

Robust temporal changes of cellular senescence and proliferation after sciatic nerve injury

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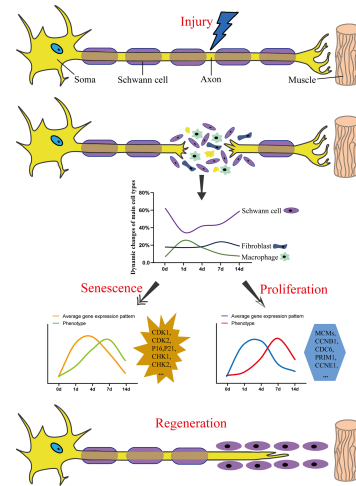
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Graphical Abstract

Dynamic changes of cellular senescence and proliferation during sciatic nerve injury and regeneration



Abstract

Cellular senescence and proliferation are essential for wound healing and tissue remodeling. However, senescence-proliferation cell fate after peripheral nerve injury has not been clearly revealed. Here, post-injury gene expression patterns in rat sciatic nerve stumps (SRP113121) and L4–5 dorsal root ganglia (SRP200823) obtained from the National Center for Biotechnology Information were analyzed to decipher cellular senescence and proliferation-associated genetic changes. We first constructed a rat sciatic nerve crush model. Then, β -galactosidase activities were determined to indicate the existence of cellular senescence in the injured sciatic nerve. Ki67 and EdU immunostaining was performed to indicate cellular proliferation in the injured sciatic nerve. Both cellular senescence and proliferation were less vigorous in the dorsal root ganglia than in sciatic nerve stumps. These results reveal the dynamic changes of injury-induced cellular senescence and proliferation from both genetic and morphological aspects, and thus extend our understanding of the biological processes following peripheral nerve injury. The study was approved by the Animal Ethics Committee of Nantong University, China (approval No. 20190226-001) on February 26, 2019.

Key Words: bioinformatic analysis; cellular senescence; dorsal root ganglia; p16; peripheral nerve regeneration; peripheral nerve trauma; proliferation; rat sciatic nerves; sciatic nerve crush; β -galactosidase activities

Chinese Library Classification No. R446; R745; R363

Introduction

Peripheral nerve trauma is a universal public health issue that causes neuropathic pain and nerve dysfunction, and seriously affects patients' quality of life. Following peripheral nerve injury, immune cells are recruited to damaged nerve stumps and dorsal root ganglia (Scholz and Woolf, 2007; Li et al., 2021; Zhang et al., 2021). Schwann cells and activated immune cells in the injured nerve stumps promote debris clearance, microenvironment reconstruction, and axon elongation (Chen et al., 2015). Injury signals that are dictated by the retrograde transport of calcium and signaling molecules activate the intrinsic growth capacity of neurons and advance nerve regeneration (Mahar and Cavalli, 2018). Emerging studies

have demonstrated the importance of cell recruitment and activation during peripheral nerve regeneration (Jessen and Mirsky, 2016; Liu et al., 2019); however, the involvement of cellular senescence remains largely undetermined.

Cellular senescence is time-related cellular function degeneration (Schmeer et al., 2019). It is a stable cell cycle arrest state that is triggered by cellular insults, including telomere shortening, irradiation, oncogene activation, genomic or epigenomic damage, and tissue injury (He and Sharpless, 2017). Cellular senescence is considered as a driver and an important hallmark of aging (Hernandez-Segura et al., 2018). Notably, senescent cells secrete cytokines, chemokines, and proteinases, which are not only associated with the aging

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process, but also engaged in tissue remodeling and wound healing processes (Demaria et al., 2014; Guo et al., 2021). Senescence-associated secretory phenotype may stimulate the plasticity and stemness of cells. Therefore, transient senescence may have pro-regenerative functions (Calcinotto et al., 2019). However, persistent senescence may lead to chronic poorly healing wounds and be harmful for tissue remodeling and regeneration (Calcinotto et al., 2019; Wang and Shi, 2020). To discover the potential management of the regeneration of injured nerves, it is important to investigate cellular senescence status after peripheral nerve injury.

When the term was initially proposed, cellular senescence was described as the finite proliferative capacity of cells (Hayflick and Moorhead, 1961). Cellular proliferation, by the contrast, indicates the initiation of the cell cycle and increase of cell numbers. Cellular proliferation normally occurs within days after tissue injury and continues throughout the regeneration process. Proliferation of cells largely contributes to tissue augmentation and wound healing (Flanagan, 2000; Velnar and Gradisnik, 2018). It has been demonstrated that, in the peripheral nervous system, molecules that modulate cellular proliferation can influence the regeneration and function recovery of injured peripheral nerves (Guseva et al., 2009; Li et al., 2015; Yi et al., 2019).

Considering the significant involvement of cellular senescence and proliferation in the wound healing process, in this study, we determined the genetic changes of cellular senescence and proliferation after sciatic nerve trauma by analyzing high-throughput data of sciatic nerves and dorsal root ganglia post-injury.

Materials and Methods

Bioinformatic analysis

High-throughput data of RNA in male Sprague-Dawley rat sciatic nerve stumps (0, 1, 4, 7, and 14 days post-injury) and L4–5 dorsal root ganglia (0, 3, 9 hours, 1, 4, and 7 days post-injury) were preserved in the National Center for Biotechnology Information with accession numbers SRP113121 (Zhao and Yi, 2019) and SRP200823 (Shen et al., 2020), respectively. Gene expressions were achieved based on the reads per kilobase transcriptome per million mapped reads method (Mortazavi et al., 2008). A schematic network of the cellular senescence pathway was built based on the Kyoto Encyclopedia of Genes and Genomes (KEGG) database (map04218; <https://www.kegg.jp/pathway/map04218>). Genes with an absolute fold change value of > 2 as well as a *P*-value < 0.05 were designated as differentially expressed as compared with uninjured control genes. The patterns of relative gene expression levels in heatmaps were normalized and generated using Multiple Experiment Viewer software (MeV; <http://mev.tm4.org>).

Animal surgery and tissue collection

A total of 15 clean rats (male, around 8 weeks, 180–220 g)

were obtained from Nantong University Experimental Animal Center (animal license Nos. SCXK [Su] 2014-0001 and SYXK [Su] 2012-0031). To remain consistent with previous sequencing data (SRP113121 (Zhao and Yi, 2019) and SRP200823 (Shen et al., 2020)), male rats were used. Surgery was approved by the Animal Ethics Committee of Nantong University, China (approval No. 20190226-001) on February 26, 2019. Sciatic nerve crush injury was performed in accordance with the Nantong University Institutional Animal Care Guidelines, as described elsewhere (Yi et al., 2015), and the experimental procedure followed the United States National Institutes of Health Guide for the Care and Use of Laboratory Animals (NIH publication No. 85-23, revised 1996).

The 15 rats were randomly divided into five groups (designated as 0, 1, 4, 7, and 14 days; *n* = 3 rats in each group). After anesthetization with mixed narcotics (Sigma-Aldrich; Merck KGaA, Darmstadt, Germany), including 42 mg/kg magnesium sulfate, 85 mg/kg trichloroacetaldehyde monohydrate, and 17 mg/kg sodium pentobarbital, rat sciatic nerves were crushed using forceps (Beaver-Visitec International, Inc., Waltham, MA, USA) (three times, 10 seconds/time). The sciatic nerve stumps at the crush site and dorsal root ganglia at lumbar vertebrae L4–5 were isolated at 1, 4, 7, and 14 days post-injury. Three slides were selected from each group for staining, and the middle segment of the wound was statistically analyzed. The day 0 group included uninjured rats, and was used as a control.

Senescence β-galactosidase staining

Sciatic nerves and dorsal root ganglia were fixed with 4% paraformaldehyde for 18–24 hours. After sucrose dehydration and cutting, tissue sections were restored to room temperature, washed with PBS, and stained with senescence β-galactosidase staining kit (Beyotime, Shanghai, China). Images were obtained using Axio Imager M2 white light microscope (Carl Zeiss Microscopy GMBH, Jena, Germany). The β-galactosidase-positive staining area was measured using ImageJ software (version 1.48; National Institutes of Health, Bethesda, MD, USA).

Immunofluorescence staining

After perfusion, sciatic nerves and dorsal root ganglia at lumbar vertebrae L4–5 were removed, fixed with 4% paraformaldehyde for 18–24 hours, and dehydrated with sucrose solution. After complete dehydration, frozen sections were cut (10 μm in thickness) and stored at –80°C. After restoring tissue sections to room temperature and treating with immunol staining blocking buffer (Beyotime), tissue sections were incubated with primary and secondary antibodies. Detailed information of antibodies is listed in **Table 1**. Cell nuclei were stained with 4',6-diamidino-2-phenylindole (DAPI) Fluoromount-G (0100-20, Southernbiotech, Birmingham, AL, USA). Images were acquired using fluorescence microscopy (Axio Imager M2).

Table 1 | List of antibodies used in this study

Antibody	Source	Catalog number	Species	RRID	Dilution	Incubation time	Temperature
Ki67	Abcam, Cambridge, MA, USA	ab16667	Rabbit	AB_302459	1:500	Overnight	4°C
p16	Signalway Antibody, College Park, MD, USA	32050	Rabbit		1:200	Overnight	4°C
CD68	Abcam, Cambridge, MA, USA	ab31630	Mouse	AB_1141557	1:100	Overnight	4°C
P4HB	Abcam, Cambridge, MA, USA	ab2792	Mouse	AB_303304	1:100	Overnight	4°C
S100β	MilliporeSigma, St Louis, MO, USA	S2532	Mouse	AB_477499	1:400	Overnight	4°C
Cy3 goat anti-rabbit IgG (H+L)	Proteintech Group, Rosemont, IL, USA	SA00009-2	Goat	AB_2890957	1:400	2 h	Room temperature
Alexa Fluor 488 goat anti-mouse IgG (H+L)	Abcam, Cambridge, MA, USA	ab150117	Goat	AB_2688012	1:400	2 h	Room temperature

P4HB: Prolyl 4-hydroxylase subunit beta.

5-Ethynyl-2'-deoxyuridine proliferation assay

5-Ethynyl-2'-deoxyuridine (EdU), a thymidine analogue that can incorporate into cellular DNA during DNA replication (Harris et al., 2018), was intraperitoneally injected into rats using an imaging kit (EdU Alexa Fluor® 647; Invitrogen, Carlsbad, CA, USA). EdU was injected at a concentration of 5 mg/kg 24 hours prior to sciatic nerve and dorsal root ganglion tissue collection. Collected tissue sections were exposed to rabbit anti-S100β (primary antibody, 1:400; Cat# ab52642, RRID AB_882426, Abcam, Cambridge, MA, USA) overnight at 4°C and Cy3 goat anti-rabbit IgG (H+L) (secondary antibody, 1:400; Cat# SA00009-2, RRID AB_2890957, Proteintech Group, Rosemont, IL, USA) for 2 hours at room temperature. DAPI Fluoromount-G was applied to stain the nuclei. EdU visualization was performed using a fluorescence microscope.

Real-time polymerase chain reaction

Gene expression quantification was determined in rat sciatic nerves using SYBR Premix Ex Taq (TaKaRa, Dalian, China) using the 2^{-ΔΔCt} method (Livak and Schmittgen, 2001) on an Applied Biosystems StepOne Real-Time system (Applied Biosystems, Foster City, CA, USA). Information of primers is shown in

Table 2.

Table 2 | List of primer sequences used in this study

Full name	Abbreviation	Forward	Reverse
Cyclin dependent kinase inhibitor 1A	<i>Cdkn1a</i>	5'-GGT GAT GTC CGA CCT GTT CC-3'	5'-ACG CTC CCA GAC GTA GTT GC-3'
Cyclin dependent kinase inhibitor 2A	<i>Cdkn2a</i>	5'-AAC ACT TTC GGT CGT ACC CC-3'	5'-CCC AGC GGA GGA GAG TAG AT-3'
ATM serine/threonine kinase	<i>Atm</i>	5'-AGG TGT GTA ATG AAG CAG GTC T-3'	5'-GAA CCG CGC TAA TGA GAG GA-3'
Cyclin dependent kinase 1	<i>Cdk1</i>	5'-AGG ACT CCA GGC TGT ATC TCA T-3'	5'-TAT CGG TAT TCC AAA CGC TCT-3'
Minichromosome maintenance complex component 5	<i>Mcm5</i>	5'-TGA GAC AAA AGG GGA GGA CA-3'	5'-GCT CGG CAG TAA GCA ATG AA-3'
Cyclin F	<i>Ccnf</i>	5'-CAC TGG GTT CTC CTA CAG CG-3'	5'-TCT CTC GCT TCC GTT TGC TT-3'
Dihydrofolate reductase	<i>Dhfr</i>	5'-GCA AGA ACG GAG ACT TAC CCT-3'	5'-GTT TTC CTA CCC ATA ATC ACC AG-3'
TIMP metalloproteinase inhibitor 1	<i>Timp1</i>	5'-CCT CTG GCA TCC TCT TGT TG-3'	5'-CGT CGA ATC CTT TGA GCA TCT-3'
Glyceraldehyde-3-phosphate dehydrogenase	<i>Gapdh</i>	5'-ACA GCA ACA GGG TGG TGG AC-3'	5'-TTT GAG GGT GCA GCG AAC TT-3'

Statistical analysis

The sample size was estimated from preliminary experiments. Data were summarized from three independent experiments and are presented as the mean ± standard error of the mean (SEM). One-way analysis of variance with Dunnett's multiple comparisons *post hoc* test was performed to compare the differences among injured nerve stumps and the uninjured control (day 0) group using GraphPad Prism 6.0 (GraphPad Software, San Diego, CA, USA). Significant differences were those with a *P*-value < 0.05.

Results

Characterization of cellular senescence in rat sciatic nerves post-injury

On investigating the involvement of cellular senescence post-injury, KEGG results showed that stress signals elicit the activation of various intracellular cascades, including mitogen-activated protein kinases and checkpoint kinases, suppress the activation of cyclin-dependent kinases, induce

an irreversible cell-cycle arrest, and cause cellular senescence (Figure 1A). The abundances of genes involved in the cellular senescence pathway in intact or injured rat sciatic nerves were screened according to previously obtained sequencing data (0, 1, 4, 7, and 14 days post-injury; Yi et al., 2015) to identify significantly differentially expressed genes. *MEK* (MAP2K1, mitogen-activated protein kinase kinase 1) and *GADD45G* (growth arrest and DNA damage inducible gamma) were increased at 1 day post-injury. *CDKN1A* p21 (cyclin-dependent kinase inhibitor 1A), *CDKN2A* p16 (cyclin-dependent kinase inhibitor 2A), *ATM* (ataxia-telangiectasia mutated), *RAD1* (cell cycle checkpoint protein RAD1), and *CHK1/2* (checkpoint kinase 1/2) were decreased post-injury. Increased amount of these genes might contribute to cellular senescence. On the contrary, *FOXO3* (forkhead box O3), a gene that functions as a trigger for cellular apoptosis, was slightly decreased at day 1 post-injury. Down-regulated *FOXO3* might exert an inhibition effect on cellular senescence. Moreover, many cell cycle-related genes, including *CDC25A* (cell division cycle 25A), *CDK1/2/4* (cyclin-dependent kinase 1/2/4), *CCND1* (cyclin D1), *CCNA2* (cyclin A2), and *CCNE1* (cyclin E1), showed elevated expressions, which indicates that cell division was robustly activated in the injured nerve stumps (Figure 1A). The dynamic patterns of genes in KEGG cellular senescence showed that genes coding for essential factors of senescence, such as p16 and p21, were up-regulated post-injury. Genes coding for checkpoint kinases, cyclin-dependent kinases, and cyclin family members were also increased (Figure 1B).

Other than the identification of transcriptome signatures, sciatic nerve sections were subjected to immunostaining to visualize β-galactosidase activity. Some β-galactosidase signals could be observed in the day 0 control group. The signals of β-galactosidase seemed to be attenuated at day 1 post-injury. However, much more intense signals were detected at later time points, especially at day 4 and day 7 post-injury (*P* < 0.05 at days 4 and 7; Figure 1C and D).

Gene expressions were additionally examined using real-time polymerase chain reaction (RT-PCR). RT-PCR results showed elevated mRNA expression levels of *Cdkn1a*, *Cdkn2a*, *Atm*, and *Cdk1* in the injured sciatic nerves as compared with the day 0 group (*P* < 0.05; Figure 2). These observations, together with sequencing outcomes, indicated a significant involvement of senescence-associated genes post-injury.

Immunopositivity of cell senescence marker p16 (Uyar et al., 2020) in rat sciatic nerve stumps were further examined using immunostaining. Consistent with the β-galactosidase signals, the immunopositivity of p16 seemed to be robustly increased at multiple time points post-injury, particularly at days 4 and 7, as compared with day 0 (Figure 3A–C). Sciatic nerve stumps were further co-immunostained with p16 and Schwann cell marker S100β (Zhang et al., 2021a) (Figure 3A), macrophage marker CD68 (Alves et al., 2018) (Figure 3B), as well as fibroblast marker P4HB (Schmid et al., 2020) (Figure 3C). Co-immunostaining of injured sciatic nerve stumps with p16 and S100β showed that the number of Schwann cells first decreased and then gradually increased post-injury, and the number of p16-positive Schwann cells was increased at days 4 and 7 post-injury as compared with the day 0 control (Figure 3A). Immunostaining with CD68 indicated that the number of macrophages was greatly increased immediately post-injury (day 1 post-injury), while the number of p16-positive macrophages seemed to be elevated at 4 and 7 days (Figure 3B). p16-positive fibroblasts also appeared to be increased post-injury (Figure 3C).

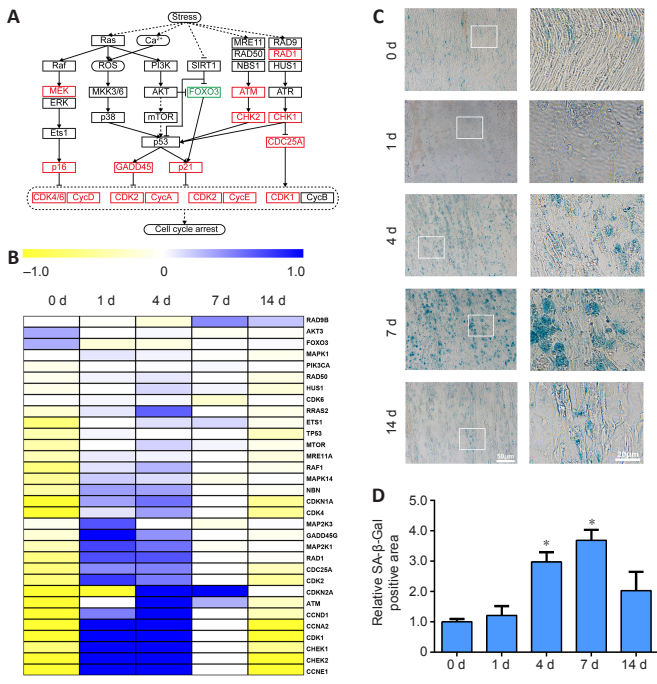


Figure 1 | Cellular senescence in sciatic nerves post-injury. (A) The schematic diagram of cellular senescence pathway. The diagram was modified from the Kyoto Encyclopedia of Genes and Genomes (KEGG) map04218. Significantly increased gene levels are presented in red, while decreased gene levels are presented in green. (B) Patterns of genes in KEGG cellular senescence signaling post-injury. Relative highly-expressed genes are presented in blue, while relative weakly-expressed genes are presented in yellow. (C) β -galactosidase staining of sciatic nerve stumps (crush sites). Elevated β -galactosidase staining was observed after nerve injury. Scale bars: 50 μ m (left) and 20 μ m (right). (D) Relative positive areas of senescence-associated (SA)- β -galactosidase in sciatic nerve stumps. Relative positive areas were normalized by the day 0 group data. Data are expressed as the mean \pm SEM ($n = 3$). * $P < 0.05$, vs. day 0 group (one-way analysis of variance followed by Dunnett's multiple comparisons *post hoc* test). The experiments were repeated three times. **ATM:** ATM serine/threonine kinase; **ATR:** ATR serine/threonine kinase; **AKT:** AKT serine/threonine kinase; **CCNE1:** cyclin E1; **CDC25A:** cell division cycle 25A; **CDK:** cyclin dependent kinase; **CHEK:** CHK, checkpoint kinase; **CycA:** CCNA2, cyclin A2; **CycB:** CCNB1, cyclin B1; **CycD:** CCND2, CYCLIN D2; **GADD45:** growth arrest and DNA damage inducible; **ERK:** mitogen-activated protein kinase 1; **Ets1:** ETS proto-oncogene 1, transcription factor; **FOXO3:** forkhead box O3; **HUS1:** HUS1 checkpoint clamp component; **MAPK1,** mitogen-activated protein kinase 1; **MAP2K:** mitogen-activated protein kinase kinase; **MEK:** mitogen-activated protein kinase kinase 1; **MKK3:** mitogen-activated protein kinase kinase 3; **MRE11:** MRE11 homolog, double strand break repair nuclease; **mTOR:** mechanistic target of rapamycin kinase; **NBN:** NBS1, nibrin; **p16:** CDKN2A, cyclin dependent kinase inhibitor 2A; **p21:** CDKN1A, cyclin dependent kinase inhibitor 1A; **p38:** mitogen-activated protein kinase 14; **p53:** tumor protein P53; **PIK3CA,** phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; **PI3K:** phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; **RAD1:** RRAD, Ras related glycolysis inhibitor and calcium channel regulator; **RAD9:** RAD9 checkpoint clamp component A; **RAD50:** RAD50 double strand break repair protein; **Raf:** Raf-1 proto-oncogene, serine/threonine kinase; **Ras:** KRAS proto-oncogene, GTPase; **RRAS2:** RAS related 2; **SIRT1:** sirtuin 1.

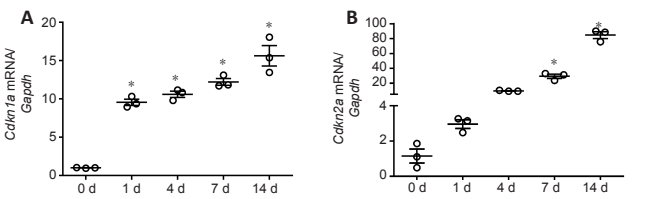


Figure 2 | Validation of the expression patterns of senescence-associated genes after sciatic nerve injury using real-time quantitative polymerase chain reaction. (A–D) The relative mRNA expression levels of *Cdkn1a* (A), *Cdkn2a* (B), *Atm* (C), and *Cdk1* (D) were normalized by *Gapdh*. Elevated mRNA expression levels of target genes were normalized by the day 0 group data. Data are expressed as the mean \pm SEM ($n = 3$). * $P < 0.05$, vs. day 0 group (one-way analysis of variance followed by Dunnett's multiple comparisons *post hoc* test). The experiments were repeated three times. **Atm:** ATM serine/threonine kinase; **Cdk1:** cyclin dependent kinase 1; **Cdkn1a:** cyclin dependent kinase inhibitor 1A; **Cdkn2a:** cyclin dependent kinase inhibitor 2A; **Gapdh:** glyceraldehyde-3-phosphate dehydrogenase.

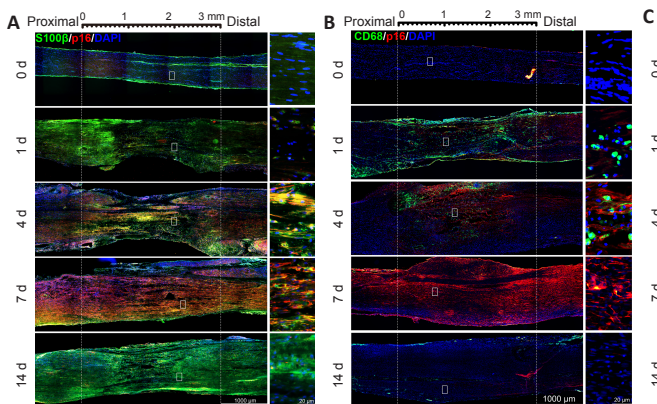


Figure 3 | Senescence activities of Schwann cells, macrophages, and fibroblasts in sciatic nerves post-injury. (A) Co-immunostaining of S100 β (Schwann cell marker; green, stained by Alexa Fluor 488) and senescence marker p16 (senescence marker; red, stained by Cy3) and DAPI (blue, nuclei) of longitudinal sections of rat sciatic nerve segments. (B) Co-immunostaining of CD68 (macrophage marker; green, stained by Alexa Fluor 488), p16 (red, stained by Cy3), and DAPI (blue) of longitudinal sections of rat sciatic nerve segments. (C) Co-immunostaining of P4HB (fibroblast marker; green, stained by Alexa Fluor 488), p16 (red, stained by Cy3), and DAPI (blue) of longitudinal sections of rat sciatic nerve segments. Elevated p16 as well as co-localized p16, S100 β , CD68, and P4HB in sciatic nerves was increased after injury. Scale bars: 1000 μ m and 200 μ m (magnification). The experiments were repeated three times. **DAPI:** 4',6-Diamidino-2-phenylindole; **P4HB:** prolyl 4-hydroxylase subunit beta.

