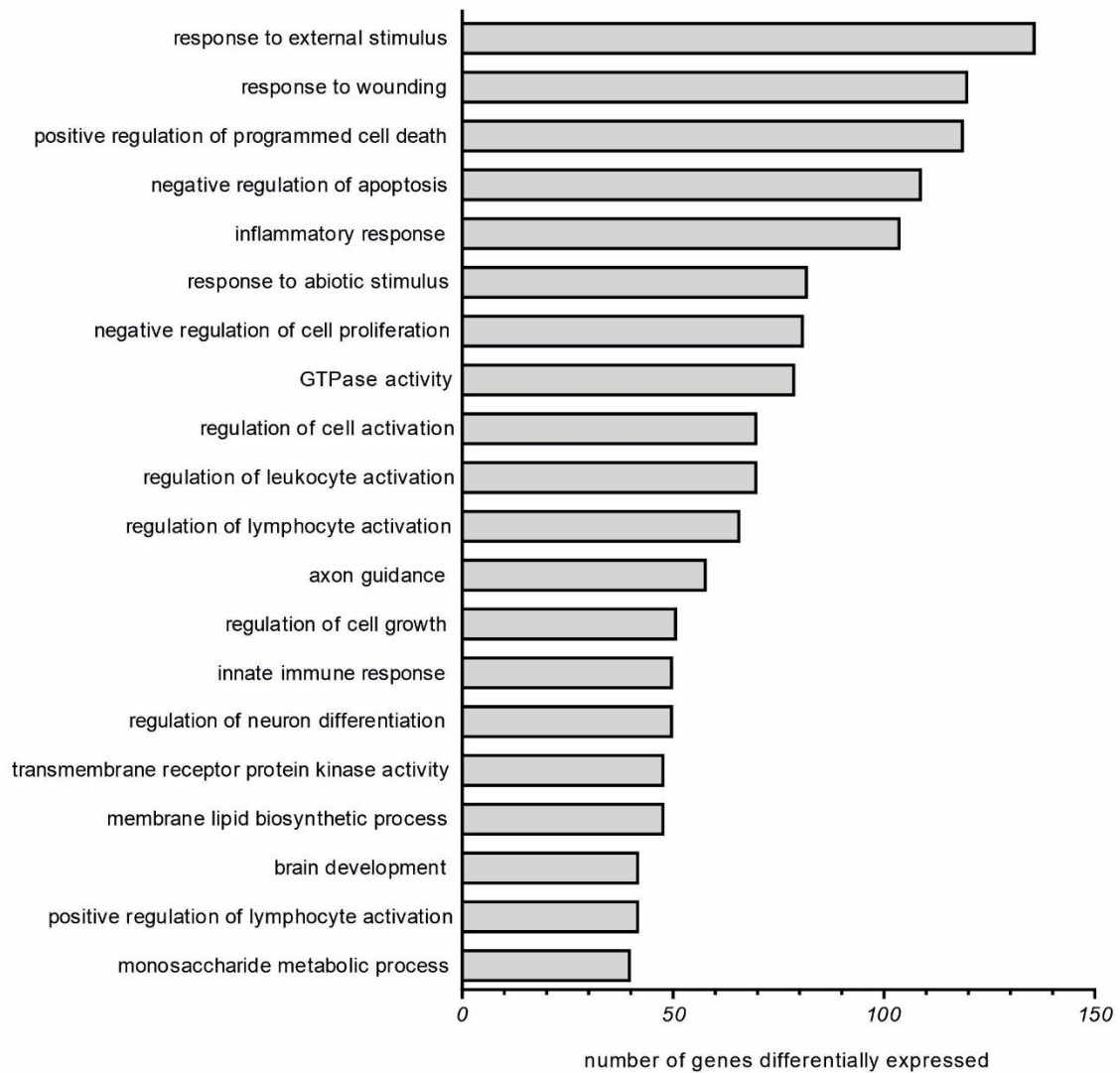


Supplementary materials



Supplementary Figure 1. Functional categories represented by genes up- or downregulated by LPS (12 h). Top 20 functional categories with p values <0.01 are shown.

