | 0.0226956242244217 | ENSMUSG00000053965/ENSMUSG00000020826/ENSMUSG00000024039/ENSMUSG00000029373/ENSMUSG00000034353/ENSMUSG00000061603/ENSMUSG00000040133/ENSMUSG00000041046/ENSMUSG00000034855/ENSMUSG00000028978/ENSMUSG00000052276 | Pde5a/Nos2/Cbs/Pf4/Ramp1/Akap6/Gpr176/Ramp3/Cxcl10/Nos3/Ostn | 11 |
| BP | GO:0032642 | regulation of chemokine production | 11/858 | 69/15881 | 0.00110360318404842 | 0.0226956242244217 | ENSMUSG00000024610/ENSMUSG00000027750/ENSMUSG00000016024/ENSMUSG00000049577/ENSMUSG00000032860/ENSMUSG00000022676/ENSMUSG00000027995/ENSMUSG00000055994/ENSMUSG00000029371/ENSMUSG00000025494/ENSMUSG00000040329 | Cd74/Postn/Lbp/Zfpm1/P2ry2/Snai2/Tlr2/Nod2/Cxcl5/Sigirr/Il7 | 11 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0010742 | macrophage derived foam cell differentiation | 6/858 | 23/15881 | 0.00111608100566222 | 0.0228497655891382 | ENSMUSG00000018800/ENSMUSG00000029373/ENSMUSG00000002944/ENSMUSG00000021108/ENSMUSG00000024030/ENSMUSG00000025044 | Abca5/Pf4/Cd36/Prkch/Abcg1/Msr1 | 6 |
| BP | GO:0007169 | transmembrane receptor protein tyrosine kinase signaling pathway | 43/858 | 489/15881 | 0.00114523803998889 | 0.0233424962283959 | ENSMUSG00000035385/ENSMUSG00000059895/ENSMUSG00000026185/ENSMUSG00000024066/ENSMUSG00000061132/ENSMUSG00000017737/ENSMUSG00000020806/ENSMUSG00000028039/ENSMUSG00000022103/ENSMUSG00000042429/ENSMUSG00000019831/ENSMUSG00000062991/ENSMUSG00000019577/ENSMUSG00000022144/ENSMUSG00000046733/ENSMUSG00000019997/ENSMUSG00000028128/ENSMUSG00000021457/ENSMUSG00000036585/ENSMUSG00000035109/ENSMUSG00000006435/ENSMUSG00000046223/ENSMUSG00000051225/ENSMUSG00000005057/ENSMUSG00000056486/ENSMUSG00000082361/ENSMUSG00000025889/ENSMUSG00000031520/ENSMUSG00000032020/ENSMUSG00000039481/ENSMUSG00000074272/ENSMUSG00000020340/ENSMUSG00000053141/ENSMUSG00000002489/ENSMUSG00000020312/ENSMUSG00000000120/ENSMUSG00000039323/ENSMUSG00000002699/ENSMUSG00000028864/ENSMUSG00000051379/ENSMUSG00000024427/ENSMUSG00000021948/ENSMUSG00000026117 | Ccl2/Ptp4a3/Igfbp5/Xdh/Blnk/Mmp9/Rhbdf2/Efna3/Gfra2/Adora1/Wasf1/Nrg1/Pdk4/Gdnf/Gprc5a/Ctgf/F3/Syk/Fgf1/Shc4/Neurl1a/Plaur/Fam83a/Sh2b2/Chn1/Btc/Snca/Vegfc/Ubash3b/Nrtn/Ceacam1/Cyfip2/Ptprt/Tiam1/Shc2/Ngfr/Igfbp2/Lcp2/Hgf/Flrt3/Spry4/Prkcd/Zap70 | 43 |
| BP | GO:0050663 | cytokine secretion | 20/858 | 174/15881 | 0.00116335624141006 | 0.0235028710269011 | ENSMUSG00000031778/ENSMUSG00000027750/ENSMUSG00000042677/ENSMUSG00000028965/ENSMUSG00000033538/ENSMUSG00000022514/ENSMUSG00000020826/ENSMUSG00000027995/ENSMUSG00000021457/ENSMUSG00000055994/ENSMUSG00000053216/ENSMUSG00000064246/ENSMUSG00000015243/ENSMUSG00000002944/ENSMUSG00000090958/ENSMUSG00000037860/ENSMUSG00000000706/ENSMUSG00000079164/ENSMUSG00000002699/ENSMUSG00000025888 | Cx3cl1/Postn/Zc3h12a/Tnfrsf9/Casp4/Il1rap/Nos2/Tlr2/Syk/Nod2/Btn2a2/Chil1/Abca1/Cd36/Lrrc32/Aim2/Btn1a1/Tlr5/Lcp2/Casp1 | 20 |
| BP | GO:0050920 | regulation of chemotaxis | 20/858 | 174/15881 | 0.00116335624141006 | 0.0235028710269011 | ENSMUSG00000024610/ENSMUSG00000029380/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000016024/ENSMUSG00000029082/ENSMUSG00000023913/ENSMUSG00000025207/ENSMUSG00000022676/ENSMUSG00000036585/ENSMUSG00000029373/ENSMUSG00000055994/ENSMUSG00000066755/ENSMUSG00000031520/ENSMUSG00000029371/ENSMUSG00000052516/ENSMUSG00000034855/ENSMUSG00000002489/ENSMUSG00000037362/ENSMUSG00000053318 | Cd74/Cxcl1/Ccl2/Cx3cl1/Lbp/Bst1/Pla2g7/Sema4g/Snai2/Fgf1/Pf4/Nod2/Tnfsf18/Vegfc/Cxcl5/Robo2/Cxcl10/Tiam1/Nov/Slamf8 | 20 |
| BP | GO:0002449 | lymphocyte mediated immunity | 21/858 | 187/15881 | 0.00119563833956626 | 0.023933413967212 | ENSMUSG00000024164/ENSMUSG00000024610/ENSMUSG00000073411/ENSMUSG00000061232/ENSMUSG00000024778/ENSMUSG00000000732/ENSMUSG00000062300/ENSMUSG00000079685/ENSMUSG00000053175/ENSMUSG00000026068/ | C3/Cd74/H2-D1/H2-K1/Fas/Icosl/Nectin2/Ulbp1/Bcl3/Il18rap/Nod2/Ctsh/Slc11a1/Ceacam1/Rsad2/ | 21 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000055994/ENSMUSG00000032359/ ENSMUSG00000026177/ENSMUSG00000074272/ ENSMUSG00000020641/ENSMUSG00000079343/ ENSMUSG00000075370/ENSMUSG00000021948/ ENSMUSG00000004266/ENSMUSG00000030707/ ENSMUSG00000034266 | C1s2/Igll1/Prkcd/Ptpn6/ Coro1a/Batf | |
| BP | GO:0006525 | arginine metabolic process | 5/858 | 16/ 15881 | 0.00120554265731051 | 0.023933413967212 | ENSMUSG00000026463/ENSMUSG00000020826/ ENSMUSG00000076441/ENSMUSG00000028978/ ENSMUSG00000046687 | Atp2b4/Nos2/Ass1/Nos3/ Gm5424 | 5 |
| BP | GO:0044144 | modulation of growth of symbiont involved in interaction with host | 5/858 | 16/ 15881 | 0.00120554265731051 | 0.023933413967212 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0050860 | negative regulation of T cell receptor signaling pathway | 5/858 | 16/ 15881 | 0.00120554265731051 | 0.023933413967212 | ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000053216/ENSMUSG00000109713/ ENSMUSG00000004266 | Lgals3/Pawr/Btn2a2/Pvrig/ Ptpn6 | 5 |
| BP | GO:0006874 | cellular calcium ion homeostasis | 32/858 | 334/ 15881 | 0.00121934418079007 | 0.0241030707461347 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000026463/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000026576/ENSMUSG00000029084/ ENSMUSG00000032839/ENSMUSG00000050541/ ENSMUSG00000044026/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000032020/ ENSMUSG00000074715/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000021070/ ENSMUSG00000041046/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000030523/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239/ ENSMUSG00000021337/ENSMUSG00000043051 | Cxcl1/Ccl2/Atp2b4/Pawr/ Ero1l/P2ry2/Atp1b1/Cd38/ Trpc1/Adra1b/Slc35g1/ Cacna1i/Mcub/Akap6/ Snca/Ubash3b/Ccl28/ Cd36/Kng2/Bdkrb2/ Ramp3/Epor/Cxcl10/ Trpm1/Ptpn6/Fxyd1/ Tnni3/Coro1a/Aplnr/Hrc/ Scgn/Disc1 | 32 |
| BP | GO:0008016 | regulation of heart contraction | 16/858 | 126/ 15881 | 0.00123736441713481 | 0.0242267883593022 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000050541/ENSMUSG00000061603/ ENSMUSG00000024065/ENSMUSG00000028978/ ENSMUSG00000041695/ENSMUSG00000036570/ ENSMUSG00000035458/ENSMUSG00000038239 | Zc3h12a/Atp2b4/Adora1/ Gch1/Pde5a/Gja5/Atp1b1/ Ctgf/Adra1b/Akap6/Ehd3/ Nos3/Kcnj2/Fxyd1/Tnni3/ Hrc | 16 |
| BP | GO:0002690 | positive regulation of leukocyte chemotaxis | 11/858 | 70/ 15881 | 0.00124673398447347 | 0.0242267883593022 | ENSMUSG00000024610/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000016024/ENSMUSG00000023913/ ENSMUSG00000029373/ENSMUSG00000066755/ ENSMUSG00000031520/ENSMUSG00000029371/ ENSMUSG00000034855 | Cd74/Cxcl1/Ccl2/Cx3cl1/ Lbp/Pla2g7/Pf4/Tnfsf18/ Vegfc/Cxcl5/Cxcl10 | 11 |
| BP | GO:0033209 | tumor necrosis factor-mediated signaling pathway | 11/858 | 70/ 15881 | 0.00124673398447347 | 0.0242267883593022 | ENSMUSG00000024778/ENSMUSG00000028965/ ENSMUSG00000033538/ENSMUSG00000028599/ ENSMUSG00000021457/ENSMUSG00000066755/ ENSMUSG00000008318/ENSMUSG00000037860/ | Fas/Tnfrsf9/Casp4/ Tnfrsf1b/Syk/Tnfsf18/Relt/ Aim2/Ngfr/Tnfrsf8/Casp1 | 11 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000000120/ENSMUSG00000028602/ ENSMUSG00000025888 | | |
| BP | GO:0050764 | regulation of phagocytosis | 11/858 | 70/ 15881 | 0.00124673398447347 | 0.0242267883593022 | ENSMUSG00000024164/ENSMUSG00000035385/ ENSMUSG00000016024/ENSMUSG00000024743/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000026177/ ENSMUSG00000041351/ENSMUSG00000002944/ ENSMUSG00000034652 | C3/Ccl2/Lbp/Syt7/Tlr2/ Syk/Nod2/Slc11a1/ Rap1gap/Cd36/Cd300a | 11 |
| BP | GO:0034121 | regulation of toll-like receptor signaling pathway | 9/858 | 50/ 15881 | 0.00127562254790761 | 0.0246835654206933 | ENSMUSG00000016024/ENSMUSG00000030921/ ENSMUSG00000019850/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000079164/ ENSMUSG00000034652 | Lbp/Trim30a/Tnfaip3/ Tlr2/Nod2/Rsad2/Cd36/ Tlr5/Cd300a | 9 |
| BP | GO:0071219 | cellular response to molecule of bacterial origin | 19/858 | 163/ 15881 | 0.00129377613459593 | 0.0247670525307079 | ENSMUSG00000035385/ENSMUSG00000016024/ ENSMUSG00000042677/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000027995/ ENSMUSG00000028599/ENSMUSG00000055994/ ENSMUSG00000075122/ENSMUSG00000015243/ ENSMUSG00000002944/ENSMUSG00000104713/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000028978/ENSMUSG00000041515/ ENSMUSG00000025888 | Ccl2/Lbp/Zc3h12a/Gch1/ Nos2/Tnfaip3/Trib1/Tlr2/ Tnfrsf1b/Nod2/Cd80/ Abca1/Cd36/Gbp6/Cxcl5/ Cxcl10/Nos3/Irf8/Casp1 | 19 |
| BP | GO:0030330 | DNA damage response, signal transduction by p53 class mediator | 10/858 | 60/ 15881 | 0.00129437102440467 | 0.0247670525307079 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000044303/ENSMUSG00000022676/ ENSMUSG00000025507/ENSMUSG00000022510/ ENSMUSG00000053175/ENSMUSG00000016526/ ENSMUSG00000025665/ENSMUSG00000034266 | Cd74/Cdkn1a/Cdkn2a/ Snai2/Pidd1/Trp63/Bcl3/ Dyrk3/Rps6ka6/Batf | 10 |
| BP | GO:0045069 | regulation of viral genome replication | 12/858 | 81/ 15881 | 0.00129679616114618 | 0.0247670525307079 | ENSMUSG00000017002/ENSMUSG00000046718/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000001166/ENSMUSG00000035692/ ENSMUSG00000074272/ENSMUSG00000032690/ ENSMUSG00000020641/ENSMUSG00000059108/ ENSMUSG00000029605/ENSMUSG00000032661 | Slpi/Bst2/Zc3h12a/Rnasel/ Oas1c/Isg15/Ceacam1/ Oas2/Rsad2/Ifitm6/Oas1b/ Oas3 | 12 |
| BP | GO:0030336 | negative regulation of cell migration | 23/858 | 214/ 15881 | 0.00130153939378557 | 0.0247670525307079 | ENSMUSG00000031778/ENSMUSG00000026185/ ENSMUSG00000000753/ENSMUSG00000031785/ ENSMUSG00000042429/ENSMUSG00000038387/ ENSMUSG00000062991/ENSMUSG00000032501/ ENSMUSG00000030220/ENSMUSG00000021596/ ENSMUSG00000026921/ENSMUSG00000029167/ ENSMUSG00000115388/ENSMUSG00000074715/ ENSMUSG00000031548/ENSMUSG00000037362/ ENSMUSG00000024451/ENSMUSG00000020121/ ENSMUSG00000021256/ENSMUSG00000026109/ ENSMUSG00000019278/ENSMUSG00000053318/ ENSMUSG00000034652 | Cx3cl1/Igfbp5/Serpinf1/ Adgrg1/Adora1/Rras/Nrg1/ Trib1/Arhgdib/Mctp1/ Egfl7/Ppargc1a/Eppk1/ Ccl28/Sfrp1/Nov/Arap3/ Srgap1/Vash1/Tmeff2/ Dpep1/Slamf8/Cd300a | 23 |
| BP | GO:1903900 | regulation of viral life cycle | 16/858 | 127/ 15881 | 0.00134652360402521 | 0.0254887351510843 | ENSMUSG00000024610/ENSMUSG00000017002/ ENSMUSG00000046718/ENSMUSG00000030921/ ENSMUSG00000042677/ENSMUSG00000066800/ ENSMUSG00000062300/ENSMUSG00000001166/ | Cd74/Slpi/Bst2/Trim30a/ Zc3h12a/Rnasel/Nectin2/ Oas1c/Isg15/Ceacam1/ | 16 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000035692/ENSMUSG00000074272/ ENSMUSG00000032690/ENSMUSG00000020641/ ENSMUSG00000059108/ENSMUSG00000029605/ ENSMUSG00000032661/ENSMUSG00000000266 | Oas2/Rsad2/Ifitm6/Oas1b/ Oas3/Mid2 | |
| BP | GO:0002315 | marginal zone B cell differentiation | 4/858 | 10/ 15881 | 0.00136681093810026 | 0.0254887351510843 | ENSMUSG00000029570/ENSMUSG00000019850/ ENSMUSG00000053175/ENSMUSG00000018169 | Lfng/Tnfaip3/Bcl3/Mfng | 4 |
| BP | GO:0010744 | positive regulation of macrophage derived foam cell differentiation | 4/858 | 10/ 15881 | 0.00136681093810026 | 0.0254887351510843 | ENSMUSG00000029373/ENSMUSG00000002944/ ENSMUSG00000021108/ENSMUSG00000025044 | Pf4/Cd36/Prkch/Msr1 | 4 |
| BP | GO:0035634 | response to stilbenoid | 4/858 | 10/ 15881 | 0.00136681093810026 | 0.0254887351510843 | ENSMUSG00000040026/ENSMUSG00000002944/ ENSMUSG00000031594/ENSMUSG00000030107 | Saa3/Cd36/Fgl1/Usp18 | 4 |
| BP | GO:2001239 | regulation of extrinsic apoptotic signaling pathway in absence of ligand | 8/858 | 41/ 15881 | 0.00136725443680042 | 0.0254887351510843 | ENSMUSG00000031778/ENSMUSG00000024778/ ENSMUSG00000022144/ENSMUSG00000022676/ ENSMUSG00000029373/ENSMUSG00000025915/ ENSMUSG00000040329/ENSMUSG00000022483 | Cx3cl1/Fas/Gdnf/Snai2/ Pf4/Sgk3/Il7/Col2a1 | 8 |
| BP | GO:2001057 | reactive nitrogen species metabolic process | 11/858 | 71/ 15881 | 0.00140477443187214 | 0.026082168196622 | ENSMUSG00000042677/ENSMUSG00000026463/ ENSMUSG00000020826/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000017969/ ENSMUSG00000076441/ENSMUSG00000002944/ ENSMUSG00000006235/ENSMUSG00000028978/ ENSMUSG00000079164 | Zc3h12a/Atp2b4/Nos2/ Ulbp1/Tlr2/Ptgis/Ass1/ Cd36/Epor/Nos3/Tlr5 | 11 |
| BP | GO:0008207 | C21-steroid hormone metabolic process | 6/858 | 24/ 15881 | 0.00142084627024591 | 0.0261686786961757 | ENSMUSG00000022150/ENSMUSG00000029167/ ENSMUSG00000033715/ENSMUSG00000027068/ ENSMUSG00000025955/ENSMUSG00000054932 | Dab2/Ppargc1a/Akr1c14/ Dhrs9/Akr1cl/Afp | 6 |
| BP | GO:0090077 | foam cell differentiation | 6/858 | 24/ 15881 | 0.00142084627024591 | 0.0261686786961757 | ENSMUSG00000018800/ENSMUSG00000029373/ ENSMUSG00000002944/ENSMUSG00000021108/ ENSMUSG00000024030/ENSMUSG00000025044 | Abca5/Pf4/Cd36/Prkch/ Abcg1/Msr1 | 6 |
| BP | GO:0040013 | negative regulation of locomotion | 27/858 | 269/ 15881 | 0.00145720336316006 | 0.0267309384938081 | ENSMUSG00000031778/ENSMUSG00000026185/ ENSMUSG00000000753/ENSMUSG00000031785/ ENSMUSG00000042429/ENSMUSG00000038387/ ENSMUSG00000062991/ENSMUSG00000025207/ ENSMUSG00000032501/ENSMUSG00000030220/ ENSMUSG00000021596/ENSMUSG00000026921/ ENSMUSG00000029167/ENSMUSG00000115388/ ENSMUSG00000074715/ENSMUSG00000052516/ ENSMUSG00000031548/ENSMUSG00000037362/ ENSMUSG00000020178/ENSMUSG00000024451/ ENSMUSG00000020121/ENSMUSG00000021256/ ENSMUSG00000000266/ENSMUSG00000026109/ ENSMUSG00000019278/ENSMUSG00000053318/ ENSMUSG00000034652 | Cx3cl1/Igfbp5/Serpinf1/ Adgrg1/Adora1/Rras/Nrg1/ Sema4g/Trib1/Arhgdib/ Mctp1/Egfl7/Ppargc1a/ Eppk1/Ccl28/Robo2/Sfrp1/ Nov/Adora2a/Arap3/ Srgap1/Vash1/Mid2/ Tmeff2/Dpep1/Slamf8/ Cd300a | 27 |
| BP | GO:0019226 | transmission of nerve impulse | 10/858 | 61/ 15881 | 0.00147468413014411 | 0.0268619575886901 | ENSMUSG00000035873/ENSMUSG00000057182/ ENSMUSG00000022416/ENSMUSG00000075318/ ENSMUSG00000026442/ENSMUSG00000064329/ ENSMUSG00000053395/ENSMUSG00000020787/ ENSMUSG00000049044/ENSMUSG00000027071 | Pawr/Scn3a/Cacna1i/ Scn2a/Nfasc/Scn1a/ Cacng8/P2rx1/Rapgef4/ P2rx3 | 10 |
| BP | GO:0097006 | regulation of plasma lipoprotein particle levels | 9/858 | 51/ 15881 | 0.00147606046933055 | 0.0268619575886901 | ENSMUSG00000018800/ENSMUSG00000057074/ ENSMUSG00000023913/ENSMUSG00000056973/ ENSMUSG00000041193/ENSMUSG00000015243/ | Abca5/Ces1g/Pla2g7/ Ces1d/Pla2g5/Abca1/ Cd36/Abcg1/Msr1 | 9 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000002944/ENSMUSG00000024030/ ENSMUSG00000025044 | | |
| BP | GO:0042326 | negative regulation of phosphorylation | 38/858 | 423/ 15881 | 0.00148197254410488 | 0.0268629489615216 | ENSMUSG00000023067/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000024066/ ENSMUSG00000044303/ENSMUSG00000006457/ ENSMUSG00000003541/ENSMUSG00000022103/ ENSMUSG00000039621/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000034570/ ENSMUSG00000096472/ENSMUSG00000021892/ ENSMUSG00000034394/ENSMUSG00000046733/ ENSMUSG00000019823/ENSMUSG00000012889/ ENSMUSG00000079363/ENSMUSG00000029167/ ENSMUSG00000025665/ENSMUSG00000026483/ ENSMUSG00000053216/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000055003/ ENSMUSG00000074272/ENSMUSG00000037664/ ENSMUSG00000021070/ENSMUSG00000031548/ ENSMUSG00000020178/ENSMUSG00000039661/ ENSMUSG00000028864/ENSMUSG00000051379/ ENSMUSG00000024427/ENSMUSG00000021948/ ENSMUSG00000004266/ENSMUSG00000034652 | Cdkn1a/Zc3h12a/Dab2/ Xdh/Cdkn2a/Actn3/Ier3/ Gfra2/Prex1/Tnfaip3/ Trib1/Inpp5j/Cdkn2d/ Sh3bp5/Lif/Gprc5a/ Mical1/Podnl1/Gbp4/ Ppargc1a/Rps6ka6/ Fam129a/Btn2a2/Snca/ Ubash3b/Lrtm2/Ceacam1/ Cdkn1c/Bdkrb2/Sfrp1/ Adora2a/Dusp26/Hgf/ Flrt3/Spry4/Prkcd/Ptpn6/ Cd300a | 38 |
| BP | GO:0032602 | chemokine production | 11/858 | 72/ 15881 | 0.00157886833822346 | 0.0284666974228401 | ENSMUSG00000024610/ENSMUSG00000027750/ ENSMUSG00000016024/ENSMUSG00000049577/ ENSMUSG00000032860/ENSMUSG00000022676/ ENSMUSG00000027995/ENSMUSG00000055994/ ENSMUSG00000029371/ENSMUSG00000025494/ ENSMUSG00000040329 | Cd74/Postn/Lbp/Zfpm1/ P2ry2/Snai2/Tlr2/Nod2/ Cxcl5/Sigirr/Il7 | 11 |