Characterization of cellular senescence in rat dorsal root ganglia post-injury

Cellular senescence status of dorsal root ganglia was also examined according to genetic and morphological aspects. Gene expression levels in rat dorsal root ganglia were screened according to previously obtained sequencing data (Gong et al., 2016). Gene changes were less robust in dorsal root ganglia than in injured sciatic nerves. Only GADD45, p21, RAD9 (cell cycle checkpoint protein RAD9), and *CycD* (cyclin D1) were significantly altered post-injury (Figure 4A). In addition, many genes in dorsal root ganglia showed reduced expressions post-injury (Figure 4B).

The expression levels of genes involved in the cellular senescence-associated GO process (GO:0090398) post-injury were also analyzed based on sequencing data. The results demonstrated dysregulation of many cellular senescence-related genes in rat sciatic nerve stumps post-injury (Additional Table 1), but the expressions of only a few related genes were altered in dorsal root ganglia (Additional Table 2). Moreover, the abundance of senescence-associated secretory phenotype genes was further determined. Many genes were dysregulated, especially up-regulated, in sciatic nerves post-injury (Additional Table 3), while fewer genes showed altered expressions in rat dorsal root ganglia (Additional Table 4).

Morphological immunostaining of β -galactosidase revealed the presence of cellular senescence in dorsal root ganglia of both uninjured and injured rats. Consistent with sequencing data that showed that the gene expressions of few cellular senescence-related genes were significantly changed in dorsal root ganglia, signals of β -galactosidase in dorsal root ganglia were not obviously altered post-injury (Figure 4C).

Characterization of cellular proliferation in rat sciatic nerves post-injury

Given that senescence is typically associated with the loss of replicative potential (Birch et al., 2018), other than cellular senescence, we also determined changes of cellular proliferation using sequencing data of sciatic nerves after nerve injury. Here, the temporal expression profiles of a series of proliferation marker genes were investigated to determine cellular proliferation status (Whitfield et al., 2006). Many proliferation marker genes, including *MKI-67*, which is a gene coding for proliferating cell nuclear antigen Ki67, were

elevated following peripheral nerve injury, especially at days 1 and 4 (Figure 5A).

Immunostaining of sciatic nerve stumps also revealed higher abundances of Ki67 than in uninjured nerves ($P < 0.05$ at day 7; Figure 5B and C). Sciatic nerves were co-immunostained with S100 β , a marker of Schwann cells. Some co-localized S100 β and Ki67 signals were detected in Ki67-positive cells at days 0-14 (Figure 5B and C).

To further visualize cell proliferation status, rats were injected with EdU. EdU incorporation was observed in day 0 sciatic nerve samples. Stronger EdU signals were detected after nerve injury. Summarized data showed that the relative number of EdU colocalized with DAPI increased at days 1, 4, and 7 post-injury ($P < 0.05$) and recovered to baseline levels at day 14 (Figure 5C-E). Immunostaining outcomes, consistent with genetic signatures, showed that peripheral nerve injury induced cellular proliferation at injured sites, especially at early time points.

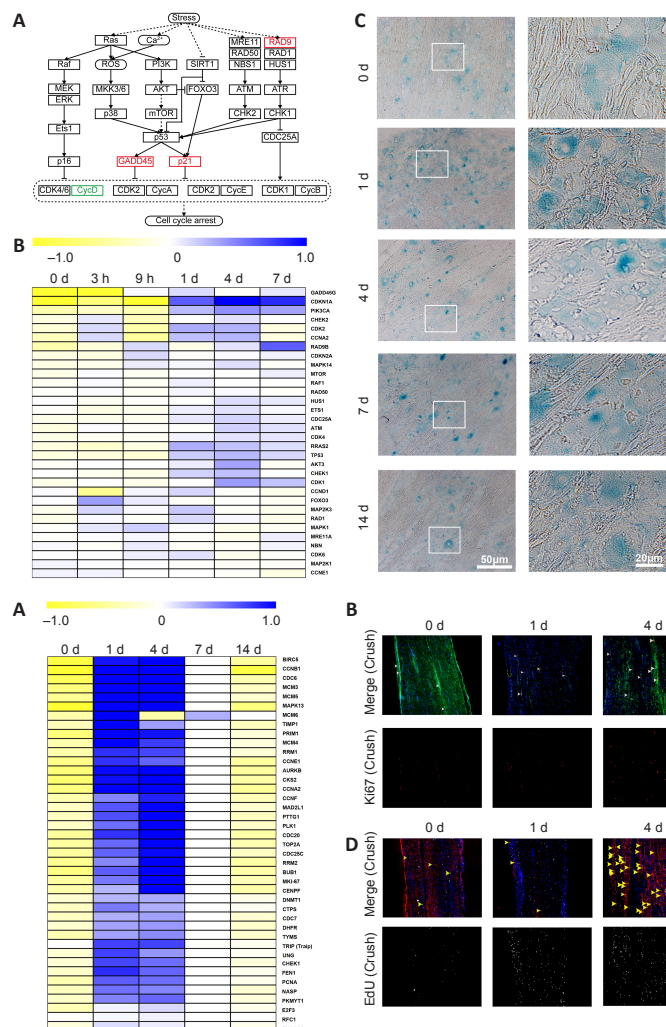
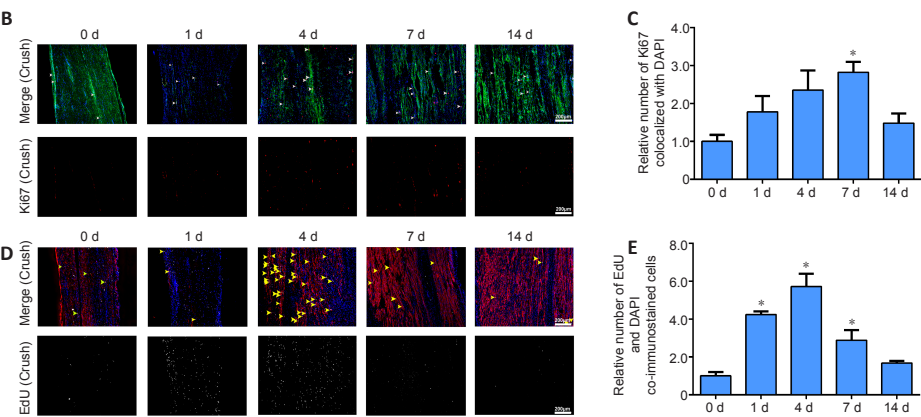


Figure 5 | Cell proliferation in sciatic nerves post-injury.

(A) Expression patterns of proliferation marker genes in rat sciatic nerves post-injury. Relative highly-expressed genes are presented in blue, while relative weakly-expressed genes are presented in yellow. (B) Co-immunostaining of Ki67 and S100 β in rat sciatic nerves. Ki67-positive cells are presented in red (stained by Cy3), while S100 β -positive cells are presented in green (stained by Alexa Fluor 488). Co-immunostained cells are marked by arrowheads in white. The cell nucleus is labeled in blue. The number of Ki67-positive cells was increased after injury. (C) Relative numbers of Ki67 and DAPI co-localized cells. An increased number of Ki67 cells colocalized with DAPI was observed after nerve injury, as compared with day 0 (control). (D) Co-immunostaining of EdU and S100 β in rat sciatic nerves. EdU-positive cells are presented in white, while S100 β -positive cells are presented in red (stained by Cy3). Co-immunostaining is marked in arrowheads in yellow. The cell nucleus is labeled in blue. The number of EdU-positive cells was increased after injury. Scale bars: 200 μ m. (E) Relative numbers of EdU and DAPI co-localized cells. An increased number of EdU colocalized with DAPI was observed after nerve injury, as compared with day 0 (control). Data in C and E are expressed as the mean \pm SEM ($n = 3$). $*P < 0.05$, vs. day 0 group (one-way analysis of variance with Dunnett's multiple comparisons *post hoc* test). The experiments were repeated three times. AURKB: Aurora kinase B; BIRC5: baculoviral IAP repeat containing 5; BUB1: BUB1 mitotic checkpoint serine/threonine kinase; CCNA2: cyclin A2; CCNB1: cyclin B1; CCNE1: cyclin E1; CCNF: cyclin F; CDC: CDC like kinase; CENPF: centromere protein F; CHEK1: checkpoint kinase 1; CKS2: CDC28 protein kinase regulatory subunit 2; CTPS: CTP synthase; DAPI: 4',6-diamidino-2-phenylindole; DHFR: dihydrofolate reductase; DNMT1: DNA methyltransferase 1; EdU: 5-ethynyl-2'-deoxyuridine; FEN1: flap structure-specific endonuclease 1; MAD2L1: mitotic arrest deficient 2 like 1; MAPK13: mitogen-activated protein kinase 13; MCM: minichromosome maintenance complex component; NASP: nuclear autoantigenic sperm protein; MKI-67: marker of proliferation Ki-67; PCNA: proliferating cell nuclear antigen; PLK1: Polo like kinase 1; PRIM1: DNA primase subunit 1; RRM: ribonucleotide reductase catalytic subunit M; PTTG1: PTTG1 regulator of sister chromatid separation, securin; TIMP1: TIMP metalloproteinase inhibitor 1; TOP2A: DNA topoisomerase II alpha; TRIP: TRAF interacting protein; TYMS: thymidylate synthetase; UNG: uracil DNA glycosylase.

Figure 4 | Cellular senescence signaling in rat dorsal root ganglia post-injury.

(A) A schematic diagram of the cellular senescence pathway. The cellular senescence pathway diagram was modified from the KEGG cellular senescence signaling (map04218). Increased gene levels are presented in red, while decreased gene levels are presented in green. (B) Expression patterns of genes in KEGG cellular senescence signaling in rat dorsal root ganglia. Relative highly-expressed genes are presented in blue, while relative weakly-expressed genes are presented in yellow. (C) β -galactosidase staining of dorsal root ganglia was presented. Cellular senescence in rat dorsal root ganglia were not obviously altered after trauma to peripheral nerves. Scale bars: 50 μ m (left) and 20 μ m (right). The experiments were repeated three times. AKT: AKT serine/threonine kinase; ATM: ATM serine/threonine kinase; ATR: ATR serine/threonine kinase; CCNE1: cyclin E1; CDC25A: cell division cycle 25A; CDK: cyclin dependent kinase; CHEK: CHK, checkpoint kinase; CycB: CCNB1, cyclin B1; CycD: CCND2, cyclin D2; CycA: CCNA2, cyclin A2; ERK: mitogen-activated protein kinase 1; Ets1: ETS proto-oncogene 1, transcription factor; FOXO3: forkhead box O3; GADD45: growth arrest and DNA damage inducible; HUS1: HUS1 checkpoint clamp component; KEGG: Kyoto Encyclopedia of Genes and Genomes; MAP2K: mitogen-activated protein kinase kinase; MAPK1: mitogen-activated protein kinase 1; MEK: mitogen-activated protein kinase kinase 1; MKK3: mitogen-activated protein kinase 3; MRE11: MRE11 homolog, double strand break repair nuclease; mTOR: mechanistic target of rapamycin kinase; NBN: NBS1, nibrin; p16: CDKN2A, cyclin dependent kinase inhibitor 2A; p21: CDKN1A, cyclin dependent kinase inhibitor 1A; p38: mitogen-activated protein kinase 14; p53: tumor protein P53; PI3K: phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PIK3CA: phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; RAD1: RRAD, Ras related glycolysis inhibitor and calcium channel regulator; RAD9: RAD9 checkpoint clamp component A; RAD50: RAD50 double strand break repair protein; Raf: Raf-1 proto-oncogene, serine/threonine kinase; Ras: KRAS proto-oncogene, GTPase; RRAS2, RAS related 2; SIRT1: sirtuin 1.



Similar to the senescence-associated genes, the temporal expressions of proliferation-associated genes were also validated using RT-PCR. RT-PCR showed that, consistent with RNA deep sequencing outcomes, mRNA expression levels of *Mcm5* (minichromosome maintenance complex component 5), *Ccnf* (cyclin F), *Dhfr* (dihydrofolate reductase), and *Timp1* (TIMP metalloproteinase inhibitor 1) were augmented in sciatic nerves post-injury (Figure 6).

Characterization of cellular proliferation in rat dorsal root ganglia post-injury

Cellular proliferation in dorsal root ganglia was assessed based on sequencing data of dorsal root ganglia at 0, 3, 9 hours, 1, 4, and 7 days after nerve injury (Gong et al., 2016). Unlike sciatic

nerve stumps, the majority of proliferation marker genes, including *MKI-67*, were not significantly changed. Only *UNG* (uracil-DNA glycosylase) and *CCNF* were elevated at 1, 4 and 7 days post-injury, *MCM5* and *DHFR* were elevated at 4 and 7 days, and *TIMP1* was elevated at 4 days. Some proliferation marker genes even exhibited reduced expressions. For instance, in dorsal root ganglia, *PLK1* (polo-like kinase 1) was down-regulated at 9 hours post-injury and *MAPK13* (mitogen activated protein kinase 13) was down-regulated at 1 day post-injury (Figure 7A).

Ki67 and EdU staining showed that although a larger number of proliferating cells appeared to exist, changes of cellular proliferation in dorsal root ganglia were less noticeable than in sciatic nerves (Figure 7B and C).

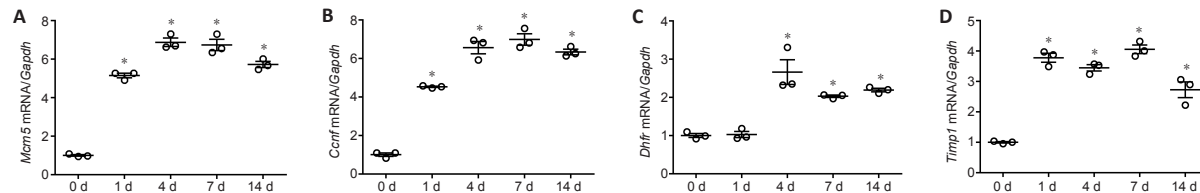


Figure 6 | Validation of the expression patterns of proliferation-associated genes after sciatic nerve injury by real-time quantitative polymerase chain reaction. (A–D) The relative expression levels of *Mcm5* (A), *Ccnf* (B), *Dhfr* (C), and *Timp1* (D) were normalized by *Gapdh* in the day 0 group. Data are expressed as the mean \pm SEM ($n = 3$). * $P < 0.05$, vs. 0 d (one-way analysis of variance followed by Dunnett’s multiple comparisons *post hoc* test). The experiments were repeated three times. CCNF: Cyclin F; DHFR: dihydrofolate reductase; GAPDH: glyceraldehyde-3-phosphate dehydrogenase; MCM5: minichromosome maintenance complex component 5; TIMP1: TIMP metalloproteinase inhibitor 1.

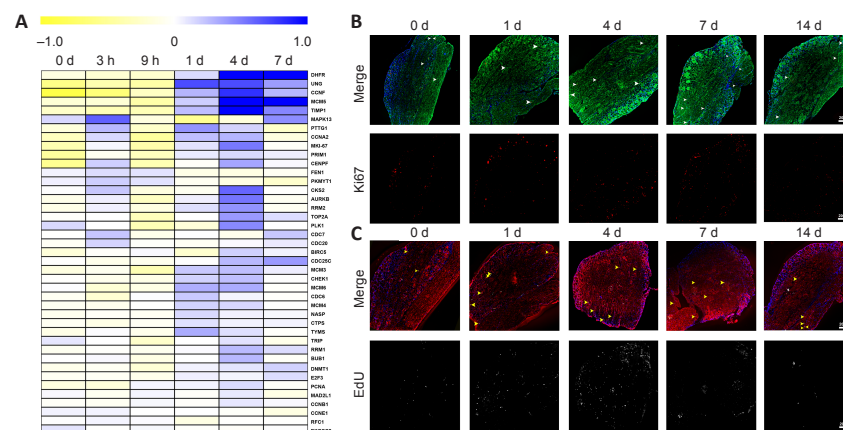


Figure 7 | Cell proliferation in rat dorsal root ganglia after sciatic nerve injury. (A) Expression patterns of proliferation marker genes in dorsal root ganglia post-injury. Relative highly-expressed genes are presented in blue, while relative weakly-expressed genes are presented in yellow. (B) Co-immunostaining of Ki67 and S100 β in rat dorsal root ganglia. Ki67-positive cells are presented in red (stained by Cy3), while S100 β -positive cells are presented in green (stained by Alexa Fluor 488). Co-immunostained cells are marked by arrowheads in white. The cell nucleus is labeled in blue. Less robust changes of Ki67-positive cells was observed in rat dorsal root ganglia after nerve injury. (C) Co-immunostaining of EdU and S100 β in rat dorsal root ganglia. EdU-positive cells are labeled in white, while S100 β -positive cells are presented in red (stained by Cy3). Co-immunostaining is marked by arrowheads in yellow. The cell nucleus is labeled in blue. Less robust changes of EdU-positive cells was observed in rat dorsal root ganglia after nerve injury. Scale bars: 200 μ m. The experiments were repeated three times. AURKB: Aurora kinase B; BIRC5: baculoviral IAP repeat containing 5; BUB1: BUB1 mitotic checkpoint serine/threonine kinase; CCNA2: cyclin A2; CCNB1: cyclin B1; CCNE1: cyclin E1; CCNF: cyclin F; CDC: CDC like kinase; CENPF: centromere protein F; K2S2: CDC28 protein kinase regulatory subunit 2; CTPS: CTP synthase; DHFR: dihydrofolate reductase; DNMT1: DNA methyltransferase 1; E2F3: E2F transcription factor 3; EdU: 5-ethynyl-2'-deoxyuridine; EXOSC9: exosome component 9; FEN1: flap structure-specific endonuclease 1; MAD2L1: mitotic arrest deficient 2 like 1; MAPK13: mitogen-activated protein kinase 13; MCM: minichromosome maintenance complex component; MKI-67: marker of proliferation Ki-67; NASP: nuclear autoantigenic sperm protein; PCNA: proliferating cell nuclear antigen; PKMYT1: protein kinase, membrane associated tyrosine/threonine 1; PLK1: Polo like kinase 1; PRIM1: DNA primase subunit 1; PTTG1: PTTG1 regulator of sister chromatid separation, securin; RFC1: replication factor C subunit 1; RRM: ribonucleotide reductase catalytic subunit M; TIMP1: TIMP metalloproteinase inhibitor 1; TRIP: TRAF interacting protein; TYMS: thymidylate synthetase; TOP2A: DNA topoisomerase II alpha; UNG: uracil DNA glycosylase.

Discussion

The degeneration and regeneration of peripheral nerves involve various sophisticated biological activities, including inflammatory and immune responses, as well as cellular growth and organ development (Yu et al., 2016; Yi et al., 2017). Together with strong and sustained inflammatory and immune responses, enhanced expressions of growth factors, proinflammatory cytokines, and matrix metalloproteinases have been observed (Xing et al., 2017; Zhang et al., 2019). These features are typical characteristics of cellular senescence (Hubackova et al., 2012; Pan et al., 2017). Observations of

these senescence-associated phenotypes demonstrated the essential participation of cellular senescence post-injury.

Using high-throughput data and KEGG pathway analysis, cellular senescence-associated gene changes were determined in this study. Sequencing data showed that *CDKN2A* was elevated by nearly 4 fold at 4 and 7 days post-injury and remained highly expressed at around 2.5-fold versus its expression in uninjured nerve stumps at 14 days post-injury. *CDKN1A* was also had a 2-fold increase from day 1 to day 7 post-injury. These findings suggest that p16 and p21 pathway-associated cellular senescence might be

induced by peripheral injury stress. β -Galactosidase activity was also found to increase at 4 and 7 days post-injury, which reveals the involvement of cellular senescence in the nerve regeneration process. Depressed β -galactosidase activity at 1 day post-injury might be due to reduced total cell populations at the injured site.

Meanwhile, many genes that promote cell cycle transition rather than cell cycle arrest, including *CDK1*, *CDK2*, and *CDK4/6*, were increased post-injury. The up-regulation of these cell cycle initiation-related genes indicates that, besides cell senescence, cell proliferation might be extensively involved in the peripheral nerve regeneration process. Consistent with this interpretation, the investigation of cell proliferation marker expressions revealed the importance of cell proliferation. These findings demonstrate the complexity of cellular transitions post-injury.

Other than genes in the canonical cellular senescence pathway, transcriptome profiles of consistently up-regulated or down-regulated senescence marker genes were also evaluated (Casella et al., 2019). A total of elevated 29 genes in senescence were discovered in rat sciatic nerve stumps. Only some of these genes, such as *Slc9a7* (solute carrier family 9 member A7), *Srpx2* (sushi repeat-containing protein X-linked 2), *Elmod1* (ELMO domain-containing protein 1), *Stat1* (signal transducer and activator of transcription 1), *Wdr63* (dynein axonemal intermediate chain 3), *Tap1* (transporter 1, ATP binding cassette subfamily B member), and *Dio2* (iodothyronine deiodinase 2), showed an elevated expression post-injury, while the expressions of other genes, such as *Dhrs7* (dehydrogenase/reductase 7), *Pam* (peptidylglycine alpha-amidating monooxygenase), *SLC16A14* (solute carrier family 16 member 14), *GPR155* (G protein-coupled receptor 155), and *CLDN1* (claudin 1), were decreased (**Additional Figure 1A**). The expression patterns of senescence marker genes that were down-regulated in senescence were also determined. However, many of these genes did not show expression reduction (**Additional Figure 1B**). A possible explanation could be that these senescence marker genes were identified in human cells (i.e., human umbilical vein endothelial cells, diploid fibroblasts, and aortic endothelial cells) and might not accurately reflect genetic changes in rats. The irregularity of senescence marker gene expressions could also be due to the mixed status of cellular senescence and proliferation at the injured site post-injury.

Cellular senescence/proliferation was also examined in dorsal root ganglia, because dorsal root ganglia receive retrograde transport of signals from the injury site and respond to injury signals (Abe and Cavalli, 2008; Allodi et al., 2012). Following peripheral nerve injury, senescence mainly occurred at the injured site, and the temporal dynamic changes of senescence/proliferation-associated genes in dorsal root ganglia were less robust than changes in sciatic nerves.

One limitation of the current study is that singles of β -galactosidase, Ki67, and EdU immunostaining in dorsal root ganglia were not quantified. Nonetheless, representative images also showed that changes of senescence-associated β -galactosidase immunostaining and proliferation-associated Ki67 and EdU immunostaining were not apparent in dorsal root ganglia.

Our results revealed that β -galactosidase signals decreased 7 days post-injury in sciatic nerves and dorsal root ganglia. The presence of transient senescent cells has been reported in the young adult rodents and acute senescent cells in adult rodents. These cells may be cleared via immunosurveillance after having executed their programmed function (Childs et

al., 2014). In addition, following nerve injury, immune cells are quickly recruited to injured sites (Benowitz and Popovich, 2011; Chen et al., 2015). Therefore, the reduced signal of senescence cells may also be due to immune clearance.

Tissue sections were co-immunostained with Ki67 and S100 β to identify the proliferation status of Schwann cells. In the peripheral nervous system, Schwann cells are unique and essential glial cells that contribute to regeneration (Ma et al., 2016; Min et al., 2021). Indeed, transplantation of Schwann cells to injured sites has been successfully used to repair peripheral nerve defects (Hood et al., 2009). The co-localization of Ki67 and S100 β at the injured site suggests that many Schwann cells undergo proliferation post-injury. Other than sciatic nerve stumps, Schwann cells are also important cell populations in dorsal root ganglia (Steffensen et al., 2018). Perineuronal satellite cells of the dorsal root ganglia are generally considered as a subtype of Schwann cells (Armati and Mathey, 2013). Unlike sciatic nerve stumps, only a few Ki67-positive cells were identified in dorsal root ganglia, and the growth conditions of Schwann cells in dorsal root ganglia were not clearly observed. Combined with previous findings (Qian et al., 2018), our results further our understanding of the dynamic changes of major cell types in peripheral nerves, cellular senescence, and cell proliferation during sciatic nerve injury and regeneration. Overall, the current study reveals more about injury-induced senescence and proliferation cell fate, and contributes to our understanding of the cellular changes that occur following peripheral nerve injury.

Author contributions: Study conception and design: SYL, SY; experiment implementation and data analysis: YYS, RRZ, QYL, SYL, SY; reagents/materials/analysis support: SYL, SY; manuscript writing: SYL, SY. All authors the final version of this manuscript for publication.

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Additional files:

Additional file 1: Open peer review reports 1–3.

Additional Table 1: Expression levels of genes involved in cellular senescence process in rat sciatic nerve stumps post-injury.

Additional Table 2: Expression levels of genes involved in cellular senescence process in rat dorsal root ganglia post-injury.

Additional Table 3: Expression levels of senescence-associated secretory

phenotype genes in rat sciatic nerve stumps post-injury.