Supplementary Table 1. The list of all genes up- or downregulated 12 h after systemic administration of LPS (FDR<0.05; FC>2)

Part A: List of all upregulated genes

Gene Symbol	Gene Title	FC
<i>Lcn2</i>	lipocalin 2	237.80
<i>Saa3</i>	serum amyloid A 3	53.09
<i>Ms4a6d</i>	membrane-spanning 4-domains, subfamily A, member 6D	26.23
<i>Gbp2</i>	guanylate binding protein 2	22.32
<i>Ctla2a</i>	cytotoxic T lymphocyte-associated protein 2 alpha	15.50
<i>Ccl5</i>	chemokine (C-C motif) ligand 5	14.31
<i>Cxcl10</i>	chemokine (C-X-C motif) ligand 10	12.15
<i>Lrg1</i>	leucine-rich alpha-2-glycoprotein 1	11.34
<i>Ch25h</i>	cholesterol 25-hydroxylase	10.43
<i>Ctla2b</i>	cytotoxic T lymphocyte-associated protein 2 beta	10.01
<i>Mpa2l</i>	macrophage activation 2 like	9.27
<i>S3-12</i>	plasma membrane associated protein, S3-12	9.19
<i>Timp1</i>	tissue inhibitor of metalloproteinase 1	8.93
<i>Ms4a6b</i>	membrane-spanning 4-domains, subfamily A, member 6B	8.91
<i>A2m</i>	alpha-2-macroglobulin	8.80
<i>Osmr</i>	oncostatin M receptor	7.58
<i>Ifitm3</i>	interferon induced transmembrane protein 3	7.15
<i>Mmp3</i>	matrix metalloproteinase 3	7.03
<i>Iigp1</i>	interferon inducible GTPase 1	6.98
<i>Prg4</i>	proteoglycan 4	6.42
<i>Spp1</i>	secreted phosphoprotein 1	6.42
<i>Igtp</i>	interferon gamma induced GTPase	6.41
<i>Rhoj</i>	ras homolog gene family, member J	6.10
<i>Oasl2</i>	2'-5' oligoadenylate synthetase-like 2	5.70
<i>Ms4a6c</i>	membrane-spanning 4-domains, subfamily A, member 6C	5.57
<i>Saa1</i>	serum amyloid A 1	5.45
<i>Gbp3</i>	guanylate binding protein 3	5.44
<i>Socs3</i>	suppressor of cytokine signaling 3	5.32
<i>Steap4</i>	STEAP family member 4	5.24
<i>Apod</i>	apolipoprotein D	5.20
<i>Cdkn1a</i>	cyclin-dependent kinase inhibitor 1A (P21)	5.18
<i>Serpina3n</i>	serine (or cysteine) peptidase inhibitor, clade A, member 3N	5.10
<i>Ifitm1</i>	interferon induced transmembrane protein 1	5.01
<i>Cp</i>	ceruloplasmin	4.81
<i>Xdh</i>	xanthine dehydrogenase	4.72
<i>Pglyrp1</i>	peptidoglycan recognition protein 1	4.64
<i>Tubb6</i>	tubulin, beta 6	4.39

