ACTA ABP BIOCHIMICA POLONICA

Supplementary Materials Epub: No 2016_1343
Vol. 63, 2016
https://doi.org/10.18388/abp.2016_ l

Regular paper

RNA-Seq-based analysis of differential gene expression associated with hepatitis C virus infection in a cell culture

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Hepatitis C virus (HCV) infections are one of the major causes of chronic liver diseases. Unfortunately, the mechanisms of HCV infection-induced liver injury and host-virus interactions are still not well recognized. To better understand these processes we determined the changes in the host gene expression that occur during HCV infection of Huh-7.5 cells. As a result, we identified genes that may contribute to the immune and metabolic cellular responses to infection. Pathway enrichment analysis indicated that HCV induced an increased expression of genes involved in mitogen-activated protein kinases signaling, adipocytokine signaling, cell cycle and nitrogen metabolism. In addition, the enrichment analyses of processes and molecular functions revealed that the up-regulated genes were mainly implicated in the negative regulation of phosphorylation. Construction of the pathway-gene-process network enabled exploration of a much more complex landscape of molecular interactions. Consequently, several essential processes altered by an HCV infection were identified: negative regulation of cell cycle, response to endoplasmic reticulum stress, response to reactive oxygen species, toll-like receptor signaling and pattern recognition receptor signaling. The analyses of genes whose expression was decreased upon HCV infection showed that the latter were engaged in the metabolism of lipids and amino acids. Moreover, we observed disturbance in the cellular antiviral defense. Altogether, our results demonstrated that the HCV infection elicits host response that includes a very wide range of cellular mechanisms. Our findings significantly broadened the understanding of complex processes that accompany the HCV infection. Consequently, they may be used for developing new host-oriented therapeutic strategies.

Key words: RNA-Seq, HCV, transcriptome

Received: 01 June, 2016; revised: 24 June, 2016; accepted: 13 July, 2016; available on-line: ?? Octobet, 2016

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Abbreviations:

Supplementary Table 1.A. The list of the significantly up-regulated genes (FC ≥ 2, P adj. value < 0.001; 72 and 96 hpi) upon HCV infection in the Huh-7.5 cells. Fold change is shown for two time points post inoculation (72 h and 96 h). Genes are presented in descending order of fold change of gene expression in HCV infected cells relative to non-infected cells at 72 h post inoculation. Newly identified differentially expressed genes are shown in bold.

Ensembl Gene ID	Gene Name	Gene Description	Fold Change 72 h	P adj. value	Fold Change 96 h	P adj. value
ENSG00000049249	TNFRSF9	tumor necrosis factor receptor superfamily, member 9	123.22	4.848E-42	12.72	2.836E-07
ENSG00000148677	ANKRD1	ankyrin repeat domain 1	93.19	8.079E-50	55.51	4.677E-247
ENSG00000163121	**NEURL3**	**neuralized homolog 3 pseudogene**	**73.17**	**2.088E-18**	**21.48**	**5.145E-32**
ENSG00000048052	HDAC9	histone deacetylase 9	49.07	5.578E-94	16.44	4.743E-83
ENSG00000109321	AREG	amphiregulin	42.68	3.713E-21	21.89	2.641E-104
ENSG00000174951	FUT1	fucosyltransferase 1	42.16	2.752E-12	39.80	2.742E-52
ENSG00000152137	HSPB8	heat shock protein 8	36.19	1.983E-69	18.10	7.738E-57
ENSG00000139269	INHBE	inhibin, beta E	34.46	7.793E-59	16.38	4.033E-153
ENSG00000146592	CREB5	cAMP responsive element binding protein 5	33.55	3.656E-89	14.91	2.601E-119
ENSG00000124882	**EREG**	**epiregulin**	**29.19**	**7.678E-12**	**7.61**	**3.325E-04**
ENSG00000184545	DUSP8	dual specificity phosphatase 8	28.64	8.244E-07	16.45	3.666E-96