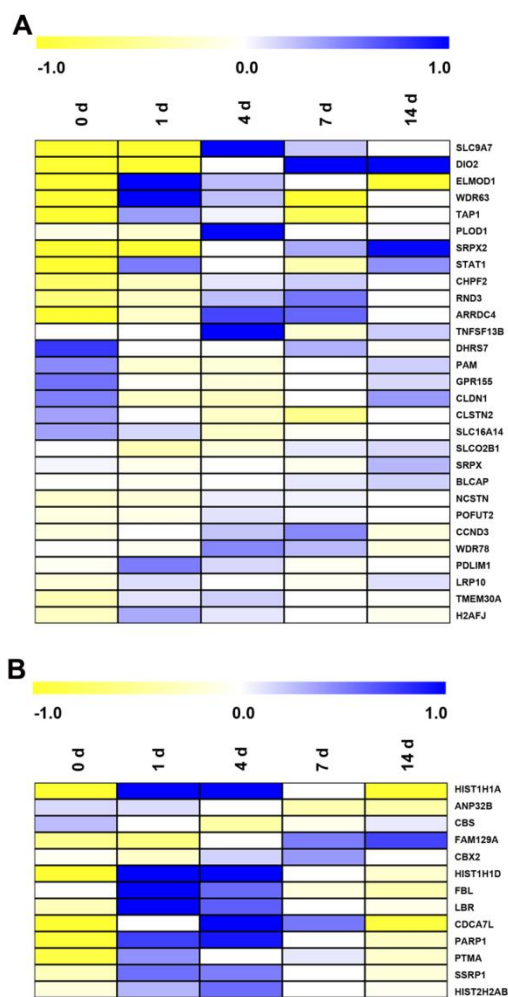
Additional Table 4: Expression levels of senescence-associated secretory phenotype genes in rat dorsal root ganglia post-injury.

Additional Figure 1: Expression levels of senescence marker genes that were elevated (A) and reduced (B) in senescence models in rat sciatic nerves.

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Additional Figure 1 Expression levels of senescence marker genes that were elevated (A) and reduced (B) in senescence models in rat sciatic nerves.

The experiments were repeated by three times. ANP32B: Acidic nuclear phosphoprotein 32 family member B; ARRDC4: arrestin domain containing 4; BLCAP: BLCAP apoptosis inducing factor; CBS: cystathionine beta-synthase; CBX2: chromobox 2; CCND3: cyclin D3; CDCA7L: cell division cycle associated 7 like; CHPF2: chondroitin polymerizing factor 2; CLDN1: claudin 1; CLSTN2: calstentenin 2; DHRS7: dehydrogenase/reductase 7; DIO2: iodothyronine deiodinase 2; ELMOD1: ELMO domain containing 1; FFAM129A: Niban apoptosis regulator 1; BL: fibrillar; GPR155: G protein-coupled receptor 155; H2AFJ: H2A.J histone; HIST1H1A: H1.1 linker histone, cluster member; HIST1H1D: H1.3 linker histone, cluster member; HIST2H2AB: H2A clustered histone 21; LBR: lamin B receptor; LRP10: LDL receptor related protein 10; NCSTN: nicastrin; PAM: peptidylglycine alpha-amidating monooxygenase; PARP1: poly(ADP-ribose) polymerase 1; PDLIM1: PDZ and LIM domain 1; PLOD1: procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1; POFUT2: protein O-fucosyltransferase 2; PTMA: prothymosin alpha; SLC9A7: solute carrier family 9 member A7; SLC16A14: solute carrier family 16 member 14; SLCO2B1: solute carrier organic anion transporter family member 2B1; SRPX: sushi repeat containing protein X-linked; STAT1: signal transducer and activator of transcription 1; RND3: Rho family GTPase 3; SSRP1: structure specific recognition protein 1; TAP1: transporter 1, ATP binding cassette subfamily B member; TMEM30A: transmembrane protein 30A; TNFSF13B: TNF superfamily member 13B; WDR: WD repeat domain.

Additional Table 2 Expression levels of genes involved in cellular senescence process in rat dorsal root ganglia post-injury

GeneID	Symbol	Description	0h_RPKM	3h_RPKM	9h_RPKM	1d_RPKM	4d_RPKM	7d_RPKM	GO Component	GO Function	GO Process	Blast nr	
24223	<i>B2m</i>	beta-2 microglobulin	674.2956402	461.1863344	613.7161195	347.3430126	497.8388766	422.3600422	GO:0005769/early endosome;GO:0009986/cell surface;GO:0012505/endo membrane system;GO:0042611;GO:0044421/extracellular region	GO:0005488/binding	GO:0001912/positive regulation of leukocyte mediated cytotoxicity;GO:0002477/antigen processing and presentation of exogenous peptide antigen via MHC class Ib;GO:0006457/protein folding;GO:0006952/defense response;GO:0009607/response to biotic stimulus;GO:0010038/response to metal ion	gij7549746[ref]NP_036644.1/8.69307e-57/beta-2-microglobulin precursor [Rattus norvegicus]	
64202	<i>Calr</i>	calreticulin	271.5521315	233.4954787	276.1615696	245.3130097	265.1907948	238.1502263	GO:0009986/cell surface;GO:0030141/secretory granule;GO:0030176/integral to endoplasmic reticulum membrane;GO:0030529/ribonucleoprotein complex;GO:0042598;GO:0044421/extracellular region	GO:0003723/RNA binding;GO:0019899/enzyme activity;GO:0030246/carbohydrate binding;GO:0030528/transcription regulator activity;GO:0035258/steroid hormone receptor	GO:0002397/MHC class I protein complex assembly;GO:0006275/regulation of DNA replication;GO:0006357/regulation of transcription from RNA polymerase II promoter;GO:0006412/translation;GO:0006605/protein targeting;GO:0007126/meiosis;GO:0007569/cell aging;GO:0008283/cell proliferation;GO:0009968/negative regulation of signal transduction;GO:0010226/response to lithium ion;GO:0030036/actin cytoskeleton organization;GO:0035051/cardiac cell differentiation;GO:0043627/response to estrogen stimulus;GO:0045596/negative regulation of cell differentiation;GO:0045807/positive regulation of endocytosis;GO:0048232/male gamete generation;GO:0051726/regulation of cell cycle	gij11693172[ref]NP_071794.1/0/calreticulin precursor [Rattus norvegicus]	
171116	<i>Opa1</i>	optic atrophy 1	62.41495819	65.83311399	64.87783338	61.31547672	61.04880491	61.59254498	GO:0005743/mitochondrial inner membrane;GO:0031224/intrinsic to membrane;GO:0043005/neurosecretory vesicle;GO:0001669/acrosomal membrane	GO:0017111/nucleoside-triphosphatase activity;GO:0032561/guanylyl ribonucleotide binding;GO:0046872/metal ion binding	GO:0006944/cellular membrane fusion;GO:0007006/mitochondrial membrane organization;GO:0008088/axon cargo transport;GO:0009207;GO:0014020;GO:0045767;GO:0050953/sensory perception of light stimulus	gij148747459[ref]NP_598269.3/0/dynamin-like 120 kDa protein, mitochondrial precursor [Rattus norvegicus]	
25404	<i>Cav1</i>	caveolin 1, caveolae protein	63.26199757	54.17141009	64.00702297	55.86820178	75.39131785	65.62107332	GO:0001669/acrosomal membrane;GO:0005624/membrane fraction;GO:0005924/cell-substrate adherens junction;GO:0012505/endo membrane system;GO:0016021/integral to membrane;GO:0032991/macromolecular complex;GO:0042995/cell projection	GO:0001499/SNARE binding;GO:0008047/enzyme activator activity;GO:0019899/enzyme binding	GO:0000122/negative regulation of transcription from RNA polymerase II promoter;GO:0000165/MAPK cascade;GO:0001765/membrane raft assembly;GO:0001933/negative regulation of protein phosphorylation;GO:0001934/positive regulation of protein phosphorylation;GO:0001935/endothelial cell proliferation;GO:0001959/regulation of cytokine-mediated signaling pathway;GO:0006631/fatty acid metabolic process;GO:0006639/acetylglucose metabolic process;GO:0006898/receptor-mediated endocytosis;GO:0006937/regulation of muscle contraction;GO:0007589/body fluid secretion;GO:0007596/blood coagulation;GO:0010038/response to metal ion;GO:0010212/response to ionizing radiation;GO:0010522/regulation of calcium ion transport into cytosol;GO:0010741/negative regulation of intracellular protein kinase cascade;GO:0014706/striated muscle tissue development;GO:0019229/regulation of vasoconstriction;GO:0030100/regulation of endocytosis;GO:0030177/positive regulation of Wnt receptor signaling pathway;GO:0030178/negative regulation of Wnt receptor signaling pathway;GO:0030301/cholesterol transport;GO:0030509/BMP signaling pathway;GO:0030855/epithelial cell differentiation;GO:0031112;GO:0031294;GO:0031669/cellular response to nutrient levels;GO:0031960/response to corticosteroid stimulus;GO:0033483;GO:0042391/regulation of membrane potential;GO:0042506/tyrosine phosphorylation of Stat5 protein;GO:0043393/regulation of	gij189083698[ref]NP_113744.2/2.3815e-100/caveolin-1 alpha isoform [Rattus norvegicus]gij189083698[ref]NP_113744.2/5.3833e-95/caveolin-1 alpha isoform [Rattus norvegicus]	
293491	<i>Ype13</i>	yippe-like 3 (Drosophila)	143.8818935	140.8995042	153.2908325	134.5089743	97.28150439	105.7788196	GO:0031981/nuclear lumen	-	-	gij112180619[gb]AAH09171.4/5.56326e-100/Ype13 protein partial [Mus musculus]gij18959250[ref]NP_579841.1/0/protein kinase C delta type [Rattus norvegicus]	
170538	<i>Prkcd</i>	protein kinase C, delta	46.49812294	48.71748337	47.51786318	42.48135362	40.5868535	38.63574343	GO:0005626/insoluble fraction;GO:0030054/cell junction;GO:0034399/nuclear periphery;GO:0044444/cytoplasmic part	GO:0004697/protein kinase C activity;GO:0019900/kinase binding;GO:0019904/protein domain specific binding;GO:0030234/enzyme regulator activity;GO:0032559;GO:004	GO:0000302/response to reactive oxygen species;GO:0001101/response to acid;GO:0001816/cytokine production;GO:0001933/negative regulation of protein phosphorylation;GO:0006915/apoptotic process;GO:0007569/cell aging;GO:0009267/cellular response to starvation;GO:0009746;GO:0009968/negative regulation of signal transduction;GO:0010740/positive regulation of intracellular protein kinase cascade;GO:0010828/positive regulation of glucose transport;GO:0012502/induction of programmed cell death;GO:0015711/organic anion transport;GO:0019724/B cell mediated immunity;GO:0032868/response to insulin stimulus;GO:0042113/B cell activation;GO:0043405/regulation of MAP kinase	gij18959250[ref]NP_579841.1/0/protein kinase C delta type [Rattus norvegicus]	
170851	<i>Map2k1</i>	mitogen activated protein kinase kinase 1	62.78672556	61.31773904	60.60721118	59.3117263	57.49600725	57.82726402	GO:0000267/cell fraction;GO:0015630/microtubule cytoskeleton;GO:0016020/membrane;GO:0030424/axon;GO:0030425/dendrite;GO:0043025/neuronal cell body;GO:0043231/intracellular membrane-bounded organelle;GO:0044444/cytoplasm;GO:0000785/chromatin;GO:0070775	GO:0004712/protein serine/threonine/tyrosine kinase activity;GO:0004725/protein tyrosine phosphatase activity;GO:0019901/protein kinase binding;GO:0031267/small GTPase binding;GO:0032559	GO:0000087/M phase of mitotic cell cycle;GO:0000165/MAPK cascade;GO:0001568/blood vessel development;GO:0002224/toll-like receptor signaling pathway;GO:0006368/transcription elongation from RNA polymerase II promoter;GO:0006470/protein dephosphorylation;GO:0006935/chemotaxis;GO:0006940/regulation of smooth muscle contraction;GO:0007030/Golgi organization;GO:0007169/transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007569/cell aging;GO:0008283/cell proliferation;GO:0009611/response to wounding;GO:0009913/epidermal cell differentiation;GO:0016477/cell migration;GO:0022408/negative regulation of cell-cell adhesion;GO:0031960/response to corticosteroid stimulus;GO:0032318/regulation of Ras GTPase activity;GO:0032401/establishment of melanosome localization;GO:0045595/regulation of cell differentiation;GO:0048858/cell projection morphogenesis;GO:0051259/protein oligomerization	gij13928886[ref]NP_113831.1/0/dual specificity mitogen-activated protein kinase kinase 1 [Rattus norvegicus]	
306571	<i>Kat6a</i>	K(lysine) acetyltransferase 6A	9.08456432	9.742527511	8.55183894	9.867991433	10.86302309	10.38177713	GO:0000785/chromatin;GO:0070775	GO:0003676/nucleic acid binding;GO:0003712/transcription cofactor activity;GO:0004468/lysine N-acetyltransferase activity;GO:0005515/protein binding;GO:0030528/transcription regulator activity;GO:0046914/transitio	GO:0003676/nucleic acid binding;GO:0008408/3'-5' exonuclease activity;GO:0016779/nucleotide transferase activity	GO:0006351/transcription, DNA-dependent;GO:0016573/histone acetylation;GO:0019827/stem cell maintenance;GO:0030097/hemopoiesis;GO:0034728/nucleosome organization;GO:0071103/DNA conformation change	gij213972547[ref]NP_001094040.1/0/histone acetyltransferase KAT6A [Rattus norvegicus]
360992	<i>Pnpt1</i>	polyribonucleotide nucleotidyltransferase 1	22.29410451	17.2423044	18.84924275	14.54865367	14.60340031	13.35823575	GO:0005740/mitochondrial envelope;GO:0016020/membrane	GO:0003676/nucleic acid binding;GO:0008408/3'-5' exonuclease activity;GO:0016779/nucleotide transferase activity	GO:0006401/RNA catabolic process;GO:0010467/gene expression	gij215277019[ref]NP_001135843.1/0/polyribonucleotide nucleotidyltransferase 1, mitochondrial [Rattus norvegicus]	
293621	<i>Hras</i>	Harvey rat sarcoma virus oncogene	54.79815249	55.17713189	58.45187345	50.91922536	50.67106551	53.5351815	GO:0012505/endomembrane system;GO:0016020/membrane;GO:0042598;GO:0043231/intracellular membrane-bounded organelle;GO:0044444/cytoplasm	GO:0005515/protein binding;GO:0017111/nucleoside-triphosphatase activity;GO:0032561/guanylyl ribonucleotide binding	GO:0000082/G1/S transition of mitotic cell cycle;GO:0002376/immune system process;GO:0006275/regulation of DNA replication;GO:0006917/induction of apoptosis;GO:0006935/chemotaxis;GO:0007169/transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007569/cell aging;GO:0007599/hemostasis;GO:0008284/positive regulation of cell proliferation;GO:0009207;GO:0009653/anatomical structure morphogenesis;GO:0016192/vesicle-mediated transport;GO:0043066/negative regulation of apoptotic process;GO:0043410/positive regulation of MAPK cascade;GO:0046578/regulation of Ras protein signal transduction;GO:0048168/regulation of	gij55778655[gb]AAH86608.1/1.88669e-99/Hras protein [Rattus norvegicus]gij55778655[gb]AAH86608.1/2.19559e-99/Hras protein [Rattus norvegicus]	
311860	<i>Abl1</i>	c-abl oncogene 1, non-receptor tyrosine kinase	10.94032618	11.85423978	11.4816429	12.49229581	14.29116607	13.35605865	GO:0005635/nuclear envelope;GO:0016020/membrane;GO:0031981/nuclear lumen;GO:0043232;GO:0044444/cytoplasmic part	GO:0003676/nucleic acid binding;GO:0004713/protein tyrosine kinase activity;GO:0019901/protein kinase binding;GO:0019904/protein domain specific binding;GO:0032559;GO:0046914/transitio	GO:0000084/S phase of mitotic cell cycle;GO:0006281/DNA repair;GO:0006351/transcription, DNA-dependent;GO:0006935/chemotaxis;GO:0007010/cytoskeleton organization;GO:0007599/hemostasis;GO:0008629;GO:0043085/positive regulation of catalytic activity;GO:0045597/positive regulation of cell differentiation	gij291167784[ref]NP_001094320.1/0/tyrosine-protein kinase ABL1 [Rattus norvegicus]	
29414	<i>Akt3</i>	v-akt murine thymoma viral oncogene homolog 3	40.83466978	42.30389129	42.530333	45.41857386	38.83999501	40.52274651	GO:0000267/cell fraction;GO:0016020/membrane;GO:0031981/nuclear lumen;GO:0044444/cytoplasmic part	GO:0004672/protein kinase activity;GO:0019901/protein kinase binding;GO:0032559	GO:0002028/regulation of sodium ion transport;GO:0006468/protein phosphorylation;GO:0023052/signaling;GO:0032868/response to insulin stimulus	gij13928778[ref]NP_113763.1/0/RAC-gamma serine/threonine-protein kinase [Rattus norvegicus]	

313961	<i>Smc6</i>	structural maintenance of chromosomes 6	15.57700821	16.40079908	16.27266779	18.16380276	18.04837023	18.0177837	GO:0043231//intracellular membrane-bounded organelle;GO:0043232	GO:0032559	GO:0006259//DNA metabolic process;GO:0033554//cellular response to stress	gij157819723[ref]NP_00110484.1//structural maintenance of chromosomes protein 6
313564	<i>Zmpste24</i>	zinc metalloproteinase STE24	27.01821477	28.2370915	27.89978765	26.95320044	30.11517139	25.93930226	GO:0005626//insoluble fraction;GO:0012505//endomembrane system;GO:0031090//organelle membrane;GO:0031224//intrinsic to membrane;GO:0043231//intracellular membrane-bounded	GO:0004175//endopeptidase activity;GO:0008237//metalloproteinase activity;GO:0043169//cation binding	GO:0006997//nucleus organization;GO:0019941//modification-dependent protein catabolic process	gij157818557[ref]NP_00110444.1//CAAX prenyl protease 1 homolog [Rattus norvegicus]
81507	<i>Bmpr1a</i>	bone morphogenetic protein receptor, type IA	17.78948549	18.44305658	16.69033308	18.1770114	17.71576227	17.39690147	GO:0031224//intrinsic to membrane;GO:0044459//plasma membrane part	GO:0004675//transmembrane receptor protein serine/threonine kinase activity;GO:0032559;GO:0042802//identical protein binding;GO:0043169//cation binding	GO:0001934//positive regulation of protein phosphorylation;GO:0002376//immune system process;GO:0003006//developmental process involved in reproduction;GO:0003203//endocardial cushion morphogenesis;GO:0007178//transmembrane receptor protein serine/threonine kinase signaling pathway;GO:0008284//positive regulation of cell proliferation;GO:0009798//axis specification;GO:0009952//anterior/posterior pattern specification;GO:0010721//negative regulation of cell development;GO:0021536//diencephalon development;GO:0030282//bone mineralization;GO:0030323//respiratory tube development;GO:0030326//embryonic limb morphogenesis;GO:0040007//growth;GO:0042307//positive regulation of protein import into nucleus;GO:0042476//odontogenesis;GO:0042661//regulation of mesodermal cell fate specification;GO:0043009//chordate embryonic development;GO:0045597//positive regulation of cell communication;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0008284//positive regulation of cell proliferation;GO:0009820//alkaloid metabolic process;GO:0009888//tissue development;GO:0010033//response to organic substance;GO:0010557//positive regulation of macromolecule biosynthetic process;GO:0019359//nicotinamide nucleotide biosynthetic process;GO:0022414//reproductive process	gij13540661[ref]NP_110476.1//bone morphogenetic protein receptor type-1A precursor [Rattus norvegicus]
297508	<i>Nampt</i>	nicotinamide phosphoribosyltransferase	20.18063236	18.90618244	16.84844367	16.25338384	16.56455546	15.54946522	GO:0043231//intracellular membrane-bounded organelle;GO:0044444//cytoplasmic part	GO:0005102//receptor binding;GO:0016763//transferase activity, transferring pentosyl groups;GO:0042802//identical protein binding;GO:0032559	GO:0006259//DNA metabolic process;GO:0033554//cellular response to stress	gij148704942[gb]EDL36889.1//pre-B-cell colony-enhancing factor 1 [Mus musculus]
293967	<i>Smc5</i>	structural maintenance of chromosomes 5	8.761302726	10.57636291	7.978608613	10.67423581	12.20335204	11.00156747	GO:0043231//intracellular membrane-bounded organelle;GO:0043232	GO:0004672//protein kinase activity;GO:0032559;GO:0060089	GO:0006464//cellular protein modification process;GO:0007049//cell cycle;GO:0007249//I-kappaB kinase/NF-kappaB cascade	gij157823069[ref]NP_001099827.1//structural maintenance of chromosomes protein 5
83722	<i>Plk2</i>	polo-like kinase 2	16.41713798	13.82479537	17.48899893	19.77834321	22.5279476	22.26392905	-	GO:0004672//protein kinase activity;GO:0032559;GO:0060089	GO:0006464//cellular protein modification process;GO:0007049//cell cycle;GO:0007249//I-kappaB kinase/NF-kappaB cascade	gij13929172[ref]NP_114009.1//serine/threonine-protein kinase PLK2 [Rattus norvegicus]
170818	<i>lcmt</i>	isoprenylcysteine carboxyl methyltransferase	25.23751924	27.81035714	25.87624612	23.40617072	19.21148814	21.26467847	GO:0005626//insoluble fraction;GO:0031090//organelle membrane;GO:0031224//intrinsic to membrane;GO:0043231//intracellular membrane-bounded	GO:0003713//transcription coactivator activity;GO:0003880//protein C-terminal carboxyl O-methyltransferase activity	GO:0006479//protein methylation;GO:0006575//cellular modified amino acid metabolic process;GO:0006605//protein targeting;GO:0006790//sulfur compound metabolic process;GO:0008283//cell proliferation;GO:0040007//growth;GO:0043009//chordate embryonic development;GO:0048513//organ development;GO:0051056//regulation of small GTPase mediated signal transduction	gij158138563[ref]NP_579844.2//2.34941e-144/protein-S-isoprenylcysteine O-methyltransferase [Rattus norvegicus]
303604	<i>Map3k3</i>	mitogen activated protein kinase kinase kinase 3	9.460931027	10.89426686	9.122773576	10.54679689	10.90403938	10.23701015	GO:0044444//cytoplasmic part	GO:0004702//receptor signaling protein serine/threonine kinase activity;GO:0032559;GO:0042802//identical protein binding	GO:0006468//protein phosphorylation;GO:0007249//I-kappaB kinase/NF-kappaB cascade	gij157817777[ref]NP_001100528.1//mitogen-activated protein kinase kinase kinase 3 [Rattus norvegicus]
81649	<i>Mapk14</i>	mitogen activated protein kinase 14	12.23301746	12.67391552	14.69373227	14.16577623	15.29413272	13.3424395	GO:0000267//cell fraction;GO:0005819//spindle lumen;GO:0031981//nuclear lumen;GO:0044444//cytoplasmic part	GO:0004702//receptor signaling protein serine/threonine kinase activity;GO:0004712//protein serine/threonine/tyrosine kinase activity;GO:0005515//protein binding;GO:0032559	GO:0000165//MAPK cascade;GO:0001775//cell activation;GO:0002224//toll-like receptor signaling pathway;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006468//protein phosphorylation;GO:0006631//fatty acid metabolic process;GO:0006974//response to DNA damage stimulus;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007264//small GTPase mediated signal transduction;GO:0007599//hemostasis;GO:0009746;GO:0010212//response to ionizing radiation;GO:0014706//striated muscle tissue development;GO:0019318//hexose metabolic process;GO:0032494//response to peptidoglycan;GO:0032989;GO:0042692//muscle cell	gij148690637[gb]EDL22584.1//mitogen activated protein kinase 14, isoform CRA_a [Mus musculus]
498183	<i>Mapkapk5</i>	mitogen-activated protein kinase-activated protein kinase 5	24.69098627	25.81205973	24.7877939	26.5786581	22.30055915	20.75596753	GO:0031981//nuclear lumen	GO:0004712//protein serine/threonine/tyrosine kinase activity;GO:0032559	GO:0006464//cellular protein modification process;GO:0023052//signaling	gij25570841[ref]NP_001157515.1//MAP kinase-activated protein kinase 5 isoform 1 [Rattus norvegicus]
302898	<i>Rsl1d1</i>	ribosomal L1 domain containing 1	10.64503204	10.68089321	10.95402444	9.143775291	10.20530886	9.997468485	GO:0030529//ribonucleoprotein complex;GO:0031981//nuclear lumen	GO:0005198//structural molecule activity	GO:0008104//protein localization;GO:0010467//gene expression	gij57114334[ref]NP_001008876.1//ribosomal L1 domain containing 1 [Rattus norvegicus]
501099	<i>Srf</i>	serum response factor (c-fos serum response element-binding transcription factor)	7.941183799	8.118468799	8.853755798	8.276448834	8.756927944	8.417452081	GO:0000785//chromatin;GO:0031981//nuclear lumen	GO:0001071//nucleic acid binding transcription factor activity;GO:0003702//RNA polymerase II transcription factor activity;GO:0010843;GO:0042802//identical protein binding;GO:0005488//binding	GO:0001702//gastrulation with mouth forming second;GO:0001704//formation of primary germ layer;GO:0001825//blastocyst formation;GO:0002040//sprouting angiogenesis;GO:0003143//embryonic heart tube morphogenesis;GO:0006939//smooth muscle contraction;GO:0007155//cell adhesion;GO:0007569//cell aging;GO:0007613//memory;GO:0008283//cell proliferation;GO:0009719;GO:0010033//response to organic substance;GO:0010552;GO:0016477//cell migration;GO:0019725//cellular homeostasis;GO:0030036//actin cytoskeleton organization;GO:0031346//positive regulation of cell projection	gij10048414[ref]NP_065239.1//serum response factor [Mus musculus]
291057	<i>Eef1e1</i>	eukaryotic translation elongation factor 1 epsilon 1	28.90603947	28.31351458	28.03304743	28.71164777	30.90853617	30.66816438	GO:0031981//nuclear lumen;GO:0043234//protein complex;GO:0044444//cytoplasmic part	GO:0005488//binding	GO:0006259//DNA metabolic process;GO:0006412//translation;GO:0006915//apoptotic process;GO:0007275//multicellular organismal development;GO:0008283//cell proliferation;GO:0009967//positive regulation of signal transduction	gij157816879[ref]NP_001099576.1//7.66796e-95/eukaryotic translation elongation factor 1 epsilon-1
299694	<i>Nuak1</i>	NUAK family, SNF1-like kinase, 1	8.620728907	8.597282505	11.45053057	7.983371069	9.69478852	8.737831025	-	GO:0004672//protein kinase activity;GO:0032559;GO:0043169//cation binding	GO:0006464//cellular protein modification process	gij157824124[ref]NP_001100244.1//NUAK family SNF1-like kinase 1 [Rattus norvegicus]
303836	<i>Bcl6</i>	B-cell CLL/lymphoma 6	6.515153609	8.840659556	8.084265682	7.568210545	7.035426246	6.647986487	GO:0031981//nuclear lumen;GO:0044427//chromosomal part	GO:0001071//nucleic acid binding transcription factor activity;GO:0003677//DNA binding;GO:0003682//chromatin binding;GO:0030528//transcription regulator activity;GO:0046914//transition	GO:0001783//B cell apoptotic process;GO:0001952//regulation of cell-matrix adhesion;GO:0002467//germinal center formation;GO:0002719;GO:0002828//regulation of type 2 immune response;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006606//protein import into nucleus;GO:0007010//cytoskeleton organization;GO:0007090//regulation of S phase of mitotic cell cycle;GO:0007266//Rho protein signal transduction;GO:0016049//cell growth;GO:0030888//regulation of B cell proliferation;GO:0031347//regulation of defense response;GO:0032318//regulation of Ras GTPase activity;GO:0032989;GO:0033554//cellular response to stress;GO:0045623//negative regulation of T-helper cell differentiation;GO:0045829;GO:0048232//male gamete generation;GO:0048468//cell	gij157819207[ref]NP_001100554.1//B-cell CLL/lymphoma 6 [Rattus norvegicus]
500538	<i>Ybx1</i>	Y box binding protein 1	12.5398116	12.7586187	13.11636552	14.10536391	13.90326882	14.45139537	GO:0005681//spliceosomal complex;GO:0043005//neuron projection;GO:0043234//protein complex	GO:0003723//RNA binding;GO:0005515//protein binding;GO:0043566//structure-specific DNA binding	GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006915//apoptotic process;GO:0008283//cell proliferation;GO:0008380//RNA splicing;GO:0009968//negative regulation of signal transduction;GO:0043009//chordate embryonic development;GO:0048255//mRNA stabilization	gij297278427[ref]XP_001088540.2//1.0175e-117/PREDICTED: hypothetical protein LOC700140 [Macaca mulatta]