<i>Icam1</i>	intercellular adhesion molecule 1	4.36
<i>Srgn</i>	serglycin	4.35
<i>Slc10a6</i>	solute carrier family 10 (sodium/bile acid cotransporter family), member 6	4.32
<i>Angptl4</i>	angiopoietin-like 4	4.23
<i>Ccl12</i>	chemokine (C-C motif) ligand 12	4.22
<i>Pla1a</i>	phospholipase A1 member A	4.21
<i>Galnt12</i>	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	4.16
<i>Ly6a</i>	lymphocyte antigen 6 complex, locus A	4.14
<i>Map3k6</i>	mitogen-activated protein kinase kinase kinase 6	4.09
<i>Mt2</i>	metallothionein 2	4.01
<i>Ifitm2</i>	interferon induced transmembrane protein 2	3.94
<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	3.91
<i>Ucp2</i>	uncoupling protein 2 (mitochondrial, proton carrier)	3.86
<i>Igsf6</i>	immunoglobulin superfamily, member 6	3.77
<i>Ada</i>	adenosine deaminase	3.77
<i>Tgm2</i>	transglutaminase 2, C polypeptide	3.65
<i>Hspb1</i>	heat shock protein 1	3.61
<i>Irf7</i>	interferon regulatory factor 7	3.56
<i>Gpr65</i>	G-protein coupled receptor 65	3.53
<i>Ifit3</i>	interferon-induced protein with tetratricopeptide repeats 3	3.50
<i>Fcgr2b</i>	Fc receptor, IgG, low affinity IIb	3.47
<i>Adamts9</i>	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 9	3.45
<i>Hspb6</i>	heat shock protein, alpha-crystallin-related, B6	3.41
<i>Gbp6</i>	guanylate binding protein 6	3.39
<i>Msr1</i>	macrophage scavenger receptor 1	3.36
<i>Rtp4</i>	receptor transporter protein 4	3.36
<i>Fcgr4</i>	Fc receptor, IgG, low affinity IV	3.35
<i>Irgm1</i>	immunity-related GTPase family M member 1	3.35
<i>Pmaip1</i>	phorbol-12-myristate-13-acetate-induced protein 1	3.32
<i>Rsad2</i>	radical S-adenosyl methionine domain containing 2	3.27
<i>Cyp1b1</i>	cytochrome P450, family 1, subfamily b, polypeptide 1	3.23
<i>Cd44</i>	CD44 antigen	3.22
<i>Adamts1</i>	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 1	3.22
<i>Arrdc2</i>	arrestin domain containing 2	3.22
<i>Ifit1</i>	interferon-induced protein with tetratricopeptide repeats 1	3.19
<i>Sult1a1</i>	sulfotransferase family 1A, phenol-preferring, member 1	3.19
<i>Maff</i>	v-maf musculoaponeurotic fibrosarcoma oncogene family, protein F (avian)	3.18
<i>Glipr2</i>	GLI pathogenesis-related 2	3.12

<i>Trim30</i>	tripartite motif-containing 30	3.07
<i>Ifi44</i>	interferon-induced protein 44	3.06
<i>Acer2</i>	alkaline ceramidase 2	3.05
<i>Pp11r</i>	placental protein 11 related	3.03
<i>Iigp2</i>	interferon inducible GTPase 2	3.02
<i>Ifi47</i>	interferon gamma inducible protein 47	3.01
<i>Cd14</i>	CD14 antigen	3.00
<i>Psmb8</i>	proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional peptidase 7)	2.96
<i>Serping1</i>	serine (or cysteine) peptidase inhibitor, clade G, member 1	2.96
<i>Sgk3</i>	serum/glucocorticoid regulated kinase 3	2.95
<i>Gpr84</i>	G protein-coupled receptor 84	2.95
<i>Lgals3bp</i>	lectin, galactoside-binding, soluble, 3 binding protein	2.94
<i>Plaur</i>	plasminogen activator, urokinase receptor	2.92
<i>Nfkbia</i>	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	2.91
<i>Cd93</i>	CD93 antigen	2.90
<i>Sgk1</i>	serum/glucocorticoid regulated kinase 1	2.89
<i>Tap1</i>	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	2.86
<i>Ccl9</i>	chemokine (C-C motif) ligand 9	2.83
<i>Tspan4</i>	tetraspanin 4	2.79
<i>Scara5</i>	scavenger receptor class A, member 5 (putative)	2.78
<i>Slfn4</i>	schlafen 4	2.77
<i>Apolo1</i>	apolipoprotein L domain containing 1	2.76
<i>Agxt2l1</i>	alanine-glyoxylate aminotransferase 2-like 1	2.76
<i>Crispld2</i>	cysteine-rich secretory protein LCCL domain containing 2	2.75
<i>Fcgr3</i>	Fc receptor, IgG, low affinity III	2.75
<i>C5ar1</i>	complement component 5a receptor 1	2.74
<i>Igfbp7</i>	insulin-like growth factor binding protein 7	2.70
<i>Bcl2a1a</i>	B-cell leukemia/lymphoma 2 related protein A1a	2.70
<i>Aspg</i>	asparaginase homolog (<i>S. cerevisiae</i>)	2.66
<i>Csf3</i>	colony stimulating factor 3 (granulocyte)	2.64
<i>Sdc4</i>	syndecan 4	2.62
<i>Ctsc</i>	cathepsin C	2.62
<i>S100a11</i>	S100 calcium binding protein A11 (calgizzarin)	2.62
<i>Xaf1</i>	XIAP associated factor 1	2.62
<i>Scgb3a1</i>	secretoglobin, family 3A, member 1	2.61
<i>Fkbp5</i>	FK506 binding protein 5	2.61
<i>Pla2g3</i>	phospholipase A2, group III	2.59
<i>Ier3</i>	immediate early response 3	2.59
<i>Ggta1</i>	glycoprotein galactosyltransferase alpha 1, 3	2.58