ENSG00000162772	ATF3	activating transcription factor 3	27.96	4.231E-90	14.50	6.114E-144
ENSG00000138670	RASGEF1B	RasGEF domain family, member 1B	25.26	8.007E-52	11.66	6.450E-34
ENSG00000093134	VNN3	vanin 3	21.95	1.362E-26	2.99	3.851E-05
ENSG00000123095	**BHLHE41**	**basic helix-loop-helix family, member e41**	**21.12**	**2.179E-30**	**7.41**	**6.502E-22**
ENSG00000105499	PLA2G4C	phospholipase A2, group IVC	19.11	6.218E-42	12.79	1.328E-39
ENSG00000169554	**ZEB2**	**zinc finger E-box binding homeobox 2**	**18.93**	**1.936E-23**	**4.16**	**3.211E-04**
ENSG00000008517	IL32	interleukin 32	18.09	3.333E-10	11.69	1.131E-53
ENSG00000081041	CXCL2	chemokine ligand 2	16.13	1.442E-32	2.76	1.900E-05
ENSG00000136826	KLF4	Kruppel-like factor 4	15.05	7.771E-40	7.45	1.195E-23
ENSG00000130487	KLHDC7B	kelch domain containing 7B	14.32	8.783E-08	10.09	2.609E-13
ENSG00000120129	DUSP1	dual specificity phosphatase 1	13.27	1.587E-59	5.14	1.041E-58
ENSG00000169429	IL8	interleukin 8	13.04	1.482E-05	4.03	9.781E-04
ENSG00000136383	ALPK3	alpha-kinase 3	12.96	4.281E-29	6.04	1.201E-40
ENSG00000112182	BACH2	BTB and CNC homology 1,	12.59	1.473E-43	5.67	5.591E-27
ENSG00000177606	JUN	jun proto-oncogene	12.10	9.251E-18	7.38	3.929E-112

ENSG00000167995	BEST1	bestrophin 1	11.40	1.503E-17	10.81	2.075E-52
ENSG00000095370	**SH2D3C**	**SH2 domain containing 3C**	**10.56**	**4.054E-10**	**5.65**	**1.259E-08**
ENSG00000099860	GADD45B	growth arrest and DNA-damage-inducible, beta	9.73	5.220E-44	4.13	1.125E-32
ENSG00000156510	HKDC1	hexokinase domain containing 1	9.39	4.414E-05	8.60	3.363E-05
ENSG00000135116	HRK	harakiri, BCL2 interacting protein	8.95	2.347E-11	8.72	8.095E-10
ENSG00000185133	**INPP5J**	**inositol polyphosphate-5-phosphatase J**	**8.76**	**4.820E-04**	**4.88**	**8.863E-32**
ENSG00000023445	BIRC3	baculoviral IAP repeat containing 3	8.45	1.381E-21	3.39	7.940E-07
ENSG00000185022	MAFF	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F	8.37	8.034E-17	6.46	2.247E-53
ENSG00000157765	SLC34A2	solute carrier family 34 (type II sodium/phosphate contransporter), member 2	8.31	6.805E-12	8.20	1.473E-05
ENSG00000156804	**FBXO32**	**F-box protein 32**	**8.29**	**2.556E-10**	**4.23**	**5.145E-07**
ENSG00000087074	PPP1R15A	protein phosphatase 1, regulatory subunit 15A	8.23	4.722E-16	5.00	4.136E-69
ENSG00000163545	NUAK2	NUAK family, SNF1-like kinase, 2	8.14	1.376E-06	2.03	2.369E-04
ENSG00000111981	ULBP1	UL16 binding protein 1	8.05	2.702E-11	6.04	9.326E-45
ENSG00000132718	SYT11	synaptotagmin XI	7.81	6.742E-33	4.94	2.828E-34
ENSG00000153029	MR1	major histocompatibility complex, class I-related	7.76	3.484E-23	3.42	4.210E-12