| BP | GO:0035150 | regulation of tube size | 16/858 | 129/ 15881 | 0.00158930886063044 | 0.0284666974228401 | ENSMUSG00000031778/ENSMUSG00000047250/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000020826/ENSMUSG00000032860/ ENSMUSG00000029084/ENSMUSG00000024039/ ENSMUSG00000050541/ENSMUSG00000021070/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000031489 | Cx3cl1/Ptgs1/Adora1/ Gch1/Pde5a/Gja5/Nos2/ P2ry2/Cd38/Cbs/Adra1b/ Bdkrb2/Nos3/Adora2a/ P2rx1/Adrb3 | 16 |
| BP | GO:0050880 | regulation of blood vessel size | 16/858 | 129/ 15881 | 0.00158930886063044 | 0.0284666974228401 | ENSMUSG00000031778/ENSMUSG00000047250/ ENSMUSG00000042429/ENSMUSG00000037580/ ENSMUSG00000053965/ENSMUSG00000057123/ ENSMUSG00000020826/ENSMUSG00000032860/ ENSMUSG00000029084/ENSMUSG00000024039/ ENSMUSG00000050541/ENSMUSG00000021070/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000031489 | Cx3cl1/Ptgs1/Adora1/ Gch1/Pde5a/Gja5/Nos2/ P2ry2/Cd38/Cbs/Adra1b/ Bdkrb2/Nos3/Adora2a/ P2rx1/Adrb3 | 16 |
| BP | GO:0050819 | negative regulation of coagulation | 8/858 | 42/ 15881 | 0.00161031321431589 | 0.0284666974228401 | ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000060459/ENSMUSG00000027611/ ENSMUSG00000026249/ENSMUSG00000021948 | Plau/Tfpi/Ubash3b/ Ceacam1/Kng2/Procr/ Serpine2/Prkcd | 8 |
| BP | GO:0034762 | regulation of transmembrane transport | 38/858 | 425/ 15881 | 0.00161247769690439 | 0.0284666974228401 | ENSMUSG00000024164/ENSMUSG00000066152/ ENSMUSG00000026463/ENSMUSG00000017737/ ENSMUSG00000005089/ENSMUSG00000057123/ | C3/Slc31a2/Atp2b4/ Mmp9/Slc1a2/Gja5/ Rnasel/Kcnab2/Atp1b1/ | 38 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000066800/ENSMUSG00000028931/ ENSMUSG00000026576/ENSMUSG00000020333/ ENSMUSG00000029851/ENSMUSG00000032839/ ENSMUSG00000029167/ENSMUSG00000005057/ ENSMUSG00000050777/ENSMUSG00000024873/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000032020/ ENSMUSG00000041245/ENSMUSG00000028214/ ENSMUSG00000041046/ENSMUSG00000009687/ ENSMUSG00000064329/ENSMUSG00000053395/ ENSMUSG00000034855/ENSMUSG00000024065/ ENSMUSG00000000120/ENSMUSG00000041695/ ENSMUSG00000018470/ENSMUSG00000052276/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000036570/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239 | Acsl6/Tcaf2/Trpc1/ Ppargc1a/Sh2b2/Tmem37/ Cnih2/Akap6/Snca/ Atp1b2/Ubash3b/Wnk3/ Gem/Ramp3/Fxyd5/Scn1a/ Cacng8/Cxcl10/Ehd3/Ngfr/ Kcnj2/Kcnab3/Ostn/Prkcd/ Ptpn6/Fxyd1/Coro1a/ Aplnr/Hrc | |
| BP | GO:0003009 | skeletal muscle contraction | 7/858 | 33/ 15881 | 0.00162837649528217 | 0.0284666974228401 | ENSMUSG00000006457/ENSMUSG00000026251/ ENSMUSG00000026253/ENSMUSG00000026418/ ENSMUSG00000041695/ENSMUSG00000027470/ ENSMUSG00000035458 | Actn3/Chrnd/Chrng/Tnni1/ Kcnj2/Mylk2/Tnni3 | 7 |
| BP | GO:0071825 | protein-lipid complex subunit organization | 7/858 | 33/ 15881 | 0.00162837649528217 | 0.0284666974228401 | ENSMUSG00000018800/ENSMUSG00000057074/ ENSMUSG00000023913/ENSMUSG00000056973/ ENSMUSG00000041193/ENSMUSG00000015243/ ENSMUSG00000024030 | Abca5/Ces1g/Pla2g7/ Ces1d/Pla2g5/Abca1/ Abcg1 | 7 |
| BP | GO:0006825 | copper ion transport | 5/858 | 17/ 15881 | 0.0016325210253395 | 0.0284666974228401 | ENSMUSG00000012428/ENSMUSG00000003617/ ENSMUSG00000023030/ENSMUSG00000066152/ ENSMUSG00000031936 | Steap4/Cp/Slc11a2/ Slc31a2/Hephl1 | 5 |
| BP | GO:0044117 | growth of symbiont in host | 5/858 | 17/ 15881 | 0.0016325210253395 | 0.0284666974228401 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0090330 | regulation of platelet aggregation | 5/858 | 17/ 15881 | 0.0016325210253395 | 0.0284666974228401 | ENSMUSG00000021457/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000026249/ ENSMUSG00000021948 | Syk/Ubash3b/Ceacam1/ Serpine2/Prkcd | 5 |
| BP | GO:1903706 | regulation of hemopoiesis | 30/858 | 313/ 15881 | 0.00169695781394299 | 0.0294782141467521 | ENSMUSG00000023367/ENSMUSG00000024610/ ENSMUSG00000029380/ENSMUSG00000029810/ ENSMUSG00000024778/ENSMUSG00000044303/ ENSMUSG00000037440/ENSMUSG00000049577/ ENSMUSG00000024014/ENSMUSG00000032501/ ENSMUSG00000034394/ENSMUSG00000034023/ ENSMUSG00000021457/ENSMUSG00000007805/ ENSMUSG00000029373/ENSMUSG00000027985/ ENSMUSG00000066755/ENSMUSG00000035692/ ENSMUSG00000035158/ENSMUSG00000053216/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000031548/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000044258/ENSMUSG00000004266/ ENSMUSG00000020325/ENSMUSG00000026117 | Tmem176a/Cd74/Cxcl1/ Tmem176b/Fas/Cdkn2a/ Vnn1/Zfpm1/Pim1/Trib1/ Lif/Fancd2/Syk/Twist2/ Pf4/Lef1/Tnfsf18/Isg15/ Mitf/Btn2a2/Ubash3b/ Ceacam1/Sfrp1/Il15/Il7/ Cyp26b1/Ctla2a/Ptpn6/ Fstl3/Zap70 | 30 |
| BP | GO:0001819 | positive regulation of cytokine production | 32/858 | 341/ 15881 | 0.00170716898164206 | 0.0295436866030584 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000035385/ENSMUSG00000031778/ | C3/Cd74/Ccl2/Cx3cl1/ Postn/Lbp/Icosl/Zfpm1/ | 32 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000027750/ENSMUSG00000016024/ ENSMUSG00000000732/ENSMUSG00000049577/ ENSMUSG00000033538/ENSMUSG00000022514/ ENSMUSG00000032860/ENSMUSG00000079685/ ENSMUSG00000026166/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000053175/ ENSMUSG00000029373/ENSMUSG00000055994/ ENSMUSG00000026177/ENSMUSG00000017830/ ENSMUSG00000020641/ENSMUSG00000002944/ ENSMUSG00000037860/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000040329/ ENSMUSG00000041515/ENSMUSG00000071203/ ENSMUSG00000079164/ENSMUSG00000028602/ ENSMUSG00000028864/ENSMUSG00000025888 | Casp4/Il1rap/P2ry2/Ulbp1/ Ccl20/Tlr2/Syk/Bcl3/Pf4/ Nod2/Slc11a1/Dhx58/ Rsad2/Cd36/Aim2/ Il12rb1/Il15/Il7/Irf8/ Naip5/Tlr5/Tnfrsf8/Hgf/ Casp1 | |
| BP | GO:0035637 | multicellular organismal signaling | 13/858 | 95/ 15881 | 0.00174885102166627 | 0.0301512435539907 | ENSMUSG00000035873/ENSMUSG00000057123/ ENSMUSG00000057182/ENSMUSG00000022416/ ENSMUSG00000075318/ENSMUSG00000026442/ ENSMUSG00000064329/ENSMUSG00000053395/ ENSMUSG00000024065/ENSMUSG00000020787/ ENSMUSG00000049044/ENSMUSG00000041695/ ENSMUSG00000027071 | Pawr/Gja5/Scn3a/Cacna1i/ Scn2a/Nfasc/Scn1a/ Cacng8/Ehd3/P2rx1/ Rapgef4/Kcnj2/P2rx3 | 13 |
| BP | GO:0003073 | regulation of systemic arterial blood pressure | 11/858 | 73/ 15881 | 0.00177021003816535 | 0.0304051806555292 | ENSMUSG00000027750/ENSMUSG00000028024/ ENSMUSG00000003541/ENSMUSG00000042429/ ENSMUSG00000057123/ENSMUSG00000050541/ ENSMUSG00000002944/ENSMUSG00000068323/ ENSMUSG00000028978/ENSMUSG00000031489/ ENSMUSG00000035458 | Postn/Enpep/Ier3/Adora1/ Gja5/Adra1b/Cd36/Slc4a5/ Nos3/Adrb3/Tnni3 | 11 |
| BP | GO:0010959 | regulation of metal ion transport | 30/858 | 314/ 15881 | 0.00178242277914055 | 0.0304329607049726 | ENSMUSG00000029380/ENSMUSG00000066152/ ENSMUSG00000026463/ENSMUSG00000050335/ ENSMUSG00000035873/ENSMUSG00000042429/ ENSMUSG00000028931/ENSMUSG00000026576/ ENSMUSG00000032839/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000041329/ ENSMUSG00000032020/ENSMUSG00000041245/ ENSMUSG00000028214/ENSMUSG00000026249/ ENSMUSG00000041046/ENSMUSG00000009687/ ENSMUSG00000034855/ENSMUSG00000024065/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000037418/ ENSMUSG00000041695/ENSMUSG00000004266/ ENSMUSG00000036570/ENSMUSG00000030707/ ENSMUSG00000044338/ENSMUSG00000038239 | Cxcl1/Slc31a2/Atp2b4/ Lgals3/Pawr/Adora1/ Kcnab2/Atp1b1/Trpc1/ Akap6/Snca/Atp1b2/ Ubash3b/Wnk3/Gem/ Serpine2/Ramp3/Fxyd5/ Cxcl10/Ehd3/Nos3/ Adora2a/P2rx1/Best1/ Kcnj2/Ptpn6/Fxyd1/ Coro1a/Aplnr/Hrc | 30 |
| BP | GO:0006939 | smooth muscle contraction | 12/858 | 84/ 15881 | 0.00178725695158576 | 0.0304329607049726 | ENSMUSG00000047250/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000022144/ ENSMUSG00000050541/ENSMUSG00000021070/ ENSMUSG00000055632/ENSMUSG00000020787/ ENSMUSG00000059588/ENSMUSG00000027071/ ENSMUSG00000035458/ENSMUSG00000020081 | Ptgs1/Pawr/Adora1/Gdnf/ Adra1b/Bdkrb2/Hmcn2/ P2rx1/Calcrl/P2rx3/Tnni3/ Tacr2 | 12 |
| BP | GO:0051345 | positive regulation of hydrolase activity | 39/858 | 442/ 15881 | 0.00179173558446197 | 0.0304329607049726 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000023030/ENSMUSG00000024778/ | Ccl2/Cx3cl1/Slc11a2/Fas/ Xdh/Cdkn2a/Ccl7/F11r/ | 39 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000024066/ENSMUSG00000044303/ ENSMUSG00000035373/ENSMUSG00000038235/ ENSMUSG00000028039/ENSMUSG00000035873/ ENSMUSG00000033538/ENSMUSG00000039621/ ENSMUSG00000026576/ENSMUSG00000019997/ ENSMUSG00000028128/ENSMUSG00000026166/ ENSMUSG00000025507/ENSMUSG00000019122/ ENSMUSG00000031292/ENSMUSG00000032359/ ENSMUSG00000079017/ENSMUSG00000057897/ ENSMUSG00000020599/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000041329/ ENSMUSG00000041193/ENSMUSG00000041351/ ENSMUSG00000003134/ENSMUSG00000039813/ ENSMUSG00000020340/ENSMUSG00000037860/ ENSMUSG00000002489/ENSMUSG00000000120/ ENSMUSG00000020787/ENSMUSG00000031780/ ENSMUSG00000021948/ENSMUSG00000025888/ ENSMUSG00000034652 | Efna3/Pawr/Casp4/Prex1/ Atp1b1/Ctgf/F3/Ccl20/ Pidd1/Ccl9/Cdkl5/Ctsh/ Ifi27l2a/Camk2b/Rgs9/ Akap6/Snca/Atp1b2/ Pla2g5/Rap1gap/Tbc1d8/ Tbc1d2/Cyfip2/Aim2/ Tiam1/Ngfr/P2rx1/Ccl17/ Prkcd/Casp1/Cd300a | |
| BP | GO:1904062 | regulation of cation transmembrane transport | 25/858 | 246/ 15881 | 0.00180931780421647 | 0.0306181972329769 | ENSMUSG00000066152/ENSMUSG00000026463/ ENSMUSG00000017737/ENSMUSG00000028931/ ENSMUSG00000026576/ENSMUSG00000032839/ ENSMUSG00000029167/ENSMUSG00000024873/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000032020/ ENSMUSG00000041245/ENSMUSG00000028214/ ENSMUSG00000041046/ENSMUSG00000009687/ ENSMUSG00000053395/ENSMUSG00000034855/ ENSMUSG00000024065/ENSMUSG00000041695/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000030707/ENSMUSG00000044338/ ENSMUSG00000038239 | Slc31a2/Atp2b4/Mmp9/ Kcnab2/Atp1b1/Trpc1/ Ppargc1a/Cnih2/Akap6/ Snca/Atp1b2/Ubash3b/ Wnk3/Gem/Ramp3/Fxyd5/ Cacng8/Cxcl10/Ehd3/ Kcnj2/Ptpn6/Fxyd1/ Coro1a/Aplnr/Hrc | 25 |
| BP | GO:0071216 | cellular response to biotic stimulus | 20/858 | 181/ 15881 | 0.0018804602633178 | 0.0317051131160862 | ENSMUSG00000035385/ENSMUSG00000016024/ ENSMUSG00000042677/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000019850/ ENSMUSG00000032501/ENSMUSG00000027995/ ENSMUSG00000028599/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000075122/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000104713/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000028978/ ENSMUSG00000041515/ENSMUSG00000025888 | Ccl2/Lbp/Zc3h12a/Gch1/ Nos2/Tnfaip3/Trib1/Tlr2/ Tnfrsf1b/Syk/Nod2/Cd80/ Abca1/Cd36/Gbp6/Cxcl5/ Cxcl10/Nos3/Irf8/Casp1 | 20 |
| BP | GO:0002274 | myeloid leukocyte activation | 18/858 | 156/ 15881 | 0.00192194680836292 | 0.0322858903412174 | ENSMUSG00000031778/ENSMUSG00000016024/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000026068/ENSMUSG00000026177/ ENSMUSG00000025889/ENSMUSG00000041193/ ENSMUSG00000035186/ENSMUSG00000029371/ ENSMUSG00000002699/ENSMUSG00000021948/ ENSMUSG00000025888/ENSMUSG00000034652/ ENSMUSG00000034266/ENSMUSG00000025279 | Cx3cl1/Lbp/Nectin2/ Ulbp1/Tlr2/Syk/Il18rap/ Slc11a1/Snca/Pla2g5/Ubd/ Cxcl5/Lcp2/Prkcd/Casp1/ Cd300a/Batf/Dnase1l3 | 18 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0015696 | ammonium transport | 12/858 | 85/15881 | 0.00198113405759571 | 0.0330381119568506 | ENSMUSG00000055368/ENSMUSG00000050335/ENSMUSG00000024743/ENSMUSG00000022144/ENSMUSG00000021457/ENSMUSG00000025889/ENSMUSG00000028825/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000007034/ENSMUSG00000034652/ENSMUSG00000020081 | Slc6a2/Lgals3/Syt7/Gdnf/Syk/Snca/Rhd/Adora2a/P2rx1/Slc44a4/Cd300a/Tacr2 | 12 |
| BP | GO:2001237 | negative regulation of extrinsic apoptotic signaling pathway | 12/858 | 85/15881 | 0.00198113405759571 | 0.0330381119568506 | ENSMUSG00000031778/ENSMUSG00000022150/ENSMUSG00000050335/ENSMUSG00000019850/ENSMUSG00000022144/ENSMUSG00000022676/ENSMUSG00000029373/ENSMUSG00000023011/ENSMUSG00000025915/ENSMUSG00000040329/ENSMUSG00000028864/ENSMUSG00000022483 | Cx3cl1/Dab2/Lgals3/Tnfaip3/Gdnf/Snai2/Pf4/Faim2/Sgk3/Il7/Hgf/Col2a1 | 12 |
| BP | GO:0016054 | organic acid catabolic process | 21/858 | 195/15881 | 0.00201875962440186 | 0.0334224968863067 | ENSMUSG00000026463/ENSMUSG00000027332/ENSMUSG00000020826/ENSMUSG00000056973/ENSMUSG00000042010/ENSMUSG00000023963/ENSMUSG00000019806/ENSMUSG00000031387/ENSMUSG00000015890/ENSMUSG00000003484/ENSMUSG00000017453/ENSMUSG00000031725/ENSMUSG00000055782/ENSMUSG00000027412/ENSMUSG00000028978/ENSMUSG00000063415/ENSMUSG00000010651/ENSMUSG00000007908/ENSMUSG00000028011/ENSMUSG00000002475/ENSMUSG00000034456 | Atp2b4/Ivd/Nos2/Ces1d/Acacb/Cyp39a1/Aig1/Renbp/Amdhd1/Cyp4f18/Pipox/Ces1f/Abcd2/Lpin3/Nos3/Cyp26b1/Acaa1b/Hmgcll1/Tdo2/Abhd3/Uroc1 | 21 |
| BP | GO:0046395 | carboxylic acid catabolic process | 21/858 | 195/15881 | 0.00201875962440186 | 0.0334224968863067 | ENSMUSG00000026463/ENSMUSG00000027332/ENSMUSG00000020826/ENSMUSG00000056973/ENSMUSG00000042010/ENSMUSG00000023963/ENSMUSG00000019806/ENSMUSG00000031387/ENSMUSG00000015890/ENSMUSG00000003484/ENSMUSG00000017453/ENSMUSG00000031725/ENSMUSG00000055782/ENSMUSG00000027412/ENSMUSG00000028978/ENSMUSG00000063415/ENSMUSG00000010651/ENSMUSG00000007908/ENSMUSG00000028011/ENSMUSG00000002475/ENSMUSG00000034456 | Atp2b4/Ivd/Nos2/Ces1d/Acacb/Cyp39a1/Aig1/Renbp/Amdhd1/Cyp4f18/Pipox/Ces1f/Abcd2/Lpin3/Nos3/Cyp26b1/Acaa1b/Hmgcll1/Tdo2/Abhd3/Uroc1 | 21 |
| BP | GO:0001820 | serotonin secretion | 4/858 | 11/15881 | 0.00205645791870863 | 0.0334429645928999 | ENSMUSG00000050335/ENSMUSG00000021457/ENSMUSG00000020787/ENSMUSG00000034652 | Lgals3/Syk/P2rx1/Cd300a | 4 |
| BP | GO:0036376 | sodium ion export across plasma membrane | 4/858 | 11/15881 | 0.00205645791870863 | 0.0334429645928999 | ENSMUSG00000026576/ENSMUSG00000040907/ENSMUSG00000041329/ENSMUSG00000036570 | Atp1b1/Atp1a3/Atp1b2/Fxyd1 | 4 |
| BP | GO:0043383 | negative T cell selection | 4/858 | 11/15881 | 0.00205645791870863 | 0.0334429645928999 | ENSMUSG00000024610/ENSMUSG00000024778/ENSMUSG00000049109/ENSMUSG00000026117 | Cd74/Fas/Themis/Zap70 | 4 |
| BP | GO:0050855 | regulation of B cell receptor signaling pathway | 4/858 | 11/15881 | 0.00205645791870863 | 0.0334429645928999 | ENSMUSG00000021108/ENSMUSG00000024696/ENSMUSG00000004266/ENSMUSG00000034652 | Prkch/Lpxn/Ptpn6/Cd300a | 4 |
| BP | GO:0090331 | negative regulation of platelet aggregation | 4/858 | 11/15881 | 0.00205645791870863 | 0.0334429645928999 | ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000026249/ENSMUSG00000021948 | Ubash3b/Ceacam1/Serpine2/Prkcd | 4 |
| BP | GO:0009636 | response to toxic substance | 27/858 | 276/15881 | 0.00211207639675461 | 0.0341055716743544 | ENSMUSG00000053279/ENSMUSG00000024778/ENSMUSG00000042677/ENSMUSG00000044303/ENSMUSG00000035373/ENSMUSG00000035873/ENSMUSG00000037580/ENSMUSG00000019850/ENSMUSG00000056973/ENSMUSG00000057182/ENSMUSG00000050541/ENSMUSG00000015709/ | Aldh1a1/Fas/Zc3h12a/Cdkn2a/Ccl7/Pawr/Gch1/Tnfaip3/Ces1d/Scn3a/Adra1b/Arnt2/Chrnd/Chrng/Ass1/Lcn2/Cd36/Cyp2f2/Epor/Nos3/ | 27 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000026251/ENSMUSG00000026253/ ENSMUSG00000076441/ENSMUSG00000026822/ ENSMUSG00000002944/ENSMUSG00000052974/ ENSMUSG00000006235/ENSMUSG00000028978/ ENSMUSG00000020178/ENSMUSG00000010651/ ENSMUSG00000003477/ENSMUSG00000025069/ ENSMUSG00000028864/ENSMUSG00000004231/ ENSMUSG00000021948 | Adora2a/Acaa1b/Inmt/ Gsto2/Hgf/Pax2/Prkcd | |
| BP | GO:0044282 | small molecule catabolic process | 27/858 | 276/ 15881 | 0.00211207639675461 | 0.0341055716743544 | ENSMUSG00000026463/ENSMUSG00000006457/ ENSMUSG00000027332/ENSMUSG00000020826/ ENSMUSG00000056973/ENSMUSG00000042010/ ENSMUSG00000023963/ENSMUSG00000028755/ ENSMUSG00000035473/ENSMUSG00000019806/ ENSMUSG00000031387/ENSMUSG00000015890/ ENSMUSG00000003484/ENSMUSG00000017453/ ENSMUSG00000031725/ENSMUSG00000055782/ ENSMUSG00000041731/ENSMUSG00000020407/ ENSMUSG00000027412/ENSMUSG00000090700/ ENSMUSG00000028978/ENSMUSG00000063415/ ENSMUSG00000010651/ENSMUSG00000007908/ ENSMUSG00000028011/ENSMUSG00000002475/ ENSMUSG00000034456 | Atp2b4/Actn3/Ivd/Nos2/ Ces1d/Acacb/Cyp39a1/ Cda/Galm/Aig1/Renbp/ Amdhd1/Cyp4f18/Pipox/ Ces1f/Abcd2/Pgm5/Upp1/ Lpin3/Cyp4f40/Nos3/ Cyp26b1/Acaa1b/Hmgcll1/ Tdo2/Abhd3/Uroc1 | 27 |