<i>Il2rg</i>	interleukin 2 receptor, gamma chain	2.57
<i>Gimap6</i>	GTPase, IMAP family member 6	2.57
<i>Ptx3</i>	pentraxin related gene	2.57
<i>Tlr2</i>	toll-like receptor 2	2.56
<i>Gp49a</i>	glycoprotein 49 A	2.56
<i>Emp1</i>	epithelial membrane protein 1	2.56
<i>C3</i>	complement component 3	2.56
<i>Herc5</i>	hect domain and RLD 5	2.56
<i>Cebpd</i>	CCAAT/enhancer binding protein (C/EBP), delta	2.55
<i>Kcna5</i>	potassium voltage-gated channel, shaker-related subfamily, member 5	2.55
<i>Cd86</i>	CD86 antigen	2.54
<i>Txnip</i>	thioredoxin interacting protein	2.53
<i>Plce1</i>	phospholipase C, epsilon 1	2.52
<i>Rnf125</i>	ring finger protein 125	2.51
<i>Ifi35</i>	interferon-induced protein 35	2.49
<i>Parp3</i>	poly (ADP-ribose) polymerase family, member 3	2.48
<i>Fcer1g</i>	Fc receptor, IgE, high affinity I, gamma polypeptide	2.48
<i>Mfsd2</i>	major facilitator superfamily domain containing 2	2.46
<i>Il1rn</i>	interleukin 1 receptor antagonist	2.46
<i>Clec4a3</i>	C-type lectin domain family 4, member a3	2.46
<i>Pnpla2</i>	patatin-like phospholipase domain containing 2	2.45
<i>Gfap</i>	glial fibrillary acidic protein	2.44
<i>Rasip1</i>	Ras interacting protein 1	2.44
<i>Nudt6</i>	nudix (nucleoside diphosphate linked moiety X)-type motif 6	2.44
<i>Csf2rb</i>	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	2.44
<i>Hif3a</i>	hypoxia inducible factor 3, alpha subunit	2.44
<i>Atp2c2</i>	ATPase, Ca ⁺⁺ transporting, type 2C, member 2	2.40
<i>Mt1</i>	metallothionein 1	2.39
<i>Il1r2</i>	interleukin 1 receptor, type II	2.38
<i>Tcfcp2l1</i>	transcription factor CP2-like 1	2.37
<i>C1r</i>	complement component 1, r subcomponent	2.36
<i>Zfp36</i>	zinc finger protein 36	2.35
<i>Cd300lf</i>	CD300 antigen like family member F	2.34
<i>Msn</i>	moesin	2.33
<i>Arpc1b</i>	actin related protein 2/3 complex, subunit 1B	2.31
<i>Tlr7</i>	toll-like receptor 7	2.31
<i>Ddc</i>	dopa decarboxylase	2.31
<i>H2-L</i>	histocompatibility 2, D region	2.31
<i>Ncf1</i>	neutrophil cytosolic factor 1	2.30
<i>H2-D1</i>	histocompatibility 2, D region locus 1	2.29