29657	<i>Arntl</i>	aryl hydrocarbon receptor nuclear translocator-like	6.137205322	5.249794401	4.787555735	4.796239134	10.0956556	9.102157059	GO:0043231//intracellular membrane-bounded organelle;GO:0043234//protein complex	GO:0001071//nucleic acid binding transcription factor activity;GO:0003676//nucleic acid binding;GO:0004871//signal transducer activity;GO:0005102//receptor binding;GO:0031072//heat	GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006606//protein import into nucleus;GO:0007623//circadian rhythm;GO:0009894;GO:0023052//signaling	gij71896600[ref]NP_077338.2//aryl hydrocarbon receptor nuclear translocator-like protein 1 [Rattus norvegicus]	
303398	<i>Tbx2</i>	T-box 2	14.21281093	11.61135786	15.17265538	14.37465919	12.60721987	12.59617911	GO:0043231//intracellular membrane-bounded organelle;GO:0043234//protein complex	GO:0001071//nucleic acid binding transcription factor activity;GO:0003677//DNA binding;GO:0030528//transcription regulator activity	GO:0001709//cell fate determination;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0007568//aging;GO:0008283//cell proliferation;GO:0009887//organ morphogenesis;GO:0014706//striated muscle tissue development;GO:0060788//ectodermal placode formation	gij157820193[ref]NP_001100503.1//3.10671e-171/T-box transcription factor TBX2 [Rattus norvegicus]	
306977	<i>Zkscan3</i>	zinc finger with KRAB and SCAN domains 3	5.835661057	6.76606486	5.501084648	6.348206953	6.669391423	6.727359278	GO:0043231//intracellular membrane-bounded organelle	GO:0001071//nucleic acid binding transcription factor activity;GO:0003676//nucleic acid binding;GO:0030528//transcription regulator activity;GO:0046914//transitio	GO:0006351//transcription, DNA-dependent	gij141803183[ref]NP_001012053.2//zinc finger protein with KRAB and SCAN domains 3 [Rattus norvegicus]	
24525	<i>Kras</i>	Kirsten rat sarcoma viral oncogene	22.00591466	16.07350941	17.65638565	20.36381041	20.61211113	20.41171011	GO:0005626//insoluble fraction;GO:0043231//intracellular membrane-bounded organelle;GO:0044425//membrane part	GO:0017111//nucleoside-triphosphatase activity;GO:0019904//protein domain specific binding;GO:0032561//guanyl ribonucleotide binding	GO:0000165//MAPK cascade;GO:0002376//immune system process;GO:0006935//chemotaxis;GO:0007010//cytoskeleton organization;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007599//hemostasis;GO:0007632//visual behavior;GO:0008283//cell proliferation;GO:0016601//Rac protein signal transduction;GO:0031960//response to corticosteroid stimulus;GO:0032770//positive regulation of monooxygenase activity;GO:0042692//muscle cell differentiation;GO:0043066//negative regulation of apoptotic process;GO:0043405//regulation of MAP kinase activity;GO:0048168//regulation of neuronal synaptic plasticity;GO:0051091//positive regulation of sequence-specific DNA binding transcription factor	GO:0006281//DNA repair;GO:0006355//regulation of transcription, DNA-dependent;GO:0034969//histone arginine methylation;GO:0035247//peptidyl-arginine omega-N-methylation;GO:0051704	gij13928698[ref]NP_113703.1//6.91668e-86/GTPase KRas [Rattus norvegicus]
295384	<i>Prmt6</i>	protein arginine methyltransferase 6	4.313079223	4.215957025	4.233574735	3.763518127	3.865269063	3.705405506	GO:0043231//intracellular membrane-bounded organelle	GO:0005515//protein binding;GO:0008469//histone-arginine N-methyltransferase activity	GO:0006281//DNA repair;GO:0006355//regulation of transcription, DNA-dependent;GO:0034969//histone arginine methylation;GO:0035247//peptidyl-arginine omega-N-methylation;GO:0051704	gij148670058[gb]EDL02005.1//protein arginine N-methyltransferase 6, isoform CRA_a [Mus musculus]	
29215	<i>Arg2</i>	arginase 2	8.241827392	8.629055309	8.056563158	8.58302604	5.99052787	7.314627742	GO:0043231//intracellular membrane-bounded organelle	GO:0016813//hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds, in linear amidines;GO:0019899//enzyme binding;GO:0043169//cation	GO:0001101//response to acid;GO:0006527//arginine catabolic process;GO:0006942//regulation of striated muscle contraction;GO:0009611//response to wounding;GO:0009746;GO:0010038//response to metal ion;GO:0010243//response to organic nitrogen;GO:0010958//regulation of amino acid import;GO:0012501//programmed cell death;GO:0019627//urea metabolic process;GO:0030323//respiratory tube development;GO:0031326;GO:0032496//response to lipopolysaccharide;GO:0032769//negative regulation of monooxygenase activity;GO:0033273//response to vitamin;GO:0034341//response to interferon-gamma;GO:0048565//digestive tract	GO:0000087//M phase of mitotic cell cycle;GO:0006464//cellular protein modification process	gij9506399[ref]NP_062041.1//arginase-2, mitochondrial precursor [Rattus norvegicus]
306252	<i>Nek4</i>	NIMA-related kinase 4	4.154892983	3.896840877	3.89229727	4.105084939	4.717135379	3.890670861	GO:0031981//nuclear lumen	GO:0004672//protein kinase activity;GO:0032559;GO:0043169//cation binding	GO:0000087//M phase of mitotic cell cycle;GO:0006464//cellular protein modification process	gij198442857[ref]NP_001013152.2//serine/threonine-protein kinase Nek4 [Rattus norvegicus]	
289353	<i>Slc30a10</i>	solute carrier family 30, member 10	4.941340314	6.077958735	5.992953447	4.841987518	4.581302335	3.815133229	GO:0031224//intrinsic to membrane	GO:0015075//ion transmembrane transporter activity	GO:0000041//transition metal ion transport	gij157787032[ref]NP_001099455.1//zinc transporter 10 [Rattus norvegicus]	
299957	<i>Nsmce2</i>	non-SMC element 2, MMS21 homolog (S. cerevisiae)	10.09555515	9.829893145	9.836912209	9.013099095	9.335785067	9.413602344	GO:0043231//intracellular membrane-bounded organelle	GO:0003824//catalytic activity;GO:0046914//transition metal ion binding	GO:0006259//DNA metabolic process;GO:0033554//cellular response to stress	gij67846030[ref]NP_001020047.1//5.875e-128/E3 SUMO-protein ligase NSE2 [Rattus norvegicus]	
353305	<i>Tbx3</i>	T-box 3	4.794193203	5.920935909	4.783873343	4.163647846	4.17521373	3.436464783	GO:0043231//intracellular membrane-bounded organelle	GO:0001071//nucleic acid binding transcription factor activity;GO:0003677//DNA binding;GO:0016564//transcription repressor activity	GO:0000578//embryonic axis specification;GO:0001944//vasculature development;GO:0003002//regionalization;GO:0003143//embryonic heart tube morphogenesis;GO:0006355//regulation of transcription, DNA-dependent;GO:0007568//aging;GO:0008283//cell proliferation;GO:0030900//forebrain development;GO:0032274//gonadotropin secretion;GO:0035051//cardiocyte differentiation;GO:0035115//embryonic forelimb morphogenesis;GO:0043009//chordate embryonic development;GO:0043066//negative regulation of apoptotic process;GO:0045661//regulation of myoblast differentiation;GO:0046545//development of primary female sexual characteristics;GO:0046546//development of primary male sexual characteristics;GO:0048732//gland	GO:0001952//regulation of cell-matrix adhesion;GO:0006464//cellular protein modification process;GO:0006796//phosphate-containing compound metabolic process;GO:0008284//positive regulation of cell proliferation;GO:0008285//negative regulation of cell proliferation;GO:0010467//gene expression;GO:0022008//neurogenesis;GO:0032844//regulation of homeostatic process;GO:0043696;GO:0045596//negative regulation of cell differentiation;GO:0048564//cellular protein modification process;GO:0051707//response to stress;GO:0001822//kidney development;GO:0002763//positive regulation of myeloid leukocyte differentiation;GO:0003164;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006629//lipid metabolic process;GO:0008285//negative regulation of cell proliferation;GO:0009605//response to external stimulus;GO:0010033//response to organic substance;GO:0010226//response to lithium ion;GO:0021700//developmental maturation;GO:0021782//glial cell development;GO:0021988//olfactory lobe development;GO:0030218//erythrocyte differentiation;GO:0043392//negative regulation of DNA binding;GO:0045165//cell fate commitment;GO:0045577//regulation of B cell differentiation;GO:0045686//negative regulation of glial cell differentiation;GO:0045687//positive regulation of glial cell differentiation;GO:0048537//mucosal-associated lymphoid tissue development;GO:0048546//digestive tract morphogenesis;GO:0048562//embryonic organ development;GO:0006342//chromatin silencing;GO:0034968//histone lysine methylation;GO:0042254//ribosome biogenesis;GO:0048869//cellular developmental process;GO:0051704;GO:0071103//DNA conformation change	gij31745146[ref]NP_853669.1//T-box transcription factor TBX3 [Rattus norvegicus]
114483	<i>Cdk6</i>	cyclin-dependent kinase 6	7.05006171	7.0804914	7.544765386	7.876144799	6.493145528	6.849426439	GO:0031252//cell leading edge;GO:0043231//intracellular membrane-bounded organelle;GO:0043234//protein complex	GO:0004674//protein serine/threonine kinase activity;GO:0005515//protein binding;GO:0032559	GO:0000060//protein import into nucleus, translocation;GO:0000079//regulation of cyclin-dependent protein serine/threonine kinase activity;GO:0002788//mitotic cell cycle;GO:0006469//negative regulation of protein kinase activity;GO:0007154//cell communication;GO:0007264//small GTPase mediated signal transduction;GO:0007569//cell aging;GO:0008284//positive regulation of cell proliferation;GO:0009416//response to light stimulus;GO:0009887//organ morphogenesis;GO:0010035//response to inorganic substance;GO:0010212//response to ionizing radiation;GO:0010467//gene expression;GO:0016049//cell growth;GO:0022402//cell cycle process;GO:0030330//DNA damage response, signal transduction by p53 class mediator;GO:0030888//regulation of B cell proliferation;GO:0045767;GO:0051052;GO:0051384//response	gij300797957[ref]NP_001178790.1//1.30568e-177/cell division protein kinase 6 [Rattus norvegicus]	
25587	<i>Id2</i>	inhibitor of DNA binding 2	14.37551533	16.40548421	14.08838807	12.76742616	15.25575737	16.87632864	GO:0031981//nuclear lumen;GO:0032991//macromolecular complex;GO:0044427//chromosomal part;GO:0044444//cytoplasmic part	GO:0030528//transcription regulator activity;GO:0046983//protein dimerization activity	GO:0000060//protein import into nucleus, translocation;GO:0000079//regulation of cyclin-dependent protein serine/threonine kinase activity;GO:0002788//mitotic cell cycle;GO:0006469//negative regulation of protein kinase activity;GO:0007154//cell communication;GO:0007264//small GTPase mediated signal transduction;GO:0007569//cell aging;GO:0008284//positive regulation of cell proliferation;GO:0009416//response to light stimulus;GO:0009887//organ morphogenesis;GO:0010035//response to inorganic substance;GO:0010212//response to ionizing radiation;GO:0010467//gene expression;GO:0016049//cell growth;GO:0022402//cell cycle process;GO:0030330//DNA damage response, signal transduction by p53 class mediator;GO:0030888//regulation of B cell proliferation;GO:0045767;GO:0051052;GO:0051384//response	gij1030074[gb]AAA79771.1//1.12065e-74/Id2 protein, partial [Mus musculus]	
302553	<i>Suv39h1</i>	suppressor of variegation 3-9 homolog 1 (Drosophila)	2.4975484	2.725313329	2.465552931	2.458903294	2.63208809	2.459148497	GO:0000790//nuclear chromatin;GO:0000792//heterochromatin;GO:0016585//chromatin remodeling complex	GO:0005515//protein binding;GO:0018024//histone-lysine N-methyltransferase activity;GO:0046914//transition metal ion binding	GO:0000060//protein import into nucleus, translocation;GO:0000079//regulation of cyclin-dependent protein serine/threonine kinase activity;GO:0002788//mitotic cell cycle;GO:0006469//negative regulation of protein kinase activity;GO:0007154//cell communication;GO:0007264//small GTPase mediated signal transduction;GO:0007569//cell aging;GO:0008284//positive regulation of cell proliferation;GO:0009416//response to light stimulus;GO:0009887//organ morphogenesis;GO:0010035//response to inorganic substance;GO:0010212//response to ionizing radiation;GO:0010467//gene expression;GO:0016049//cell growth;GO:0022402//cell cycle process;GO:0030330//DNA damage response, signal transduction by p53 class mediator;GO:0030888//regulation of B cell proliferation;GO:0045767;GO:0051052;GO:0051384//response	gij7339838[gb]AAF60970.1 AF193862_1//position-effect variegation 3-9 homolog [Mus musculus]	
114851	<i>Cdkn1a</i>	cyclin-dependent kinase inhibitor 1A	4.005355985	6.26145636	4.352747919	11.41972595	15.17518168	12.19798316	GO:0031981//nuclear lumen;GO:0043234//protein complex;GO:0044444//cytoplasmic part	GO:0005515//protein binding;GO:0016538//cyclin-dependent protein kinase regulator activity;GO:0016772//transferase activity, transferring phosphorus-containing groups;GO:0043169//cation binding	GO:0000060//protein import into nucleus, translocation;GO:0000079//regulation of cyclin-dependent protein serine/threonine kinase activity;GO:0002788//mitotic cell cycle;GO:0006469//negative regulation of protein kinase activity;GO:0007154//cell communication;GO:0007264//small GTPase mediated signal transduction;GO:0007569//cell aging;GO:0008284//positive regulation of cell proliferation;GO:0009416//response to light stimulus;GO:0009887//organ morphogenesis;GO:0010035//response to inorganic substance;GO:0010212//response to ionizing radiation;GO:0010467//gene expression;GO:0016049//cell growth;GO:0022402//cell cycle process;GO:0030330//DNA damage response, signal transduction by p53 class mediator;GO:0030888//regulation of B cell proliferation;GO:0045767;GO:0051052;GO:0051384//response	gij18158451[ref]NP_542960.1//1.01626e-92/cyclin-dependent kinase inhibitor 1 [Rattus norvegicus]	
500047	<i>Wnt16</i>	wingless-type MMTV integration site family, member 16	4.501653282	4.980201232	4.362718983	4.459977605	5.906501067	5.560284022	GO:0016020//membrane;GO:0031012//extracellular matrix;GO:0044424//intracellular part	GO:0001664//G-protein coupled receptor binding;GO:0060089	GO:0000122//negative regulation of transcription from RNA polymerase II promoter;GO:0001837//epithelial to mesenchymal transition;GO:0002072//optic cup morphogenesis involved in camera-type eye development;GO:0003002//regionalization;GO:0008283//cell proliferation;GO:0009913//epidermal cell differentiation;GO:0010941//regulation of cell death;GO:0034599//cellular response to oxidative stress;GO:0035567//non-canonical Wnt receptor signaling pathway;GO:0044444//cytoplasmic part	gij157822931[ref]NP_001102693.1//protein Wnt-16 precursor [Rattus norvegicus]	

361403	<i>Terf2</i>	telomeric repeat binding factor 2	3.44125633	3.474261421	3.349306335	4.242275187	3.775000803	4.075076613	GO:0000782//telomere cap complex;GO:0031981//nuclear lumen;GO:0043073//germ cell nucleus;GO:0043234//protein complex	GO:0003690//double-stranded DNA binding;GO:0042802//identical protein binding;GO:0043565//sequence-specific DNA binding	GO:0001304;GO:0006278//RNA-dependent DNA replication;GO:0016233//telomere capping;GO:0032201//telomere maintenance via semi-conservative replication;GO:0034502//protein localization to chromosome;GO:0043009//chordate embryonic development	gij148679452[gb][EDL11399.1]/1.95553e-149/telomeric repeat binding factor 2, isoform CRA_a [Mus musculus]/gij157823369[ref] NP_0011101918.1/0/telomeric repeat-binding factor 2
680111	<i>Rbl1</i>	retinoblastoma-like 1 (p107)	1.844890181	1.915534062	1.497781475	2.007803517	2.952362338	2.370439102	GO:0043231//intracellular membrane-bounded organelle;GO:0043234//protein complex	GO:0005515//protein binding	GO:0006325//chromatin organization;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0007049//cell cycle;GO:0019216//regulation of lipid metabolic process;GO:0051704	gij300797136[ref]NP_001177995.1/0/retinoblastoma-like protein 1 [Rattus norvegicus]
85489	<i>Twist1</i>	twist family bHLH transcription factor 1	2.75998626	1.505578228	2.199233174	1.986489714	2.883632158	2.308771046	GO:0043231//intracellular membrane-bounded organelle	GO:0001071//nucleic acid binding transcription factor activity;GO:0010843;GO:0042802//identical protein binding;GO:0046983//protein dissociation activity	GO:0001503//ossification;GO:0001818//negative regulation of cytokine production;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0012501//programmed cell death;GO:0014020;GO:0016202//regulation of striated muscle tissue development;GO:0016477//cell migration;GO:0030326//embryonic limb morphogenesis;GO:0045596//negative regulation of cell differentiation;GO:0048704//embryonic skeletal system morphogenesis;GO:0065009	gij148704924[gb][EDL36871.1]/7.22751e-59/twist gene homolog 1 (Drosophila) [Mus musculus]
361567	<i>Bcl2l12</i>	BCL2-like 12 (proline rich)	2.056668248	1.747107068	2.044843503	1.40581119	2.25059142	1.988057863	-	-	GO:0006915//apoptotic process	gij157824188[ref]NP_001101950.1/1.00776e-104/bcl-2-like protein 12 [Rattus norvegicus]
64513	<i>Pawr</i>	PRKC, apoptosis, WT1, regulator	1.500514915	1.753635594	1.817710391	1.894299996	2.38068803	2.160052429	GO:0015629//actin cytoskeleton;GO:0016020//membrane;GO:0043231//intracellular membrane-bounded organelle	GO:0003712//transcription cofactor activity;GO:0008092//cytoskeletal protein binding;GO:0030275//LRR domain binding	GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006915//apoptotic process;GO:0007015//actin filament organization;GO:0010560//positive regulation of glycoprotein biosynthetic process;GO:0012502//induction of programmed cell death;GO:0030888//regulation of B cell proliferation;GO:0032623//interleukin-2 production;GO:0042098//T cell proliferation;GO:0050856//regulation of T cell receptor signaling pathway	gij15741228[ref]NP_277020.1/1.64984e-171/PRKC apoptosis WT1 regulator protein [Rattus norvegicus]
295631	<i>Pla2r1</i>	phospholipase A2 receptor 1	0.472354141	0.543498737	0.366627778	0.711346056	0.49556597	0.564473599	GO:0016021//integral to membrane;GO:0044421//extracellular region part	GO:0004871//signal transducer activity;GO:0030246//carbohydrate binding	GO:0016192//vesicle-mediated transport	gij282154817[ref]NP_001094307.1/0/secretory phospholipase A2 receptor precursor [Rattus norvegicus]
292263	<i>Fbxo5</i>	F-box protein 5	0.912397136	1.422475724	0.729193421	0.667169282	1.394787505	1.211482963	GO:0015630//microtubule cytoskeleton;GO:0031981//nuclear lumen;GO:0044444//cytoplasmic part	GO:0046914//transition metal ion binding	GO:0000082//G1/S transition of mitotic cell cycle;GO:0003006//developmental process involved in reproduction;GO:0007056//spindle assembly involved in female meiosis;GO:0007067//mitosis;GO:0007127//meiosis I;GO:0031109//microtubule polymerization or depolymerization;GO:0043161//proteasomal ubiquitin-dependent protein catabolic process;GO:0051420//regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	gij157818927[ref]NP_001099676.1/0/F-box only protein 5 [Rattus norvegicus]
494500	<i>Gsta5</i>	glutathione S-transferase alpha 3	1.025322574	1.04022608	1.374608656	1.333535681	0.717588068	0.676587275	GO:0044424//intracellular part;GO:0044444//cytoplasmic part	GO:0016765//transferase activity, transferring alkyl or aryl (other than methyl) groups	GO:0006790//sulfur compound metabolic process	gij58331159[ref]NP_001009920.1/4.27431e-123/glutathione S-transferase alpha-5 [Rattus norvegicus]/gij58331159[ref] NP_001009920.1/4.6696e-123
25163	<i>Cdkn2a</i>	cyclin-dependent kinase inhibitor 2A	1.378171357	1.377334961	1.779542346	1.538757711	1.596895654	1.646945117	GO:0043234//protein complex;GO:0044444//cytoplasmic part;GO:0044451//nucleoplasmic part;GO:0044452	GO:0001071//nucleic acid binding transcription factor activity;GO:0003676//nucleic acid binding;GO:0008134//transcription factor binding;GO:0016538//cyclin-dependent protein kinase regulator activity;GO:0016772//transferase activity, transferring phosphorus-containing groups;GO:0019900//kinase binding;GO:0030528//transcription regulator activity;GO:0003720//telomerase activity;GO:0003723//RNA binding;GO:0042802//identical protein binding;GO:0043565//sequence-specific DNA binding	GO:0000079//regulation of cyclin-dependent protein serine/threonine kinase activity;GO:0000086//G2/M transition of mitotic cell cycle;GO:0000209//protein polyubiquitination;GO:0000737//DNA catabolic process, endonucleolytic;GO:0001952//regulation of cell-matrix adhesion;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0007050//cell cycle arrest;GO:0007264//small GTPase mediated signal transduction;GO:0009719;GO:0009967//positive regulation of signal transduction;GO:0010033//response to organic substance;GO:0010661;GO:0012502//induction of programmed cell death;GO:0016049//cell growth;GO:0016925//protein sumoylation;GO:0017145//stem cell division;GO:0022603//regulation of anatomical structure morphogenesis;GO:0030888//regulation of B cell proliferation;GO:0031397//negative regulation of protein ubiquitination;GO:0031647//regulation of protein stability;GO:0032583;GO:0033028//myeloid cell apoptotic process;GO:0033080//immature T cell proliferation in thymus;GO:0033157//regulation of intracellular protein transport;GO:0033598//mammary gland epithelial cell proliferation;GO:0033673//negative regulation of kinase activity;GO:0042254//ribosome biogenesis;GO:0043388//positive regulation of DNA binding;GO:0043433//negative regulation of sequence-specific DNA binding transcription factor activity;GO:0051318//G1 phase;GO:0071989//membrane apoptotic process	gij13928746[ref]NP_2113738.1/6.96361e-74/cyclin-dependent kinase inhibitor 2A [Rattus norvegicus]
301965	<i>Tert</i>	telomerase reverse transcriptase	0.154524098	0.283122251	0.166622413	0.300220738	0.254915832	0.284512721	GO:0000782//telomere cap complex;GO:0016604//nuclear body;GO:0030529//ribonucleoprotein complex	GO:0003720//telomerase activity;GO:0003723//RNA binding;GO:0042802//identical protein binding;GO:0043565//sequence-specific DNA binding	GO:0006278//RNA-dependent DNA replication;GO:0043066//negative regulation of apoptotic process	gij55741827[ref]NP_445875.1/0/telomerase reverse transcriptase [Rattus norvegicus]
25164	<i>Cdkn2b</i>	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	0.046131896	0.092207798	0.036576286	0.008148039	0.109926586	0.016334409	GO:0043231//intracellular membrane-bounded organelle;GO:0044444//cytoplasmic part	GO:0016538//cyclin-dependent protein kinase regulator activity;GO:0016772//transferase activity, transferring phosphorus-containing groups;GO:0019900//kinase binding	GO:0000082//G1/S transition of mitotic cell cycle;GO:0006469//negative regulation of protein kinase activity;GO:0007154//cell communication;GO:0007179//transforming growth factor beta receptor signaling pathway;GO:0007584//response to nutrient;GO:0008285//negative regulation of cell proliferation;GO:0010033//response to organic substance;GO:0030099//myeloid cell differentiation;GO:0030855//epithelial cell differentiation;GO:0051318//G1 phase;GO:0051726//regulation of cell cycle	gij18677739[ref]NP_570825.1/4.82017e-68/cyclin-dependent kinase 4 inhibitor B [Rattus norvegicus]
84017	<i>Hmga2</i>	high mobility group AT-hook 2	-	-	0.02064143	0.229912866	-	0.0691361	GO:0043231//intracellular membrane-bounded organelle;GO:0044427//chromosomal part	GO:0005515//protein binding;GO:0043565//sequence-specific DNA binding	GO:0000087//M phase of mitotic cell cycle;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0010741//negative regulation of intracellular protein kinase cascade;GO:0032501//multicellular organismal process;GO:0043388//positive regulation of DNA binding;GO:0051276//chromosome organization	gij14091756[ref]NP_114459.1/8.38419e-32/high mobility group protein HMGI-C [Rattus norvegicus]