| BP | GO:0030193 | regulation of blood coagulation | 10/858 | 64/ 15881 | 0.00214118879501847 | 0.0341713105640575 | ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000021457/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000026249/ENSMUSG00000021948 | Plau/Tfpi/Syk/Ubash3b/ Ceacam1/Cd36/Kng2/Selp/ Serpine2/Prkcd | 10 |
| BP | GO:1900046 | regulation of hemostasis | 10/858 | 64/ 15881 | 0.00214118879501847 | 0.0341713105640575 | ENSMUSG00000021822/ENSMUSG00000027082/ ENSMUSG00000021457/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000002944/ ENSMUSG00000060459/ENSMUSG00000026580/ ENSMUSG00000026249/ENSMUSG00000021948 | Plau/Tfpi/Syk/Ubash3b/ Ceacam1/Cd36/Kng2/Selp/ Serpine2/Prkcd | 10 |
| BP | GO:0007266 | Rho protein signal transduction | 20/858 | 183/ 15881 | 0.00214374906163245 | 0.0341713105640575 | ENSMUSG00000031785/ENSMUSG00000039960/ ENSMUSG00000054855/ENSMUSG00000039621/ ENSMUSG00000020021/ENSMUSG00000030220/ ENSMUSG00000037999/ENSMUSG00000050541/ ENSMUSG00000034226/ENSMUSG00000031442/ ENSMUSG00000024013/ENSMUSG00000015243/ ENSMUSG00000028841/ENSMUSG00000002489/ ENSMUSG00000021895/ENSMUSG00000000120/ ENSMUSG00000024451/ENSMUSG00000020121/ ENSMUSG00000037509/ENSMUSG00000030433 | Adgrg1/Rhou/Rnd1/Prex1/ Fgd6/Arhgdib/Arap2/ Adra1b/Rhov/Mcf2l/Fgd2/ Abca1/Cnksr1/Tiam1/ Arhgef3/Ngfr/Arap3/ Srgap1/Arhgef4/Sbk2 | 20 |
| BP | GO:0044110 | growth involved in symbiotic interaction | 5/858 | 18/ 15881 | 0.00216085478926661 | 0.0341713105640575 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |
| BP | GO:0044116 | growth of symbiont involved in interaction with host | 5/858 | 18/ 15881 | 0.00216085478926661 | 0.0341713105640575 | ENSMUSG00000016024/ENSMUSG00000027995/ ENSMUSG00000055994/ENSMUSG00000002944/ ENSMUSG00000041515 | Lbp/Tlr2/Nod2/Cd36/Irf8 | 5 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0071677 | positive regulation of mononuclear cell migration | 5/858 | 18/15881 | 0.00216085478926661 | 0.0341713105640575 | ENSMUSG00000035385/ENSMUSG00000050335/ENSMUSG00000023913/ENSMUSG00000066755/ENSMUSG00000034855 | Ccl2/Lgals3/Pla2g7/Tnfsf18/Cxcl10 | 5 |
| BP | GO:2000379 | positive regulation of reactive oxygen species metabolic process | 12/858 | 86/15881 | 0.00219190357541935 | 0.0345315442876197 | ENSMUSG00000029380/ENSMUSG00000023067/ENSMUSG00000042677/ENSMUSG00000024066/ENSMUSG00000021822/ENSMUSG00000079685/ENSMUSG00000027995/ENSMUSG00000025889/ENSMUSG00000076441/ENSMUSG00000002944/ENSMUSG00000079164/ENSMUSG00000021948 | Cxcl1/Cdkn1a/Zc3h12a/Xdh/Plau/Ulbp1/Tlr2/Snca/Ass1/Cd36/Tlr5/Prkcd | 12 |
| BP | GO:0035296 | regulation of tube diameter | 15/858 | 121/15881 | 0.00220622382823213 | 0.0345315442876197 | ENSMUSG00000031778/ENSMUSG00000047250/ENSMUSG00000042429/ENSMUSG00000037580/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000020826/ENSMUSG00000032860/ENSMUSG00000029084/ENSMUSG00000050541/ENSMUSG00000021070/ENSMUSG00000028978/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000031489 | Cx3cl1/Ptgs1/Adora1/Gch1/Pde5a/Gja5/Nos2/P2ry2/Cd38/Adra1b/Bdkrb2/Nos3/Adora2a/P2rx1/Adrb3 | 15 |
| BP | GO:0097746 | regulation of blood vessel diameter | 15/858 | 121/15881 | 0.00220622382823213 | 0.0345315442876197 | ENSMUSG00000031778/ENSMUSG00000047250/ENSMUSG00000042429/ENSMUSG00000037580/ENSMUSG00000053965/ENSMUSG00000057123/ENSMUSG00000020826/ENSMUSG00000032860/ENSMUSG00000029084/ENSMUSG00000050541/ENSMUSG00000021070/ENSMUSG00000028978/ENSMUSG00000020178/ENSMUSG00000020787/ENSMUSG00000031489 | Cx3cl1/Ptgs1/Adora1/Gch1/Pde5a/Gja5/Nos2/P2ry2/Cd38/Adra1b/Bdkrb2/Nos3/Adora2a/P2rx1/Adrb3 | 15 |
| BP | GO:0036230 | granulocyte activation | 6/858 | 26/15881 | 0.00221601371584453 | 0.0345667989825273 | ENSMUSG00000021457/ENSMUSG00000026068/ENSMUSG00000029371/ENSMUSG00000021948/ENSMUSG00000034652/ENSMUSG00000025279 | Syk/Il18rap/Cxcl5/Prkcd/Cd300a/Dnase1l3 | 6 |
| BP | GO:0009611 | response to wounding | 35/858 | 390/15881 | 0.00227353553332968 | 0.0353438439181353 | ENSMUSG00000024164/ENSMUSG00000035385/ENSMUSG00000031778/ENSMUSG00000005089/ENSMUSG00000019850/ENSMUSG00000021822/ENSMUSG00000024743/ENSMUSG00000022144/ENSMUSG00000027082/ENSMUSG00000022676/ENSMUSG00000028128/ENSMUSG00000021457/ENSMUSG00000029373/ENSMUSG00000115388/ENSMUSG00000021469/ENSMUSG00000026177/ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000002944/ENSMUSG00000060459/ENSMUSG00000026580/ENSMUSG00000027611/ENSMUSG00000026249/ENSMUSG00000030468/ENSMUSG00000037362/ENSMUSG00000000120/ENSMUSG00000021256/ENSMUSG00000020787/ENSMUSG00000026109/ENSMUSG00000051379/ENSMUSG00000028475/ENSMUSG00000021948/ENSMUSG00000004266/ENSMUSG00000021998/ENSMUSG00000097636 | C3/Ccl2/Cx3cl1/Slc1a2/Tnfaip3/Plau/Syt7/Gdnf/Tfpi/Snai2/F3/Syk/Pf4/Eppk1/Msx2/Slc11a1/Ubash3b/Ceacam1/Cd36/Kng2/Selp/Procr/Serpine2/Siglecg/Nov/Ngfr/Vash1/P2rx1/Tmeff2/Flrt3/Spaar/Prkcd/Ptpn6/Lcp1/Mirt1 | 35 |
| BP | GO:0043062 | extracellular structure organization | 24/858 | 237/15881 | 0.00231645124249755 | 0.0358512656051958 | ENSMUSG00000027750/ENSMUSG00000059901/ENSMUSG00000026574/ENSMUSG00000017737/ENSMUSG00000050335/ENSMUSG00000021831/ENSMUSG00000018800/ENSMUSG00000057074/ | Postn/Adamts14/Dpt/Mmp9/Lgals3/Ero1l/Abca5/Ces1g/Pla2g7/Ces1d/Ctgf/Bcl3/Dmp1/ | 24 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000023913/ENSMUSG00000056973/ ENSMUSG00000019997/ENSMUSG00000053175/ ENSMUSG00000029307/ENSMUSG00000003051/ ENSMUSG00000033327/ENSMUSG00000041193/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000035258/ENSMUSG00000063765/ ENSMUSG00000024030/ENSMUSG00000050578/ ENSMUSG00000022483/ENSMUSG00000021998 | Elf3/Tnxb/Pla2g5/Abca1/ Cd36/Abi3bp/Chadl/ Abcg1/Mmp13/Col2a1/ Lcp1 | |
| BP | GO:0050906 | detection of stimulus involved in sensory perception | 13/858 | 98/ 15881 | 0.0023218111392811 | 0.0358512656051958 | ENSMUSG00000035873/ENSMUSG00000042429/ ENSMUSG00000035504/ENSMUSG00000062168/ ENSMUSG00000035916/ENSMUSG00000026249/ ENSMUSG00000042774/ENSMUSG00000064329/ ENSMUSG00000037418/ENSMUSG00000045381/ ENSMUSG00000062873/ENSMUSG00000046493/ ENSMUSG00000061972 | Pawr/Adora1/Reep6/ Ppef1/Ptprq/Serpine2/ Olfr1353/Scn1a/Best1/ Olfr433/Olfr1355/ Olfr1352/Olfr99 | 13 |
| BP | GO:0050856 | regulation of T cell receptor signaling pathway | 7/858 | 35/ 15881 | 0.00233332864309985 | 0.0359082052256909 | ENSMUSG00000050335/ENSMUSG00000035873/ ENSMUSG00000062300/ENSMUSG00000053216/ ENSMUSG00000109713/ENSMUSG00000004266/ ENSMUSG00000034652 | Lgals3/Pawr/Nectin2/ Btn2a2/Pvrig/Ptpn6/ Cd300a | 7 |
| BP | GO:0042391 | regulation of membrane potential | 32/858 | 348/ 15881 | 0.00235557361622772 | 0.0361292996789978 | ENSMUSG00000031778/ENSMUSG00000044303/ ENSMUSG00000035873/ENSMUSG00000042429/ ENSMUSG00000057123/ENSMUSG00000026576/ ENSMUSG00000040907/ENSMUSG00000057182/ ENSMUSG00000026251/ENSMUSG00000022416/ ENSMUSG00000024873/ENSMUSG00000031654/ ENSMUSG00000026253/ENSMUSG00000023243/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000075318/ ENSMUSG00000070570/ENSMUSG00000027674/ ENSMUSG00000064329/ENSMUSG00000024065/ ENSMUSG00000032066/ENSMUSG00000000120/ ENSMUSG00000020178/ENSMUSG00000020787/ ENSMUSG00000049044/ENSMUSG00000028020/ ENSMUSG00000041695/ENSMUSG00000027071/ ENSMUSG00000025888/ENSMUSG00000036570 | Cx3cl1/Cdkn2a/Pawr/ Adora1/Gja5/Atp1b1/ Atp1a3/Scn3a/Chrnd/ Cacna1i/Cnih2/Cbln1/ Chrng/Kcnk5/Akap6/Snca/ Atp1b2/Scn2a/Slc17a7/ Pex5l/Scn1a/Ehd3/Bco2/ Ngfr/Adora2a/P2rx1/ Rapgef4/Glrb/Kcnj2/ P2rx3/Casp1/Fxyd1 | 32 |
| BP | GO:0001505 | regulation of neurotransmitter levels | 25/858 | 251/ 15881 | 0.00238007276199455 | 0.0363833789550234 | ENSMUSG00000042677/ENSMUSG00000055368/ ENSMUSG00000026463/ENSMUSG00000006764/ ENSMUSG00000037580/ENSMUSG00000005089/ ENSMUSG00000020826/ENSMUSG00000024743/ ENSMUSG00000022144/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000025889/ ENSMUSG00000017969/ENSMUSG00000076441/ ENSMUSG00000002944/ENSMUSG00000070570/ ENSMUSG00000006235/ENSMUSG00000040046/ ENSMUSG00000028978/ENSMUSG00000020178/ ENSMUSG00000079164/ENSMUSG00000007034/ ENSMUSG00000054423/ENSMUSG00000043943/ ENSMUSG00000020081 | Zc3h12a/Slc6a2/Atp2b4/ Tph2/Gch1/Slc1a2/Nos2/ Syt7/Gdnf/Ulbp1/Tlr2/ Snca/Ptgis/Ass1/Cd36/ Slc17a7/Epor/Tph1/Nos3/ Adora2a/Tlr5/Slc44a4/ Cadps/Naalad2/Tacr2 | 25 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| BP | GO:0030168 | platelet activation | 10/858 | 65/15881 | 0.00241066331419337 | 0.0367285779365142 | ENSMUSG00000031778/ENSMUSG00000021457/ENSMUSG00000029373/ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000026580/ENSMUSG00000026249/ENSMUSG00000020787/ENSMUSG00000021948/ENSMUSG00000004266 | Cx3cl1/Syk/Pf4/Ubash3b/Ceacam1/Selp/Serpine2/P2rx1/Prkcd/Ptpn6 | 10 |
| BP | GO:0019724 | B cell mediated immunity | 12/858 | 87/15881 | 0.00242064114459723 | 0.0367584777785526 | ENSMUSG00000024164/ENSMUSG00000024610/ENSMUSG00000024778/ENSMUSG00000000732/ENSMUSG00000062300/ENSMUSG00000053175/ENSMUSG00000055994/ENSMUSG00000079343/ENSMUSG00000075370/ENSMUSG00000021948/ENSMUSG00000004266/ENSMUSG00000034266 | C3/Cd74/Fas/Icosl/Nectin2/Bcl3/Nod2/C1s2/Igll1/Prkcd/Ptpn6/Batf | 12 |
| BP | GO:0000041 | transition metal ion transport | 11/858 | 76/15881 | 0.00246041213609845 | 0.037116612026801 | ENSMUSG00000012428/ENSMUSG00000003617/ENSMUSG00000023030/ENSMUSG00000020432/ENSMUSG00000066152/ENSMUSG00000022032/ENSMUSG00000032839/ENSMUSG00000026177/ENSMUSG00000063354/ENSMUSG00000029716/ENSMUSG00000031936 | Steap4/Cp/Slc11a2/Tcn2/Slc31a2/Scara5/Trpc1/Slc11a1/Slc39a4/Tfr2/Hephl1 | 11 |
| BP | GO:1902106 | negative regulation of leukocyte differentiation | 11/858 | 76/15881 | 0.00246041213609845 | 0.037116612026801 | ENSMUSG00000023367/ENSMUSG00000024610/ENSMUSG00000029810/ENSMUSG00000044303/ENSMUSG00000049577/ENSMUSG00000032501/ENSMUSG00000066755/ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000031548/ENSMUSG00000020325 | Tmem176a/Cd74/Tmem176b/Cdkn2a/Zfpm1/Trib1/Tnfsf18/Ubash3b/Ceacam1/Sfrp1/Fstl3 | 11 |
| BP | GO:0045428 | regulation of nitric oxide biosynthetic process | 9/858 | 55/15881 | 0.00254469654133343 | 0.037960058516757 | ENSMUSG00000042677/ENSMUSG00000026463/ENSMUSG00000079685/ENSMUSG00000027995/ENSMUSG00000017969/ENSMUSG00000076441/ENSMUSG00000002944/ENSMUSG00000006235/ENSMUSG00000079164 | Zc3h12a/Atp2b4/Ulbp1/Tlr2/Ptgis/Ass1/Cd36/Epor/Tlr5 | 9 |
| BP | GO:0060401 | cytosolic calcium ion transport | 16/858 | 135/15881 | 0.00254828427618717 | 0.037960058516757 | ENSMUSG00000035873/ENSMUSG00000021831/ENSMUSG00000019997/ENSMUSG00000032839/ENSMUSG00000022416/ENSMUSG00000027994/ENSMUSG00000061603/ENSMUSG00000025889/ENSMUSG00000032020/ENSMUSG00000041046/ENSMUSG00000034855/ENSMUSG00000030523/ENSMUSG00000004266/ENSMUSG00000030707/ENSMUSG00000044338/ENSMUSG00000038239 | Pawr/Ero1l/Ctgf/Trpc1/Cacna1i/Mcub/Akap6/Snca/Ubash3b/Ramp3/Cxcl10/Trpm1/Ptpn6/Coro1a/Aplnr/Hrc | 16 |
| BP | GO:0098742 | cell-cell adhesion via plasma-membrane adhesion molecules | 16/858 | 135/15881 | 0.00254828427618717 | 0.037960058516757 | ENSMUSG00000031778/ENSMUSG00000090523/ENSMUSG00000022636/ENSMUSG00000019850/ENSMUSG00000054793/ENSMUSG00000062300/ENSMUSG00000022512/ENSMUSG00000031654/ENSMUSG00000051375/ENSMUSG00000074272/ENSMUSG00000026580/ENSMUSG00000052516/ENSMUSG00000053141/ENSMUSG00000008153/ENSMUSG00000051379/ENSMUSG00000028519 | Cx3cl1/Gypc/Alcam/Tnfaip3/Cadm4/Nectin2/Cldn1/Cbln1/Pcdh1/Ceacam1/Selp/Robo2/Ptprt/Clstn3/Flrt3/Dab1 | 16 |
| BP | GO:0032651 | regulation of interleukin-1 beta production | 8/858 | 45/15881 | 0.0025494326260709 | 0.037960058516757 | ENSMUSG00000042677/ENSMUSG00000033538/ENSMUSG00000019850/ENSMUSG00000027995/ENSMUSG00000055994/ENSMUSG00000037860/ENSMUSG00000071203/ENSMUSG00000025888 | Zc3h12a/Casp4/Tnfaip3/Tlr2/Nod2/Aim2/Naip5/Casp1 | 8 |
| BP | GO:0048871 | multicellular organismal homeostasis | 27/858 | 280/15881 | 0.00258892284483278 | 0.0382842032084685 | ENSMUSG00000023030/ENSMUSG00000042429/ENSMUSG00000040612/ENSMUSG00000019577/ | Slc11a2/Adora1/Ildr2/Pdk4/Cd38/Acacb/Ctgf/ | 27 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000029084/ENSMUSG00000042010/ ENSMUSG00000019997/ENSMUSG00000021457/ ENSMUSG00000022510/ENSMUSG00000022512/ ENSMUSG00000029167/ENSMUSG00000055994/ ENSMUSG00000032359/ENSMUSG00000026177/ ENSMUSG00000032020/ENSMUSG00000074272/ ENSMUSG00000028825/ENSMUSG00000002944/ ENSMUSG00000020892/ENSMUSG00000072437/ ENSMUSG00000040329/ENSMUSG00000063415/ ENSMUSG00000034829/ENSMUSG00000022483/ ENSMUSG00000031489/ENSMUSG00000002204/ ENSMUSG00000030707 | Syk/Trp63/Cldn1/ Ppargc1a/Nod2/Ctsh/ Slc11a1/Ubash3b/ Ceacam1/Rhd/Cd36/ Aloxe3/Nanos1/Il7/ Cyp26b1/Nxnl1/Col2a1/ Adrb3/Napsa/Coro1a | |
| BP | GO:0002244 | hematopoietic progenitor cell differentiation | 15/858 | 123/ 15881 | 0.00259317707209265 | 0.0382842032084685 | ENSMUSG00000071637/ENSMUSG00000028931/ ENSMUSG00000022034/ENSMUSG00000029851/ ENSMUSG00000048826/ENSMUSG00000035916/ ENSMUSG00000048416/ENSMUSG00000031548/ ENSMUSG00000030468/ENSMUSG00000031125/ ENSMUSG00000043157/ENSMUSG00000004266/ ENSMUSG00000020325/ENSMUSG00000068748/ ENSMUSG00000034266 | Cebpd/Kcnab2/Esco2/ Tcaf2/Dact2/Ptprq/Mlf1/ Sfrp1/Siglecg/ 3830403N18Rik/Arl11/ Ptpn6/Fstl3/Ptprz1/Batf | 15 |
| BP | GO:0050671 | positive regulation of lymphocyte proliferation | 14/858 | 111/ 15881 | 0.0025962466632869 | 0.0382842032084685 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000074272/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000039323/ ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Cdkn1a/Icosl/Bst1/ Cd38/Syk/Cd80/Ceacam1/ Il12rb1/Il15/Il7/Igfbp2/ Coro1a/Zap70 | 14 |
| BP | GO:0051271 | negative regulation of cellular component movement | 25/858 | 253/ 15881 | 0.00264789280319661 | 0.0388493871732586 | ENSMUSG00000031778/ENSMUSG00000026185/ ENSMUSG00000000753/ENSMUSG00000031785/ ENSMUSG00000042429/ENSMUSG00000038387/ ENSMUSG00000062991/ENSMUSG00000025207/ ENSMUSG00000032501/ENSMUSG00000030220/ ENSMUSG00000021596/ENSMUSG00000026921/ ENSMUSG00000029167/ENSMUSG00000115388/ ENSMUSG00000024873/ENSMUSG00000074715/ ENSMUSG00000031548/ENSMUSG00000037362/ ENSMUSG00000024451/ENSMUSG00000020121/ ENSMUSG00000021256/ENSMUSG00000026109/ ENSMUSG00000019278/ENSMUSG00000053318/ ENSMUSG00000034652 | Cx3cl1/Igfbp5/Serpinf1/ Adgrg1/Adora1/Rras/Nrg1/ Sema4g/Trib1/Arhgdib/ Mctp1/Egfl7/Ppargc1a/ Eppk1/Cnih2/Ccl28/Sfrp1/ Nov/Arap3/Srgap1/Vash1/ Tmeff2/Dpep1/Slamf8/ Cd300a | 25 |
| BP | GO:2000146 | negative regulation of cell motility | 23/858 | 226/ 15881 | 0.00265308653152312 | 0.0388493871732586 | ENSMUSG00000031778/ENSMUSG00000026185/ ENSMUSG00000000753/ENSMUSG00000031785/ ENSMUSG00000042429/ENSMUSG00000038387/ ENSMUSG00000062991/ENSMUSG00000032501/ ENSMUSG00000030220/ENSMUSG00000021596/ ENSMUSG00000026921/ENSMUSG00000029167/ ENSMUSG00000115388/ENSMUSG00000074715/ ENSMUSG00000031548/ENSMUSG00000037362/ ENSMUSG00000024451/ENSMUSG00000020121/ ENSMUSG00000021256/ENSMUSG00000026109/ | Cx3cl1/Igfbp5/Serpinf1/ Adgrg1/Adora1/Rras/Nrg1/ Trib1/Arhgdib/Mctp1/ Egfl7/Ppargc1a/Eppk1/ Ccl28/Sfrp1/Nov/Arap3/ Srgap1/Vash1/Tmeff2/ Dpep1/Slamf8/Cd300a | 23 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000019278/ENSMUSG00000053318/ ENSMUSG00000034652 | | |
| BP | GO:0002526 | acute inflammatory response | 12/858 | 88/ 15881 | 0.00266845986907467 | 0.0388493871732586 | ENSMUSG00000024164/ENSMUSG00000029380/ ENSMUSG00000016024/ENSMUSG00000037440/ ENSMUSG00000042429/ENSMUSG00000028128/ ENSMUSG00000040026/ENSMUSG00000021070/ ENSMUSG00000025494/ENSMUSG00000060063/ ENSMUSG00000074115/ENSMUSG00000025279 | C3/Cxcl1/Lbp/Vnn1/ Adora1/F3/Saa3/Bdkrb2/ Sigirr/Alox5ap/Saa1/ Dnase1l3 | 12 |