ENSG00000130513	GDF15	growth differentiation factor 15	7.07	1.227E-04	8.02	1.561E-76
ENSG00000109819	PPARGC1A	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha	6.99	1.016E-24	2.72	1.980E-21
ENSG00000187720	THSD4	thrombospondin, type I, domain containing 4	6.98	4.198E-18	3.99	8.095E-12
ENSG00000108551	RASD1	RAS, dexamethasone-induced 1	6.81	1.329E-05	5.26	1.956E-07
ENSG00000120833	SOCS2	suppressor of cytokine signaling 2	6.80	4.762E-16	3.61	1.111E-09
ENSG00000155090	KLF10	Kruppel-like factor 10	6.70	8.933E-35	2.45	3.140E-19
ENSG00000137801	THBS1	thrombospondin 1	6.68	1.910E-31	4.13	2.219E-23
ENSG00000128965	CHAC1	ChaC, cation transport regulator homolog 1	6.55	3.444E-05	5.66	1.746E-31
ENSG00000137628	**DDX60**	**DEAD box polypeptide 60**	**6.43**	**1.518E-04**	**8.62**	**9.413E-11**
ENSG00000112183	RBM24	RNA binding motif protein 24	6.43	7.144E-04	5.28	1.356E-10
ENSG00000166046	TCP11L2	t-complex 11, 2	6.09	4.618E-24	2.92	2.626E-17
ENSG00000189157	**FAM47E**	**family with sequence similarity 47, member E**	**6.04**	**1.312E-12**	**3.11**	**1.651E-06**
ENSG00000138772	ANXA3	annexin A3	5.88	2.458E-22	4.34	2.339E-30
ENSG00000118503	TNFAIP3	tumor necrosis factor, alpha-induced protein 3	5.83	9.824E-29	2.49	1.058E-15
ENSG00000221869	CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	5.81	7.858E-20	2.09	1.548E-07

ENSG00000165046	**LETM2**	**leucine zipper-EF-hand containing transmembrane protein 2**	**5.69**	**3.844E-12**	**3.59**	**7.227E-05**
ENSG00000173210	ABLIM3	actin binding LIM protein family, member 3	5.62	4.807E-26	4.25	3.469E-38
ENSG00000168209	DDIT4	DNA-damage-inducible transcript 4	5.45	1.601E-09	3.69	3.311E-45
ENSG00000125347	IRF1	interferon regulatory factor 1	5.42	5.632E-13	3.62	2.315E-17
ENSG00000020577	SAMD4A	sterile alpha motif domain containing 4A	5.35	4.709E-26	2.68	3.948E-17
ENSG00000104450	SPAG1	sperm associated antigen 1	5.32	2.605E-09	2.25	1.487E-04
ENSG00000067082	KLF6	Kruppel-like factor 6	5.30	7.851E-23	3.37	6.363E-45
ENSG00000134769	DTNA	dystrobrevin, alpha	5.06	1.826E-25	3.48	1.202E-37
ENSG00000198208	RPS6KL1	ribosomal protein S6 kinase-like 1	5.05	1.045E-08	9.89	1.033E-22
ENSG00000175197	DDIT3	DNA-damage-inducible transcript 3	5.02	3.316E-24	4.72	2.866E-51
ENSG00000163435	ELF3	E74-like factor 3 (ets domain transcription factor, epithelial-specific)	4.95	8.579E-08	3.56	4.185E-31
ENSG00000087266	SH3BP2	SH3-domain binding protein 2	4.91	5.986E-16	2.70	2.213E-20
ENSG00000147883	CDKN2B	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	4.87	4.956E-22	2.47	1.505E-09
ENSG00000134107	**BHLHE40**	**basic helix-loop-helix family, member e40**	**4.82**	**1.826E-25**	**2.57**	**1.630E-26**
ENSG00000184371	CSF1	colony stimulating factor 1	4.72	1.004E-07	3.67	2.029E-27