Up-regulated genes as compared with the uninjured control (0 hour) were labeled in red color while down-regulated genes were labeled in green color.

Additional Table 3 Expression levels of senescence-associated secretory phenotype genes in rat sciatic nerve stumps post-injury

GeneID	Symbol	Description	0d_RPKM	1d_RPKM	4d_RPKM	7d_RPKM	14d_RPKM	GO Component	GO Function	GO Process	Blast nr
25641	<i>Igfbp6</i>	insulin-like growth factor binding protein 6	886.0780559	227.8608091	289.7139774	440.9400041	706.3236195	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0005520//insulin-like growth factor binding	GO:0008283//cell proliferation;GO:0016049//cell growth;GO:0023052//signaling	gi 6981090 ref NP_037236.1 /2.01742e-130/insulin-like growth factor-binding protein 6 precursor [Rattus norvegicus]gi 149059343 gb EDM10350.1 /0/rCG44468, isoform CRA_b [Rattus norvegicus]
25205	<i>Il6st</i>	interleukin 6 signal transducer	100.2454365	127.5963966	142.8575383	137.3101558	144.8722262	GO:0005887//integral to plasma membrane;GO:0009986//cell surface;GO:0043005//neuron projection;GO:0043235//receptor complex;GO:0044297//cellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0004897//ciliary neurotrophic factor receptor activity;GO:0005126//cytokine receptor binding;GO:0019838//growth factor binding;GO:0042802//identical ligand binding;GO:0004866//endopeptidase inhibitor activity;GO:0005102//receptor binding;GO:0043169//cation binding;GO:0070011//peptidase activity, acting on L-amino acid peptides	GO:0001819//positive regulation of cytokine production;GO:0001960//negative regulation of cytokine-mediated signaling pathway;GO:0002250//adaptive immune response;GO:0002526//acute inflammatory response;GO:0003300//cardiac muscle hypertrophy;GO:0006073//cellular glucan metabolic process;GO:0006641//triglyceride metabolic process;GO:0007167//enzyme linked receptor protein signaling pathway;GO:0007219//Notch signaling pathway;GO:0014909//smooth muscle cell migration;GO:0016049//cell growth;GO:0031667//response to nutrient levels;GO:0042098//T cell proliferation;GO:0042503//tyrosine phosphorylation of Stat3 protein;GO:0042508//tyrosine phosphorylation	gi 267133 sp P25785.2 TIMP2_MOUSE/2.32006e-114/RecName: Full=Metalloproteinase inhibitor 2; AltName: Full=Tissue inhibitor of metalloproteinases 2; Short=TIMP-2; Flags: gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus]gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus]gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus]gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Mus musculus]gi 25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
29543	<i>Timp2</i>	TIMP metalloproteinase inhibitor 2	358.5257833	154.7693291	228.0174192	266.8470103	279.9282891	GO:0005578//proteinaceous extracellular matrix;GO:0030427//site of polarized growth;GO:0042995//cell projection;GO:0043231//intracellular membrane-bounded organelle;GO:0044297//cellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0004866//endopeptidase inhibitor activity;GO:0005102//receptor binding;GO:0043169//cation binding;GO:0070011//peptidase activity, acting on L-amino acid peptides	GO:0007346//regulation of mitotic cell cycle;GO:0008283//cell proliferation;GO:0010033//response to organic substance;GO:0010466//negative regulation of peptidase activity;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0030162//regulation of proteolysis;GO:0031281;GO:0032486//Rap protein signal transduction;GO:0045597//positive regulation of cell differentiation;GO:0046058//cAMP metabolic process;GO:0046578//regulation of Ras protein signal transduction;GO:0048232//male gamete generation;GO:0050767//regulation of neurogenesis	gi 267133 sp P25785.2 TIMP2_MOUSE/2.32006e-114/RecName: Full=Metalloproteinase inhibitor 2; AltName: Full=Tissue inhibitor of metalloproteinases 2; Short=TIMP-2; Flags: gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus]gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus]gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus]gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Mus musculus]gi 25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
360622	<i>Igfbp4</i>	insulin-like growth factor binding protein 4	98.45083882	107.31853	184.2263055	180.4757758	157.7722662	GO:0044421//extracellular region part	GO:0019838//growth factor binding	GO:0006006//glucose metabolic process;GO:0006952//defense response;GO:0008283//cell proliferation;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0016049//cell growth;GO:0044260;GO:0048731	gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus]gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus]gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus]gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Mus musculus]gi 25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
308444	<i>Axl</i>	Axl receptor tyrosine kinase	75.08247163	114.2581879	103.7658821	93.26450471	97.05451718	GO:0016021//integral to membrane	GO:0004713//protein tyrosine kinase activity;GO:0004871//signal transducer activity;GO:0017022//myosin binding;GO:0019900//kinase binding;GO:0032559;GO:0046983//protein dimerization	GO:0000904//cell morphogenesis involved in differentiation;GO:0001818//negative regulation of cytokine production;GO:0002695;GO:0006464//cellular protein modification process;GO:0006796//phosphate-containing compound metabolic process;GO:0006909//phagocytosis;GO:0006952//defense response;GO:0007154//cell communication;GO:0007166//cell surface receptor signaling pathway;GO:0007243//intracellular protein kinase cascade;GO:0009887//organ morphogenesis;GO:0009888//tissue development;GO:0016477//cell migration;GO:0030098//lymphocyte differentiation;GO:0034614//cellular response to reactive oxygen species;GO:0043066//negative regulation of apoptotic process;GO:0046903//secretion;GO:0048232//male gamete generation;GO:0048511//rhythmic process;GO:0001525//angiogenesis;GO:0001935//endothelial cell proliferation;GO:0002548//monocyte chemotaxis;GO:0003006//developmental process involved in reproduction;GO:0003013;GO:0006875//cellular metal ion homeostasis;GO:0006950//response to stress;GO:0007166//cell surface receptor signaling pathway;GO:0007276//gamete generation;GO:0007411//axon guidance;GO:0007626//locomotory behavior;GO:0009628//response to abiotic stimulus;GO:0009725//response to hormone stimulus;GO:0009887//organ morphogenesis;GO:0014046;GO:0021537//telencephalon development;GO:0030832//regulation of actin filament length;GO:0032414//positive regulation of ion transmembrane transporter activity;GO:0042110//T cell activation;GO:0045773//positive regulation of axon extension;GO:0050927//positive regulation of positive chemotaxis;GO:0051707//response to other organism	gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Mus musculus]gi 25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
24772	<i>Cxcl12</i>	chemokine (C-X-C motif) ligand 12	33.16458567	30.53379627	20.03816385	32.31435715	41.74343291	GO:0009986//cell surface;GO:0016020//membrane;GO:0044421//extracellular region part	GO:0005125//cytokine activity;GO:0060089	GO:0001525//angiogenesis;GO:0001935//endothelial cell proliferation;GO:0002548//monocyte chemotaxis;GO:0003006//developmental process involved in reproduction;GO:0003013;GO:0006875//cellular metal ion homeostasis;GO:0006950//response to stress;GO:0007166//cell surface receptor signaling pathway;GO:0007276//gamete generation;GO:0007411//axon guidance;GO:0007626//locomotory behavior;GO:0009628//response to abiotic stimulus;GO:0009725//response to hormone stimulus;GO:0009887//organ morphogenesis;GO:0014046;GO:0021537//telencephalon development;GO:0030832//regulation of actin filament length;GO:0032414//positive regulation of ion transmembrane transporter activity;GO:0042110//T cell activation;GO:0045773//positive regulation of axon extension;GO:0050927//positive regulation of positive chemotaxis;GO:0051707//response to other organism	gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus]gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Mus musculus]gi 25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
24329	<i>Egfr</i>	epidermal growth factor receptor	22.45466311	16.43506179	23.30099529	25.00522507	29.61533889	GO:0005635//nuclear envelope;GO:0030128//clathrin coat of endocytic vesicle;GO:0031224//intrinsic to membrane;GO:0044421//extracellular region part;GO:0044459//plasma membrane part	GO:0003779//actin binding;GO:0004709//MAP kinase kinase kinase activity;GO:0004714//transmembrane receptor protein tyrosine kinase activity;GO:0019838//growth factor binding;GO:0019902//phosphatase binding;GO:0030234//enzyme regulator activity;GO:0032559;GO:0043566//structure-specific DNA binding;GO:0046983//protein receptor binding	GO:0000165//MAPK cascade;GO:0001701//in utero embryonic development;GO:0001775//cell activation;GO:0002009//morphogenesis of an epithelium;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0006950//response to stress;GO:0007155//cell adhesion;GO:0007173//epidermal growth factor receptor signaling pathway;GO:0007346//regulation of mitotic cell cycle;GO:0007423//sensory organ development;GO:0007431//salivary gland development;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009411//response to UV;GO:0010033//response to organic substance;GO:0010038//response to metal ion;GO:0010467//gene expression;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0010863//positive regulation of phospholipase C activity;GO:0016477//cell migration;GO:0019722//calcium-mediated signaling;GO:0021987//cerebral cortex development;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031657;GO:0032768;GO:0035411//catenin import into nucleus;GO:0043405//regulation of MAP kinase activity;GO:0048511//rhythmic process;GO:0048858//cell projection morphogenesis;GO:0050806//positive regulation of synaptic transmission	gi 213417659 ref NP_068616.1 /4.79492e-120/kit ligand isoform 2 precursor [Rattus norvegicus]gi 33667068 ref NP_068615.1 /8.30177e-128/kit ligand isoform 1 precursor [Rattus norvegicus]gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus]gi 11559943 ref NP_071518.1 /1.87163e-100/fibroblast growth factor 7 precursor [Rattus norvegicus]
60427	<i>Kitlg</i>	KIT ligand	13.40503319	12.01319658	7.850388328	9.568220128	10.19312542	GO:0031224//intrinsic to membrane;GO:0043232;GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0001667//ameboidal cell migration;GO:0001934//positive regulation of protein phosphorylation;GO:0002573//myeloid leukocyte differentiation;GO:0006275//regulation of DNA replication;GO:0008406//gonad development;GO:0022602//ovulation cycle process;GO:0033024;GO:0043405//regulation of MAP kinase activity;GO:0045634//regulation of melanocyte differentiation;GO:0046578//regulation of Ras protein signal transduction;GO:0070665	gi 213417659 ref NP_068616.1 /4.79492e-120/kit ligand isoform 2 precursor [Rattus norvegicus]gi 33667068 ref NP_068615.1 /8.30177e-128/kit ligand isoform 1 precursor [Rattus norvegicus]gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus]gi 11559943 ref NP_071518.1 /1.87163e-100/fibroblast growth factor 7 precursor [Rattus norvegicus]
116510	<i>Timp1</i>	TIMP metalloproteinase inhibitor 1	91.90100502	780.8513993	291.0485971	185.4777932	97.38230119	GO:0005578//proteinaceous extracellular matrix;GO:0031091//platelet alpha granule	GO:0004866//endopeptidase inhibitor activity;GO:0043169//cation binding	GO:0001775//cell activation;GO:0006887//exocytosis;GO:0006915//apoptotic process;GO:0007599//hemostasis;GO:0008202//steroid metabolic process;GO:0008283//cell proliferation;GO:0009611//response to wounding;GO:0009725//response to hormone stimulus;GO:0009888//tissue development;GO:0010466//negative regulation of peptidase activity;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0010863//positive regulation of phospholipase C activity;GO:0016477//cell migration;GO:0019722//calcium-mediated signaling;GO:0021987//cerebral cortex development;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031657;GO:0032768;GO:0035411//catenin import into nucleus;GO:0043405//regulation of MAP kinase activity;GO:0048511//rhythmic process;GO:0048858//cell projection morphogenesis;GO:0050806//positive regulation of synaptic transmission	gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus]gi 11559943 ref NP_071518.1 /1.87163e-100/fibroblast growth factor 7 precursor [Rattus norvegicus]
29348	<i>Fgf7</i>	fibroblast growth factor 7	69.82551556	51.33988557	18.07696854	21.0348728	38.01539352	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0005104//fibroblast growth factor receptor binding;GO:0005539//glycosaminoglycan binding	GO:0001934//positive regulation of protein phosphorylation;GO:0001942//hair follicle development;GO:0006935//chemotaxis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009611//response to wounding;GO:0022602//ovulation cycle process;GO:0030036//actin cytoskeleton organization;GO:0030323//respiratory tube development;GO:0030335//positive regulation of cell migration;GO:0032940//secretion by cell;GO:0034613//cellular protein localization;GO:0046470//phosphatidylcholine metabolic process;GO:0048875//chemical homeostasis within a tissue;GO:0050679//positive regulation of epithelial cell proliferation	gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus]gi 11559943 ref NP_071518.1 /1.87163e-100/fibroblast growth factor 7 precursor [Rattus norvegicus]

83785	<i>Vegfa</i>	vascular endothelial growth factor A	10.45166886	9.838930007	14.05134502	15.58977878	14.33532189	GO:0005578//proteinaceous extracellular matrix;GO:0016020/membrane;GO:0016023//cytoplasmic membrane-bounded vesicle	GO:0005172//vascular endothelial growth factor receptor binding;GO:0005539//glycosaminoglycan binding;GO:0042802//identical protein binding;GO:0046983//protein dimerization activity	GO:0001658//branching involved in ureteric bud morphogenesis;GO:0001666//response to hypoxia;GO:0001754//eye photoreceptor cell differentiation;GO:0001934//positive regulation of protein phosphorylation;GO:0001935//endothelial cell proliferation;GO:0002460//adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains;GO:0002690//positive regulation of leukocyte chemotaxis;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007589//body fluid secretion;GO:0008284//positive regulation of cell proliferation;GO:0009791//post-embryonic development;GO:0009967//positive regulation of signal transduction;GO:0010595//positive regulation of endothelial cell migration;GO:0021700//developmental maturation;GO:0022602//ovulation cycle process;GO:0030218//erythrocyte differentiation;GO:0030323//respiratory tube development;GO:0032845;GO:0043009//chordate embryonic development;GO:0043066//negative regulation of apoptotic process;GO:0043114//regulation of vascular permeability;GO:0043488//regulation of mRNA stability;GO:0045765//regulation of angiogenesis;GO:0048747//muscle fiber development;GO:0048771//tissue remodeling;GO:0048875//chemical homeostasis within a tissue;GO:0050927//positive regulation of positive chemotaxis	gi 160358789 ref NP_114024.2 /9.31992e-165/vascular endothelial growth factor A isoform 1 precursor [Rattus norvegicus]/gi 160358793 ref NP_001103804.1 /3.23555e-166/vascular endothelial growth factor A isoform 2 precursor [Rattus norvegicus]/gi 160358797 ref NP_001103804.1 /3.81434e-136/vascular endothelial growth factor A isoform 3 precursor [Rattus norvegicus]/gi 160358811 ref NP_001103736.1 /2.25432e-56/vascular endothelial growth factor A isoform 4 precursor [Mus musculus]/gi 160358815 ref NP_001103737.1 /1.97191e-57/vascular endothelial growth factor A isoform 5 precursor [Mus musculus]
24617	<i>Serpine1</i>	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	10.64362398	134.9637984	49.90453678	20.20066458	10.49680871	GO:0000267//cell fraction;GO:0016020/membrane;GO:0031091//platelet alpha granule;GO:0044421//extracellular region part	GO:0004175//endopeptidase activity;GO:0004866//endopeptidase inhibitor activity;GO:0019899//enzyme binding	GO:0001775//cell activation;GO:0001819//positive regulation of cytokine production;GO:0001953//negative regulation of cell-matrix adhesion;GO:0002540//leukotriene production involved in inflammatory response;GO:0002548//monocyte chemotaxis;GO:0006887//exocytosis;GO:0006915//apoptotic process;GO:0006979//response to oxidative stress;GO:0007569//cell aging;GO:0008283//cell proliferation;GO:0009629//response to gravity;GO:0009888//tissue development;GO:0009966//regulation of signal transduction;GO:0010466//negative regulation of peptidase activity;GO:0010755;GO:0014909//smooth muscle cell migration;GO:0016525//negative regulation of angiogenesis;GO:0030194//positive regulation of blood coagulation;GO:0030195//negative regulation of blood coagulation;GO:0031349//positive regulation of defense response;GO:0031960//response to corticosteroid stimulus;GO:0032102;GO:0032496//response to	gi 6981332 ref NP_036752.1 /0/plasminogen activator inhibitor 1 precursor [Rattus norvegicus]
25341	<i>Tnfrsf11b</i>	tumor necrosis factor receptor superfamily, member 11b	8.290654779	6.87706135	3.373635481	4.709679584	7.241249031	GO:0031012//extracellular matrix	GO:0004871//signal transducer activity;GO:0005102//receptor binding	GO:0002762//negative regulation of myeloid leukocyte differentiation;GO:0010038//response to metal ion;GO:0012501//programmed cell death;GO:0023052//signaling;GO:0031667//response to nutrient levels;GO:0032845;GO:0042475//odontogenesis of dentin-containing tooth;GO:0043062//extracellular matrix organization;GO:0048545//response to steroid hormone stimulus;GO:0001101//response to acid;GO:0001666//response to hypoxia;GO:0001678//cellular glucose homeostasis;GO:0002286//T cell activation involved in immune response;GO:0002456//T cell mediated immunity;GO:0002687//positive regulation of leukocyte migration;GO:0007568//aging;GO:0009314//response to radiation;GO:0009725//response to hormone stimulus;GO:0010038//response to metal ion;GO:0014075//response to amine stimulus;GO:0016337//cell-cell adhesion;GO:0019229//regulation of vasoconstriction;GO:0022406//membrane docking;GO:0022415;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031667//response to nutrient levels;GO:0032496//response to lipopolysaccharide;GO:0034612//response to tumor necrosis factor;GO:0043271//negative regulation of ion	gi 6981306 ref NP_037002.1 /0/tumor necrosis factor receptor superfamily member 11B precursor [Rattus norvegicus]/gi 6981068 ref NP_037099.1 /0/intercellular adhesion molecule 1 precursor [Rattus norvegicus]
25464	<i>Icam1</i>	intercellular adhesion molecule 1	8.937367792	28.41965752	19.85024843	19.32450926	18.89047842	GO:0009986//cell surface;GO:0031224//intracellular membrane;GO:0044421//extracellular region part;GO:0044459//plasma membrane part	GO:0005102//receptor binding	GO:0001666//response to hypoxia;GO:0001934//positive regulation of protein phosphorylation;GO:0001976//neurological system process involved in regulation of systemic arterial blood pressure;GO:0002237//response to molecule of bacterial origin;GO:0002526//acute inflammatory response;GO:0002684//positive regulation of immune system process;GO:0006110//regulation of glycolysis;GO:0006693//prostaglandin metabolic process;GO:0006813//potassium ion transport;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0007050//cell cycle arrest;GO:0007417//central nervous system development;GO:0007568//aging;GO:0007631//feeding behavior;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009968//negative regulation of signal transduction;GO:0010467//gene expression;GO:0010737//protein kinase A signaling cascade;GO:0010828//positive regulation of glucose transport;GO:0014909//smooth muscle cell migration;GO:0030888//regulation of B cell proliferation;GO:0031960//response to corticosteroid stimulus;GO:0032103;GO:0032571//response to vitamin K;GO:0034614//cellular response to reactive oxygen species;GO:0042770//signal transduction in response to DNA damage;GO:0043410//positive regulation of MAPK cascade;GO:0043434//response to peptide hormone stimulus;GO:0043627//response to estrogen stimulus;GO:0044223//male gamete	gi 13591985 ref NP_112313.1 /1.29889e-61/macrophage migration inhibitory factor [Rattus norvegicus]
81683	<i>Mif</i>	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	41.42298192	43.83675942	28.03294889	20.06502169	21.1885679	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0005102//receptor binding;GO:0016862//intracellular oxidoreductase activity, interconverting keto- and enol-groups;GO:0016863//intracellular oxidoreductase activity, transposing C=C bonds	GO:0001666//response to hypoxia;GO:0001934//positive regulation of protein phosphorylation;GO:0001976//neurological system process involved in regulation of systemic arterial blood pressure;GO:0002237//response to molecule of bacterial origin;GO:0002526//acute inflammatory response;GO:0002684//positive regulation of immune system process;GO:0006110//regulation of glycolysis;GO:0006693//prostaglandin metabolic process;GO:0006813//potassium ion transport;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0007050//cell cycle arrest;GO:0007417//central nervous system development;GO:0007568//aging;GO:0007631//feeding behavior;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009968//negative regulation of signal transduction;GO:0010467//gene expression;GO:0010737//protein kinase A signaling cascade;GO:0010828//positive regulation of glucose transport;GO:0014909//smooth muscle cell migration;GO:0030888//regulation of B cell proliferation;GO:0031960//response to corticosteroid stimulus;GO:0032103;GO:0032571//response to vitamin K;GO:0034614//cellular response to reactive oxygen species;GO:0042770//signal transduction in response to DNA damage;GO:0043410//positive regulation of MAPK cascade;GO:0043434//response to peptide hormone stimulus;GO:0043627//response to estrogen stimulus;GO:0044223//male gamete	gi 13591985 ref NP_112313.1 /1.29889e-61/macrophage migration inhibitory factor [Rattus norvegicus]
25021	<i>Itgam</i>	integrin, alpha M	5.242445874	64.48722048	40.79614761	29.86704437	28.51357979	GO:0005887//integral to plasma membrane;GO:0009986//cell surface;GO:0043231//intracellular membrane-bounded organelle	GO:0004871//signal transducer activity;GO:0005539//glycosaminoglycan binding;GO:0043394//proteoglycan binding;GO:0046983//protein binding;GO:0051427	GO:0001666//response to hypoxia;GO:0001934//positive regulation of protein phosphorylation;GO:0001976//neurological system process involved in regulation of systemic arterial blood pressure;GO:0002237//response to molecule of bacterial origin;GO:0002526//acute inflammatory response;GO:0002684//positive regulation of immune system process;GO:0006110//regulation of glycolysis;GO:0006693//prostaglandin metabolic process;GO:0006813//potassium ion transport;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0007050//cell cycle arrest;GO:0007417//central nervous system development;GO:0007568//aging;GO:0007631//feeding behavior;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009968//negative regulation of signal transduction;GO:0010467//gene expression;GO:0010737//protein kinase A signaling cascade;GO:0010828//positive regulation of glucose transport;GO:0014909//smooth muscle cell migration;GO:0030888//regulation of B cell proliferation;GO:0031960//response to corticosteroid stimulus;GO:0032103;GO:0032571//response to vitamin K;GO:0034614//cellular response to reactive oxygen species;GO:0042770//signal transduction in response to DNA damage;GO:0043410//positive regulation of MAPK cascade;GO:0043434//response to peptide hormone stimulus;GO:0043627//response to estrogen stimulus;GO:0044223//male gamete	gi 29789036 ref NP_036843.1 /0/integrin alpha-M precursor [Rattus norvegicus]
25608	<i>Lep</i>	leptin	2.55698922	0.109850243	0.038572957	0.233197358	0.390860521	GO:0044421//extracellular region part	GO:0005102//receptor binding	GO:0001816//cytokine production;GO:0006071//glycerol metabolic process;GO:0006094//gluconeogenesis;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006606//protein import into nucleus;GO:0006631//fatty acid metabolic process;GO:0006694//steroid biosynthetic process;GO:0006811//ion transport;GO:0006915//apoptotic process;GO:0006950//response to stress;GO:0007159//leukocyte cell-cell adhesion;GO:0007631//feeding behavior;GO:0008283//cell proliferation;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0014897;GO:0015980//energy derivation by oxidation of organic compounds;GO:0016125//sterol metabolic process;GO:0019216//regulation of lipid metabolic process;GO:0019221//cytokine-mediated signaling pathway;GO:0019229//regulation of vasoconstriction;GO:0019935//cyclic-nucleotide-mediated signaling;GO:0021953//central nervous system neuron differentiation;GO:0022602//ovulation cycle process;GO:0030073//insulin secretion;GO:0030282//bone mineralization;GO:0030299//intestinal cholesterol absorption;GO:0032096//negative regulation of response to food;GO:0032275//luteinizing hormone secretion;GO:0032278;GO:0032526//response to retinoic acid;GO:0032891;GO:0033591//response to L-ascorbic acid;GO:0042503//tyrosine phosphorylation of Stat3 protein;GO:0043434//response to peptide hormone stimulus;GO:0043627//response to estrogen stimulus;GO:0044223//male gamete	gi 6981148 ref NP_037208.1 /1.03323e-69/leptin precursor [Rattus norvegicus]
246097	<i>Fas</i>	Fas cell surface death receptor	2.477137674	5.715285519	3.982197154	3.281282505	3.411854079	GO:0000267//cell fraction;GO:0009986//cell surface;GO:0031224//intracellular membrane;GO:0031264//death-inducing signaling complex;GO:0044444//cytoplasmic part	GO:0005035//death receptor activity;GO:0019899//enzyme binding	GO:0002237//response to molecule of bacterial origin;GO:0002440;GO:0002449;GO:0003008;GO:0008283//cell proliferation;GO:0008624;GO:0009612//response to mechanical stimulus;GO:0010226//response to lithium ion;GO:0010939//regulation of necrotic cell death;GO:0019221//cytokine-mediated signaling pathway;GO:0031102//neuron projection regeneration;GO:0031960//response to corticosteroid stimulus;GO:0043029//T cell homeostasis;GO:0043066//negative regulation of apoptotic process;GO:0043170;GO:0043383//negative T cell selection;GO:0045595//regulation of cell differentiation;GO:0048232//male gamete generation;GO:0048511//rhythmic	gi 59624977 ref NP_631933.2 /1.41511e-180/tumor necrosis factor receptor superfamily member 6 precursor [Rattus norvegicus]
25662	<i>Igfbp2</i>	insulin-like growth factor binding protein 2	4.296580247	1.190044295	1.997528122	0.523199201	0.437146636	GO:0031982//vesicle;GO:0044421//extracellular region part;GO:0044459//plasma membrane part	GO:0005520//insulin-like growth factor binding	GO:0009966//regulation of signal transduction;GO:0010038//response to metal ion;GO:0016049//cell growth;GO:0022414//reproductive process;GO:0031960//response to corticosteroid stimulus;GO:0032501//multicellular organismal process;GO:0032502//developmental process;GO:0033189//response to vitamin A;GO:0040008//regulation of growth;GO:0043627//response to peptide hormone stimulus	gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]