| BP | GO:0042089 | cytokine biosynthetic process | 12/858 | 88/ 15881 | 0.00266845986907467 | 0.0388493871732586 | ENSMUSG00000016024/ENSMUSG00000000732/ ENSMUSG00000049577/ENSMUSG00000035873/ ENSMUSG00000022514/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000053175/ENSMUSG00000025494/ ENSMUSG00000031438/ENSMUSG00000028602 | Lbp/Icosl/Zfpm1/Pawr/ Il1rap/Ccl20/Tlr2/Syk/ Bcl3/Sigirr/Rnf128/Tnfrsf8 | 12 |
| BP | GO:0050730 | regulation of peptidyl-tyrosine phosphorylation | 22/858 | 213/ 15881 | 0.00270711722506927 | 0.0392380339179686 | ENSMUSG00000024610/ENSMUSG00000029082/ ENSMUSG00000042429/ENSMUSG00000062991/ ENSMUSG00000022144/ENSMUSG00000021892/ ENSMUSG00000034394/ENSMUSG00000046733/ ENSMUSG00000021457/ENSMUSG00000006435/ ENSMUSG00000055994/ENSMUSG00000075122/ ENSMUSG00000066755/ENSMUSG00000031520/ ENSMUSG00000002944/ENSMUSG00000031548/ ENSMUSG00000031712/ENSMUSG00000028864/ ENSMUSG00000021948/ENSMUSG00000004266/ ENSMUSG00000068748/ENSMUSG00000034652 | Cd74/Bst1/Adora1/Nrg1/ Gdnf/Sh3bp5/Lif/Gprc5a/ Syk/Neurl1a/Nod2/Cd80/ Tnfsf18/Vegfc/Cd36/Sfrp1/ Il15/Hgf/Prkcd/Ptpn6/ Ptprz1/Cd300a | 22 |
| BP | GO:0002455 | humoral immune response mediated by circulating immunoglobulin | 6/858 | 27/ 15881 | 0.00272082311075316 | 0.0392380339179686 | ENSMUSG00000024164/ENSMUSG00000053175/ ENSMUSG00000055994/ENSMUSG00000079343/ ENSMUSG00000075370/ENSMUSG00000004266 | C3/Bcl3/Nod2/C1s2/Igll1/ Ptpn6 | 6 |
| BP | GO:0043171 | peptide catabolic process | 6/858 | 27/ 15881 | 0.00272082311075316 | 0.0392380339179686 | ENSMUSG00000028024/ENSMUSG00000006344/ ENSMUSG00000032359/ENSMUSG00000024481/ ENSMUSG00000040471/ENSMUSG00000050578 | Enpep/Ggt5/Ctsh/Lvrn/ Ggt6/Mmp13 | 6 |
| BP | GO:0006140 | regulation of nucleotide metabolic process | 16/858 | 136/ 15881 | 0.00274727768142211 | 0.0392409591224036 | ENSMUSG00000006457/ENSMUSG00000016194/ ENSMUSG00000003541/ENSMUSG00000053965/ ENSMUSG00000020826/ENSMUSG00000024039/ ENSMUSG00000028755/ENSMUSG00000029167/ ENSMUSG00000029373/ENSMUSG00000034353/ ENSMUSG00000061603/ENSMUSG00000040133/ ENSMUSG00000041046/ENSMUSG00000034855/ ENSMUSG00000028978/ENSMUSG00000052276 | Actn3/Hsd11b1/Ier3/ Pde5a/Nos2/Cbs/Cda/ Ppargc1a/Pf4/Ramp1/ Akap6/Gpr176/Ramp3/ Cxcl10/Nos3/Ostn | 16 |
| BP | GO:0030801 | positive regulation of cyclic nucleotide metabolic process | 7/858 | 36/ 15881 | 0.00276380937560758 | 0.0392409591224036 | ENSMUSG00000020826/ENSMUSG00000029373/ ENSMUSG00000034353/ENSMUSG00000041046/ ENSMUSG00000034855/ENSMUSG00000028978/ ENSMUSG00000052276 | Nos2/Pf4/Ramp1/Ramp3/ Cxcl10/Nos3/Ostn | 7 |
| BP | GO:0032732 | positive regulation of interleukin-1 production | 7/858 | 36/ 15881 | 0.00276380937560758 | 0.0392409591224036 | ENSMUSG00000033538/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000055994/ ENSMUSG00000037860/ENSMUSG00000071203/ ENSMUSG00000025888 | Casp4/Ccl20/Tlr2/Nod2/ Aim2/Naip5/Casp1 | 7 |
| BP | GO:0048247 | lymphocyte chemotaxis | 7/858 | 36/ 15881 | 0.00276380937560758 | 0.0392409591224036 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000026166/ | Ccl2/Cx3cl1/Ccl7/Ccl20/ Ccl9/Cxcl10/Ccl17 | 7 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000019122/ENSMUSG00000034855/ ENSMUSG00000031780 | | |
| BP | GO:0050853 | B cell receptor signaling pathway | 7/858 | 36/ 15881 | 0.00276380937560758 | 0.0392409591224036 | ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000075370/ENSMUSG00000021108/ ENSMUSG00000024696/ENSMUSG00000004266/ ENSMUSG00000034652 | Cd38/Syk/Igll1/Prkch/ Lpxn/Ptpn6/Cd300a | 7 |
| BP | GO:0010884 | positive regulation of lipid storage | 5/858 | 19/ 15881 | 0.00280361384375021 | 0.0395953814769855 | ENSMUSG00000024164/ENSMUSG00000042677/ ENSMUSG00000042010/ENSMUSG00000002944/ ENSMUSG00000025044 | C3/Zc3h12a/Acacb/Cd36/ Msr1 | 5 |
| BP | GO:0043270 | positive regulation of ion transport | 23/858 | 227/ 15881 | 0.00280603989969915 | 0.0395953814769855 | ENSMUSG00000029380/ENSMUSG00000050335/ ENSMUSG00000037685/ENSMUSG00000042429/ ENSMUSG00000032860/ENSMUSG00000026576/ ENSMUSG00000020333/ENSMUSG00000032839/ ENSMUSG00000003484/ENSMUSG00000061603/ ENSMUSG00000025889/ENSMUSG00000041329/ ENSMUSG00000041245/ENSMUSG00000041046/ ENSMUSG00000034855/ENSMUSG00000024065/ ENSMUSG00000020178/ENSMUSG00000020787/ ENSMUSG00000041695/ENSMUSG00000021948/ ENSMUSG00000036570/ENSMUSG00000044338/ ENSMUSG00000020081 | Cxcl1/Lgals3/Atp8a1/ Adora1/P2ry2/Atp1b1/ Acsl6/Trpc1/Cyp4f18/ Akap6/Snca/Atp1b2/ Wnk3/Ramp3/Cxcl10/ Ehd3/Adora2a/P2rx1/ Kcnj2/Prkcd/Fxyd1/Aplnr/ Tacr2 | 23 |
| BP | GO:0019935 | cyclic-nucleotide-mediated signaling | 14/858 | 112/ 15881 | 0.00282356237197936 | 0.0397204203616483 | ENSMUSG00000026463/ENSMUSG00000050541/ ENSMUSG00000029373/ENSMUSG00000034353/ ENSMUSG00000015243/ENSMUSG00000002944/ ENSMUSG00000027674/ENSMUSG00000041046/ ENSMUSG00000034855/ENSMUSG00000020178/ ENSMUSG00000049044/ENSMUSG00000059588/ ENSMUSG00000031489/ENSMUSG00000044338 | Atp2b4/Adra1b/Pf4/ Ramp1/Abca1/Cd36/ Pex5l/Ramp3/Cxcl10/ Adora2a/Rapgef4/Calcrl/ Adrb3/Aplnr | 14 |
| BP | GO:0001676 | long-chain fatty acid metabolic process | 9/858 | 56/ 15881 | 0.00288974515629302 | 0.0404035709962189 | ENSMUSG00000047250/ENSMUSG00000020333/ ENSMUSG00000019806/ENSMUSG00000025002/ ENSMUSG00000003484/ENSMUSG00000002944/ ENSMUSG00000052974/ENSMUSG00000020892/ ENSMUSG00000025197 | Ptgs1/Acsl6/Aig1/ Cyp2c55/Cyp4f18/Cd36/ Cyp2f2/Aloxe3/Cyp2c23 | 9 |
| BP | GO:0032890 | regulation of organic acid transport | 9/858 | 56/ 15881 | 0.00288974515629302 | 0.0404035709962189 | ENSMUSG00000042429/ENSMUSG00000032860/ ENSMUSG00000020333/ENSMUSG00000021457/ ENSMUSG00000003484/ENSMUSG00000025889/ ENSMUSG00000020178/ENSMUSG00000025557/ ENSMUSG00000036570 | Adora1/P2ry2/Acsl6/Syk/ Cyp4f18/Snca/Adora2a/ Slc15a1/Fxyd1 | 9 |
| BP | GO:0046851 | negative regulation of bone remodeling | 4/858 | 12/ 15881 | 0.00295369428976226 | 0.0410474000389386 | ENSMUSG00000029084/ENSMUSG00000032020/ ENSMUSG00000074272/ENSMUSG00000031548 | Cd38/Ubash3b/Ceacam1/ Sfrp1 | 4 |
| BP | GO:0055119 | relaxation of cardiac muscle | 4/858 | 12/ 15881 | 0.00295369428976226 | 0.0410474000389386 | ENSMUSG00000053965/ENSMUSG00000026576/ ENSMUSG00000061603/ENSMUSG00000041695 | Pde5a/Atp1b1/Akap6/ Kcnj2 | 4 |
| BP | GO:0031644 | regulation of neurological system process | 10/858 | 67/ 15881 | 0.00303104895763129 | 0.0419951375217435 | ENSMUSG00000032561/ENSMUSG00000035873/ ENSMUSG00000042429/ENSMUSG00000062991/ ENSMUSG00000037362/ENSMUSG00000000120/ ENSMUSG00000049044/ENSMUSG00000028602/ ENSMUSG00000027071/ENSMUSG00000028864 | Acpp/Pawr/Adora1/Nrg1/ Nov/Ngfr/Rapgef4/Tnfrsf8/ P2rx3/Hgf | 10 |
| BP | GO:0032946 | positive regulation of mononuclear cell proliferation | 14/858 | 113/ 15881 | 0.00306696343098743 | 0.0423647418509288 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000029084/ENSMUSG00000021457/ | Cd74/Cdkn1a/Icosl/Bst1/ Cd38/Syk/Cd80/Ceacam1/ | 14 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000075122/ENSMUSG00000074272/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000039323/ ENSMUSG00000030707/ENSMUSG00000026117 | Il12rb1/Il15/Il7/Igfbp2/ Coro1a/Zap70 | |
| BP | GO:0002699 | positive regulation of immune effector process | 18/858 | 163/ 15881 | 0.0031172595275525 | 0.0429301867668341 | ENSMUSG00000024164/ENSMUSG00000024610/ ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000016024/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000026068/ ENSMUSG00000055994/ENSMUSG00000017830/ ENSMUSG00000074272/ENSMUSG00000020641/ ENSMUSG00000002944/ENSMUSG00000034652 | C3/Cd74/Cxcl1/H2-D1/ Ccl2/H2-K1/Lbp/Nectin2/ Ulbp1/Tlr2/Syk/Il18rap/ Nod2/Dhx58/Ceacam1/ Rsad2/Cd36/Cd300a | 18 |
| BP | GO:0007204 | positive regulation of cytosolic calcium ion concentration | 23/858 | 229/ 15881 | 0.00313436383782651 | 0.0430365046714741 | ENSMUSG00000029380/ENSMUSG00000035873/ ENSMUSG00000021831/ENSMUSG00000032860/ ENSMUSG00000029084/ENSMUSG00000032839/ ENSMUSG00000050541/ENSMUSG00000022416/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000032020/ENSMUSG00000074715/ ENSMUSG00000002944/ENSMUSG00000060459/ ENSMUSG00000021070/ENSMUSG00000041046/ ENSMUSG00000006235/ENSMUSG00000034855/ ENSMUSG00000030523/ENSMUSG00000004266/ ENSMUSG00000030707/ENSMUSG00000044338/ ENSMUSG00000038239 | Cxcl1/Pawr/Ero1l/P2ry2/ Cd38/Trpc1/Adra1b/ Cacna1i/Akap6/Snca/ Ubash3b/Ccl28/Cd36/ Kng2/Bdkrb2/Ramp3/ Epor/Cxcl10/Trpm1/ Ptpn6/Coro1a/Aplnr/Hrc | 23 |
| BP | GO:0034765 | regulation of ion transmembrane transport | 31/858 | 341/ 15881 | 0.00324649881831469 | 0.0443456499979914 | ENSMUSG00000066152/ENSMUSG00000026463/ ENSMUSG00000017737/ENSMUSG00000057123/ ENSMUSG00000028931/ENSMUSG00000026576/ ENSMUSG00000020333/ENSMUSG00000029851/ ENSMUSG00000032839/ENSMUSG00000029167/ ENSMUSG00000050777/ENSMUSG00000024873/ ENSMUSG00000061603/ENSMUSG00000025889/ ENSMUSG00000041329/ENSMUSG00000032020/ ENSMUSG00000041245/ENSMUSG00000028214/ ENSMUSG00000041046/ENSMUSG00000009687/ ENSMUSG00000064329/ENSMUSG00000053395/ ENSMUSG00000034855/ENSMUSG00000024065/ ENSMUSG00000041695/ENSMUSG00000018470/ ENSMUSG00000004266/ENSMUSG00000036570/ ENSMUSG00000030707/ENSMUSG00000044338/ ENSMUSG00000038239 | Slc31a2/Atp2b4/Mmp9/ Gja5/Kcnab2/Atp1b1/ Acsl6/Tcaf2/Trpc1/ Ppargc1a/Tmem37/Cnih2/ Akap6/Snca/Atp1b2/ Ubash3b/Wnk3/Gem/ Ramp3/Fxyd5/Scn1a/ Cacng8/Cxcl10/Ehd3/ Kcnj2/Kcnab3/Ptpn6/ Fxyd1/Coro1a/Aplnr/Hrc | 31 |
| BP | GO:0001912 | positive regulation of leukocyte mediated cytotoxicity | 7/858 | 37/ 15881 | 0.00325264204988118 | 0.0443456499979914 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000062300/ENSMUSG00000079685/ ENSMUSG00000026068 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nectin2/Ulbp1/Il18rap | 7 |
| BP | GO:0002532 | production of molecular mediator involved in inflammatory response | 9/858 | 57/ 15881 | 0.00327070499203229 | 0.0443456499979914 | ENSMUSG00000016024/ENSMUSG00000042677/ ENSMUSG00000020826/ENSMUSG00000021457/ ENSMUSG00000055994/ENSMUSG00000060063/ ENSMUSG00000020787/ENSMUSG00000053318/ ENSMUSG00000034652 | Lbp/Zc3h12a/Nos2/Syk/ Nod2/Alox5ap/P2rx1/ Slamf8/Cd300a | 9 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| BP | GO:0010543 | regulation of platelet activation | 6/858 | 28/15881 | 0.00330706766230114 | 0.0443456499979914 | ENSMUSG00000021457/ENSMUSG00000032020/ENSMUSG00000074272/ENSMUSG00000026580/ENSMUSG00000026249/ENSMUSG00000021948 | Syk/Ubash3b/Ceacam1/Selp/Serpine2/Prkcd | 6 |
| BP | GO:0019369 | arachidonic acid metabolic process | 6/858 | 28/15881 | 0.00330706766230114 | 0.0443456499979914 | ENSMUSG00000047250/ENSMUSG00000025002/ENSMUSG00000003484/ENSMUSG00000052974/ENSMUSG00000020892/ENSMUSG00000025197 | Ptgs1/Cyp2c55/Cyp4f18/Cyp2f2/Aloxe3/Cyp2c23 | 6 |
| BP | GO:0043368 | positive T cell selection | 6/858 | 28/15881 | 0.00330706766230114 | 0.0443456499979914 | ENSMUSG00000024610/ENSMUSG00000066755/ENSMUSG00000049109/ENSMUSG00000048251/ENSMUSG00000034266/ENSMUSG00000026117 | Cd74/Tnfsf18/Themis/Bcl11b/Batf/Zap70 | 6 |
| BP | GO:0046633 | alpha-beta T cell proliferation | 6/858 | 28/15881 | 0.00330706766230114 | 0.0443456499979914 | ENSMUSG00000021457/ENSMUSG00000075122/ENSMUSG00000074272/ENSMUSG00000031712/ENSMUSG00000052013/ENSMUSG00000026117 | Syk/Cd80/Ceacam1/Il15/Btla/Zap70 | 6 |
| BP | GO:0050706 | regulation of interleukin-1 beta secretion | 6/858 | 28/15881 | 0.00330706766230114 | 0.0443456499979914 | ENSMUSG00000042677/ENSMUSG00000033538/ENSMUSG00000027995/ENSMUSG00000055994/ENSMUSG00000037860/ENSMUSG00000025888 | Zc3h12a/Casp4/Tlr2/Nod2/Aim2/Casp1 | 6 |
| BP | GO:0050803 | regulation of synapse structure or activity | 18/858 | 164/15881 | 0.00333005811052573 | 0.0444418604677112 | ENSMUSG00000026825/ENSMUSG00000022514/ENSMUSG00000027995/ENSMUSG00000006435/ENSMUSG00000057897/ENSMUSG00000031654/ENSMUSG00000025889/ENSMUSG00000055003/ENSMUSG00000070570/ENSMUSG00000027296/ENSMUSG00000002104/ENSMUSG00000002489/ENSMUSG00000033214/ENSMUSG00000008153/ENSMUSG00000051379/ENSMUSG00000036295/ENSMUSG00000002341/ENSMUSG00000043051 | Dnm1/Il1rap/Tlr2/Neurl1a/Camk2b/Cbln1/Snca/Lrtm2/Slc17a7/Itpka/Rapsn/Tiam1/Slitrk5/Clstn3/Flrt3/Lrrn3/Ncan/Disc1 | 18 |
| BP | GO:0050673 | epithelial cell proliferation | 32/858 | 356/15881 | 0.00334574204581342 | 0.0444418604677112 | ENSMUSG00000035385/ENSMUSG00000026185/ENSMUSG00000000753/ENSMUSG00000022150/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000019850/ENSMUSG00000021822/ENSMUSG00000022676/ENSMUSG00000028128/ENSMUSG00000022510/ENSMUSG00000036585/ENSMUSG00000026921/ENSMUSG00000007805/ENSMUSG00000055994/ENSMUSG00000115388/ENSMUSG00000056758/ENSMUSG00000028640/ENSMUSG00000031520/ENSMUSG00000041351/ENSMUSG00000074272/ENSMUSG00000029754/ENSMUSG00000017724/ENSMUSG00000031548/ENSMUSG00000037362/ENSMUSG00000000120/ENSMUSG00000021256/ENSMUSG00000004231/ENSMUSG00000048251/ENSMUSG00000012350/ENSMUSG00000038259/ENSMUSG00000044338 | Ccl2/Igfbp5/Serpinf1/Dab2/Xdh/Cdkn2a/Tnfaip3/Plau/Snai2/F3/Trp63/Fgf1/Egfl7/Twist2/Nod2/Eppk1/Hmga2/Tfap2c/Vegfc/Rap1gap/Ceacam1/Dlx6/Etv4/Sfrp1/Nov/Ngfr/Vash1/Pax2/Bcl11b/Ehf/Gdf5/Aplnr | 32 |
| BP | GO:0042100 | B cell proliferation | 11/858 | 79/15881 | 0.00335355768919327 | 0.0444418604677112 | ENSMUSG00000024610/ENSMUSG00000023067/ENSMUSG00000044303/ENSMUSG00000029082/ENSMUSG00000035873/ENSMUSG00000029084/ENSMUSG00000027985/ENSMUSG00000040329/ENSMUSG00000052013/ENSMUSG00000021948/ENSMUSG00000034652 | Cd74/Cdkn1a/Cdkn2a/Bst1/Pawr/Cd38/Lef1/Il7/Btla/Prkcd/Cd300a | 11 |
| BP | GO:0001933 | negative regulation of protein phosphorylation | 34/858 | 385/15881 | 0.00336844405070206 | 0.0444418604677112 | ENSMUSG00000023067/ENSMUSG00000042677/ENSMUSG00000022150/ENSMUSG00000024066/ENSMUSG00000044303/ENSMUSG00000022103/ENSMUSG00000039621/ENSMUSG00000019850/ | Cdkn1a/Zc3h12a/Dab2/Xdh/Cdkn2a/Gfra2/Prex1/Tnfaip3/Trib1/Inpp5j/Sh3bp5/Lif/Gprc5a/ | 34 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000032501/ENSMUSG00000034570/ ENSMUSG00000021892/ENSMUSG00000034394/ ENSMUSG00000046733/ENSMUSG00000019823/ ENSMUSG00000012889/ENSMUSG00000079363/ ENSMUSG00000029167/ENSMUSG00000025665/ ENSMUSG00000026483/ENSMUSG00000053216/ ENSMUSG00000025889/ENSMUSG00000032020/ ENSMUSG00000055003/ENSMUSG00000074272/ ENSMUSG00000021070/ENSMUSG00000031548/ ENSMUSG00000020178/ENSMUSG00000039661/ ENSMUSG00000028864/ENSMUSG00000051379/ ENSMUSG00000024427/ENSMUSG00000021948/ ENSMUSG00000004266/ENSMUSG00000034652 | Mical1/Podnl1/Gbp4/ Ppargc1a/Rps6ka6/ Fam129a/Btn2a2/Snca/ Ubash3b/Lrtm2/Ceacam1/ Bdkrb2/Sfrp1/Adora2a/ Dusp26/Hgf/Flrt3/Spry4/ Prkcd/Ptpn6/Cd300a | |
| BP | GO:0006801 | superoxide metabolic process | 8/858 | 47/ 15881 | 0.00338207791173816 | 0.0444418604677112 | ENSMUSG00000029380/ENSMUSG00000037580/ ENSMUSG00000020826/ENSMUSG00000021457/ ENSMUSG00000024039/ENSMUSG00000002944/ ENSMUSG00000028978/ENSMUSG00000021948 | Cxcl1/Gch1/Nos2/Syk/ Cbs/Cd36/Nos3/Prkcd | 8 |
| BP | GO:0031343 | positive regulation of cell killing | 8/858 | 47/ 15881 | 0.00338207791173816 | 0.0444418604677112 | ENSMUSG00000029380/ENSMUSG00000073411/ ENSMUSG00000035385/ENSMUSG00000061232/ ENSMUSG00000020826/ENSMUSG00000062300/ ENSMUSG00000079685/ENSMUSG00000026068 | Cxcl1/H2-D1/Ccl2/H2-K1/ Nos2/Nectin2/Ulbp1/ Il18rap | 8 |
| BP | GO:0032720 | negative regulation of tumor necrosis factor production | 8/858 | 47/ 15881 | 0.00338207791173816 | 0.0444418604677112 | ENSMUSG00000029816/ENSMUSG00000016024/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000019850/ENSMUSG00000053175/ ENSMUSG00000007805/ENSMUSG00000055994 | Gpnmb/Lbp/Trim30a/ Zc3h12a/Tnfaip3/Bcl3/ Twist2/Nod2 | 8 |
| BP | GO:0051048 | negative regulation of secretion | 20/858 | 191/ 15881 | 0.0035293658472873 | 0.0462268956322619 | ENSMUSG00000024610/ENSMUSG00000031778/ ENSMUSG00000042677/ENSMUSG00000028965/ ENSMUSG00000020806/ENSMUSG00000047250/ ENSMUSG00000042429/ENSMUSG00000034394/ ENSMUSG00000004347/ENSMUSG00000053216/ ENSMUSG00000003484/ENSMUSG00000025889/ ENSMUSG00000020641/ENSMUSG00000090958/ ENSMUSG00000041245/ENSMUSG00000031548/ ENSMUSG00000037362/ENSMUSG00000000706/ ENSMUSG00000034652/ENSMUSG00000020081 | Cd74/Cx3cl1/Zc3h12a/ Tnfrsf9/Rhbdf2/Ptgs1/ Adora1/Lif/Pde1c/Btn2a2/ Cyp4f18/Snca/Rsad2/ Lrrc32/Wnk3/Sfrp1/Nov/ Btn1a1/Cd300a/Tacr2 | 20 |