<i>Anubl1</i>	AN1, ubiquitin-like, homolog (<i>Xenopus laevis</i>)	2.28
<i>C3ar1</i>	complement component 3a receptor 1	2.27
<i>Map3k8</i>	mitogen-activated protein kinase kinase kinase 8	2.26
<i>Ezr</i>	ezrin	2.25
<i>Tnfrsf1a</i>	tumor necrosis factor receptor superfamily, member 1a	2.23
<i>Parp14</i>	poly (ADP-ribose) polymerase family, member 14	2.22
<i>Cirbp</i>	cold inducible RNA binding protein	2.21
<i>Lgals9</i>	lectin, galactose binding, soluble 9	2.21
<i>H2-K1</i>	histocompatibility 2, K1, K region	2.20
<i>Cd274</i>	CD274 antigen	2.18
<i>Mgp</i>	matrix Gla protein	2.18
<i>Rbm3</i>	RNA binding motif protein 3	2.18
<i>Selp</i>	selectin, platelet	2.17
<i>Gpr182</i>	G protein-coupled receptor 182	2.16
<i>Procr</i>	protein C receptor, endothelial	2.15
<i>Angpt2</i>	angiopoietin 2	2.14
<i>Tmbim1</i>	transmembrane BAX inhibitor motif containing 1	2.13
<i>Tspo</i>	translocator protein	2.12
<i>Alox12b</i>	arachidonate 12-lipoxygenase, 12R type	2.12
<i>Parp9</i>	poly (ADP-ribose) polymerase family, member 9	2.11
<i>Tsc22d3</i>	TSC22 domain family, member 3	2.10
<i>Adm</i>	adrenomedullin	2.10
<i>Tmem176a</i>	transmembrane protein 176A	2.10
<i>Capg</i>	capping protein (actin filament), gelsolin-like	2.10
<i>Lyve1</i>	lymphatic vessel endothelial hyaluronan receptor 1	2.07
<i>Irf9</i>	interferon regulatory factor 9	2.07
<i>Vim</i>	vimentin	2.07
<i>Il13ra1</i>	interleukin 13 receptor, alpha 1	2.07
<i>Clic1</i>	chloride intracellular channel 1	2.06
<i>Hck</i>	hemopoietic cell kinase	2.06
<i>Cxcl9</i>	chemokine (C-X-C motif) ligand 9	2.06
<i>Akap12</i>	A kinase (PRKA) anchor protein (gravin) 12	2.06
<i>Synpo</i>	synaptopodin	2.05
<i>Rhou</i>	ras homolog gene family, member U	2.05
<i>Col5a3</i>	collagen, type V, alpha 3	2.05
<i>Ddit4</i>	DNA-damage-inducible transcript 4	2.04
<i>Anxa2</i>	annexin A2	2.04
<i>Psmb9</i>	proteasome (prosome, macropain) subunit, beta type 9	2.03
<i>Bcl3</i>	B-cell leukemia/lymphoma 3	2.01
<i>Pycard</i>	PYD and CARD domain containing	2.01

Part B: List of all downregulated genes (FDR<0.05)

Gene Symbol	Gene Title	FC
<i>Gpr34</i>	G protein-coupled receptor 34	-7.85
<i>P2ry12</i>	purinergic receptor P2Y, G-protein coupled 12	-4.61
<i>Serpinb1a</i>	serine (or cysteine) peptidase inhibitor, clade B, member 1a	-3.75
<i>Akr1c14</i>	aldo-keto reductase family 1, member C14	-3.56
<i>Itm2a</i>	integral membrane protein 2A	-3.51
<i>Cxcl12</i>	chemokine (C-X-C motif) ligand 12	-3.45
<i>Ugt8a</i>	UDP galactosyltransferase 8A	-3.10
<i>Tek</i>	endothelial-specific receptor tyrosine kinase	-3.06
<i>Slco1c1</i>	solute carrier organic anion transporter family, member 1c1	-2.88
<i>Slc40a1</i>	solute carrier family 40 (iron-regulated transporter), member 1	-2.71
<i>Myoc</i>	myocilin	-2.66
<i>Abcb1a</i>	ATP-binding cassette, sub-family B (MDR/TAP), member 1A	-2.61
<i>Slc22a8</i>	solute carrier family 22 (organic anion transporter), member 8	-2.60
<i>Fabp7</i>	fatty acid binding protein 7, brain	-2.60
<i>Pllp</i>	plasma membrane proteolipid	-2.60
<i>Aspa</i>	aspartoacylase	-2.56
<i>Pltp</i>	phospholipid transfer protein	-2.52
<i>Slc47a1</i>	solute carrier family 47, member 1	-2.44
<i>Ptprb</i>	protein tyrosine phosphatase, receptor type, B	-2.44
<i>Olfml3</i>	olfactomedin-like 3	-2.39
<i>Hist1h3b</i>	histone cluster 1, H3b	-2.36
<i>Gjb1</i>	gap junction protein, beta 1	-2.34
<i>Slc19a3</i>	solute carrier family 19 (sodium/hydrogen exchanger), member 3	-2.33
<i>Gjc2</i>	gap junction protein, gamma 2	-2.31
<i>Gulp1</i>	GULP, engulfment adaptor PTB domain containing 1	-2.29
<i>Hist1h4a</i>	histone cluster 1, H4a	-2.24
<i>Rlbp1</i>	retinaldehyde binding protein 1	-2.21
<i>Opalin</i>	oligodendrocytic myelin paranodal and inner loop protein	-2.21
<i>Tst</i>	thiosulfate sulfurtransferase, mitochondrial	-2.20
<i>Hist2h3c2</i>	histone cluster 2, H3c2	-2.17
<i>Rasgrp3</i>	RAS, guanyl releasing protein 3	-2.14
<i>Tnc</i>	tenascin C	-2.07
<i>Ranbp3l</i>	RAN binding protein 3-like	-2.06
<i>Ppp1r14a</i>	protein phosphatase 1, regulatory (inhibitor) subunit 14A	-2.06
<i>Gng11</i>	guanine nucleotide binding protein (G protein), gamma 11	-2.06
<i>Gldc</i>	glycine decarboxylase	-2.05
<i>Hist1h3a</i>	histone cluster 1, H3a	-2.01