24446	<i>Hgf</i>	hepatocyte growth factor	1.926760379	4.567548794	11.35586631	7.349915596	6.054365127	GO:0044421//extracellular region part	GO:0004175//endopeptidase activity;GO:0046983//protein dimerization activity;GO:0070851//growth factor receptor binding	GO:0000165//MAPK cascade;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0008283//cell proliferation;GO:0009887//organ morphogenesis;GO:0019538//protein metabolic process;GO:0032989;GO:0043066//negative regulation of apoptotic process;GO:0060638//mesenchymal-epithelial cell signaling	gi 433431 emb CAA51054.1 /0/hepatocyte growth factor [Mus musculus]
29397	<i>Ccl11</i>	chemokine (C-C motif) ligand 11	4.615361145	5.455810031	3.47734628	3.773303663	8.029040428	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0000165//MAPK cascade;GO:0001935//endothelial cell proliferation;GO:0006464//cellular protein modification process;GO:0006875//cellular metal ion homeostasis;GO:0006954//inflammatory response;GO:0009628//response to abiotic stimulus;GO:0030041//actin filament polymerization;GO:0030595//leukocyte chemotaxis;GO:0032321//positive regulation of Rho GTPase activity;GO:0034097//response to cytokine stimulus;GO:0045765//regulation of angiogenesis;GO:0048754//branching morphogenesis of an epithelial tube;GO:0051707//response to other	gi 11276089 ref NP_062078.1 /2.69204e-39/eotaxin precursor [Rattus norvegicus]
24770	<i>Ccl2</i>	chemokine (C-C motif) ligand 2	4.508587865	368.486145	74.23711713	27.71775211	27.78808634	GO:0044297//cell body;GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005125//cytokine activity;GO:0005539//glycosaminoglycan binding;GO:0048020//CCR chemokine receptor binding	GO:0001101//response to acid;GO:0001525//angiogenesis;GO:0001817//regulation of cytokine production;GO:0001935//endothelial cell proliferation;GO:0002436;GO:0002690//positive regulation of leukocyte chemotaxis;GO:0006875//cellular metal ion homeostasis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007178//transmembrane receptor protein serine/threonine kinase signaling pathway;GO:0008347//glial cell migration;GO:0009887//organ morphogenesis;GO:0010212//response to ionizing radiation;GO:0019221//cytokine-mediated signaling pathway;GO:0031960//response to corticosteroid stimulus;GO:0032496//response to lipopolysaccharide;GO:0033273//response to vitamin;GO:0034341//response to interferon-gamma;GO:0034612//response to tumor necrosis factor;GO:0042465;GO:0043066//negative regulation of apoptotic process;GO:0048609//multicellular organismal reproductive process;GO:0050804//regulation of	gi 13928714 ref NP_113718.1 /1.69689e-66/C-C motif chemokine 2 precursor [Rattus norvegicus]
25313	<i>Egf</i>	epidermal growth factor	0.6750425	0.434936692	0.521108515	1.077653042	0.747150803	GO:0000267//cell fraction;GO:0031224//intrinsic to membrane;GO:0044421//extracellular region part	GO:0046872//metal ion binding;GO:0070851//growth factor receptor binding	GO:0000165//MAPK cascade;GO:0001763//morphogenesis of a branching structure;GO:0007088//regulation of mitosis;GO:0007176//regulation of epidermal growth factor-activated receptor activity;GO:0021930//cerebellar granule cell precursor proliferation;GO:0032880//regulation of protein localization;GO:0034765//regulation of ion transmembrane transport;GO:0035411//catenin import into nucleus;GO:0043405//regulation of MAP kinase activity;GO:0048646//anatomical structure formation	gi 6978797 ref NP_036974.1 /0/pro-epidermal growth factor precursor [Rattus norvegicus]
50692	<i>Plaur</i>	plasminogen activator, urokinase receptor	2.078905732	20.67565463	16.45406953	10.16735424	6.306961327	GO:0031224//intrinsic to membrane	GO:0004872//receptor activity;GO:0005515//protein binding;GO:0016772//transferase activity, transferring phosphorus-containing groups	GO:0003006//developmental process involved in reproduction;GO:0006464//cellular protein modification process;GO:0006796//phosphate-containing compound metabolic process;GO:0006915//apoptotic process;GO:0010467//gene expression;GO:0023052//signaling;GO:0030154//cell differentiation;GO:0042246//tissue regeneration	gi 20128772 ref NP_599179.1 /1.32836e-164/urokinase plasminogen activator surface receptor isoform 1 precursor [Rattus norvegicus]/gi 8394516 ref NP_059046.1 /8.55082e-164/urokinase plasminogen activator surface receptor isoform 2 precursor [Rattus norvegicus]
54250	<i>Fgf2</i>	fibroblast growth factor 2	1.628855273	3.023584681	2.569505629	2.226686362	1.548792915	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0003713//transcription coactivator activity;GO:0005123//death receptor binding;GO:0005262//calcium channel activity;GO:0005539//glycosaminoglycan binding;GO:0019838//growth factor binding;GO:0070851//growth factor receptor binding	GO:0001708//cell fate specification;GO:0001932//regulation of protein phosphorylation;GO:0001935//endothelial cell proliferation;GO:0002040//sprouting angiogenesis;GO:0003156//regulation of organ formation;GO:0006694//steroid biosynthetic process;GO:0006816//calcium ion transport;GO:0007049//cell cycle;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007264//small GTPase mediated signal transduction;GO:0007267//cell-cell signaling;GO:0008284//positive regulation of cell proliferation;GO:0009611//response to wounding;GO:0010518//positive regulation of phospholipase activity;GO:0010551;GO:0010595//positive regulation of endothelial cell migration;GO:0010596//negative regulation of endothelial cell migration;GO:0016049//cell growth;GO:0017156//calcium ion-dependent exocytosis;GO:0021539//subthalamus development;GO:0021930//cerebellar granule cell precursor proliferation;GO:0030323//respiratory tube development;GO:0030855//epithelial cell differentiation;GO:0032412//regulation of ion transmembrane transporter activity;GO:0042221//response to chemical stimulus;GO:0043067//regulation of programmed cell death;GO:0043410//positive regulation of MAPK cascade;GO:0043551//regulation of phosphatidylinositol 3-kinase activity;GO:0043647//inositol phosphate metabolic process;GO:0045507//positive regulation of cell	gi 9506599 ref NP_062178.1 /1.82528e-83/fibroblast growth factor 2 precursor [Rattus norvegicus]
310738	<i>Ngf</i>	nerve growth factor (beta polypeptide)	1.395133482	10.72081598	10.35477571	7.356521449	3.352549908	GO:0044421//extracellular region part;GO:0044431//Golgi apparatus part;GO:0044432//endoplasmic reticulum part	GO:0004871//signal transducer activity;GO:0005123//death receptor binding	GO:0001934//positive regulation of protein phosphorylation;GO:0002237//response to molecule of bacterial origin;GO:0006917//induction of apoptosis;GO:0006952//defense response;GO:0007167//enzyme linked receptor protein signaling pathway;GO:0007264//small GTPase mediated signal transduction;GO:0007600//sensory perception;GO:0007611//learning or memory;GO:0007626//locomotory behavior;GO:0008283//cell proliferation;GO:0009605//response to external stimulus;GO:0009628//response to abiotic stimulus;GO:0009967//positive regulation of signal transduction;GO:0010769//regulation of cell morphogenesis involved in differentiation;GO:0014070//response to organic cyclic compound;GO:0016486//peptide hormone processing;GO:0030307//positive regulation of cell growth;GO:0031346//positive regulation of cell projection organization;GO:0031960//response to corticosteroid stimulus;GO:0043066//negative regulation of apoptotic process;GO:0043388//positive regulation of DNA binding;GO:0050767//regulation of	gi 202515 gb AAA40599.1 /5.82075e-160/nerve growth factor [Mastomys natalensis]
25670	<i>Il15</i>	interleukin 15	2.009421152	1.970864613	1.482968484	2.132170485	2.318302247	GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005102//receptor binding	GO:0001779//natural killer cell differentiation;GO:0001787//natural killer cell proliferation;GO:0001819//positive regulation of cytokine production;GO:0002684//positive regulation of immune system process;GO:0008285//negative regulation of cell proliferation;GO:0014891;GO:0030203//glycosaminoglycan metabolic process;GO:0033280//response to vitamin D;GO:0042503//tyrosine phosphorylation of Stat3 protein;GO:0045058//T cell activation;GO:0045071//regulation of hematopoietic differentiation;GO:0045072//T cell differentiation;GO:0002763//positive regulation of myeloid leukocyte differentiation;GO:0006952//defense response;GO:0008283//cell proliferation;GO:0030595//leukocyte chemotaxis;GO:0051480//cytosolic calcium ion homeostasis	gi 6981092 ref NP_037261.1 /1.94732e-80/interleukin-15 precursor [Rattus norvegicus]
25542	<i>Ccl3</i>	chemokine (C-C motif) ligand 3	0.89047684	24.78525401	7.948072711	10.03156507	15.97889308	GO:0000267//cell fraction;GO:0044421//extracellular region part	GO:0005125//cytokine activity;GO:0005539//glycosaminoglycan binding	GO:0002763//positive regulation of myeloid leukocyte differentiation;GO:0006952//defense response;GO:0008283//cell proliferation;GO:0030595//leukocyte chemotaxis;GO:0051480//cytosolic calcium ion homeostasis	gi 40254794 ref NP_037157.2 /9.73979e-48/C-C motif chemokine 3 precursor [Rattus norvegicus]
81503	<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	0.66802353	23.34169849	2.771107793	1.503479641	0.509972115	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0006952//defense response;GO:0030595//leukocyte chemotaxis	gi 13540652 ref NP_110472.1 /4.80618e-48/growth-regulated alpha protein precursor [Rattus norvegicus]
25647	<i>Il7</i>	interleukin 7	0.412628896	0.587393659	0.867891529	0.715038908	0.840007261	GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0001894//tissue homeostasis;GO:0010467//gene expression;GO:0016049//cell growth;GO:0030888//regulation of B cell proliferation;GO:0043066//negative regulation of apoptotic process;GO:0044092//negative regulation of molecular function;GO:0045580//regulation of T cell differentiation;GO:0045977//positive regulation of growth	gi 40254788 ref NP_037242.2 /1.75329e-77/interleukin-7 precursor [Rattus norvegicus]
24494	<i>Il1b</i>	interleukin 1 beta	0.283235103	21.75761306	3.195304237	2.938355481	2.868463927	GO:0016023//cytoplasmic membrane-bounded vesicle;GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0001660//fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//I-kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of	gi 158186736 ref NP_113700.2 /1.51739e-142/interleukin-1 beta precursor [Rattus norvegicus]

305236	<i>Cxcl11</i>	chemokine (C-X-C motif) ligand 11	0.261688323	0.781029898	0.963226019	0.709247645	2.07087179	GO:0044421//extracellular region part	GO:0001664//G-protein coupled receptor binding;GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0006952//defense response;GO:0007154//cell communication;GO:0023052//signaling;GO:0042221//response to chemical stimulus	gj 33636734 ref NP_891997.1 /2.82897e-50/C-X-C motif chemokine 11 precursor [Rattus norvegicus]
171040	<i>Il11</i>	interleukin 11	0.123575042	3.946070661	0.563155953	0.423059999	0.323443656	GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005126//cytokine receptor binding	GO:0001934//positive regulation of protein phosphorylation;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0008283//cell proliferation;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0030098//lymphocyte differentiation;GO:0030099//myeloid cell differentiation;GO:0046883//regulation of hormone secretion	gj 340805851 ref NP_598203.4 /3.22599e-71/interleukin-11 precursor [Rattus norvegicus]
24498	<i>Il6</i>	interleukin 6	0.131971049	4.111704511	1.66546585	0.508279262	0.226681385	GO:0005887//integral to plasma membrane;GO:0009986//cell surface;GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0000060//protein import into nucleus, translocation;GO:0001101//response to acid;GO:0001562//response to protozoan;GO:0001780//neutrophil homeostasis;GO:0001819//positive regulation of cytokine production;GO:0001934//positive regulation of protein phosphorylation;GO:0002237//response to molecule of bacterial origin;GO:0002251;GO:0002526//acute inflammatory response;GO:0006111//regulation of gluconeogenesis;GO:0006275//regulation of DNA replication;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006412//transcription;GO:0008284//positive regulation of cell proliferation;GO:0009620//response to fungus;GO:0009628//response to abiotic stimulus;GO:0009991//response to extracellular stimulus;GO:0010038//response to metal ion;GO:0010466//negative regulation of peptidase activity;GO:0014074//response to purine-containing compound;GO:0019221//cytokine-mediated signaling pathway;GO:0019725//cellular homeostasis;GO:0030030//cell projection organization;GO:0030072//peptide hormone secretion;GO:0031016//pancreas development;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031960//response to corticosteroid stimulus;GO:0032583;GO:0033673//negative regulation of kinase activity;GO:0040007//growth;GO:0042036//negative regulation of cytokine biosynthetic process;GO:0042098//T cell proliferation;GO:0042503//tyrosine phosphorylation of Stat3 protein;GO:0042742//defense response to bacterium;GO:0043410//positive regulation of MAPK cascade;GO:0043434//response to peptide hormone stimulus;GO:0043523//regulation of neuron apoptotic process;GO:0045187//regulation of circadian sleep/wake cycle, sleep;GO:0045624//positive regulation of T-helper cell differentiation;GO:0045767;GO:0046883//regulation of hormone secretion;GO:0048634;GO:0048771//tissue remodeling;GO:0050673//epithelial cell	gj 7549769 ref NP_036721.1 /3.82161e-116/interleukin-6 precursor [Rattus norvegicus]
360750	<i>Ccl25</i>	chemokine (C-C motif) ligand 25	0.050590516	0.117847004	0.079806118	0.043299244	0.024827801	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0007166//cell surface receptor signaling pathway;GO:0042221//response to chemical stimulus	gj 82524292 ref NP_001032280.1 /1.81593e-82/C-C motif chemokine 25 precursor [Rattus norvegicus]
29538	<i>Ccl20</i>	chemokine (C-C motif) ligand 20	0.042251761	0.442901101	0.022217267	0.072324595	0.020735473	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0006952//defense response;GO:0007154//cell communication;GO:0023052//signaling;GO:0042221//response to chemical stimulus;GO:0042465	gj 9507069 ref NP_062106.1 /4.14841e-50/C-C motif chemokine 20 precursor [Rattus norvegicus]
24493	<i>Il1a</i>	interleukin 1 alpha	0.01730795	0.917226242	1.63818883	0.750549215	0.305785776	GO:0044421//extracellular region part;GO:0044444//cytoplasmic part	GO:0005149//interleukin-1 receptor binding;GO:0046914//transition metal ion binding	GO:0001819//positive regulation of cytokine production;GO:0002237//response to molecule of bacterial origin;GO:0002376//immune system process;GO:0006694//steroid biosynthetic process;GO:0006953//acute-phase response;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//I-kappaB kinase/NF-kappaB cascade;GO:0008283//cell proliferation;GO:0009408//response to heat;GO:0009719;GO:0010038//response to metal ion;GO:0010212//response to ionizing radiation;GO:0030216//keratinocyte differentiation;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0043066//negative regulation of apoptotic process;GO:0043410//positive regulation of MAPK cascade;GO:0045765//regulation of	gj 8393593 ref NP_058715.1 /5.6272e-150/interleukin-1 alpha precursor [Rattus norvegicus]
685958	<i>Ccl26</i>	chemokine (C-C motif) ligand 26	-	-	-	0.153990528	0.066223664	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0001935//endothelial cell proliferation;GO:0002376//immune system process;GO:0016477//cell migration;GO:0030041//actin filament polymerization;GO:0032321//positive regulation of Rho GTPase activity	gj 157823491 ref NP_001102958.1 /1.96257e-52/chemokine (C-C motif) ligand 26 precursor [Rattus norvegicus]
300339	<i>Mmp1</i>	matrix metalloproteinase 1	-	0.019869553	0.01794091	0.019467877	-	GO:0031012//extracellular region part	GO:0004175//endopeptidase activity	GO:0002376//immune system process;GO:0007599//hemostasis;GO:0019538//protein metabolic process;GO:0006952//defense response;GO:0007154//cell communication;GO:0023052//signaling;GO:0032501//multicellular organismal process;GO:0042221//response to chemical stimulus	gj 197384336 ref NP_001128gj 11559996 ref NP_071550.1 /1.76645e-50/C-X-C motif chemokine 5 precursor [Rattus norvegicus]
171551	<i>Cxcl3</i>	chemokine (C-X-C motif) ligand 3	-	2.293798382	0.403470839	0.583747476	0.376561118	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0006952//defense response;GO:0030595//leukocyte chemotaxis	gj 149033777 gb EDL88573.1 /1.95119e-59/gene model 1960, (NCBI), isoform CRA 1 [Rattus norvegicus]
688605	<i>Ccl1</i>	chemokine (C-C motif) ligand 1	-	-	0.160436192	0.130568296	0.187169759	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0042221//response to chemical stimulus	gj 300797687 ref NP_001178021.1 /1.27329e-48/C-C motif chemokine 1 precursor [Rattus norvegicus]
114105	<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 2	-	5.580312508	0.526918502	0.946985801	0.169047783	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0006952//defense response;GO:0030595//leukocyte chemotaxis	gj 16758460 ref NP_446099.1 /1.76289e-42/C-X-C motif chemokine 2 precursor [Rattus norvegicus]
59325	<i>Ereg</i>	epiregulin	-	0.120372801	-	-	-	GO:0016021//integral to membrane;GO:0044421//extracellular region part	GO:0070851//growth factor receptor binding	GO:0001547//antral ovarian follicle growth;GO:0006275//regulation of DNA replication;GO:0006351//transcription, DNA-dependent;GO:0007088//regulation of mitosis;GO:0007126//meiosis;GO:0007154//cell communication;GO:0007176//regulation of epidermal growth factor-activated receptor activity;GO:0007186//G-protein coupled receptor signaling pathway;GO:0008284//positive regulation of cell proliferation;GO:0008285//negative regulation of cell proliferation;GO:0009611//response to wounding;GO:0009725//response to hormone stimulus;GO:0009913//epidermal cell differentiation;GO:0022605//oogenesis stage;GO:0031349//positive regulation of defense response;GO:0033674//positive regulation of kinase activity;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0045765//regulation of angiogenesis;GO:0051148//negative regulation of cell proliferation	gj 11078689 ref NP_067721.1 /5.53766e-82/proepiregulin preproprotein [Rattus norvegicus]
25685	<i>Igf1bp1</i>	insulin-like growth factor binding protein 1	-	-	0.012086193	-	-	GO:0044421//extracellular region part	GO:0019838//growth factor binding	GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009888//tissue development;GO:0016049//cell growth;GO:0019318//hexose metabolic process;GO:0048017//inositol lipid-mediated signaling	gj 6981080 ref NP_037276.1 /2.38401e-163/insulin-like growth factor-binding protein 1 precursor [Rattus norvegicus]

Up-regulated genes as compared with the uninjured control (0 day) were labeled in red color while down-regulated genes were labeled in green color.