| BP | GO:0042107 | cytokine metabolic process | 12/858 | 91/ 15881 | 0.00353808119645092 | 0.0462268956322619 | ENSMUSG00000016024/ENSMUSG00000000732/ ENSMUSG00000049577/ENSMUSG00000035873/ ENSMUSG00000022514/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000053175/ENSMUSG00000025494/ ENSMUSG00000031438/ENSMUSG00000028602 | Lbp/Icosl/Zfpm1/Pawr/ Il1rap/Ccl20/Tlr2/Syk/ Bcl3/Sigirr/Rnf128/Tnfrsf8 | 12 |
| BP | GO:1905952 | regulation of lipid localization | 14/858 | 115/ 15881 | 0.00360538405126218 | 0.0469426198710991 | ENSMUSG00000024164/ENSMUSG00000042677/ ENSMUSG00000022150/ENSMUSG00000037685/ ENSMUSG00000032860/ENSMUSG00000020333/ ENSMUSG00000042010/ENSMUSG00000021457/ ENSMUSG00000003484/ENSMUSG00000015243/ ENSMUSG00000002944/ENSMUSG00000024030/ ENSMUSG00000025044/ENSMUSG00000021948 | C3/Zc3h12a/Dab2/Atp8a1/ P2ry2/Acsl6/Acacb/Syk/ Cyp4f18/Abca1/Cd36/ Abcg1/Msr1/Prkcd | 14 |
| BP | GO:0009187 | cyclic nucleotide metabolic process | 13/858 | 103/ 15881 | 0.00361333292945879 | 0.0469426198710991 | ENSMUSG00000053965/ENSMUSG00000020826/ ENSMUSG00000024039/ENSMUSG00000029373/ | Pde5a/Nos2/Cbs/Pf4/ Pde1c/Ramp1/Akap6/ | 13 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000004347/ENSMUSG00000034353/ ENSMUSG00000061603/ENSMUSG00000040133/ ENSMUSG00000041046/ENSMUSG00000034855/ ENSMUSG00000028978/ENSMUSG00000059173/ ENSMUSG00000052276 | Gpr176/Ramp3/Cxcl10/ Nos3/Pde1a/Ostn | |
| BP | GO:0050678 | regulation of epithelial cell proliferation | 28/858 | 301/ 15881 | 0.00363776690419702 | 0.0471265509114338 | ENSMUSG00000035385/ENSMUSG00000000753/ ENSMUSG00000022150/ENSMUSG00000024066/ ENSMUSG00000044303/ENSMUSG00000019850/ ENSMUSG00000021822/ENSMUSG00000022676/ ENSMUSG00000028128/ENSMUSG00000022510/ ENSMUSG00000036585/ENSMUSG00000026921/ ENSMUSG00000007805/ENSMUSG00000055994/ ENSMUSG00000115388/ENSMUSG00000056758/ ENSMUSG00000031520/ENSMUSG00000041351/ ENSMUSG00000074272/ENSMUSG00000029754/ ENSMUSG00000017724/ENSMUSG00000031548/ ENSMUSG00000000120/ENSMUSG00000021256/ ENSMUSG00000004231/ENSMUSG00000048251/ ENSMUSG00000038259/ENSMUSG00000044338 | Ccl2/Serpinf1/Dab2/Xdh/ Cdkn2a/Tnfaip3/Plau/ Snai2/F3/Trp63/Fgf1/ Egfl7/Twist2/Nod2/Eppk1/ Hmga2/Vegfc/Rap1gap/ Ceacam1/Dlx6/Etv4/Sfrp1/ Ngfr/Vash1/Pax2/Bcl11b/ Gdf5/Aplnr | 28 |
| BP | GO:0030888 | regulation of B cell proliferation | 9/858 | 58/ 15881 | 0.00369008577218431 | 0.0476696714119359 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000044303/ENSMUSG00000029082/ ENSMUSG00000035873/ENSMUSG00000029084/ ENSMUSG00000040329/ENSMUSG00000052013/ ENSMUSG00000034652 | Cd74/Cdkn1a/Cdkn2a/ Bst1/Pawr/Cd38/Il7/Btla/ Cd300a | 9 |
| BP | GO:2000027 | regulation of organ morphogenesis | 18/858 | 166/ 15881 | 0.00379191908610651 | 0.0488475868788889 | ENSMUSG00000022150/ENSMUSG00000044303/ ENSMUSG00000024014/ENSMUSG00000019850/ ENSMUSG00000021822/ENSMUSG00000022144/ ENSMUSG00000034394/ENSMUSG00000022676/ ENSMUSG00000029307/ENSMUSG00000036585/ ENSMUSG00000056758/ENSMUSG00000074272/ ENSMUSG00000017724/ENSMUSG00000031548/ ENSMUSG00000033227/ENSMUSG00000000120/ ENSMUSG00000028864/ENSMUSG00000004231 | Dab2/Cdkn2a/Pim1/ Tnfaip3/Plau/Gdnf/Lif/ Snai2/Dmp1/Fgf1/Hmga2/ Ceacam1/Etv4/Sfrp1/ Wnt6/Ngfr/Hgf/Pax2 | 18 |
| BP | GO:0042108 | positive regulation of cytokine biosynthetic process | 8/858 | 48/ 15881 | 0.00387041031930306 | 0.0495801724143124 | ENSMUSG00000016024/ENSMUSG00000000732/ ENSMUSG00000049577/ENSMUSG00000026166/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000053175/ENSMUSG00000028602 | Lbp/Icosl/Zfpm1/Ccl20/ Tlr2/Syk/Bcl3/Tnfrsf8 | 8 |
| BP | GO:1903556 | negative regulation of tumor necrosis factor superfamily cytokine production | 8/858 | 48/ 15881 | 0.00387041031930306 | 0.0495801724143124 | ENSMUSG00000029816/ENSMUSG00000016024/ ENSMUSG00000030921/ENSMUSG00000042677/ ENSMUSG00000019850/ENSMUSG00000053175/ ENSMUSG00000007805/ENSMUSG00000055994 | Gpnmb/Lbp/Trim30a/ Zc3h12a/Tnfaip3/Bcl3/ Twist2/Nod2 | 8 |
| BP | GO:0070665 | positive regulation of leukocyte proliferation | 14/858 | 116/ 15881 | 0.00390214261942506 | 0.0498474263305942 | ENSMUSG00000024610/ENSMUSG00000023067/ ENSMUSG00000000732/ENSMUSG00000029082/ ENSMUSG00000029084/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000074272/ ENSMUSG00000000791/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000039323/ ENSMUSG00000030707/ENSMUSG00000026117 | Cd74/Cdkn1a/Icosl/Bst1/ Cd38/Syk/Cd80/Ceacam1/ Il12rb1/Il15/Il7/Igfbp2/ Coro1a/Zap70 | 14 |
| CC | GO:0009897 | external side of plasma membrane | 37/852 | 239/ 15881 | 5.46E-09 | 2.51E-06 | ENSMUSG00000024610/ENSMUSG00000073411/ ENSMUSG00000075602/ENSMUSG00000061232/ | Cd74/H2-D1/Ly6a/H2-K1/ Fas/Alcam/Tnfrsf9/Ly6c1/ | 37 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000024778/ENSMUSG00000022636/ ENSMUSG00000028965/ENSMUSG00000079018/ ENSMUSG00000000732/ENSMUSG00000050335/ ENSMUSG00000028024/ENSMUSG00000022103/ ENSMUSG00000062991/ENSMUSG00000026980/ ENSMUSG00000079685/ENSMUSG00000027995/ ENSMUSG00000075122/ENSMUSG00000053216/ ENSMUSG00000015243/ENSMUSG00000074272/ ENSMUSG00000068227/ENSMUSG00000027070/ ENSMUSG00000002944/ENSMUSG00000026580/ ENSMUSG00000026249/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000000791/ ENSMUSG00000000120/ENSMUSG00000020787/ ENSMUSG00000000706/ENSMUSG00000075370/ ENSMUSG00000029716/ENSMUSG00000005947/ ENSMUSG00000028020/ENSMUSG00000052013/ ENSMUSG00000024030 | Icosl/Lgals3/Enpep/Gfra2/ Nrg1/Ly75/Ulbp1/Tlr2/ Cd80/Btn2a2/Abca1/ Ceacam1/Il2rb/Lrp2/Cd36/ Selp/Serpine2/Epor/ Cxcl10/Il12rb1/Ngfr/ P2rx1/Btn1a1/Igll1/Tfr2/ Itgae/Glrb/Btla/Abcg1 | |
| CC | GO:0098552 | side of membrane | 50/852 | 413/ 15881 | 5.79E-08 | 1.03E-05 | ENSMUSG00000024610/ENSMUSG00000073411/ ENSMUSG00000075602/ENSMUSG00000043004/ ENSMUSG00000061232/ENSMUSG00000024778/ ENSMUSG00000022636/ENSMUSG00000028965/ ENSMUSG00000079018/ENSMUSG00000000732/ ENSMUSG00000050335/ENSMUSG00000028024/ ENSMUSG00000022103/ENSMUSG00000062991/ ENSMUSG00000026980/ENSMUSG00000028931/ ENSMUSG00000027669/ENSMUSG00000079685/ ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000075122/ENSMUSG00000031442/ ENSMUSG00000053216/ENSMUSG00000020599/ ENSMUSG00000015243/ENSMUSG00000074272/ ENSMUSG00000068227/ENSMUSG00000027070/ ENSMUSG00000041731/ENSMUSG00000002944/ ENSMUSG00000026580/ENSMUSG00000028214/ ENSMUSG00000026249/ENSMUSG00000006235/ ENSMUSG00000034855/ENSMUSG00000041361/ ENSMUSG00000002489/ENSMUSG00000000791/ ENSMUSG00000031506/ENSMUSG00000000120/ ENSMUSG00000020787/ENSMUSG00000000706/ ENSMUSG00000075370/ENSMUSG00000029716/ ENSMUSG00000005947/ENSMUSG00000038811/ ENSMUSG00000028020/ENSMUSG00000052013/ ENSMUSG00000024030/ENSMUSG00000026117 | Cd74/H2-D1/Ly6a/Gng2/ H2-K1/Fas/Alcam/Tnfrsf9/ Ly6c1/Icosl/Lgals3/Enpep/ Gfra2/Nrg1/Ly75/Kcnab2/ Gnb4/Ulbp1/Tlr2/Syk/ Cd80/Mcf2l/Btn2a2/Rgs9/ Abca1/Ceacam1/Il2rb/ Lrp2/Pgm5/Cd36/Selp/ Gem/Serpine2/Epor/ Cxcl10/Myzap/Tiam1/ Il12rb1/Ptpn7/Ngfr/P2rx1/ Btn1a1/Igll1/Tfr2/Itgae/ Gngt2/Glrb/Btla/Abcg1/ Zap70 | 50 |
| CC | GO:0065010 | extracellular membrane-bounded organelle | 8/852 | 13/ 15881 | 6.72E-08 | 1.03E-05 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000028766/ENSMUSG00000029298/ ENSMUSG00000054072/ENSMUSG00000028268/ ENSMUSG00000104713/ENSMUSG00000050860 | Gbp7/Pf4/Alpl/Gbp9/ Iigp1/Gbp3/Gbp6/ Phospho1 | 8 |
| CC | GO:0020003 | symbiont-containing vacuole | 6/852 | 11/ 15881 | 8.58E-06 | 0.000986574387421807 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| CC | GO:0098797 | plasma membrane protein complex | 43/852 | 402/15881 | 1.25E-05 | 0.00115366663755321 | ENSMUSG00000024610/ENSMUSG00000073411/ENSMUSG00000043004/ENSMUSG00000061232/ENSMUSG00000024778/ENSMUSG00000022150/ENSMUSG00000022636/ENSMUSG00000035929/ENSMUSG00000029082/ENSMUSG00000057123/ENSMUSG00000028931/ENSMUSG00000026576/ENSMUSG00000027669/ENSMUSG00000027995/ENSMUSG00000021457/ENSMUSG00000040907/ENSMUSG00000071715/ENSMUSG00000057182/ENSMUSG00000038403/ENSMUSG00000026251/ENSMUSG00000024873/ENSMUSG00000020599/ENSMUSG00000026253/ENSMUSG00000034353/ENSMUSG00000041329/ENSMUSG00000075318/ENSMUSG00000074272/ENSMUSG00000041731/ENSMUSG00000041046/ENSMUSG00000064329/ENSMUSG00000053395/ENSMUSG00000000791/ENSMUSG00000035296/ENSMUSG00000029716/ENSMUSG00000005947/ENSMUSG00000038811/ENSMUSG00000028020/ENSMUSG00000041695/ENSMUSG00000062157/ENSMUSG00000059588/ENSMUSG00000004266/ENSMUSG00000050623/ENSMUSG00000026117 | Cd74/H2-D1/Gng2/H2-K1/Fas/Dab2/Alcam/H2-Q4/Bst1/Gja5/Kcnab2/Atp1b1/Gnb4/Tlr2/Syk/Atp1a3/Ncf4/Scn3a/Hfe2/Chrnd/Cnih2/Rgs9/Chrng/Ramp1/Atp1b2/Scn2a/Ceacam1/Pgm5/Ramp3/Scn1a/Cacng8/Il12rb1/Sgcg/Tfr2/Itgae/Gngt2/Glrb/Kcnj2/Ifnlr1/Calcrl/Ptpn6/Catsperz/Zap70 | 43 |
| CC | GO:0005578 | proteinaceous extracellular matrix | 34/852 | 301/15881 | 3.34E-05 | 0.00223125368093994 | ENSMUSG00000027750/ENSMUSG00000000753/ENSMUSG00000026574/ENSMUSG00000017737/ENSMUSG00000050335/ENSMUSG00000048126/ENSMUSG00000043822/ENSMUSG00000019997/ENSMUSG00000012889/ENSMUSG00000029436/ENSMUSG00000029307/ENSMUSG00000036585/ENSMUSG00000028766/ENSMUSG00000033327/ENSMUSG00000002020/ENSMUSG00000019846/ENSMUSG00000035258/ENSMUSG00000055632/ENSMUSG00000042501/ENSMUSG00000031548/ENSMUSG00000037362/ENSMUSG00000033227/ENSMUSG00000050860/ENSMUSG00000063765/ENSMUSG00000033214/ENSMUSG00000021613/ENSMUSG00000028339/ENSMUSG00000030606/ENSMUSG00000050578/ENSMUSG00000030170/ENSMUSG00000036295/ENSMUSG00000022483/ENSMUSG00000002341/ENSMUSG00000068748 | Postn/Serpinf1/Dpt/Mmp9/Lgals3/Col6a3/Adamtsl5/Ctgf/Podnl1/Mmp17/Dmp1/Fgf1/Alpl/Tnxb/Ltbp2/Lama4/Abi3bp/Hmcn2/Cpa6/Sfrp1/Nov/Wnt6/Phospho1/Chadl/Slitrk5/Hapln1/Col15a1/Hapln3/Mmp13/Wnt5b/Lrrn3/Col2a1/Ncan/Ptprz1 | 34 |
| CC | GO:0044304 | main axon | 13/852 | 65/15881 | 3.40E-05 | 0.00223125368093994 | ENSMUSG00000026825/ENSMUSG00000042429/ENSMUSG00000005089/ENSMUSG00000062991/ENSMUSG00000028931/ENSMUSG00000028599/ENSMUSG00000075318/ENSMUSG00000026442/ENSMUSG00000064329/ENSMUSG00000052516/ENSMUSG00000002489/ENSMUSG00000020178/ENSMUSG00000024044 | Dnm1/Adora1/Slc1a2/Nrg1/Kcnab2/Tnfrsf1b/Scn2a/Nfasc/Scn1a/Robo2/Tiam1/Adora2a/Epb41l3 | 13 |
| CC | GO:0098802 | plasma membrane receptor complex | 20/852 | 137/15881 | 4.20E-05 | 0.00223125368093994 | ENSMUSG00000022150/ENSMUSG00000022636/ENSMUSG00000029082/ENSMUSG00000027995/ENSMUSG00000021457/ENSMUSG00000038403/ENSMUSG00000026251/ENSMUSG00000024873/ | Dab2/Alcam/Bst1/Tlr2/Syk/Hfe2/Chrnd/Cnih2/Chrng/Ramp1/Ceacam1/Ramp3/Cacng8/Il12rb1/ | 20 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000026253/ENSMUSG00000034353/ ENSMUSG00000074272/ENSMUSG00000041046/ ENSMUSG00000053395/ENSMUSG00000000791/ ENSMUSG00000029716/ENSMUSG00000005947/ ENSMUSG00000062157/ENSMUSG00000059588/ ENSMUSG00000004266/ENSMUSG00000026117 | Tfr2/Itgae/Ifnlr1/Calcrl/ Ptpn6/Zap70 | |
| CC | GO:0030430 host cell cytoplasm | 6/852 | 14/ 15881 | 4.85E-05 | 0.00223125368093994 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |
| CC | GO:0033655 host cell cytoplasm part | 6/852 | 14/ 15881 | 4.85E-05 | 0.00223125368093994 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |
| CC | GO:0031012 extracellular matrix | 38/852 | 367/ 15881 | 8.00E-05 | 0.00334368252198233 | ENSMUSG00000017002/ENSMUSG00000027750/ ENSMUSG00000000753/ENSMUSG00000026574/ ENSMUSG00000017737/ENSMUSG00000050335/ ENSMUSG00000048126/ENSMUSG00000043822/ ENSMUSG00000019997/ENSMUSG00000028128/ ENSMUSG00000012889/ENSMUSG00000029436/ ENSMUSG00000029307/ENSMUSG00000036585/ ENSMUSG00000028766/ENSMUSG00000033327/ ENSMUSG00000002020/ENSMUSG00000060459/ ENSMUSG00000019846/ENSMUSG00000035258/ ENSMUSG00000055632/ENSMUSG00000042501/ ENSMUSG00000026249/ENSMUSG00000031548/ ENSMUSG00000037362/ENSMUSG00000033227/ ENSMUSG00000050860/ENSMUSG00000063765/ ENSMUSG00000033214/ENSMUSG00000021613/ ENSMUSG00000028339/ENSMUSG00000030606/ ENSMUSG00000050578/ENSMUSG00000030170/ ENSMUSG00000036295/ENSMUSG00000022483/ ENSMUSG00000002341/ENSMUSG00000068748 | Slpi/Postn/Serpinf1/Dpt/ Mmp9/Lgals3/Col6a3/ Adamtsl5/Ctgf/F3/Podnl1/ Mmp17/Dmp1/Fgf1/Alpl/ Tnxb/Ltbp2/Kng2/Lama4/ Abi3bp/Hmcn2/Cpa6/ Serpine2/Sfrp1/Nov/Wnt6/ Phospho1/Chadl/Slitrk5/ Hapln1/Col15a1/Hapln3/ Mmp13/Wnt5b/Lrrn3/ Col2a1/Ncan/Ptprz1 | 38 |
| CC | GO:0043235 receptor complex | 32/852 | 290/ 15881 | 8.82E-05 | 0.00338227559290138 | ENSMUSG00000024610/ENSMUSG00000038146/ ENSMUSG00000022150/ENSMUSG00000022636/ ENSMUSG00000029082/ENSMUSG00000022103/ ENSMUSG00000022144/ENSMUSG00000027995/ ENSMUSG00000021457/ENSMUSG00000032839/ ENSMUSG00000038403/ENSMUSG00000026251/ ENSMUSG00000024873/ENSMUSG00000026253/ ENSMUSG00000034353/ENSMUSG00000074272/ ENSMUSG00000027070/ENSMUSG00000002944/ ENSMUSG00000027674/ENSMUSG00000041046/ ENSMUSG00000053395/ENSMUSG00000000791/ ENSMUSG00000033214/ENSMUSG00000029716/ ENSMUSG00000005947/ENSMUSG00000062157/ ENSMUSG00000059588/ENSMUSG00000027071/ ENSMUSG00000041633/ENSMUSG00000004266/ ENSMUSG00000031489/ENSMUSG00000026117 | Cd74/Notch3/Dab2/ Alcam/Bst1/Gfra2/Gdnf/ Tlr2/Syk/Trpc1/Hfe2/ Chrnd/Cnih2/Chrng/ Ramp1/Ceacam1/Lrp2/ Cd36/Pex5l/Ramp3/ Cacng8/Il12rb1/Slitrk5/ Tfr2/Itgae/Ifnlr1/Calcrl/ P2rx3/Kctd12b/Ptpn6/ Adrb3/Zap70 | 32 |
| CC | GO:0061702 inflammasome complex | 6/852 | 16/ 15881 | 0.000117894815338806 | 0.0041716626966039 | ENSMUSG00000033538/ENSMUSG00000078945/ ENSMUSG00000078942/ENSMUSG00000037860/ ENSMUSG00000071203/ENSMUSG00000025888 | Casp4/Naip2/Naip6/Aim2/ Naip5/Casp1 | 6 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CC | GO:0030673 | axolemma | 6/852 | 17/15881 | 0.000173960348538133 | 0.00500136002047131 | ENSMUSG00000042429/ENSMUSG00000005089/ENSMUSG00000062991/ENSMUSG00000052516/ENSMUSG00000020178/ENSMUSG00000024044 | Adora1/Slc1a2/Nrg1/Robo2/Adora2a/Epb41l3 | 6 |
| CC | GO:0033646 | host intracellular part | 6/852 | 17/15881 | 0.000173960348538133 | 0.00500136002047131 | ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/Gbp3/Gbp6 | 6 |
| CC | GO:0043656 | intracellular region of host | 6/852 | 17/15881 | 0.000173960348538133 | 0.00500136002047131 | ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/Gbp3/Gbp6 | 6 |
| CC | GO:0031225 | anchored component of membrane | 17/852 | 123/15881 | 0.00030248262793128 | 0.00754829604168526 | ENSMUSG00000003617/ENSMUSG00000075602/ENSMUSG00000046718/ENSMUSG00000037440/ENSMUSG00000079018/ENSMUSG00000029082/ENSMUSG00000028039/ENSMUSG00000022103/ENSMUSG00000022583/ENSMUSG00000020010/ENSMUSG00000079685/ENSMUSG00000029436/ENSMUSG00000046223/ENSMUSG00000038403/ENSMUSG00000028766/ENSMUSG00000019278/ENSMUSG00000034842 | Cp/Ly6a/Bst2/Vnn1/Ly6c1/Bst1/Efna3/Gfra2/Ly6f/Vnn3/Ulbp1/Mmp17/Plaur/Hfe2/Alpl/Dpep1/Art3 | 17 |
| CC | GO:0005911 | cell-cell junction | 39/852 | 408/15881 | 0.00034325123941767 | 0.00754829604168526 | ENSMUSG00000090523/ENSMUSG00000036718/ENSMUSG00000026208/ENSMUSG00000038235/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000054793/ENSMUSG00000062300/ENSMUSG00000022512/ENSMUSG00000050541/ENSMUSG00000115388/ENSMUSG00000028970/ENSMUSG00000061603/ENSMUSG00000049109/ENSMUSG00000075318/ENSMUSG00000051375/ENSMUSG00000074272/ENSMUSG00000041731/ENSMUSG00000041245/ENSMUSG00000026442/ENSMUSG00000064329/ENSMUSG00000002489/ENSMUSG00000037362/ENSMUSG00000000120/ENSMUSG00000022286/ENSMUSG00000041695/ENSMUSG00000024044/ENSMUSG00000021108/ENSMUSG00000002699/ENSMUSG00000034917/ENSMUSG00000001739/ENSMUSG00000051379/ENSMUSG00000050578/ENSMUSG00000021948/ENSMUSG00000030064/ENSMUSG00000004266/ENSMUSG00000036570/ENSMUSG00000030707/ENSMUSG00000026117 | Gypc/Micall2/Des/F11r/Gja5/Atp1b1/Cadm4/Nectin2/Cldn1/Adra1b/Eppk1/Abcb1b/Akap6/Themis/Scn2a/Pcdh1/Ceacam1/Pgm5/Wnk3/Nfasc/Scn1a/Tiam1/Nov/Ngfr/Grhl2/Kcnj2/Epb41l3/Prkch/Lcp2/Tjp3/Cldn15/Flrt3/Mmp13/Prkcd/Frmd4b/Ptpn6/Fxyd1/Coro1a/Zap70 | 39 |
| CC | GO:0018995 | host | 6/852 | 19/15881 | 0.00034770844064436 | 0.00754829604168526 | ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/Gbp3/Gbp6 | 6 |
| CC | GO:0033643 | host cell part | 6/852 | 19/15881 | 0.00034770844064436 | 0.00754829604168526 | ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/Gbp3/Gbp6 | 6 |