Supplementary Table 2. List of the genes in most significantly altered top ten canonical pathways.

Ingenuity Canonical Pathways	-log (p-value)	Ratio	Genes
Granulocyte adhesion and diapedesis	1.13E+01	1.07E-01	<i>C5ar1, Icam1, Mmp3, Tnfrsf1a, Ccl5, Sdc4, Csf3, Ccl9, Cxcl10, Il1r2, Selp, Ccl12, Il1rn, Ezr, Cxcl12, MMP12, CXCL2, Msn, Hspb1</i>
Agranulocyte adhesion and diapedesis	8.07E+00	8.47E-02	<i>C5ar1, Icam1, Mmp3, Tnfrsf1a, Sdc4, Ccl5, Ccl9, Cxcl10, Ccl12, Selp, Il1rn, Ezr, Cxcl12, MMP12, CXCL2, Msn</i>
Communication between innate and adaptive immune cells	6.85E+00	9.17E-02	<i>Cxcl10, Tlr2, Il1rn, HLA-B, Tlr7, Fcer1g, Cd86, Ccl5, HLA-E, Ccl9</i>
Acute phase response signaling	6.20E+00	7.78E-02	<i>C1r, Socs3, Serping1, Nfkbia, C3, Il1rn, Tnfrsf1a, Saa3, Saa1, Osmr, Serpina3n, Cp, LBP, A2m</i>
Dendritic cell maturation	5.85E+00	6.22E-02	<i>Tlr2, Col5a3, Nfkbia, Plce1, Icam1, Il1rn, Tnfrsf1a, FCGR2A, HLA-B, Fcer1g, Cd86, Fcgr2b, FCGR3A</i>
LXR/RXR activation	5.63E+00	8.09E-02	<i>Il1r2, C3, Msr1, Ccl12, Il1rn, Tnfrsf1a, Saa1, Cd14, LBP, PLTP, Apod</i>
Antigen presentation pathway	5.29E+00	1.50E-01	<i>Psmb9, NLRC5, HLA-B, Psmb8, Tap1, HLA-E</i>
Interferon signaling	5.09E+00	1.67E-01	<i>Ifit3, Ifitm1, Ifi35, Irf9, Psmb8, Tap1</i>
IL-10 signaling	4.84E+00	1.03E-01	<i>Il1r2, Socs3, Nfkbia, FCGR2A, Il1rn, Cd14, LBP, Fcgr2b</i>
Atherosclerosis signaling	4.76E+00	7.30E-02	<i>Alox12b, Col5a3, Icam1, Msr1, Ccl12, Mmp3, Selp, Il1rn, Pla2g3, Apod</i>

Ingenuity Pathway Analysis software (Ingenuity Systems) was used to analyze affected genes ($p < 0.05$, $FC > 2$) to identify the number of genes significantly associated with canonical pathways in the Ingenuity database. Top 10 pathways are presented.