Additional Table 4 Expression levels of senescence-associated secretory phenotype genes in rat dorsal root ganglia post-injury

GeneID	Symbol	Description	0h_RPKM	3h_RPKM	9h_RPKM	1d_RPKM	4d_RPKM	7d_RPKM	GO Component	GO Function	GO Process	Blast nr	
25205	<i>Il6st</i>	interleukin 6 signal transducer	65.41236399	70.64950896	70.97260773	78.23840462	76.27574165	69.00519844	GO:0005887/integral to plasma membrane;GO:0009986/cell surface;GO:0043005/neuron projection;GO:0043235/receptor complex;GO:0044297/cell matrix;GO:0030427/site of polarized growth;GO:0042995/cell projection;GO:0043231/intracellular membrane-bounded organelle;GO:0044297/cell	GO:0004897/ciliary neurotrophic factor receptor activity;GO:0005126/cytokine receptor binding;GO:0019838/growth factor binding;GO:0042802/identical binding;GO:0005578/proteinaceous extracellular matrix;GO:0030427/site of polarized growth;GO:0042995/cell projection;GO:0043231/intracellular membrane-bounded organelle;GO:0044297/cell	GO:0001819/positive regulation of cytokine production;GO:0001960/negative regulation of cytokine-mediated signaling pathway;GO:0002250/adaptive immune response;GO:0002526/acute inflammatory response;GO:0003300/cardiac muscle hypertrophy;GO:0006073/cellular glucan metabolic process;GO:0006641/triglyceride metabolic process;GO:0007167/enzyme linked receptor protein signaling pathway;GO:0007219/Notch signaling pathway;GO:0014909/smooth muscle cell migration;GO:0016049/cell growth;GO:0031667/response to nutrient levels;GO:0042098/T cell proliferation;GO:0042503/tyrosine phosphorylation of Stat3 protein;GO:0042508/tyrosine phosphorylation	gi 149059343 gb EDM10350.1 /O/CG44468, isoform CRA_b [Rattus norvegicus]	
29543	<i>Timp2</i>	TIMP metalloproteinase inhibitor 2	158.5700162	152.7930029	156.0374688	152.8121976	149.4455151	153.3278941	GO:0005578/proteinaceous extracellular matrix;GO:0030427/site of polarized growth;GO:0042995/cell projection;GO:0043231/intracellular membrane-bounded organelle;GO:0044297/cell	GO:0004866/endopeptidase inhibitor activity;GO:0005102/receptor binding;GO:0043169/cation binding;GO:0070011/peptidase activity, acting on L-amino acid peptides	GO:0007346/regulation of mitotic cell cycle;GO:0008283/cell proliferation;GO:0010033/response to organic substance;GO:0010466/negative regulation of peptidase activity;GO:0010740/positive regulation of intracellular protein kinase cascade;GO:0030162/regulation of proteolysis;GO:0031281;GO:0032486/Rap protein signal transduction;GO:0045597/positive regulation of cell differentiation;GO:0046058/cAMP metabolic process;GO:0046578/regulation of Ras protein signal transduction;GO:0048232/male gamete generation;GO:0050767/regulation of neurogenesis	gi 267133 sp P25785.2 TIMP2_MOUSE/2.32006e-114/RecName: Full=Metalloproteinase inhibitor 2; AltName: Full=Tissue inhibitor of metalloproteinases 2; Short=TIMP-2; Flags: gi 6981090 ref NP_037236.1 /2.01742e-130/insulin-like growth factor-binding protein 6 precursor [Rattus norvegicus] gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus] gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus] gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus] gi 213417659 ref NP_068616.1 /4.79492e-120/kit ligand isoform 2 precursor [Rattus norvegicus] gi 33667068 ref NP_068615.1 /8.30177e-128/kit ligand isoform 1	
25641	<i>Igfbp6</i>	insulin-like growth factor binding protein 6	146.6436175	161.8023849	167.6207153	136.9027672	192.7220797	158.4082816	GO:0043231/intracellular membrane-bounded organelle;GO:0044421/extracellular region part	GO:0005520/insulin-like growth factor binding	GO:0008283/cell proliferation;GO:0016049/cell growth;GO:0023052/signaling	gi 6981090 ref NP_037236.1 /2.01742e-130/insulin-like growth factor-binding protein 6 precursor [Rattus norvegicus] gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus] gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus] gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus] gi 213417659 ref NP_068616.1 /4.79492e-120/kit ligand isoform 2 precursor [Rattus norvegicus] gi 33667068 ref NP_068615.1 /8.30177e-128/kit ligand isoform 1	
308444	<i>Axl</i>	Axl receptor tyrosine kinase	29.96456905	28.77930297	28.36660315	29.14843424	39.02473694	39.74370932	GO:0016021/integral to membrane	GO:0004713/protein tyrosine kinase activity;GO:0004871/signal transducer activity;GO:0017022/myosin binding;GO:0019900/kinase binding;GO:0032559;GO:0046983/protein dimerization	GO:0000904/cell morphogenesis involved in differentiation;GO:0001818/negative regulation of cytokine production;GO:0002695;GO:0006466/cellular protein modification process;GO:0006796/phosphate-containing compound metabolic process;GO:0006909/phagocytosis;GO:0006952/defense response;GO:0007154/cell communication;GO:0007166/cell surface receptor signaling pathway;GO:0007243/intracellular protein kinase cascade;GO:0009887/organ morphogenesis;GO:0009888/tissue development;GO:0016477/cell migration;GO:0030098/lymphocyte differentiation;GO:0034614/cellular response to reactive oxygen species;GO:0043066/negative regulation of apoptotic process;GO:0046903/secretion;GO:0048232/male gamete generation;GO:0048511/rhythmic	GO:0006006/glucose metabolic process;GO:0006952/defense response;GO:0008283/cell proliferation;GO:0010740/positive regulation of intracellular protein kinase cascade;GO:0016049/cell growth;GO:0044260;GO:0048731	gi 61557097 ref NP_001013165.1 /0/tyrosine-protein kinase receptor UFO isoform 2 precursor [Rattus norvegicus] gi 93204849 ref NP_113982.1 /0/tyrosine-protein kinase receptor UFO isoform 1 precursor [Rattus norvegicus] gi 51948524 ref NP_001004274.1 /2.96753e-131/insulin-like growth factor-binding protein 4 precursor [Rattus norvegicus] gi 213417659 ref NP_068616.1 /4.79492e-120/kit ligand isoform 2 precursor [Rattus norvegicus] gi 33667068 ref NP_068615.1 /8.30177e-128/kit ligand isoform 1
360622	<i>Igfbp4</i>	insulin-like growth factor binding protein 4	33.13343168	36.25187678	31.19234298	39.32367212	37.64339231	31.5565227	GO:0044421/extracellular region part	GO:0019838/growth factor binding	GO:0001667/ameboidal cell migration;GO:0001934/positive regulation of protein phosphorylation;GO:0002573/myeloid leukocyte differentiation;GO:0006275/regulation of DNA replication;GO:0008406/gonad development;GO:0022602/ovulation cycle process;GO:0033024;GO:0043405/regulation of MAP kinase activity;GO:0045634/regulation of melanocyte differentiation;GO:0046578/regulation of Ras protein signal transduction;GO:0070665	GO:0006006/glucose metabolic process;GO:0006952/defense response;GO:0008283/cell proliferation;GO:0010740/positive regulation of intracellular protein kinase cascade;GO:0016049/cell growth;GO:0044260;GO:0048731	gi 160358789 ref NP_114024.2 /9.31992e-165/vascular endothelial growth factor A isoform 1 precursor [Rattus norvegicus] gi 160358793 ref NP_001103803.1 /8.23555e-166/vascular endothelial growth factor A isoform 2 precursor [Rattus norvegicus] gi 160358797 ref NP_001103804.1 /3.81434e-136/vascular endothelial growth factor A isoform 3 precursor [Rattus norvegicus] gi 160358811 ref NP_001103736.1 /2.25432e-56/vascular endothelial growth factor A isoform 4 precursor [Mus musculus] gi 160358815 ref NP_001103737.1 /1.97191e-57/vascular endothelial growth factor A isoform 5 precursor [Mus musculus] gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Rattus norvegicus] gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus] gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]
60427	<i>Kitlg</i>	KIT ligand	10.54352512	11.11134786	11.13717596	14.78217054	14.30892029	14.71004674	GO:0031224/intrinsic to membrane;GO:0043232;GO:0044421/extracellular region part	GO:0005126/cytokine receptor binding	GO:0001667/ameboidal cell migration;GO:0001934/positive regulation of protein phosphorylation;GO:0002573/myeloid leukocyte differentiation;GO:0006275/regulation of DNA replication;GO:0008406/gonad development;GO:0022602/ovulation cycle process;GO:0033024;GO:0043405/regulation of MAP kinase activity;GO:0045634/regulation of melanocyte differentiation;GO:0046578/regulation of Ras protein signal transduction;GO:0070665	GO:0001667/ameboidal cell migration;GO:0001934/positive regulation of protein phosphorylation;GO:0002573/myeloid leukocyte differentiation;GO:0006275/regulation of DNA replication;GO:0008406/gonad development;GO:0022602/ovulation cycle process;GO:0033024;GO:0043405/regulation of MAP kinase activity;GO:0045634/regulation of melanocyte differentiation;GO:0046578/regulation of Ras protein signal transduction;GO:0070665	gi 160358789 ref NP_114024.2 /9.31992e-165/vascular endothelial growth factor A isoform 1 precursor [Rattus norvegicus] gi 160358793 ref NP_001103803.1 /8.23555e-166/vascular endothelial growth factor A isoform 2 precursor [Rattus norvegicus] gi 160358797 ref NP_001103804.1 /3.81434e-136/vascular endothelial growth factor A isoform 3 precursor [Rattus norvegicus] gi 160358811 ref NP_001103736.1 /2.25432e-56/vascular endothelial growth factor A isoform 4 precursor [Mus musculus] gi 160358815 ref NP_001103737.1 /1.97191e-57/vascular endothelial growth factor A isoform 5 precursor [Mus musculus] gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Rattus norvegicus] gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus] gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]
83785	<i>Vegfa</i>	vascular endothelial growth factor A	14.81955091	15.59185915	15.41081857	13.79430713	13.35359992	13.01188905	GO:0005578/proteinaceous extracellular matrix;GO:0016020/membrane;GO:0016023/cytoplasmic membrane-bounded vesicle	GO:0005172/vascular endothelial growth factor receptor binding;GO:0005539/glycosaminoglycan binding;GO:0042802/identical protein binding;GO:0046983/protein dimerization activity	GO:0001658/branching involved in ureteric bud morphogenesis;GO:0001666/response to hypoxia;GO:0001754/eye photoreceptor cell differentiation;GO:0001934/positive regulation of protein phosphorylation;GO:0001935/endothelial cell proliferation;GO:0002460/adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains;GO:0002690/positive regulation of leukocyte chemotaxis;GO:0006357/regulation of transcription from RNA polymerase II promoter;GO:0007169/transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007589/body fluid secretion;GO:0008284/positive regulation of cell proliferation;GO:0009791/post-embryonic development;GO:0009967/positive regulation of signal transduction;GO:0010595/positive regulation of endothelial cell migration;GO:0021700/developmental maturation;GO:0022602/ovulation cycle process;GO:0030218/erythrocyte differentiation;GO:0030323/respiratory tube development;GO:0032845;GO:0043009/chordate embryonic development;GO:0043066/negative regulation of apoptotic process;GO:0043114/regulation of vascular permeability;GO:0043488/regulation of mRNA stability;GO:0045765/regulation of angiogenesis;GO:0048747/muscle fiber development;GO:0048771/tissue remodeling;GO:0048875/chemical homeostasis within a tissue;GO:0050927/positive regulation of positive chemotaxis	GO:0001658/branching involved in ureteric bud morphogenesis;GO:0001666/response to hypoxia;GO:0001754/eye photoreceptor cell differentiation;GO:0001934/positive regulation of protein phosphorylation;GO:0001935/endothelial cell proliferation;GO:0002460/adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains;GO:0002690/positive regulation of leukocyte chemotaxis;GO:0006357/regulation of transcription from RNA polymerase II promoter;GO:0007169/transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007589/body fluid secretion;GO:0008284/positive regulation of cell proliferation;GO:0009791/post-embryonic development;GO:0009967/positive regulation of signal transduction;GO:0010595/positive regulation of endothelial cell migration;GO:0021700/developmental maturation;GO:0022602/ovulation cycle process;GO:0030218/erythrocyte differentiation;GO:0030323/respiratory tube development;GO:0032845;GO:0043009/chordate embryonic development;GO:0043066/negative regulation of apoptotic process;GO:0043114/regulation of vascular permeability;GO:0043488/regulation of mRNA stability;GO:0045765/regulation of angiogenesis;GO:0048747/muscle fiber development;GO:0048771/tissue remodeling;GO:0048875/chemical homeostasis within a tissue;GO:0050927/positive regulation of positive chemotaxis	gi 160358789 ref NP_114024.2 /9.31992e-165/vascular endothelial growth factor A isoform 1 precursor [Rattus norvegicus] gi 160358793 ref NP_001103803.1 /8.23555e-166/vascular endothelial growth factor A isoform 2 precursor [Rattus norvegicus] gi 160358797 ref NP_001103804.1 /3.81434e-136/vascular endothelial growth factor A isoform 3 precursor [Rattus norvegicus] gi 160358811 ref NP_001103736.1 /2.25432e-56/vascular endothelial growth factor A isoform 4 precursor [Mus musculus] gi 160358815 ref NP_001103737.1 /1.97191e-57/vascular endothelial growth factor A isoform 5 precursor [Mus musculus] gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Rattus norvegicus] gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus] gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]
24772	<i>Cxcl12</i>	chemokine (C-X-C motif) ligand 12	8.335547846	8.407445118	6.969160325	8.218161854	9.576662449	8.758939168	GO:0009986/cell surface;GO:0016020/membrane;GO:0044421/extracellular region part	GO:0005125/cytokine activity;GO:0060089	GO:0001525/angiogenesis;GO:0001935/endothelial cell proliferation;GO:0002548/monocyte chemotaxis;GO:0003006/developmental process involved in reproduction;GO:0003013;GO:0006875/cellular metal ion homeostasis;GO:0006950/response to stress;GO:0007166/cell surface receptor signaling pathway;GO:0007276/gamete generation;GO:0007411/axon guidance;GO:0007626/locomotory behavior;GO:0009628/response to abiotic stimulus;GO:0009725/response to hormone stimulus;GO:0009887/organ morphogenesis;GO:0014046;GO:0021537/telencephalon development;GO:0030832/regulation of actin filament length;GO:0032414/positive regulation of ion transmembrane transporter activity;GO:0042110/T cell activation;GO:0045773/positive regulation of axon extension;GO:0050927/positive regulation of positive chemotaxis;GO:0051707/response to other organism	GO:0001525/angiogenesis;GO:0001935/endothelial cell proliferation;GO:0002548/monocyte chemotaxis;GO:0003006/developmental process involved in reproduction;GO:0003013;GO:0006875/cellular metal ion homeostasis;GO:0006950/response to stress;GO:0007166/cell surface receptor signaling pathway;GO:0007276/gamete generation;GO:0007411/axon guidance;GO:0007626/locomotory behavior;GO:0009628/response to abiotic stimulus;GO:0009725/response to hormone stimulus;GO:0009887/organ morphogenesis;GO:0014046;GO:0021537/telencephalon development;GO:0030832/regulation of actin filament length;GO:0032414/positive regulation of ion transmembrane transporter activity;GO:0042110/T cell activation;GO:0045773/positive regulation of axon extension;GO:0050927/positive regulation of positive chemotaxis;GO:0051707/response to other organism	gi 148667157 gb EDK99573.1 /1.72649e-48/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 148667157 gb EDK99573.1 /2.25105e-49/chemokine (C-X-C motif) ligand 12, isoform CRA_c [Mus musculus] gi 149049654 gb EDM02108.1 /1.73942e-52/chemokine (C-X-C motif) ligand 12, isoform CRA_b [Rattus norvegicus] gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus] gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]
116510	<i>Timp1</i>	TIMP metalloproteinase inhibitor 1	60.99199772	55.52684016	55.27836309	92.7183287	151.9993753	105.8990656	GO:0005578/proteinaceous extracellular matrix;GO:0031091/platelet alpha granule	GO:0004866/endopeptidase inhibitor activity;GO:0043169/cation binding	GO:0001775/cell activation;GO:0006887/exocytosis;GO:0006915/apoptotic process;GO:0007599/hemostasis;GO:0008202/steroid metabolic process;GO:0008283/cell proliferation;GO:0009611/response to wounding;GO:0009725/response to hormone stimulus;GO:0009888/tissue development;GO:0010466/negative regulation of peptidase activity;GO:0012300;GO:0018460/cell maturation	GO:0001775/cell activation;GO:0006887/exocytosis;GO:0006915/apoptotic process;GO:0007599/hemostasis;GO:0008202/steroid metabolic process;GO:0008283/cell proliferation;GO:0009611/response to wounding;GO:0009725/response to hormone stimulus;GO:0009888/tissue development;GO:0010466/negative regulation of peptidase activity;GO:0012300;GO:0018460/cell maturation	gi 16758666 ref NP_446271.1 /1.01374e-110/metalloproteinase inhibitor 1 precursor [Rattus norvegicus] gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]
25662	<i>Igfbp2</i>	insulin-like growth factor binding protein 2	31.33480981	28.924165	33.05853624	28.77943041	21.54945323	20.71543809	GO:0031982/vesicle;GO:004421/extracellular region part;GO:0044459/plasma membrane part	GO:0005520/insulin-like growth factor binding	GO:0009966/regulation of signal transduction;GO:0010038/response to metal ion;GO:0016049/cell growth;GO:0022414/reproductive process;GO:0031960/response to corticosteroid stimulus;GO:0032501/multicellular organismal process;GO:0032502/developmental process;GO:0033189/response to vitamin A;GO:0040008/regulation of growth;GO:0043627/response to estrogen stimulus	gi 148747421 ref NP_037254.2 /6.857e-156/insulin-like growth factor-binding protein 2 precursor [Rattus norvegicus]	

81683	<i>Mif</i>	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	57.44016868	59.10947971	64.2347814	54.31309673	46.57159586	55.01108876	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0005102//receptor binding;GO:0016862//intracellular oxidoreductase activity, interconverting keto- and enol- groups;GO:0016863//intracellular oxidoreductase activity, transposing C=C bonds	GO:0001666//response to hypoxia;GO:0001934//positive regulation of protein phosphorylation;GO:0001976//neurological system process involved in regulation of systemic arterial blood pressure;GO:0002237//response to molecule of bacterial origin;GO:0002526//acute inflammatory response;GO:0002684//positive regulation of immune system process;GO:0006110//regulation of glycolysis;GO:0006693//prostaglandin metabolic process;GO:0006813//potassium ion transport;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0007050//cell cycle arrest;GO:0007417//central nervous system development;GO:0007568//aging;GO:0007631//feeding behavior;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009968//negative regulation of signal transduction;GO:0010467//gene expression;GO:0010737//protein kinase A signaling cascade;GO:0010828//positive regulation of glucose transport;GO:0014909//smooth muscle cell migration;GO:0030888//regulation of B cell proliferation;GO:0031960//response to corticosteroid stimulus;GO:0032103;GO:0032571//response to vitamin K;GO:0034614//cellular response to reactive oxygen species;GO:0042770//signal transduction in response to DNA damage;GO:0043410//positive regulation of MAPK cascade;GO:0043434//response to peptide hormone stimulus;GO:0043627//response to nitrogen stimulus;GO:0048223//male gamete production;GO:0000165//MAPK cascade;GO:0001701//in utero embryonic development;GO:0001775//cell activation;GO:0002009//morphogenesis of an epithelium;GO:0006915//apoptotic process;GO:0006935//chemotaxis;GO:0006950//response to stress;GO:0007155//cell adhesion;GO:0007173//epidermal growth factor receptor signaling pathway;GO:0007346//regulation of mitotic cell cycle;GO:0007423//sensory organ development;GO:0007431//salivary gland development;GO:0008284//positive regulation of cell proliferation;GO:0008544//epidermis development;GO:0009411//response to UV;GO:0010033//response to organic substance;GO:0010038//response to metal ion;GO:0010467//gene expression;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0010863//positive regulation of phospholipase C activity;GO:0016477//cell migration;GO:0019722//calcium-mediated signaling;GO:0021987//cerebral cortex development;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031657;GO:0032768;GO:0035411//catenin import into nucleus;GO:0043405//regulation of MAP kinase activity;GO:0048511//rhythmic process;GO:0048858//cell projection morphogenesis;GO:0050806//positive regulation of synaptic transmission	gij13591985 ref NP_112313.1 /1.29889e-61/macrophage migration inhibitory factor [Rattus norvegicus]
24329	<i>Egfr</i>	epidermal growth factor receptor	5.895980021	6.09717323	7.758022665	6.367906774	9.579337955	9.874150403	GO:0005635//nuclear envelope;GO:0030128//clathrin coat of endocytic vesicle;GO:0031224//intrinsic to membrane;GO:0044421//extracellular region part;GO:0044459//plasma membrane part	GO:0003779//actin binding;GO:0004709//MAP kinase kinase activity;GO:0004714//transmembrane receptor protein tyrosine kinase activity;GO:0019838//growth factor binding;GO:0019902//phosphatase activity;GO:0030234//enzyme regulator activity;GO:0032559;GO:0043566//structure-specific DNA binding;GO:0046092//protein activity;GO:0005539//glycosaminoglycan binding;GO:0048020//CCR chemokine receptor binding	GO:0001101//response to acid;GO:0001525//angiogenesis;GO:0001817//regulation of cytokine production;GO:0001935//endothelial cell proliferation;GO:0002436;GO:0002690//positive regulation of leukocyte chemotaxis;GO:0006875//cellular metal ion homeostasis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007178//transmembrane receptor protein serine/threonine kinase signaling pathway;GO:0008347//glial cell migration;GO:0009887//organ morphogenesis;GO:0010212//response to ionizing radiation;GO:0019221//cytokine-mediated signaling pathway;GO:0031960//response to corticosteroid stimulus;GO:0032496//response to lipopolysaccharide;GO:0033273//response to vitamin;GO:0034341//response to interferon-gamma;GO:0034612//response to tumor necrosis factor;GO:0042465;GO:0043066//negative regulation of apoptotic process;GO:0048609//multicellular organismal reproductive process;GO:0050804//regulation of GO:0001934//positive regulation of protein phosphorylation;GO:0001942//hair follicle development;GO:0006935//chemotaxis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009611//response to wounding;GO:0022602//ovulation cycle process;GO:0030036//actin cytoskeleton organization;GO:0030323//respiratory tube development;GO:0030335//positive regulation of cell migration;GO:0032940//secretion by cell;GO:0034613//cellular protein localization;GO:0046470//phosphatidylcholine metabolic process;GO:0048875//chemical homeostasis within a tissue;GO:0050679//positive regulation of epithelial	gij25742617 ref NP_113695.1 /0/epidermal growth factor receptor precursor [Rattus norvegicus]
24770	<i>Ccl2</i>	chemokine (C-C motif) ligand 2	21.21390016	14.7805258	71.54483696	36.64162619	62.41176224	48.81245029	GO:0044297//cell body;GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005125//cytokine activity;GO:0005539//glycosaminoglycan binding;GO:0048020//CCR chemokine receptor binding	GO:0001101//response to acid;GO:0001525//angiogenesis;GO:0001817//regulation of cytokine production;GO:0001935//endothelial cell proliferation;GO:0002436;GO:0002690//positive regulation of leukocyte chemotaxis;GO:0006875//cellular metal ion homeostasis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007178//transmembrane receptor protein serine/threonine kinase signaling pathway;GO:0008347//glial cell migration;GO:0009887//organ morphogenesis;GO:0010212//response to ionizing radiation;GO:0019221//cytokine-mediated signaling pathway;GO:0031960//response to corticosteroid stimulus;GO:0032496//response to lipopolysaccharide;GO:0033273//response to vitamin;GO:0034341//response to interferon-gamma;GO:0034612//response to tumor necrosis factor;GO:0042465;GO:0043066//negative regulation of apoptotic process;GO:0048609//multicellular organismal reproductive process;GO:0050804//regulation of GO:0001934//positive regulation of protein phosphorylation;GO:0001942//hair follicle development;GO:0006935//chemotaxis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009611//response to wounding;GO:0022602//ovulation cycle process;GO:0030036//actin cytoskeleton organization;GO:0030323//respiratory tube development;GO:0030335//positive regulation of cell migration;GO:0032940//secretion by cell;GO:0034613//cellular protein localization;GO:0046470//phosphatidylcholine metabolic process;GO:0048875//chemical homeostasis within a tissue;GO:0050679//positive regulation of epithelial	gij13928714 ref NP_113718.1 /1.69689e-66/C-C motif chemokine 2 precursor [Rattus norvegicus]
29348	<i>Fgf7</i>	fibroblast growth factor 7	14.66270911	10.38814647	14.26117289	17.74721635	13.25415191	16.40211575	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0005104//fibroblast growth factor receptor binding;GO:0005539//glycosaminoglycan binding	GO:0001101//response to acid;GO:0001525//angiogenesis;GO:0001817//regulation of cytokine production;GO:0001935//endothelial cell proliferation;GO:0002436;GO:0002690//positive regulation of leukocyte chemotaxis;GO:0006875//cellular metal ion homeostasis;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009611//response to wounding;GO:0022602//ovulation cycle process;GO:0030036//actin cytoskeleton organization;GO:0030323//respiratory tube development;GO:0030335//positive regulation of cell migration;GO:0032940//secretion by cell;GO:0034613//cellular protein localization;GO:0046470//phosphatidylcholine metabolic process;GO:0048875//chemical homeostasis within a tissue;GO:0050679//positive regulation of epithelial	gij11559943 ref NP_071518.1 /1.87163e-100/fibroblast growth factor 7 precursor [Rattus norvegicus]
25464	<i>Icam1</i>	intercellular adhesion molecule 1	3.851676444	3.007296021	4.129063416	4.804631077	6.324629656	4.886963971	GO:0009986//cell surface;GO:0031224//intrinsic to membrane;GO:0044421//extracellular region part;GO:0044459//plasma membrane part	GO:0005102//receptor binding	GO:0001101//response to acid;GO:0001666//response to hypoxia;GO:0001678//cellular glucose homeostasis;GO:0002286//T cell activation involved in immune response;GO:0002456//T cell mediated immunity;GO:0002687//positive regulation of leukocyte migration;GO:0007568//aging;GO:0009314//response to radiation;GO:0009725//response to hormone stimulus;GO:0010038//response to metal ion;GO:0014075//response to amine stimulus;GO:0016337//cell-cell adhesion;GO:0019229//regulation of vasoconstriction;GO:0022406//membrane docking;GO:0022415;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031667//response to nutrient levels;GO:0032496//response to lipopolysaccharide;GO:0034612//response to tumor necrosis factor;GO:0043271//negative regulation of ion	gij6981068 ref NP_037099.1 /0/intercellular adhesion molecule 1 precursor [Rattus norvegicus]
24617	<i>Serpine1</i>	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	3.237100164	5.416573875	2.553925658	7.94212271	3.886053956	3.904729033	GO:0000267//cell fraction;GO:0016020//membrane;GO:0031091//platelet alpha granule;GO:0044421//extracellular region part	GO:0004175//endopeptidase activity;GO:0004866//endopeptidase inhibitor activity;GO:0019899//enzyme binding	GO:0001101//response to acid;GO:0001666//response to hypoxia;GO:0001678//cellular glucose homeostasis;GO:0002286//T cell activation involved in immune response;GO:0002456//T cell mediated immunity;GO:0002687//positive regulation of leukocyte migration;GO:0007568//aging;GO:0009314//response to radiation;GO:0009725//response to hormone stimulus;GO:0010038//response to metal ion;GO:0014075//response to amine stimulus;GO:0016337//cell-cell adhesion;GO:0019229//regulation of vasoconstriction;GO:0022406//membrane docking;GO:0022415;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031667//response to nutrient levels;GO:0032496//response to lipopolysaccharide;GO:0034612//response to tumor necrosis factor;GO:0043271//negative regulation of ion	gij6981332 ref NP_036752.1 /0/plasminogen activator inhibitor 1 precursor [Rattus norvegicus]
50692	<i>Plaur</i>	plasminogen activator, urokinase receptor	6.907989495	8.115706275	8.426293999	13.38524982	9.964940024	10.29050516	GO:0031224//intrinsic to membrane	GO:0004872//receptor activity;GO:0005515//protein binding;GO:0016772//transferase activity, transferring phosphorus-containing groups	GO:0001101//response to acid;GO:0001666//response to hypoxia;GO:0001678//cellular glucose homeostasis;GO:0002286//T cell activation involved in immune response;GO:0002456//T cell mediated immunity;GO:0002687//positive regulation of leukocyte migration;GO:0007568//aging;GO:0009314//response to radiation;GO:0009725//response to hormone stimulus;GO:0010038//response to metal ion;GO:0014075//response to amine stimulus;GO:0016337//cell-cell adhesion;GO:0019229//regulation of vasoconstriction;GO:0022406//membrane docking;GO:0022415;GO:0031328//positive regulation of cellular biosynthetic process;GO:0031667//response to nutrient levels;GO:0032496//response to lipopolysaccharide;GO:0034612//response to tumor necrosis factor;GO:0043271//negative regulation of ion	gij20128772 ref NP_599179.1 /1.32836e-164/urokinase plasminogen activator surface receptor isoform 1 precursor [Rattus norvegicus]//gij8394516 ref NP_059046.1 /8.55082e-164/urokinase plasminogen activator surface receptor isoform 2 precursor [Rattus norvegicus]
24446	<i>Hgf</i>	hepatocyte growth factor	2.638773594	3.426950271	2.961751719	2.745461091	3.438679	3.627861332	GO:0044421//extracellular region part	GO:0004175//endopeptidase activity;GO:0046983//protein dimerization activity;GO:0070851//growth factor receptor binding	GO:0000165//MAPK cascade;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0008283//cell proliferation;GO:0009887//organ morphogenesis;GO:0019538//protein metabolic process;GO:0032989;GO:0043066//negative regulation of apoptotic process;GO:0060638//mesenchymal-epithelial cell signaling	gij433431 emb CAA51054.1 /0/hepatocyte growth factor [Mus musculus]
25021	<i>Itgam</i>	integrin, alpha M	1.918164496	1.806307449	1.925601731	2.352894746	4.457240702	5.123299756	GO:0005887//integral to plasma membrane;GO:0009986//cell surface;GO:0043231//intracellular membrane-bounded organelle	GO:0004871//signal transducer activity;GO:0005539//glycosaminoglycan binding;GO:0043394//proteoglycan binding;GO:0046983//protein	GO:0007166//cell surface receptor signaling pathway;GO:0007599//hemostasis;GO:0016337//cell-cell adhesion;GO:0030595//leukocyte chemotaxis;GO:0042098//T cell proliferation	gij29789036 ref NP_036843.1 /0/integrin alpha-M precursor [Rattus norvegicus]
246097	<i>Fas</i>	Fas cell surface death receptor	2.377601907	3.104666159	2.411216437	2.425805793	1.843139283	2.134809439	GO:0000267//cell fraction;GO:0009986//cell surface;GO:0031224//intrinsic to membrane;GO:0031264//death-inducing signaling complex;GO:0044444//cytoplasmic part	GO:0005035//death receptor activity;GO:0019899//enzyme binding	GO:0002237//response to molecule of bacterial origin;GO:0002440;GO:0002449;GO:0003008;GO:0008283//cell proliferation;GO:0008624;GO:0009612//response to mechanical stimulus;GO:0010226//response to lithium ion;GO:0010939//regulation of necrotic cell death;GO:0019221//cytokine-mediated signaling pathway;GO:0031102//neuron projection regeneration;GO:0031960//response to corticosteroid stimulus;GO:0043029//T cell homeostasis;GO:0043066//negative regulation of apoptotic process;GO:0043170;GO:0043383//negative T cell selection;GO:0045595//regulation of cell differentiation;GO:0048232//male gamete generation;GO:0048511//rhythmic	gij59624977 ref NP_631933.2 /1.41511e-180/tumor necrosis factor receptor superfamily member 6 precursor [Rattus norvegicus]