| CC | GO:0043657 | host cell | 6/852 | 19/15881 | 0.00034770844064436 | 0.00754829604168526 | ENSMUSG00000040253/ENSMUSG00000029373/ENSMUSG00000029298/ENSMUSG00000054072/ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/Gbp3/Gbp6 | 6 |
| CC | GO:0044291 | cell-cell contact zone | 12/852 | 71/15881 | 0.000361005462863208 | 0.00754829604168526 | ENSMUSG00000026208/ENSMUSG00000057123/ENSMUSG00000026576/ENSMUSG00000062300/ENSMUSG00000050541/ENSMUSG00000061603/ | Des/Gja5/Atp1b1/Nectin2/Adra1b/Akap6/Scn2a/ | 12 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000075318/ENSMUSG00000041731/ ENSMUSG00000064329/ENSMUSG00000002489/ ENSMUSG00000041695/ENSMUSG00000036570 | Pgm5/Scn1a/Tiam1/Kcnj2/ Fxyd1 | |
| CC | GO:0042101 | T cell receptor complex | 5/852 | 14/ 15881 | 0.000585642909125921 | 0.0116257490482953 | ENSMUSG00000022636/ENSMUSG00000021457/ ENSMUSG00000074272/ENSMUSG00000004266/ ENSMUSG00000026117 | Alcam/Syk/Ceacam1/ Ptpn6/Zap70 | 5 |
| CC | GO:0014704 | intercalated disc | 10/852 | 55/ 15881 | 0.000606560819911058 | 0.0116257490482953 | ENSMUSG00000026208/ENSMUSG00000057123/ ENSMUSG00000026576/ENSMUSG00000050541/ ENSMUSG00000061603/ENSMUSG00000075318/ ENSMUSG00000041731/ENSMUSG00000064329/ ENSMUSG00000041695/ENSMUSG00000036570 | Des/Gja5/Atp1b1/Adra1b/ Akap6/Scn2a/Pgm5/Scn1a/ Kcnj2/Fxyd1 | 10 |
| CC | GO:0044215 | other organism | 6/852 | 23/ 15881 | 0.00107601595409398 | 0.0183321236623419 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |
| CC | GO:0044216 | other organism cell | 6/852 | 23/ 15881 | 0.00107601595409398 | 0.0183321236623419 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |
| CC | GO:0044217 | other organism part | 6/852 | 23/ 15881 | 0.00107601595409398 | 0.0183321236623419 | ENSMUSG00000040253/ENSMUSG00000029373/ ENSMUSG00000029298/ENSMUSG00000054072/ ENSMUSG00000028268/ENSMUSG00000104713 | Gbp7/Pf4/Gbp9/Iigp1/ Gbp3/Gbp6 | 6 |
| MF | GO:0004771 | sterol esterase activity | 9/846 | 16/ 15605 | 3.14E-08 | 2.43E-05 | ENSMUSG00000031877/ENSMUSG00000031886/ ENSMUSG00000057074/ENSMUSG00000056973/ ENSMUSG00000071047/ENSMUSG00000062826/ ENSMUSG00000031725/ENSMUSG00000061825/ ENSMUSG00000050097 | Ces2g/Ces2e/Ces1g/Ces1d/ Ces1a/Ces2f/Ces1f/Ces2c/ Ces2b | 9 |
| MF | GO:0008009 | chemokine activity | 11/846 | 29/ 15605 | 1.57E-07 | 6.05E-05 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000035373/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000029373/ENSMUSG00000074715/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000031780 | Cxcl1/Ccl2/Cx3cl1/Ccl7/ Ccl20/Ccl9/Pf4/Ccl28/ Cxcl5/Cxcl10/Ccl17 | 11 |
| MF | GO:0030414 | peptidase inhibitor activity | 23/846 | 134/ 15605 | 8.02E-07 | 0.000127054805142688 | ENSMUSG00000024164/ENSMUSG00000017002/ ENSMUSG00000046718/ENSMUSG00000000753/ ENSMUSG00000078945/ENSMUSG00000042842/ ENSMUSG00000027082/ENSMUSG00000041481/ ENSMUSG00000078942/ENSMUSG00000031387/ ENSMUSG00000027985/ENSMUSG00000021403/ ENSMUSG00000079014/ENSMUSG00000025889/ ENSMUSG00000060459/ENSMUSG00000078949/ ENSMUSG00000026315/ENSMUSG00000026249/ ENSMUSG00000027834/ENSMUSG00000071203/ ENSMUSG00000051029/ENSMUSG00000019278/ ENSMUSG00000079012 | C3/Slpi/Bst2/Serpinf1/ Naip2/Serpinb6b/Tfpi/ Serpina3g/Naip6/Renbp/ Lef1/Serpinb9b/Serpina3i/ Snca/Kng2/R3hdml/ Serpinb8/Serpine2/ Serpini1/Naip5/Serpinb1b/ Dpep1/Serpina3m | 23 |
| MF | GO:0042379 | chemokine receptor binding | 12/846 | 40/ 15605 | 8.14E-07 | 0.000127054805142688 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000035373/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000029373/ENSMUSG00000074715/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000031780/ENSMUSG00000043953 | Cxcl1/Ccl2/Cx3cl1/Ccl7/ Ccl20/Ccl9/Pf4/Ccl28/ Cxcl5/Cxcl10/Ccl17/Ccrl2 | 12 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| MF | GO:0004806 | triglyceride lipase activity | 9/846 | 22/15605 | 1.02E-06 | 0.000127054805142688 | ENSMUSG00000031877/ENSMUSG00000031886/ENSMUSG00000057074/ENSMUSG00000056973/ENSMUSG00000071047/ENSMUSG00000062826/ENSMUSG00000031725/ENSMUSG00000061825/ENSMUSG00000050097 | Ces2g/Ces2e/Ces1g/Ces1d/Ces1a/Ces2f/Ces1f/Ces2c/Ces2b | 9 |
| MF | GO:0004497 | monooxygenase activity | 16/846 | 72/15605 | 1.14E-06 | 0.000127054805142688 | ENSMUSG00000006764/ENSMUSG00000020826/ENSMUSG00000023963/ENSMUSG00000019823/ENSMUSG00000025002/ENSMUSG00000033715/ENSMUSG00000003484/ENSMUSG00000017969/ENSMUSG00000052974/ENSMUSG00000040046/ENSMUSG00000090700/ENSMUSG00000050103/ENSMUSG00000028978/ENSMUSG00000063415/ENSMUSG00000025955/ENSMUSG00000025197 | Tph2/Nos2/Cyp39a1/Mical1/Cyp2c55/Akr1c14/Cyp4f18/Ptgis/Cyp2f2/Tph1/Cyp4f40/Agmo/Nos3/Cyp26b1/Akr1cl/Cyp2c23 | 16 |
| MF | GO:0005539 | glycosaminoglycan binding | 25/846 | 157/15605 | 1.15E-06 | 0.000127054805142688 | ENSMUSG00000035385/ENSMUSG00000027750/ENSMUSG00000029816/ENSMUSG00000031785/ENSMUSG00000035373/ENSMUSG00000043822/ENSMUSG00000019997/ENSMUSG00000027995/ENSMUSG00000053475/ENSMUSG00000036585/ENSMUSG00000029373/ENSMUSG00000055994/ENSMUSG00000033327/ENSMUSG00000002020/ENSMUSG00000041193/ENSMUSG00000026580/ENSMUSG00000035258/ENSMUSG00000026249/ENSMUSG00000031548/ENSMUSG00000034855/ENSMUSG00000037362/ENSMUSG00000021613/ENSMUSG00000074115/ENSMUSG00000030606/ENSMUSG00000002341 | Ccl2/Postn/Gpnmb/Adgrg1/Ccl7/Adamtsl5/Ctgf/Tlr2/Tnfaip6/Fgf1/Pf4/Nod2/Tnxb/Ltbp2/Pla2g5/Selp/Abi3bp/Serpine2/Sfrp1/Cxcl10/Nov/Hapln1/Saa1/Hapln3/Ncan | 25 |
| MF | GO:0004866 | endopeptidase inhibitor activity | 22/846 | 128/15605 | 1.35E-06 | 0.000130565521725583 | ENSMUSG00000024164/ENSMUSG00000017002/ENSMUSG00000046718/ENSMUSG00000000753/ENSMUSG00000078945/ENSMUSG00000042842/ENSMUSG00000027082/ENSMUSG00000041481/ENSMUSG00000078942/ENSMUSG00000031387/ENSMUSG00000027985/ENSMUSG00000021403/ENSMUSG00000079014/ENSMUSG00000025889/ENSMUSG00000060459/ENSMUSG00000026315/ENSMUSG00000026249/ENSMUSG00000027834/ENSMUSG00000071203/ENSMUSG00000051029/ENSMUSG00000019278/ENSMUSG00000079012 | C3/Slpi/Bst2/Serpinf1/Naip2/Serpinb6b/Tfpi/Serpina3g/Naip6/Renbp/Lef1/Serpinb9b/Serpina3i/Snca/Kng2/Serpinb8/Serpine2/Serpini1/Naip5/Serpinb1b/Dpep1/Serpina3m | 22 |
| MF | GO:0061135 | endopeptidase regulator activity | 22/846 | 134/15605 | 2.98E-06 | 0.000255644265339066 | ENSMUSG00000024164/ENSMUSG00000017002/ENSMUSG00000046718/ENSMUSG00000000753/ENSMUSG00000078945/ENSMUSG00000042842/ENSMUSG00000027082/ENSMUSG00000041481/ENSMUSG00000078942/ENSMUSG00000031387/ENSMUSG00000027985/ENSMUSG00000021403/ENSMUSG00000079014/ENSMUSG00000025889/ENSMUSG00000060459/ENSMUSG00000026315/ENSMUSG00000026249/ENSMUSG00000027834/ENSMUSG00000071203/ENSMUSG00000051029/ENSMUSG00000019278/ENSMUSG00000079012 | C3/Slpi/Bst2/Serpinf1/Naip2/Serpinb6b/Tfpi/Serpina3g/Naip6/Renbp/Lef1/Serpinb9b/Serpina3i/Snca/Kng2/Serpinb8/Serpine2/Serpini1/Naip5/Serpinb1b/Dpep1/Serpina3m | 22 |
| MF | GO:0061134 | peptidase regulator activity | 24/846 | 163/15605 | 7.61E-06 | 0.000587861742518015 | ENSMUSG00000024164/ENSMUSG00000017002/ENSMUSG00000046718/ENSMUSG00000000753/ | C3/Slpi/Bst2/Serpinf1/Naip2/Serpinb6b/Tfpi/ | 24 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000078945/ENSMUSG00000042842/ ENSMUSG00000027082/ENSMUSG00000041481/ ENSMUSG00000078942/ENSMUSG00000031387/ ENSMUSG00000027985/ENSMUSG00000032359/ ENSMUSG00000021403/ENSMUSG00000079014/ ENSMUSG00000025889/ENSMUSG00000060459/ ENSMUSG00000078949/ENSMUSG00000026315/ ENSMUSG00000026249/ENSMUSG00000027834/ ENSMUSG00000071203/ENSMUSG00000051029/ ENSMUSG00000019278/ENSMUSG00000079012 | Serpina3g/Naip6/Renbp/ Lef1/Ctsh/Serpinb9b/ Serpina3i/Snca/Kng2/ R3hdml/Serpinb8/ Serpine2/Serpini1/Naip5/ Serpinb1b/Dpep1/ Serpina3m | |
| MF | GO:0008201 | heparin binding | 19/846 | 117/ 15605 | 1.63E-05 | 0.0011458430265883 | ENSMUSG00000035385/ENSMUSG00000027750/ ENSMUSG00000029816/ENSMUSG00000031785/ ENSMUSG00000035373/ENSMUSG00000043822/ ENSMUSG00000019997/ENSMUSG00000036585/ ENSMUSG00000029373/ENSMUSG00000033327/ ENSMUSG00000002020/ENSMUSG00000041193/ ENSMUSG00000026580/ENSMUSG00000035258/ ENSMUSG00000026249/ENSMUSG00000031548/ ENSMUSG00000034855/ENSMUSG00000037362/ ENSMUSG00000074115 | Ccl2/Postn/Gpnmb/ Adgrg1/Ccl7/Adamtsl5/ Ctgf/Fgf1/Pf4/Tnxb/Ltbp2/ Pla2g5/Selp/Abi3bp/ Serpine2/Sfrp1/Cxcl10/ Nov/Saa1 | 19 |
| MF | GO:0048018 | receptor ligand activity | 35/846 | 308/ 15605 | 2.80E-05 | 0.00180012997301589 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000029816/ ENSMUSG00000096188/ENSMUSG00000035373/ ENSMUSG00000050335/ENSMUSG00000062991/ ENSMUSG00000025207/ENSMUSG00000022144/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000066755/ENSMUSG00000082361/ ENSMUSG00000031520/ENSMUSG00000040026/ ENSMUSG00000074715/ENSMUSG00000039481/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000037362/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000038508/ ENSMUSG00000006488/ENSMUSG00000074115/ ENSMUSG00000028864/ENSMUSG00000051379/ ENSMUSG00000031780/ENSMUSG00000052276/ ENSMUSG00000038259 | Cxcl1/Ccl2/Cx3cl1/ Gpnmb/Cmtm4/Ccl7/ Lgals3/Nrg1/Sema4g/Gdnf/ Lif/Ctgf/Ccl20/Ccl9/Fgf1/ Pf4/Tnfsf18/Btc/Vegfc/ Saa3/Ccl28/Nrtn/Cxcl5/ Cxcl10/Nov/Il15/Il7/ Gdf15/Prl7a1/Saa1/Hgf/ Flrt3/Ccl17/Ostn/Gdf5 | 35 |
| MF | GO:0005126 | cytokine receptor binding | 27/846 | 217/ 15605 | 4.80E-05 | 0.00285019267355016 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000035373/ ENSMUSG00000022514/ENSMUSG00000022144/ ENSMUSG00000034394/ENSMUSG00000026166/ ENSMUSG00000019122/ENSMUSG00000029373/ ENSMUSG00000066755/ENSMUSG00000031520/ ENSMUSG00000074715/ENSMUSG00000026875/ ENSMUSG00000074272/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000000791/ ENSMUSG00000031712/ENSMUSG00000000120/ ENSMUSG00000040329/ENSMUSG00000038508/ ENSMUSG00000079164/ENSMUSG00000006488/ | Cxcl1/Ccl2/Cx3cl1/Ccl7/ Il1rap/Gdnf/Lif/Ccl20/ Ccl9/Pf4/Tnfsf18/Vegfc/ Ccl28/Traf1/Ceacam1/ Cxcl5/Cxcl10/Il12rb1/Il15/ Ngfr/Il7/Gdf15/Tlr5/ Prl7a1/Ccl17/Ccrl2/Gdf5 | 27 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000031780/ENSMUSG00000043953/ ENSMUSG00000038259 | | |
| MF | GO:1901681 | sulfur compound binding | 25/846 | 195/ 15605 | 5.52E-05 | 0.00304371692630842 | ENSMUSG00000035385/ENSMUSG00000027750/ ENSMUSG00000029816/ENSMUSG00000031785/ ENSMUSG00000035373/ENSMUSG00000050737/ ENSMUSG00000042010/ENSMUSG00000043822/ ENSMUSG00000019997/ENSMUSG00000024039/ ENSMUSG00000040907/ENSMUSG00000036585/ ENSMUSG00000029373/ENSMUSG00000033327/ ENSMUSG00000002020/ENSMUSG00000041193/ ENSMUSG00000026580/ENSMUSG00000035258/ ENSMUSG00000004540/ENSMUSG00000026249/ ENSMUSG00000031548/ENSMUSG00000034855/ ENSMUSG00000032348/ENSMUSG00000037362/ ENSMUSG00000074115 | Ccl2/Postn/Gpnmb/ Adgrg1/Ccl7/Ptges/Acacb/ Adamtsl5/Ctgf/Cbs/ Atp1a3/Fgf1/Pf4/Tnxb/ Ltbp2/Pla2g5/Selp/ Abi3bp/Psg17/Serpine2/ Sfrp1/Cxcl10/Gsta4/Nov/ Saa1 | 25 |
| MF | GO:0004857 | enzyme inhibitor activity | 34/846 | 310/ 15605 | 7.42E-05 | 0.00382079903837775 | ENSMUSG00000024164/ENSMUSG00000017002/ ENSMUSG00000046718/ENSMUSG00000000753/ ENSMUSG00000023067/ENSMUSG00000044303/ ENSMUSG00000026463/ENSMUSG00000078945/ ENSMUSG00000032501/ENSMUSG00000042842/ ENSMUSG00000096472/ENSMUSG00000021892/ ENSMUSG00000027082/ENSMUSG00000012889/ ENSMUSG00000041481/ENSMUSG00000078942/ ENSMUSG00000031387/ENSMUSG00000027985/ ENSMUSG00000021403/ENSMUSG00000079014/ ENSMUSG00000037166/ENSMUSG00000025889/ ENSMUSG00000055003/ENSMUSG00000037664/ ENSMUSG00000060459/ENSMUSG00000078949/ ENSMUSG00000026315/ENSMUSG00000026249/ ENSMUSG00000027834/ENSMUSG00000071203/ ENSMUSG00000051029/ENSMUSG00000019278/ ENSMUSG00000051379/ENSMUSG00000079012 | C3/Slpi/Bst2/Serpinf1/ Cdkn1a/Cdkn2a/Atp2b4/ Naip2/Trib1/Serpinb6b/ Cdkn2d/Sh3bp5/Tfpi/ Podnl1/Serpina3g/Naip6/ Renbp/Lef1/Serpinb9b/ Serpina3i/Ppp1r14a/Snca/ Lrtm2/Cdkn1c/Kng2/ R3hdml/Serpinb8/ Serpine2/Serpini1/Naip5/ Serpinb1b/Dpep1/Flrt3/ Serpina3m | 34 |
| MF | GO:0005506 | iron ion binding | 18/846 | 121/ 15605 | 8.90E-05 | 0.00429472702214898 | ENSMUSG00000023030/ENSMUSG00000024066/ ENSMUSG00000006764/ENSMUSG00000020826/ ENSMUSG00000023963/ENSMUSG00000025002/ ENSMUSG00000062168/ENSMUSG00000003484/ ENSMUSG00000025889/ENSMUSG00000017969/ ENSMUSG00000026822/ENSMUSG00000052974/ ENSMUSG00000020892/ENSMUSG00000040046/ ENSMUSG00000050103/ENSMUSG00000028978/ ENSMUSG00000064294/ENSMUSG00000063415 | Slc11a2/Xdh/Tph2/Nos2/ Cyp39a1/Cyp2c55/Ppef1/ Cyp4f18/Snca/Ptgis/Lcn2/ Cyp2f2/Aloxe3/Tph1/ Agmo/Nos3/Aox3/Cyp26b1 | 18 |
| MF | GO:0022890 | inorganic cation transmembrane transporter activity | 44/846 | 448/ 15605 | 9.98E-05 | 0.00453035536083189 | ENSMUSG00000023030/ENSMUSG00000055368/ ENSMUSG00000026463/ENSMUSG00000036067/ ENSMUSG00000005089/ENSMUSG00000028931/ ENSMUSG00000026576/ENSMUSG00000040907/ ENSMUSG00000032839/ENSMUSG00000057182/ ENSMUSG00000035694/ENSMUSG00000030313/ ENSMUSG00000026251/ENSMUSG00000060961/ ENSMUSG00000022416/ENSMUSG00000027994/ ENSMUSG00000050777/ENSMUSG00000026177/ | Slc11a2/Slc6a2/Atp2b4/ Slc2a6/Slc1a2/Kcnab2/ Atp1b1/Atp1a3/Trpc1/ Scn3a/Caps2/Dennd5b/ Chrnd/Slc4a4/Cacna1i/ Mcub/Tmem37/Slc11a1/ Chrng/Kcnk5/Atp1b2/ Scn2a/Slc17a7/Slc4a8/ Pex5l/Slc39a4/Scn1a/ | 44 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000026253/ENSMUSG00000023243/ ENSMUSG00000041329/ENSMUSG00000075318/ ENSMUSG00000070570/ENSMUSG00000023032/ ENSMUSG00000027674/ENSMUSG00000063354/ ENSMUSG00000064329/ENSMUSG00000053395/ ENSMUSG00000026435/ENSMUSG00000068323/ ENSMUSG00000030109/ENSMUSG00000000794/ ENSMUSG00000036298/ENSMUSG00000020787/ ENSMUSG00000025557/ENSMUSG00000022899/ ENSMUSG00000029716/ENSMUSG00000038600/ ENSMUSG00000041695/ENSMUSG00000018470/ ENSMUSG00000030523/ENSMUSG00000027071/ ENSMUSG00000042686/ENSMUSG00000052387 | Cacng8/Slc45a3/Slc4a5/ Slc6a12/Kcnn3/Slc2a13/ P2rx1/Slc15a1/Slc15a2/ Tfr2/Atp6v0a4/Kcnj2/ Kcnab3/Trpm1/P2rx3/ Jph1/Trpm3 | |
| MF | GO:0008324 | cation transmembrane transporter activity | 47/846 | 492/ 15605 | 0.000113848727372682 | 0.00488284541842836 | ENSMUSG00000023030/ENSMUSG00000055368/ ENSMUSG00000026463/ENSMUSG00000036067/ ENSMUSG00000005089/ENSMUSG00000028931/ ENSMUSG00000026576/ENSMUSG00000040907/ ENSMUSG00000032839/ENSMUSG00000057182/ ENSMUSG00000035694/ENSMUSG00000030313/ ENSMUSG00000026251/ENSMUSG00000060961/ ENSMUSG00000022416/ENSMUSG00000027994/ ENSMUSG00000050777/ENSMUSG00000026177/ ENSMUSG00000026253/ENSMUSG00000023243/ ENSMUSG00000041329/ENSMUSG00000075318/ ENSMUSG00000028825/ENSMUSG00000070570/ ENSMUSG00000023032/ENSMUSG00000027674/ ENSMUSG00000063354/ENSMUSG00000064329/ ENSMUSG00000053395/ENSMUSG00000026435/ ENSMUSG00000068323/ENSMUSG00000030109/ ENSMUSG00000000794/ENSMUSG00000054753/ ENSMUSG00000036298/ENSMUSG00000020787/ ENSMUSG00000025557/ENSMUSG00000022899/ ENSMUSG00000029716/ENSMUSG00000038600/ ENSMUSG00000041695/ENSMUSG00000018470/ ENSMUSG00000030523/ENSMUSG00000007034/ ENSMUSG00000027071/ENSMUSG00000042686/ ENSMUSG00000052387 | Slc11a2/Slc6a2/Atp2b4/ Slc2a6/Slc1a2/Kcnab2/ Atp1b1/Atp1a3/Trpc1/ Scn3a/Caps2/Dennd5b/ Chrnd/Slc4a4/Cacna1i/ Mcub/Tmem37/Slc11a1/ Chrng/Kcnk5/Atp1b2/ Scn2a/Rhd/Slc17a7/ Slc4a8/Pex5l/Slc39a4/ Scn1a/Cacng8/Slc45a3/ Slc4a5/Slc6a12/Kcnn3/ AU018091/Slc2a13/P2rx1/ Slc15a1/Slc15a2/Tfr2/ Atp6v0a4/Kcnj2/Kcnab3/ Trpm1/Slc44a4/P2rx3/ Jph1/Trpm3 | 47 |
| MF | GO:0030545 | receptor regulator activity | 35/846 | 332/ 15605 | 0.000129472773523971 | 0.00526068321897399 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000029816/ ENSMUSG00000096188/ENSMUSG00000035373/ ENSMUSG00000050335/ENSMUSG00000062991/ ENSMUSG00000025207/ENSMUSG00000022144/ ENSMUSG00000034394/ENSMUSG00000019997/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000036585/ENSMUSG00000029373/ ENSMUSG00000066755/ENSMUSG00000082361/ ENSMUSG00000031520/ENSMUSG00000040026/ ENSMUSG00000074715/ENSMUSG00000039481/ ENSMUSG00000029371/ENSMUSG00000034855/ ENSMUSG00000037362/ENSMUSG00000031712/ | Cxcl1/Ccl2/Cx3cl1/ Gpnmb/Cmtm4/Ccl7/ Lgals3/Nrg1/Sema4g/Gdnf/ Lif/Ctgf/Ccl20/Ccl9/Fgf1/ Pf4/Tnfsf18/Btc/Vegfc/ Saa3/Ccl28/Nrtn/Cxcl5/ Cxcl10/Nov/Il15/Il7/ Gdf15/Prl7a1/Saa1/Hgf/ Flrt3/Ccl17/Ostn/Gdf5 | 35 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000040329/ENSMUSG00000038508/ ENSMUSG00000006488/ENSMUSG00000074115/ ENSMUSG00000028864/ENSMUSG00000051379/ ENSMUSG00000031780/ENSMUSG00000052276/ ENSMUSG00000038259 | | |