ENSG00000166173	LARP6	La ribonucleoprotein domain family, member 6	4.72	2.088E-18	4.26	2.427E-26
ENSG00000130766	SESN2	sestrin 2	4.71	5.183E-04	3.95	1.930E-42
ENSG00000101255	TRIB3	tribbles homolog 3	4.66	1.068E-07	4.51	4.935E-65
ENSG00000101928	MOSPD1	motile sperm domain containing 1	4.64	2.044E-07	2.94	4.518E-25
ENSG00000164938	TP53INP1	tumor protein p53 inducible nuclear protein 1	4.61	2.980E-10	2.17	1.492E-10
ENSG00000146859	TMEM140	transmembrane protein 140	4.53	1.631E-18	3.59	1.994E-25
ENSG00000163393	SLC22A15	solute carrier family 22, member 15	4.52	1.398E-20	3.50	1.302E-24
ENSG00000143507	DUSP10	dual specificity phosphatase 10	4.49	3.373E-17	2.58	6.064E-12
ENSG00000080031	PTPRH	protein tyrosine phosphatase, receptor type, H	4.30	1.755E-07	2.23	1.552E-08
ENSG00000010818	HIVEP2	human immunodeficiency virus type I enhancer binding protein 2	4.30	7.183E-21	2.41	8.086E-19
ENSG00000116717	GADD45A	growth arrest and DNA-damage-inducible, alpha	4.17	4.182E-19	2.76	8.295E-25
ENSG00000139289	PHLDA1	pleckstrin homology-like domain, family A, member 1	4.15	8.850E-20	2.76	3.436E-25
ENSG00000163735	CXCL5	chemokine (C-X-C motif) ligand 5	4.12	1.621E-10	2.68	2.470E-27
ENSG00000114019	AMOTL2	angiomotin like 2	4.07	5.986E-16	3.16	2.860E-33
ENSG00000075426	FOSL2	FOS-like antigen 2	4.05	2.557E-13	2.74	1.546E-16

ENSG00000133134	BEX2	brain expressed X-linked 2	4.05	3.023E-12	3.74	2.249E-16
ENSG00000128683	GAD1	glutamate decarboxylase 1	3.99	3.719E-09	2.23	1.183E-04
ENSG00000156232	**WHAMM**	**WAS protein homolog associated with actin**	**3.84**	**2.363E-17**	**2.11**	**1.226E-11**
ENSG00000104081	BMF	Bcl2 modifying factor	3.82	4.343E-18	2.15	1.058E-15
ENSG00000129474	**AJUBA**	**ajuba LIM protein**	**3.81**	**3.731E-19**	**2.39**	**5.812E-23**
ENSG00000104361	**NIPAL2**	**NIPA-like domain containing 2**	**3.80**	**5.153E-13**	**2.30**	**1.633E-10**
ENSG00000135046	ANXA1	annexin A1	3.73	8.977E-12	3.65	6.931E-07
ENSG00000100100	**PIK3IP1**	**phosphoinositide-3-kinase interacting protein 1**	**3.72**	**1.455E-10**	**2.55**	**2.535E-08**
ENSG00000125845	BMP2	bone morphogenetic protein 2	3.70	4.706E-18	2.18	2.986E-18
ENSG00000153071	DAB2	Dab, mitogen-responsive phosphoprotein, homolog 2	3.69	9.915E-18	2.71	5.603E-30
ENSG00000079335	CDC14A	cell division cycle 14A	3.66	1.654E-15	2.12	4.019E-09
ENSG00000168003	SLC3A2	solute carrier family 3, member 2	3.56	1.622E-12	4.08	8.623E-61
ENSG00000115844	DLX2	distal-less homeobox 2	3.54	1.412E-04	2.63	5.365E-05
ENSG00000170537	TMC7	transmembrane channel-like 7	3.52	9.373E-15	3.04	6.035E-20
ENSG00000136603	SKIL	SKI-like oncogene	3.46	2.201E-16	2.25	2.771E-19