25313	<i>Egf</i>	epidermal growth factor	0.72120043	1.213344314	0.779275247	0.718203546	0.988470963	1.112561758	GO:0000267//cell fraction;GO:0031224//intracellular region part	GO:0046872//metal ion binding;GO:0070851//growth factor receptor binding	GO:0000165//MAPK cascade;GO:0001763//morphogenesis of a branching structure;GO:0007088//regulation of mitosis;GO:0007176//regulation of epidermal growth factor-activated factor precursor [Rattus norvegicus]	gij6978797[ref]NP_036974.1
25341	<i>Tnfrsf11b</i>	tumor necrosis factor receptor superfamily, member 11b	0.964586123	0.73067571	0.794986599	0.794335964	1.195980114	1.109465147	GO:0031012//extracellular matrix	GO:0004871//signal transducer activity;GO:0005102//receptor binding	GO:0002762//negative regulation of myeloid leukocyte differentiation;GO:0010038//response to metal ion;GO:0012501//programmed cell death;GO:0023052//signaling;GO:0031667//response to nutrient levels;GO:0032845;GO:0042475//odontogenesis of dentin-containing tooth;GO:0043062//extracellular structure organization;GO:0048545//response to steroid hormone stimulus	gij6981306[ref]NP_037002.1
25647	<i>Il7</i>	interleukin 7	1.480801139	1.387408554	1.394211479	1.324077981	1.679461436	2.048136535	GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0001894//tissue homeostasis;GO:0010467//gene expression;GO:0016049//cell growth;GO:0030888//regulation of B cell proliferation;GO:0043066//negative regulation of apoptotic process;GO:0044092//negative regulation of molecular function;GO:0045580//regulation of T cell differentiation;GO:0045897//intrinsic regulation of growth	gij40254788[ref]NP_037242.2
54250	<i>Fgf2</i>	fibroblast growth factor 2	1.387157957	2.019571612	2.949164621	7.749466611	9.398331917	10.36905407	GO:0043231//intracellular membrane-bounded organelle;GO:0044421//extracellular region part	GO:0003713//transcription coactivator activity;GO:0005123//death receptor binding;GO:0005262//calcium channel activity;GO:0005539//glycosaminoglycan binding;GO:0019838//growth factor binding;GO:0070851//growth factor receptor binding	GO:0001708//cell fate specification;GO:0001932//regulation of protein phosphorylation;GO:0001935//endothelial cell proliferation;GO:0002040//sprouting angiogenesis;GO:0003156//regulation of organ formation;GO:0006694//steroid biosynthetic process;GO:0006816//calcium ion transport;GO:0007049//cell cycle;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0007264//small GTPase mediated signal transduction;GO:0007267//cell-cell signaling;GO:0008284//positive regulation of cell proliferation;GO:0009611//response to wounding;GO:0010518//positive regulation of phospholipase activity;GO:0010551;GO:0010595//positive regulation of endothelial cell migration;GO:0010596//negative regulation of endothelial cell migration;GO:0016049//cell growth;GO:0017156//calcium ion-dependent exocytosis;GO:0021539//subthalamus development;GO:0021930//cerebellar granule cell precursor proliferation;GO:0030323//respiratory tube development;GO:0030855//epithelial cell differentiation;GO:0032412//regulation of ion transmembrane transporter activity;GO:0042221//response to chemical stimulus;GO:0043067//regulation of programmed cell death;GO:0043410//positive regulation of MAPK cascade;GO:0043551//regulation of phosphatidylinositol 3-kinase activity;GO:0043647//inositol phosphate metabolic process;GO:0045897//intrinsic regulation of cell growth	gij9506599[ref]NP_062178.1
305236	<i>Cxcl11</i>	chemokine (C-X-C motif) ligand 11	0.940954993	0.098987783	0.329832034	0.40236933	0.326795325	0.14028375	GO:0044421//extracellular region part	GO:0001664//G-protein coupled receptor binding;GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0006952//defense response;GO:0007154//cell communication;GO:0023052//signaling;GO:0042221//response to chemical stimulus	gij33636734[ref]NP_891997.1
310738	<i>Ngf</i>	nerve growth factor (beta polypeptide)	0.906388046	0.485270341	0.908568542	3.087462456	2.420886258	2.131921513	GO:0044421//extracellular region part;GO:0044431//Golgi apparatus part;GO:0044432//endoplasmic reticulum part	GO:0004871//signal transducer activity;GO:0005123//death receptor binding	GO:0001934//positive regulation of protein phosphorylation;GO:0002237//response to molecule of bacterial origin;GO:0006917//induction of apoptosis;GO:0006952//defense response;GO:0007167//enzyme linked receptor protein signaling pathway;GO:0007264//small GTPase mediated signal transduction;GO:0007600//sensory perception;GO:0007611//learning or memory;GO:0007626//locomotory behavior;GO:0008283//cell proliferation;GO:0009605//response to external stimulus;GO:0009628//response to abiotic stimulus;GO:0009967//positive regulation of signal transduction;GO:0010769//regulation of cell morphogenesis involved in differentiation;GO:0014070//response to organic cyclic compound;GO:0016486//peptide hormone processing;GO:0030307//positive regulation of cell growth;GO:0031346//positive regulation of cell projection organization;GO:0031960//response to corticosteroid stimulus;GO:0043066//negative regulation of apoptotic process;GO:0043388//positive regulation of DNA binding;GO:0050767//regulation of fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of cell growth	gij202515[gb]AAA40599.1
24494	<i>Il1b</i>	interleukin 1 beta	0.649716706	0.480498576	0.766523124	0.537058599	0.971789667	1.490737477	GO:0016023//cytoplasmic membrane-bounded vesicle;GO:0044421//extracellular region part	GO:0005126//cytokine receptor binding	GO:0001660//fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of cell growth	gij158186736[ref]NP_113700.2
25670	<i>Il15</i>	interleukin 15	1.245356786	1.422401135	1.387998977	1.583718813	1.17396821	1.28507374	GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005102//receptor binding	GO:0001660//fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of cell growth	gij6981092[ref]NP_037261.1
29397	<i>Ccl11</i>	chemokine (C-C motif) ligand 11	0.573607035	0.677487814	0.578826113	0.810506017	1.567558351	1.200154811	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0001660//fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of cell growth	gij11276089[ref]NP_062078.1
81503	<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	0.430771268	0.224613828	1.229553768	0.516054154	0.308972258	0.318318779	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0001660//fever generation;GO:0002237//response to molecule of bacterial origin;GO:0002437//inflammatory response to antigenic stimulus;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//kappaB kinase/NF-kappaB cascade;GO:0007292//female gamete generation;GO:0007611//learning or memory;GO:0009612//response to mechanical stimulus;GO:0009895;GO:0009968//negative regulation of signal transduction;GO:0010212//response to ionizing radiation;GO:0010551;GO:0010827//regulation of glucose transport;GO:0014047//glutamate secretion;GO:0014072;GO:0019915//lipid storage;GO:0030073//insulin secretion;GO:0030595//leukocyte chemotaxis;GO:0031331;GO:0031960//response to corticosteroid stimulus;GO:0032305//positive regulation of icosanoid secretion;GO:0032612;GO:0032722//positive regulation of chemokine production;GO:0032770//positive regulation of monooxygenase activity;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0035504;GO:0042098//T cell proliferation;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0042345//regulation of NF-kappaB import into nucleus;GO:0042493//response to drug;GO:0043066//negative regulation of apoptotic process;GO:0043406//positive regulation of MAP kinase activity;GO:0043410//positive regulation of MAPK cascade;GO:0043627//response to estrogen stimulus;GO:0045765//regulation of cell growth	gij13540652[ref]NP_110472.1
25542	<i>Ccl3</i>	chemokine (C-C motif) ligand 3	0.507002774	0.322442324	0.548159829	0.464028114	0.532250753	0.195839831	GO:0000267//cell fraction;GO:0044421//extracellular region part	GO:0005125//cytokine activity;GO:0005539//glycosaminoglycan binding	GO:0002763//positive regulation of myeloid leukocyte differentiation;GO:0006952//defense response;GO:0008283//cell proliferation;GO:0030595//leukocyte chemotaxis;GO:0051480//cytosolic calcium ion homeostasis	gij40254794[ref]NP_037157.2
114105	<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 2	0.221245947	-	0.09021486	0.016747513	-	0.016786907	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0006952//defense response;GO:0030595//leukocyte chemotaxis	gij16758460[ref]NP_446099.1
171040	<i>Il11</i>	interleukin 11	0.103939148	0.083100855	0.108780582	0.209283886	0.20576002	0.231857865	GO:0044421//extracellular region part;GO:0044424//intracellular part	GO:0005126//cytokine receptor binding	GO:0001934//positive regulation of protein phosphorylation;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0008283//cell proliferation;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0030098//lymphocyte differentiation;GO:0030099//myeloid cell differentiation;GO:0048883//regulation of hormone secretion	gij340805851[ref]NP_598203.4
360750	<i>Ccl25</i>	chemokine (C-C motif) ligand 25	0.076593162	-	-	-	0.02807877	-	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0007166//cell surface receptor signaling pathway;GO:0042221//response to chemical stimulus	gij82524292[ref]NP_001032280.1

24493	<i>Il1a</i>	interleukin 1 alpha	0.043673226	-	0.01662091	0.694239905	0.470707033	0.380410516	GO:0044421//extracellular region part;GO:0044444//cytoplasmic part	GO:0005149//interleukin-1 receptor binding;GO:0046914//transition metal ion binding	GO:0001819//positive regulation of cytokine production;GO:0002237//response to molecule of bacterial origin;GO:0002376//immune system process;GO:0006694//steroid biosynthetic process;GO:0006953//acute-phase response;GO:0007088//regulation of mitosis;GO:0007166//cell surface receptor signaling pathway;GO:0007249//I-kappaB kinase/NF-kappaB cascade;GO:0008283//cell proliferation;GO:0009408//response to heat;GO:0009719;GO:0010038//response to metal ion;GO:0010212//response to ionizing radiation;GO:0030216//keratinocyte differentiation;GO:0032872//regulation of stress-activated MAPK cascade;GO:0033273//response to vitamin;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0043066//negative regulation of apoptotic process;GO:0043410//positive regulation of MAPK cascade;GO:0045765//regulation of defense response;GO:0030595//leukocyte chemotaxis	gij8393593[ref][NP_058715.1]/5.6272e-150/interleukin-1 alpha precursor [Rattus norvegicus]
171551	<i>Cxcl3</i>	chemokine (C-X-C motif) ligand 3	0.103260614	0.103197946	0.024561464	-	-	0.027421935	GO:0044421//extracellular region part	GO:0005125//cytokine activity		gij149033777[gb][EDL88573.1]/1.95119e-59/gene model 1960, (NCBI), isoform CBA-1 [Rattus norvegicus]
300339	<i>Mmp1</i>	matrix metalloproteinase 1 (interstitial collagenase)	0.017218618	-	-	-	-	0.036580671	GO:0031012//extracellular matrix	GO:0004175//endopeptidase activity;GO:0046914//transition metal ion binding	GO:0002376//immune system process;GO:0007599//hemostasis;GO:0019538//protein metabolic process;GO:0032963//collagen metabolic process	gij197384336[ref][NP_001128002.1]/0/matrix metalloproteinase 1a precursor [Rattus norvegicus]
24498	<i>Il6</i>	interleukin 6	0.033300313	0.033280103	0.221781795	3.793672303	2.801683558	2.652973793	GO:0005887//integral to membrane;GO:0044421//extracellular region part	GO:0005126//cytokine activity;GO:0005125//cytokine activity	GO:0000060//protein import into nucleus, translocation;GO:0001101//response to stress;GO:0006952//defense response;GO:0007154//cell proliferation;GO:0001935//endothelial cell proliferation;GO:0002376//immune system process;GO:0016477//cell migration;GO:0030041//actin filament polymerization;GO:0032321//positive regulation of Rho GTPase activity	gij7549769[ref][NP_036721.1]/11559996[ref][NP_071550.1]/157823491[ref][NP_001102958.1]/1.96257e-52/chemokine (C-C motif) ligand 26 precursor [Rattus norvegicus]
60665	<i>Cxcl5</i>	chemokine (C-X-C motif) ligand 5	0.088546633	0.35397158	0.168492894	-	0.438221721	0.188115869	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0042221//response to chemical stimulus	gij9507069[ref][NP_062106.1]/4.14841e-50/C-C motif chemokine 20 precursor [Rattus norvegicus]
685958	<i>Ccl26</i>	chemokine (C-C motif) ligand 26	-	0.102087205	0.064792277	0.036084172	0.037447518	0.108507147	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0042221//response to chemical stimulus	gij300797687[ref][NP_001178021.1]/1.27329e-48/C-C motif chemokine 1 precursor [Rattus norvegicus]
29538	<i>Ccl20</i>	chemokine (C-C motif) ligand 20	-	-	0.081149151	0.045193657	-	-	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0006952//defense response;GO:0007154//cell communication;GO:0023052//signaling;GO:0042221//response to chemical stimulus;GO:0042465	gij6981148[ref][NP_037208.1]/1.03323e-69/leptin precursor [Rattus norvegicus]
688605	<i>Ccl1</i>	chemokine (C-C motif) ligand 1	-	0.26929641	0.512747734	0.20397137	0.381020213	0.163560921	GO:0044421//extracellular region part	GO:0005125//cytokine activity	GO:0002376//immune system process;GO:0042221//response to chemical stimulus	gij11078689[ref][NP_067721.1]/5.53766e-82/preproepiregulin [Rattus norvegicus]
25608	<i>Lep</i>	leptin	-	0.02642683	0.025158703	0.011209126	0.0697958	0.011235492	GO:0044421//extracellular region part	GO:0051427	GO:0001816//cytokine production;GO:0006071//glycerol metabolic process;GO:0006094//gluconeogenesis;GO:0006357//regulation of transcription from RNA polymerase II promoter;GO:0006606//protein import into nucleus;GO:0006631//fatty acid metabolic process;GO:0006694//steroid biosynthetic process;GO:0006811//ion transport;GO:0006915//apoptotic process;GO:0006950//response to stress;GO:0007159//leukocyte cell-cell adhesion;GO:0007631//feeding behavior;GO:0008283//cell proliferation;GO:0010740//positive regulation of intracellular protein kinase cascade;GO:0014897;GO:0015980//energy derivation by oxidation of organic compounds;GO:0016125//steroid metabolic process;GO:0019216//regulation of lipid metabolic process;GO:0019221//cytokine-mediated signaling pathway;GO:0019229//regulation of vasoconstriction;GO:0019935//cyclic-nucleotide-mediated signaling;GO:0021953//central nervous system neuron differentiation;GO:0022602//ovulation cycle process;GO:0030073//insulin secretion;GO:0030282//bone mineralization;GO:0030299//intestinal cholesterol absorption;GO:0032096//negative regulation of response to food;GO:0032275//luteinizing hormone secretion;GO:0032278;GO:0032526//response to retinoic acid;GO:0032891;GO:0033591//response to L-ascorbic acid;GO:0042503//tyrosine phosphorylation of Stat3 protein;GO:0043434//response to peptide hormone stimulus;GO:0045607//positive regulation of cell differentiation;GO:0046007//positive regulation of antral ovarian follicle growth;GO:0006275//regulation of DNA replication;GO:0006351//transcription, DNA-dependent;GO:0007088//regulation of mitosis;GO:0007126//meiosis;GO:0007154//cell communication;GO:0007176//regulation of epidermal growth factor-activated receptor activity;GO:0007186//G-protein coupled receptor signaling pathway;GO:0008284//positive regulation of cell proliferation;GO:0008285//negative regulation of cell proliferation;GO:0009611//response to wounding;GO:0009725//response to hormone stimulus;GO:0009913//epidermal cell differentiation;GO:0022605//oogenesis stage;GO:0031349//positive regulation of defense response;GO:0033674//positive regulation of kinase activity;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0045765//regulation of angiogenesis;GO:0051148//negative regulation of cytoskeleton organization;GO:0051149//positive regulation of cytoskeleton organization;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009888//tissue development;GO:0016049//cell growth;GO:0019318//hexose metabolic process;GO:0048017//inositol lipid-mediated signaling	
59325	<i>Ereg</i>	epiregulin	-	-	0.039698865	-	-	-	GO:0016021//integral to membrane;GO:0044421//extracellular region part	GO:0070851//growth factor receptor binding	GO:0001547//antral ovarian follicle growth;GO:0006275//regulation of DNA replication;GO:0006351//transcription, DNA-dependent;GO:0007088//regulation of mitosis;GO:0007126//meiosis;GO:0007154//cell communication;GO:0007176//regulation of epidermal growth factor-activated receptor activity;GO:0007186//G-protein coupled receptor signaling pathway;GO:0008284//positive regulation of cell proliferation;GO:0008285//negative regulation of cell proliferation;GO:0009611//response to wounding;GO:0009725//response to hormone stimulus;GO:0009913//epidermal cell differentiation;GO:0022605//oogenesis stage;GO:0031349//positive regulation of defense response;GO:0033674//positive regulation of kinase activity;GO:0042108//positive regulation of cytokine biosynthetic process;GO:0045765//regulation of angiogenesis;GO:0051148//negative regulation of cytoskeleton organization;GO:0051149//positive regulation of cytoskeleton organization;GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009888//tissue development;GO:0016049//cell growth;GO:0019318//hexose metabolic process;GO:0048017//inositol lipid-mediated signaling	gij11078689[ref][NP_067721.1]/5.53766e-82/preproepiregulin [Rattus norvegicus]
25685	<i>Igfbp1</i>	insulin-like growth factor binding protein 1	-	-	-	-	0.051028485	-	GO:0044421//extracellular region part	GO:0019838//growth factor binding	GO:0007169//transmembrane receptor protein tyrosine kinase signaling pathway;GO:0009888//tissue development;GO:0016049//cell growth;GO:0019318//hexose metabolic process;GO:0048017//inositol lipid-mediated signaling	gij6981080[ref][NP_037276.1]/2.38401e-163/insulin-like growth factor-binding protein 1 precursor [Rattus norvegicus]

Up-regulated genes as compared with the uninjured control (0 hour) were labeled in red color while down-regulated genes were labeled in green color.