| MF | GO:0048020 | CCR chemokine receptor binding | 7/846 | 23/ 15605 | 0.000153085172772263 | 0.00590908766900936 | ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000026166/ ENSMUSG00000019122/ENSMUSG00000031780/ ENSMUSG00000043953 | Ccl2/Cx3cl1/Ccl7/Ccl20/ Ccl9/Ccl17/Ccrl2 | 7 |
| MF | GO:0001664 | G-protein coupled receptor binding | 25/846 | 210/ 15605 | 0.000183331439190674 | 0.00646390795870355 | ENSMUSG00000024164/ENSMUSG00000029380/ ENSMUSG00000035385/ENSMUSG00000031778/ ENSMUSG00000035373/ENSMUSG00000026825/ ENSMUSG00000042429/ENSMUSG00000032860/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000040907/ENSMUSG00000029373/ ENSMUSG00000074715/ENSMUSG00000021070/ ENSMUSG00000029371/ENSMUSG00000031548/ ENSMUSG00000034855/ENSMUSG00000033227/ ENSMUSG00000020178/ENSMUSG00000024232/ ENSMUSG00000074115/ENSMUSG00000031780/ ENSMUSG00000043953/ENSMUSG00000030170/ ENSMUSG00000031489 | C3/Cxcl1/Ccl2/Cx3cl1/ Ccl7/Dnm1/Adora1/P2ry2/ Ccl20/Ccl9/Atp1a3/Pf4/ Ccl28/Bdkrb2/Cxcl5/Sfrp1/ Cxcl10/Wnt6/Adora2a/ Bambi/Saa1/Ccl17/Ccrl2/ Wnt5b/Adrb3 | 25 |
| MF | GO:0015295 | solute:proton symporter activity | 6/846 | 17/ 15605 | 0.00018420463094751 | 0.00646390795870355 | ENSMUSG00000023030/ENSMUSG00000036067/ ENSMUSG00000026435/ENSMUSG00000036298/ ENSMUSG00000025557/ENSMUSG00000022899 | Slc11a2/Slc2a6/Slc45a3/ Slc2a13/Slc15a1/Slc15a2 | 6 |
| MF | GO:0022804 | active transmembrane transporter activity | 32/846 | 304/ 15605 | 0.000254750056302953 | 0.00846484020591681 | ENSMUSG00000023030/ENSMUSG00000055368/ ENSMUSG00000026463/ENSMUSG00000020620/ ENSMUSG00000018800/ENSMUSG00000036067/ ENSMUSG00000005089/ENSMUSG00000026576/ ENSMUSG00000040907/ENSMUSG00000037762/ ENSMUSG00000035694/ENSMUSG00000060961/ ENSMUSG00000027994/ENSMUSG00000028970/ ENSMUSG00000026177/ENSMUSG00000041329/ ENSMUSG00000015243/ENSMUSG00000055782/ ENSMUSG00000070570/ENSMUSG00000023032/ ENSMUSG00000070280/ENSMUSG00000026435/ ENSMUSG00000068323/ENSMUSG00000020600/ ENSMUSG00000030109/ENSMUSG00000036298/ ENSMUSG00000025557/ENSMUSG00000022899/ ENSMUSG00000038963/ENSMUSG00000038600/ ENSMUSG00000024030/ENSMUSG00000025938 | Slc11a2/Slc6a2/Atp2b4/ Abca8b/Abca5/Slc2a6/ Slc1a2/Atp1b1/Atp1a3/ Slc16a9/Caps2/Slc4a4/ Mcub/Abcb1b/Slc11a1/ Atp1b2/Abca1/Abcd2/ Slc17a7/Slc4a8/Slc22a14/ Slc45a3/Slc4a5/Slc7a15/ Slc6a12/Slc2a13/Slc15a1/ Slc15a2/Slco4a1/ Atp6v0a4/Abcg1/Slco5a1 | 32 |
| MF | GO:0035325 | Toll-like receptor binding | 5/846 | 12/ 15605 | 0.000266206031848792 | 0.00846484020591681 | ENSMUSG00000027995/ENSMUSG00000021457/ ENSMUSG00000040026/ENSMUSG00000074272/ ENSMUSG00000002944 | Tlr2/Syk/Saa3/Ceacam1/ Cd36 | 5 |
| MF | GO:0016298 | lipase activity | 15/846 | 99/ 15605 | 0.000274120472989534 | 0.00846484020591681 | ENSMUSG00000031877/ENSMUSG00000031886/ ENSMUSG00000057074/ENSMUSG00000042429/ ENSMUSG00000023913/ENSMUSG00000056973/ ENSMUSG00000002847/ENSMUSG00000071047/ ENSMUSG00000041193/ENSMUSG00000062826/ ENSMUSG00000031725/ENSMUSG00000061825/ | Ces2g/Ces2e/Ces1g/ Adora1/Pla2g7/Ces1d/ Pla1a/Ces1a/Pla2g5/Ces2f/ Ces1f/Ces2c/Ces2b/Plch1/ Abhd3 | 15 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ENSMUSG00000050097/ENSMUSG00000036834/ ENSMUSG00000002475 | | |
| MF | GO:0016709 | oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, NAD(P)H as one donor, and incorporation of one atom of oxygen | 8/846 | 33/ 15605 | 0.000298129910973567 | 0.00864413413439358 | ENSMUSG00000020826/ENSMUSG00000019823/ ENSMUSG00000033715/ENSMUSG00000003484/ ENSMUSG00000090700/ENSMUSG00000028978/ ENSMUSG00000063415/ENSMUSG00000025955 | Nos2/Mical1/Akr1c14/ Cyp4f18/Cyp4f40/Nos3/ Cyp26b1/Akr1cl | 8 |
| MF | GO:0015294 | solute:cation symporter activity | 13/846 | 79/ 15605 | 0.000302320753404957 | 0.00864413413439358 | ENSMUSG00000023030/ENSMUSG00000055368/ ENSMUSG00000036067/ENSMUSG00000005089/ ENSMUSG00000060961/ENSMUSG00000070570/ ENSMUSG00000023032/ENSMUSG00000026435/ ENSMUSG00000068323/ENSMUSG00000030109/ ENSMUSG00000036298/ENSMUSG00000025557/ ENSMUSG00000022899 | Slc11a2/Slc6a2/Slc2a6/ Slc1a2/Slc4a4/Slc17a7/ Slc4a8/Slc45a3/Slc4a5/ Slc6a12/Slc2a13/Slc15a1/ Slc15a2 | 13 |
| MF | GO:0035586 | purinergic receptor activity | 6/846 | 19/ 15605 | 0.000367824312343666 | 0.0101414417546182 | ENSMUSG00000042429/ENSMUSG00000032860/ ENSMUSG00000048779/ENSMUSG00000020178/ ENSMUSG00000020787/ENSMUSG00000027071 | Adora1/P2ry2/P2ry6/ Adora2a/P2rx1/P2rx3 | 6 |
| MF | GO:0005125 | cytokine activity | 18/846 | 136/ 15605 | 0.000396851415705717 | 0.0105644583767177 | ENSMUSG00000029380/ENSMUSG00000035385/ ENSMUSG00000031778/ENSMUSG00000096188/ ENSMUSG00000035373/ENSMUSG00000034394/ ENSMUSG00000026166/ENSMUSG00000019122/ ENSMUSG00000029373/ENSMUSG00000066755/ ENSMUSG00000074715/ENSMUSG00000029371/ ENSMUSG00000034855/ENSMUSG00000031712/ ENSMUSG00000040329/ENSMUSG00000038508/ ENSMUSG00000031780/ENSMUSG00000038259 | Cxcl1/Ccl2/Cx3cl1/ Cmtm4/Ccl7/Lif/Ccl20/ Ccl9/Pf4/Tnfsf18/Ccl28/ Cxcl5/Cxcl10/Il15/Il7/ Gdf15/Ccl17/Gdf5 | 18 |
| MF | GO:0004867 | serine-type endopeptidase inhibitor activity | 12/846 | 72/ 15605 | 0.000452873276147785 | 0.0116539389728697 | ENSMUSG00000017002/ENSMUSG00000000753/ ENSMUSG00000042842/ENSMUSG00000027082/ ENSMUSG00000041481/ENSMUSG00000021403/ ENSMUSG00000079014/ENSMUSG00000026315/ ENSMUSG00000026249/ENSMUSG00000027834/ ENSMUSG00000051029/ENSMUSG00000079012 | Slpi/Serpinf1/Serpinb6b/ Tfpi/Serpina3g/Serpinb9b/ Serpina3i/Serpinb8/ Serpine2/Serpini1/ Serpinb1b/Serpina3m | 12 |
| MF | GO:0005031 | tumor necrosis factor-activated receptor activity | 6/846 | 21/ 15605 | 0.000670191001447566 | 0.0161683579099225 | ENSMUSG00000024778/ENSMUSG00000028965/ ENSMUSG00000028599/ENSMUSG00000008318/ ENSMUSG00000000120/ENSMUSG00000028602 | Fas/Tnfrsf9/Tnfrsf1b/Relt/ Ngfr/Tnfrsf8 | 6 |
| MF | GO:0005035 | death receptor activity | 6/846 | 21/ 15605 | 0.000670191001447566 | 0.0161683579099225 | ENSMUSG00000024778/ENSMUSG00000028965/ ENSMUSG00000028599/ENSMUSG00000008318/ ENSMUSG00000000120/ENSMUSG00000028602 | Fas/Tnfrsf9/Tnfrsf1b/Relt/ Ngfr/Tnfrsf8 | 6 |
| MF | GO:0016705 | oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen | 17/846 | 131/ 15605 | 0.000715350847136183 | 0.0167348743633071 | ENSMUSG00000047250/ENSMUSG00000006764/ ENSMUSG00000020826/ENSMUSG00000023963/ ENSMUSG00000019823/ENSMUSG00000025002/ ENSMUSG00000033715/ENSMUSG00000003484/ ENSMUSG00000017969/ENSMUSG00000052974/ ENSMUSG00000040046/ENSMUSG00000090700/ ENSMUSG00000050103/ENSMUSG00000028978/ ENSMUSG00000063415/ENSMUSG00000025955/ ENSMUSG00000025197 | Ptgs1/Tph2/Nos2/ Cyp39a1/Mical1/Cyp2c55/ Akr1c14/Cyp4f18/Ptgis/ Cyp2f2/Tph1/Cyp4f40/ Agmo/Nos3/Cyp26b1/ Akr1cl/Cyp2c23 | 17 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | |
| MF | GO:0005216 | ion channel activity | 29/846 | 287/15605 | 0.00093941190219142 | 0.0213301761321111 | ENSMUSG00000028931/ENSMUSG00000054720/ENSMUSG00000032839/ENSMUSG00000057182/ENSMUSG00000030313/ENSMUSG00000026251/ENSMUSG00000022416/ENSMUSG00000027994/ENSMUSG00000050777/ENSMUSG00000026253/ENSMUSG00000023243/ENSMUSG00000075318/ENSMUSG00000070570/ENSMUSG00000027674/ENSMUSG00000028255/ENSMUSG00000009687/ENSMUSG00000064329/ENSMUSG00000053395/ENSMUSG00000000794/ENSMUSG00000020787/ENSMUSG00000037418/ENSMUSG00000028020/ENSMUSG00000041695/ENSMUSG00000018470/ENSMUSG00000030523/ENSMUSG00000027071/ENSMUSG00000036570/ENSMUSG00000042686/ENSMUSG00000052387 | Kcnab2/Lrrc8c/Trpc1/Scn3a/Dennd5b/Chrnd/Cacna1i/Mcub/Tmem37/Chrng/Kcnk5/Scn2a/Slc17a7/Pex5l/Clca1/Fxyd5/Scn1a/Cacng8/Kcnn3/P2rx1/Best1/Glrb/Kcnj2/Kcnab3/Trpm1/P2rx3/Fxyd1/Jph1/Trpm3 | 29 |
| MF | GO:0003924 | GTPase activity | 27/846 | 263/15605 | 0.0010957252557679 | 0.0241685684986519 | ENSMUSG00000043004/ENSMUSG00000028278/ENSMUSG00000026825/ENSMUSG00000039960/ENSMUSG00000038387/ENSMUSG00000054855/ENSMUSG00000037580/ENSMUSG00000030220/ENSMUSG00000027669/ENSMUSG00000020486/ENSMUSG00000022456/ENSMUSG00000069893/ENSMUSG00000034226/ENSMUSG00000054072/ENSMUSG00000019845/ENSMUSG00000028268/ENSMUSG00000031504/ENSMUSG00000000386/ENSMUSG00000048852/ENSMUSG00000071723/ENSMUSG00000028214/ENSMUSG00000020732/ENSMUSG00000068606/ENSMUSG00000078922/ENSMUSG00000058163/ENSMUSG00000021062/ENSMUSG00000078921 | Gng2/Rragd/Dnm1/Rhou/Rras/Rnd1/Gch1/Arhgdib/Gnb4/Sept4/Sept3/9930111J21Rik1/Rhov/Iigp1/Tube1/Gbp3/Rab20/Mx1/Gm12185/Gspt2/Gem/Rab37/Gm4841/Tgtp1/Gm5431/Rab15/Tgtp2 | 27 |
| MF | GO:0015081 | sodium ion transmembrane transporter activity | 15/846 | 114/15605 | 0.00124872331537827 | 0.0260631823713061 | ENSMUSG00000055368/ENSMUSG00000005089/ENSMUSG00000026576/ENSMUSG00000040907/ENSMUSG00000057182/ENSMUSG00000035694/ENSMUSG00000060961/ENSMUSG00000022416/ENSMUSG00000041329/ENSMUSG00000075318/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000064329/ENSMUSG00000068323/ENSMUSG00000030109 | Slc6a2/Slc1a2/Atp1b1/Atp1a3/Scn3a/Caps2/Slc4a4/Cacna1i/Atp1b2/Scn2a/Slc17a7/Slc4a8/Scn1a/Slc4a5/Slc6a12 | 15 |
| MF | GO:0015077 | monovalent inorganic cation transmembrane transporter activity | 28/846 | 279/15605 | 0.00126527383713634 | 0.0260631823713061 | ENSMUSG00000023030/ENSMUSG00000055368/ENSMUSG00000036067/ENSMUSG00000005089/ENSMUSG00000028931/ENSMUSG00000026576/ENSMUSG00000040907/ENSMUSG00000057182/ENSMUSG00000035694/ENSMUSG00000060961/ENSMUSG00000022416/ENSMUSG00000026177/ENSMUSG00000023243/ENSMUSG00000041329/ENSMUSG00000075318/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000064329/ENSMUSG00000026435/ENSMUSG00000068323/ENSMUSG00000030109/ENSMUSG00000000794/ENSMUSG00000036298/ENSMUSG00000025557/ | Slc11a2/Slc6a2/Slc2a6/Slc1a2/Kcnab2/Atp1b1/Atp1a3/Scn3a/Caps2/Slc4a4/Cacna1i/Slc11a1/Kcnk5/Atp1b2/Scn2a/Slc17a7/Slc4a8/Scn1a/Slc45a3/Slc4a5/Slc6a12/Kcnn3/Slc2a13/Slc15a1/Slc15a2/Atp6v0a4/Kcnj2/Kcnab3 | 28 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000022899/ENSMUSG00000038600/ ENSMUSG00000041695/ENSMUSG00000018470 | | |
| MF | GO:0022838 | substrate-specific channel activity | 29/846 | 293/ 15605 | 0.0012966616620637 | 0.0260631823713061 | ENSMUSG00000028931/ENSMUSG00000054720/ ENSMUSG00000032839/ENSMUSG00000057182/ ENSMUSG00000030313/ENSMUSG00000026251/ ENSMUSG00000022416/ENSMUSG00000027994/ ENSMUSG00000050777/ENSMUSG00000026253/ ENSMUSG00000023243/ENSMUSG00000075318/ ENSMUSG00000070570/ENSMUSG00000027674/ ENSMUSG00000028255/ENSMUSG00000009687/ ENSMUSG00000064329/ENSMUSG00000053395/ ENSMUSG00000000794/ENSMUSG00000020787/ ENSMUSG00000037418/ENSMUSG00000028020/ ENSMUSG00000041695/ENSMUSG00000018470/ ENSMUSG00000030523/ENSMUSG00000027071/ ENSMUSG00000036570/ENSMUSG00000042686/ ENSMUSG00000052387 | Kcnab2/Lrrc8c/Trpc1/ Scn3a/Dennd5b/Chrnd/ Cacna1i/Mcub/Tmem37/ Chrng/Kcnk5/Scn2a/ Slc17a7/Pex5l/Clca1/ Fxyd5/Scn1a/Cacng8/ Kcnn3/P2rx1/Best1/Glrb/ Kcnj2/Kcnab3/Trpm1/ P2rx3/Fxyd1/Jph1/Trpm3 | 29 |
| MF | GO:0001730 | 2′-5′-oligoadenylate synthetase activity | 4/846 | 10/ 15605 | 0.00138440459790158 | 0.0260631823713061 | ENSMUSG00000001166/ENSMUSG00000032690/ ENSMUSG00000029605/ENSMUSG00000032661 | Oas1c/Oas2/Oas1b/Oas3 | 4 |
| MF | GO:0015267 | channel activity | 30/846 | 308/ 15605 | 0.00139014896321833 | 0.0260631823713061 | ENSMUSG00000057123/ENSMUSG00000028931/ ENSMUSG00000054720/ENSMUSG00000032839/ ENSMUSG00000057182/ENSMUSG00000030313/ ENSMUSG00000026251/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000050777/ ENSMUSG00000026253/ENSMUSG00000023243/ ENSMUSG00000075318/ENSMUSG00000070570/ ENSMUSG00000027674/ENSMUSG00000028255/ ENSMUSG00000009687/ENSMUSG00000064329/ ENSMUSG00000053395/ENSMUSG00000000794/ ENSMUSG00000020787/ENSMUSG00000037418/ ENSMUSG00000028020/ENSMUSG00000041695/ ENSMUSG00000018470/ENSMUSG00000030523/ ENSMUSG00000027071/ENSMUSG00000036570/ ENSMUSG00000042686/ENSMUSG00000052387 | Gja5/Kcnab2/Lrrc8c/ Trpc1/Scn3a/Dennd5b/ Chrnd/Cacna1i/Mcub/ Tmem37/Chrng/Kcnk5/ Scn2a/Slc17a7/Pex5l/ Clca1/Fxyd5/Scn1a/ Cacng8/Kcnn3/P2rx1/ Best1/Glrb/Kcnj2/Kcnab3/ Trpm1/P2rx3/Fxyd1/Jph1/ Trpm3 | 30 |
| MF | GO:0022803 | passive transmembrane transporter activity | 30/846 | 308/ 15605 | 0.00139014896321833 | 0.0260631823713061 | ENSMUSG00000057123/ENSMUSG00000028931/ ENSMUSG00000054720/ENSMUSG00000032839/ ENSMUSG00000057182/ENSMUSG00000030313/ ENSMUSG00000026251/ENSMUSG00000022416/ ENSMUSG00000027994/ENSMUSG00000050777/ ENSMUSG00000026253/ENSMUSG00000023243/ ENSMUSG00000075318/ENSMUSG00000070570/ ENSMUSG00000027674/ENSMUSG00000028255/ ENSMUSG00000009687/ENSMUSG00000064329/ ENSMUSG00000053395/ENSMUSG00000000794/ ENSMUSG00000020787/ENSMUSG00000037418/ ENSMUSG00000028020/ENSMUSG00000041695/ ENSMUSG00000018470/ENSMUSG00000030523/ ENSMUSG00000027071/ENSMUSG00000036570/ ENSMUSG00000042686/ENSMUSG00000052387 | Gja5/Kcnab2/Lrrc8c/ Trpc1/Scn3a/Dennd5b/ Chrnd/Cacna1i/Mcub/ Tmem37/Chrng/Kcnk5/ Scn2a/Slc17a7/Pex5l/ Clca1/Fxyd5/Scn1a/ Cacng8/Kcnn3/P2rx1/ Best1/Glrb/Kcnj2/Kcnab3/ Trpm1/P2rx3/Fxyd1/Jph1/ Trpm3 | 30 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| upregulated DEGs | | | | | | | | | |
| MF | GO:0046873 | metal ion transmembrane transporter activity | 32/846 | 336/15605 | 0.00141794515491562 | 0.0260631823713061 | ENSMUSG00000023030/ENSMUSG00000055368/ENSMUSG00000026463/ENSMUSG00000005089/ENSMUSG00000028931/ENSMUSG00000026576/ENSMUSG00000040907/ENSMUSG00000032839/ENSMUSG00000057182/ENSMUSG00000035694/ENSMUSG00000030313/ENSMUSG00000060961/ENSMUSG00000022416/ENSMUSG00000027994/ENSMUSG00000050777/ENSMUSG00000026177/ENSMUSG00000023243/ENSMUSG00000041329/ENSMUSG00000075318/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000063354/ENSMUSG00000064329/ENSMUSG00000053395/ENSMUSG00000068323/ENSMUSG00000030109/ENSMUSG00000000794/ENSMUSG00000029716/ENSMUSG00000041695/ENSMUSG00000018470/ENSMUSG00000030523/ENSMUSG00000042686 | Slc11a2/Slc6a2/Atp2b4/Slc1a2/Kcnab2/Atp1b1/Atp1a3/Trpc1/Scn3a/Caps2/Dennd5b/Slc4a4/Cacna1i/Mcub/Tmem37/Slc11a1/Kcnk5/Atp1b2/Scn2a/Slc17a7/Slc4a8/Slc39a4/Scn1a/Cacng8/Slc4a5/Slc6a12/Kcnn3/Tfr2/Kcnj2/Kcnab3/Trpm1/Jph1 | 32 |
| MF | GO:0046906 | tetrapyrrole binding | 13/846 | 93/15605 | 0.00148025937170051 | 0.0265758194175068 | ENSMUSG00000020432/ENSMUSG00000047250/ENSMUSG00000020826/ENSMUSG00000023963/ENSMUSG00000024039/ENSMUSG00000025002/ENSMUSG00000003484/ENSMUSG00000017969/ENSMUSG00000052974/ENSMUSG00000028978/ENSMUSG00000063415/ENSMUSG00000028011/ENSMUSG00000025197 | Tcn2/Ptgs1/Nos2/Cyp39a1/Cbs/Cyp2c55/Cyp4f18/Ptgis/Cyp2f2/Nos3/Cyp26b1/Tdo2/Cyp2c23 | 13 |
| MF | GO:0015291 | secondary active transmembrane transporter activity | 21/846 | 191/15605 | 0.00162665559214818 | 0.0285404117531454 | ENSMUSG00000023030/ENSMUSG00000055368/ENSMUSG00000036067/ENSMUSG00000005089/ENSMUSG00000037762/ENSMUSG00000035694/ENSMUSG00000060961/ENSMUSG00000027994/ENSMUSG00000026177/ENSMUSG00000070570/ENSMUSG00000023032/ENSMUSG00000070280/ENSMUSG00000026435/ENSMUSG00000068323/ENSMUSG00000020600/ENSMUSG00000030109/ENSMUSG00000036298/ENSMUSG00000025557/ENSMUSG00000022899/ENSMUSG00000038963/ENSMUSG00000025938 | Slc11a2/Slc6a2/Slc2a6/Slc1a2/Slc16a9/Caps2/Slc4a4/Mcub/Slc11a1/Slc17a7/Slc4a8/Slc22a14/Slc45a3/Slc4a5/Slc7a15/Slc6a12/Slc2a13/Slc15a1/Slc15a2/Slco4a1/Slco5a1 | 21 |
| MF | GO:0020037 | heme binding | 12/846 | 84/15605 | 0.00183869457335977 | 0.0315438269029721 | ENSMUSG00000047250/ENSMUSG00000020826/ENSMUSG00000023963/ENSMUSG00000024039/ENSMUSG00000025002/ENSMUSG00000003484/ENSMUSG00000017969/ENSMUSG00000052974/ENSMUSG00000028978/ENSMUSG00000063415/ENSMUSG00000028011/ENSMUSG00000025197 | Ptgs1/Nos2/Cyp39a1/Cbs/Cyp2c55/Cyp4f18/Ptgis/Cyp2f2/Nos3/Cyp26b1/Tdo2/Cyp2c23 | 12 |
| MF | GO:0004861 | cyclin-dependent protein serine/threonine kinase inhibitor activity | 4/846 | 11/15605 | 0.00208261827768964 | 0.0334954439661751 | ENSMUSG00000023067/ENSMUSG00000044303/ENSMUSG00000096472/ENSMUSG00000037664 | Cdkn1a/Cdkn2a/Cdkn2d/Cdkn1c | 4 |

(*continued on next page*)

**Table 3** (*continued*)

| upregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| MF | GO:0008391 | arachidonic acid monooxygenase activity | 4/846 | 11/15605 | 0.00208261827768964 | 0.0334954439661751 | ENSMUSG00000025002/ENSMUSG00000003484/ENSMUSG00000052974/ENSMUSG00000025197 | Cyp2c55/Cyp4f18/Cyp2f2/Cyp2c23 | 4 |
| MF | GO:0045236 | CXCR chemokine receptor binding | 4/846 | 11/15605 | 0.00208261827768964 | 0.0334954439661751 | ENSMUSG00000029380/ENSMUSG00000029373/ENSMUSG00000029371/ENSMUSG00000034855 | Cxcl1/Pf4/Cxcl5/Cxcl10 | 4 |
| MF | GO:0004869 | cysteine-type endopeptidase inhibitor activity | 8/846 | 44/15605 | 0.00224560158573312 | 0.0348113229720445 | ENSMUSG00000078945/ENSMUSG00000041481/ENSMUSG00000078942/ENSMUSG00000027985/ENSMUSG00000025889/ENSMUSG00000060459/ENSMUSG00000071203/ENSMUSG00000019278 | Naip2/Serpina3g/Naip6/Lef1/Snca/Kng2/Naip5/Dpep1 | 8 |
| MF | GO:0043027 | cysteine-type endopeptidase inhibitor activity involved in apoptotic process | 6/846 | 26/15605 | 0.00225461936347438 | 0.0348113229720445 | ENSMUSG00000078945/ENSMUSG00000078942/ENSMUSG00000027985/ENSMUSG00000025889/ENSMUSG00000071203/ENSMUSG00000019278 | Naip2/Naip6/Lef1/Snca/Naip5/Dpep1 | 6 |
| MF | GO:0004364 | glutathione transferase activity | 6/846 | 27/15605 | 0.00276779322467024 | 0.0418245580919213 | ENSMUSG00000050737/ENSMUSG00000026688/ENSMUSG00000074604/ENSMUSG00000032348/ENSMUSG00000060063/ENSMUSG00000025069 | Ptges/Mgst3/Mgst2/Gsta4/Alox5ap/Gsto2 | 6 |
| MF | GO:0043028 | cysteine-type endopeptidase regulator activity involved in apoptotic process | 7/846 | 36/15605 | 0.00281719821344548 | 0.0418245580919213 | ENSMUSG00000078945/ENSMUSG00000078942/ENSMUSG00000027985/ENSMUSG00000032359/ENSMUSG00000025889/ENSMUSG00000071203/ENSMUSG00000019278 | Naip2/Naip6/Lef1/Ctsh/Snca/Naip5/Dpep1 | 7 |
| MF | GO:0003906 | DNA-(apurinic or apyrimidinic site) endonuclease activity | 4/846 | 12/15605 | 0.00299082440061008 | 0.0435644610805845 | ENSMUSG00000046711/ENSMUSG00000039396/ENSMUSG00000056758/ENSMUSG00000078249 | Hmga1/Neil3/Hmga2/Hmga1b | 4 |

| downregulated DEGs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Category | GOID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | Count |
| CC | GO:0005578 | proteinaceous extracellular matrix | 19/186 | 301/15881 | 2.60E-09 | 6.73E-07 | ENSMUSG00000041559/ENSMUSG00000042254/ENSMUSG00000036040/ENSMUSG00000041577/ENSMUSG00000030116/ENSMUSG00000019929/ENSMUSG00000058571/ENSMUSG00000019899/ENSMUSG00000045672/ENSMUSG00000024330/ENSMUSG00000027111/ENSMUSG00000048915/ENSMUSG00000031849/ENSMUSG00000028600/ENSMUSG00000017344/ENSMUSG00000021388/ENSMUSG00000025784/ENSMUSG00000026668/ENSMUSG00000027966 | Fmod/Cilp/Adamtsl2/Prelp/Mfap5/Dcn/Gpc6/Lama2/Col27a1/Col11a2/Itga6/Efna5/Comp/Podn/Vtn/Aspn/Clec3b/Ucma/Col11a1 | 19 |
| CC | GO:0031012 | extracellular matrix | 20/186 | 367/15881 | 1.20E-08 | 1.55E-06 | ENSMUSG00000041559/ENSMUSG00000042254/ENSMUSG00000036040/ENSMUSG00000041577/ENSMUSG00000030116/ENSMUSG00000019929/ENSMUSG00000058571/ENSMUSG00000019899/ENSMUSG00000045672/ENSMUSG00000024330/ENSMUSG00000027111/ENSMUSG00000048915/ENSMUSG00000031849/ENSMUSG00000028600/ENSMUSG00000017344/ENSMUSG00000021388/ | Fmod/Cilp/Adamtsl2/Prelp/Mfap5/Dcn/Gpc6/Lama2/Col27a1/Col11a2/Itga6/Efna5/Comp/Podn/Vtn/Aspn/Clec3b/Ucma/Cpxm2/Col11a1 | 20 |

(*continued on next page*)

**Table 3** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| downregulated DEGs | | | | | | | | |
| | | | | | | | ENSMUSG00000025784/ENSMUSG00000026668/ ENSMUSG00000030862/ENSMUSG00000027966 | |
| CC | GO:0044420 | extracellular matrix component | 7/186 | 119/ 15881 | 0.00050175587003438 | 0.0433182567796348 | ENSMUSG00000030116/ENSMUSG00000019899/ ENSMUSG00000045672/ENSMUSG00000027111/ ENSMUSG00000048915/ENSMUSG00000017344/ ENSMUSG00000027966 | Mfap5/Lama2/Col27a1/Itga6/ Efna5/Vtn/Col11a1 | 7 |
| MF | GO:0005044 | scavenger receptor activity | 6/183 | 36/ 15605 | 3.48E-06 | 0.000869278969210754 | ENSMUSG00000024593/ENSMUSG00000017344/ ENSMUSG00000032268/ENSMUSG00000008845/ ENSMUSG00000038188/ENSMUSG00000024034 | Megf10/Vtn/Tmprss5/Cd163/ Scarf1/Tmprss3 | 6 |
| MF | GO:0005201 | extracellular matrix structural constituent | 6/183 | 38/ 15605 | 4.84E-06 | 0.000869278969210754 | ENSMUSG00000041577/ENSMUSG00000030116/ ENSMUSG00000045672/ENSMUSG00000024330/ ENSMUSG00000031849/ENSMUSG00000027966 | Prelp/Mfap5/Col27a1/Col11a2/ Comp/Col11a1 | 6 |
| MF | GO:0038024 | cargo receptor activity | 7/183 | 66/ 15605 | 1.18E-05 | 0.00141386955310093 | ENSMUSG00000024593/ENSMUSG00000017344/ ENSMUSG00000032268/ENSMUSG00000008845/ ENSMUSG00000001247/ENSMUSG00000038188/ ENSMUSG00000024034 | Megf10/Vtn/Tmprss5/Cd163/Lsr/ Scarf1/Tmprss3 | 7 |
| MF | GO:0017147 | Wnt-protein binding | 4/183 | 27/ 15605 | 0.000260074704252757 | 0.023341704706685 | ENSMUSG00000027253/ENSMUSG00000018822/ ENSMUSG00000070867/ENSMUSG00000022297 | Lrp4/Sfrp5/Trabd2b/Fzd6 | 4 |
| MF | GO:0005518 | collagen binding | 5/183 | 57/ 15605 | 0.000536670339370086 | 0.0385329303667722 | ENSMUSG00000019929/ENSMUSG00000031849/ ENSMUSG00000028600/ENSMUSG00000017344/ ENSMUSG00000021388 | Dcn/Comp/Podn/Vtn/Aspn | 5 |
| MF | GO:0097110 | scaffold protein binding | 5/183 | 62/ 15605 | 0.000791196372794239 | 0.0473399163055219 | ENSMUSG00000022840/ENSMUSG00000029361/ ENSMUSG00000032511/ENSMUSG00000027253/ ENSMUSG00000074657 | Adcy5/Nos1/Scn5a/Lrp4/Kif5a | 5 |

**Table 4**
KEGG pathways significantly enriched for differentially expressed genes (DEGs) in differentiated C17.2 cells.

| KEGGID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | keggID | Count |
|---|---|---|---|---|---|---|---|---|---|
| mmu00983 | Drug metabolism - other enzymes | 15/385 | 58/5966 | 2.45E-06 | 0.000678458232980981 | ENSMUSG00000031877/ ENSMUSG00000024066/ ENSMUSG00000031886/ ENSMUSG00000056973/ ENSMUSG00000026688/ ENSMUSG00000028755/ ENSMUSG00000074604/ ENSMUSG00000031725/ ENSMUSG00000061825/ ENSMUSG00000020407/ ENSMUSG00000032348/ ENSMUSG00000090145/ ENSMUSG00000050097/ ENSMUSG00000025069/ ENSMUSG00000054545 | Ces2g/Xdh/Ces2e/ Ces1d/Mgst3/Cda/ Mgst2/Ces1f/Ces2c/ Upp1/Gsta4/ Ugt1a6b/Ces2b/ Gsto2/Ugt1a6a | mmu:72361/mmu:22436/ mmu:234673/ mmu:104158/ mmu:66447/mmu:72269/ mmu:211666/ mmu:234564/ mmu:234671/ mmu:22271/mmu:14860/ mmu:394435/ mmu:234669/ mmu:68214/mmu:94284 | 15 |
| mmu04060 | Cytokine-cytokine receptor interaction | 30/385 | 194/5966 | 5.36E-06 | 0.00074232585500892 | ENSMUSG00000029380/ ENSMUSG00000035385/ ENSMUSG00000031778/ ENSMUSG00000024778/ ENSMUSG00000035373/ ENSMUSG00000028965/ ENSMUSG00000022514/ ENSMUSG00000034394/ ENSMUSG00000026166/ ENSMUSG00000028599/ ENSMUSG00000019122/ ENSMUSG00000026068/ ENSMUSG00000029373/ ENSMUSG00000066755/ ENSMUSG00000008318/ ENSMUSG00000074715/ ENSMUSG00000068227/ ENSMUSG00000029371/ ENSMUSG00000006235/ ENSMUSG00000034855/ ENSMUSG00000000791/ ENSMUSG00000031712/ ENSMUSG00000000120/ ENSMUSG00000040329/ ENSMUSG00000038508/ ENSMUSG00000060548/ ENSMUSG00000062157/ ENSMUSG00000028602/ ENSMUSG00000031780/ ENSMUSG00000038259 | Cxcl1/Ccl2/Cx3cl1/ Fas/Ccl7/Tnfrsf9/ Il1rap/Lif/Ccl20/ Tnfrsf1b/Ccl9/ Il18rap/Pf4/Tnfsf18/ Relt/Ccl28/Il2rb/ Cxcl5/Epor/Cxcl10/ Il12rb1/Il15/Ngfr/ Il7/Gdf15/Tnfrsf19/ Ifnlr1/Tnfrsf8/ Ccl17/Gdf5 | mmu:14825/mmu:20296/ mmu:20312/mmu:14102/ mmu:20306/mmu:21942/ mmu:16180/mmu:16878/ mmu:20297/mmu:21938/ mmu:20308/mmu:16174/ mmu:56744/ mmu:240873/ mmu:320100/ mmu:56838/mmu:16185/ mmu:20311/mmu:13857/ mmu:15945/mmu:16161/ mmu:16168/mmu:18053/ mmu:16196/mmu:23886/ mmu:29820/ mmu:242700/ mmu:21941/mmu:20295/ mmu:14563 | 30 |
| mmu04668 | TNF signaling pathway | 17/385 | 106/5966 | 0.00039117767481587 | 0.036118738641332 | ENSMUSG00000029380/ ENSMUSG00000035385/ ENSMUSG00000031778/ ENSMUSG00000024778/ | Cxcl1/Ccl2/Cx3cl1/ Fas/Mmp9/Tnfaip3/ Creb5/Lif/Ccl20/ Map3k8/Tnfrsf1b/ | mmu:14825/mmu:20296/ mmu:20312/mmu:14102/ mmu:17395/mmu:21929/ mmu:231991/ | 17 |

(*continued on next page*)

**Table 4** (*continued*)

| KEGGID | Description | GeneRatio | BgRatio | pvalue | padj | geneID | geneName | keggID | Count |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | ENSMUSG00000017737/ ENSMUSG00000019850/ ENSMUSG00000053007/ ENSMUSG00000034394/ ENSMUSG00000026166/ ENSMUSG00000024235/ ENSMUSG00000028599/ ENSMUSG00000053175/ ENSMUSG00000055994/ ENSMUSG00000026875/ ENSMUSG00000034855/ ENSMUSG00000031712/ ENSMUSG00000058163 | Bcl3/Nod2/Traf1/ Cxcl10/Il15/Gm5431 | mmu:16878/mmu:20297/ mmu:26410/mmu:21938/ mmu:12051/ mmu:257632/ mmu:22029/mmu:15945/ mmu:16168/ mmu:432555 | |
| mmu00830 | Retinol metabolism | 9/385 | 39/ 5966 | 0.000660315483169279 | 0.0457268472094726 | ENSMUSG00000053279/ ENSMUSG00000025002/ ENSMUSG00000027068/ ENSMUSG00000090145/ ENSMUSG00000064294/ ENSMUSG00000063415/ ENSMUSG00000024747/ ENSMUSG00000054545/ ENSMUSG00000025197 | Aldh1a1/Cyp2c55/ Dhrs9/Ugt1a6b/ Aox3/Cyp26b1/ Aldh1a7/Ugt1a6a/ Cyp2c23 | mmu:11668/mmu:72082/ mmu:241452/ mmu:394435/ mmu:71724/ mmu:232174/ mmu:26358/mmu:94284/ mmu:226143 | 9 |

A

| gene_name | log2FoldChange | padj |
|---|---|---|
| Ucma | -4.64239 | 2.68E-08 |
| Cdkn1a | 1.485774 | 6.36E-101 |
| Tnfsf18 | 3.380902 | 7.03E-11 |
| Cd74 | 3.472131 | 0 |
| Btn2a2 | 6.641648 | 8.96E-09 |
| Vnn1 | 7.754756 | 1.96E-70 |

B

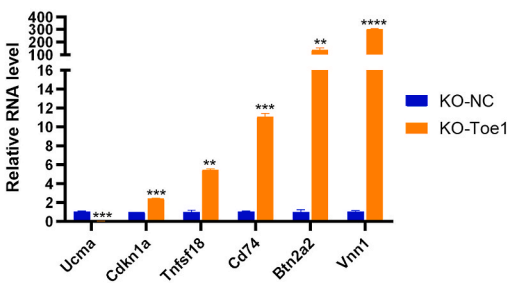



**Fig. 6.** Validation of Gene Expression
(A) Names of genes to be validated, along with their fold-change values and padj values from differential expression analysis.
(B) qPCR validation of mRNA expression levels for the selected genes, **p < 0.01, ***p < 0.001, ****p < 0.0001.

## 4. Discussion

PCH7 is an autosomal recessive neurodegenerative disorder characterized by severe cerebellar and brainstem underdevelopment and atrophy. Currently, there are no effective treatments and supportive care remains the primary approach [23]. During brain development, NSCs undergo rapid symmetric division to expand their cell pool, followed by differentiation to generate neuronal and glial cell progeny. Therefore, understanding the molecular mechanisms of NSC proliferation and differentiation is crucial to identify potential therapeutic targets for neurodegenerative diseases.

Our study focused on the NSC line C17.2 to investigate the effect of Toe1 on the proliferation and differentiation of NSCs. The findings revealed that Toe1 plays a considerable regulatory role in the proliferation and differentiation of NSCs, with Toe1 knockout inhibiting the proliferation and differentiation of C17.2 cells. The RNA-seq results indicated that (1) in undifferentiated C17.2 cells, Toe1 primarily affects biological metabolic processes such as calcium ion binding, the ECM, and alpha-amino acid catabolism. (2) In differentiated C17.2 cells, Toe1 predominantly influences biological functions related to peptidase activity, chemotactic factors, the ECM, and the TNF signaling pathway. We validated the expression of selected genes to confirm the accuracy and reliability of the RNA-seq results. In future studies, we will focus on validating the expression of other genes associated with peptidase activity, chemotactic factors, extracellular matrix, and the TNF signaling pathway.

Peptidases are enzymes capable of hydrolyzing peptide chains and disrupting protein hydrolysis cascades, including those involving hormones, cytokines, membrane receptors, and ECM structures. This disruption leads to the transmission of downstream signals that regulate various functions of bioactive molecules.

Chemokines constitute a class of small secreted proteins that exert biological effects by interacting with G protein-coupled transmembrane receptors. Owing to their ability to guide the migration or aggregation of cells, they are referred to as chemotactic cytokines, and this process is chemotaxis. Chemokines regulate multiple cell signaling pathways, including actin polymerization, cytoskeletal rearrangement, adhesion plaque assembly, and disaggregation. They play important roles in cell survival, proliferation, and other biological activities.

The ECM is a product secreted by cells that remains in the extracellular space and is primarily composed of fibronectin and glycoproteins. The ECM dynamically responds to changes in the microenvironment of an organism, influencing cell behavior by determining the cell shape, affecting cell survival, and controlling cell differentiation.

The TNF signaling pathway is involved in normal inflammatory and immune responses and acts synergistically to coordinate tissue homeostasis by regulating the production of other cytokines. TNF also promotes cell proliferation and differentiation. TNF facilitates MHC class I antigen expression in T cells, enhances IL-2-dependent thymocyte and T-cell proliferative capacity, and stimulates the production of lymphokines such as IL-2, CSF, and IFN-γ. TNF-α exhibits growth factor-like effects on specific tumor cells and collaborates with EGF, PDGF, and insulin to promote proliferation, thereby enhancing EGF receptor expression.

Peptidase activity, chemotactic factors, extracellular matrix (ECM), and TNF signaling pathways, while representing distinct biological processes, intricately interplay to collectively regulate cellular activities. In our investigation, we have identified eight overlapping genes implicated in the TNF signaling pathway, cytokine-cytokine receptor interaction, and cytokine-mediated signaling pathway (refer to Supplementary Fig. 2). Notably, these genes possess multifaceted functions, including the regulation of cell growth, migration, adhesion, and chemotaxis. Moving forward, our research endeavors will be directed towards unraveling the pivotal molecular mechanisms through which Toe1 governs NSC differentiation, with a particular focus on these identified genes.

Of significant relevance is the classical signaling cascade orchestrated by the Notch pathway, which plays a pivotal role in modulating various facets of neural differentiation and function. Therefore, our future investigations will incorporate additional experiments aimed at elucidating the intricate involvement of Toe1 in NSC proliferation and differentiation via the Notch pathway. Our commitment lies in conducting comprehensive research endeavors aimed at advancing our understanding of the intricate mechanisms underlying neurodevelopment, with a particular emphasis on unraveling the regulatory role of Toe1 within this intricate framework.

Our overarching objective is to delineate the intricate crosstalk within the Toe1 regulatory network, thereby laying the foundation for the development of innovative therapeutic strategies targeted towards addressing neurodegenerative diseases, including Pontocerebellar Hypoplasia type 7 (PCH7).

## CRediT authorship contribution statement

**Tingting Deng:** Writing – original draft. **Xingxing Wu:** Visualization, Software, Methodology. **Yujie Wang:** Project administration. **Xiaoqin Fan:** Validation, Methodology. **Bing Hu:** Writing – review & editing, Supervision.

## Data availability statement

The RNA sequencing data were uploaded to the GEO database with accession number GSE254608 and GSE254609, respectively. The another original datasets supporting the conclusions of this article will be made available by the authors. Data will be made available on request.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39535.

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