ENSG00000141682	PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	3.46	7.905E-04	2.65	3.570E-15
ENSG00000150687	PRSS23	protease, serine, 23	3.37	1.208E-12	2.64	7.789E-14
ENSG00000090339	ICAM1	intercellular adhesion molecule 1	3.37	1.353E-15	2.84	3.460E-29
ENSG00000105991	HOXA1	homeobox A1	3.34	1.836E-07	2.65	7.186E-05
ENSG00000059728	MXD1	MAX dimerization protein 1	3.29	2.950E-13	2.24	1.248E-12
ENSG00000049449	RCN1	reticulocalbin 1, EF-hand calcium binding domain	3.26	7.195E-06	2.21	1.481E-11
ENSG00000173334	TRIB1	tribbles homolog 1	3.24	2.608E-13	2.00	1.120E-09
ENSG00000065911	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	3.24	5.519E-12	3.91	2.259E-56
ENSG00000120875	DUSP4	dual specificity phosphatase 4	3.20	1.070E-11	3.19	6.248E-18
ENSG00000069667	RORA	RAR-related orphan receptor A	3.14	1.157E-07	2.06	4.614E-04
ENSG00000172348	RCAN2	regulator of calcineurin 2	3.13	9.960E-10	2.66	1.408E-09
ENSG00000070669	ASNS	asparagine synthetase	3.11	6.138E-14	3.19	7.823E-43
ENSG00000168280	KIF5C	kinesin family member 5C	3.11	1.202E-09	2.09	4.620E-15
ENSG00000172059	KLF11	Kruppel-like factor 11	3.11	4.400E-11	2.45	1.847E-12
ENSG00000116761	CTH	cystathionase (cystathionine gamma-lyase)	3.09	5.632E-13	2.55	4.094E-23

ENSG00000156030	**ELMSAN1**	**ELM2 and Myb/SANT-like domain containing 1**	**3.08**	**4.790E-06**	**2.69**	**7.461E-24**
ENSG00000175175	PPM1E	protein phosphatase, Mg2+/Mn2+ dependent, 1E	3.06	4.140E-10	2.21	1.522E-08
ENSG00000148339	SLC25A25	solute carrier family 25, member 25	3.05	3.531E-05	2.57	2.524E-15
ENSG00000171867	PRNP	prion protein	3.01	7.558E-05	3.43	4.077E-05
ENSG00000154447	SH3RF1	SH3 domain containing ring finger 1	2.97	1.220E-11	2.37	3.369E-15
ENSG00000151012	SLC7A11	solute carrier family 7, member 11	2.97	1.619E-06	2.69	2.388E-29
ENSG00000144837	PLA1A	phospholipase A1 member A	2.96	6.030E-08	2.68	2.230E-16
ENSG00000173276	**ZBTB21**	**zinc finger and BTB domain containing 21**	**2.94**	**1.834E-11**	**2.18**	**2.613E-14**
ENSG00000151726	ACSL1	acyl-CoA synthetase long-chain family member 1	2.94	8.779E-12	2.10	3.233E-15
ENSG00000140941	**MAP1LC3B**	**microtubule-associated protein 1 light chain 3 beta**	**2.93**	**2.097E-12**	**2.11**	**1.105E-17**
ENSG00000174738	NR1D2	nuclear receptor subfamily 1, group D, member 2	2.91	4.784E-05	2.09	7.551E-17
ENSG00000140297	GCNT3	glucosaminyl (N-acetyl) transferase 3, mucin type	2.89	1.232E-09	2.76	4.014E-17
ENSG00000106546	AHR	aryl hydrocarbon receptor	2.89	4.796E-12	2.14	2.968E-18
ENSG00000100906	NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	2.88	2.186E-11	2.45	2.421E-18
ENSG00000051108	HERPUD1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	2.87	1.328E-11	2.33	3.069E-20

ENSG00000139793	MBNL2	muscleblind-like splicing regulator 2	2.82	6.362E-11	2.36	8.860E-19
ENSG00000116584	ARHGEF2	Rho/Rac guanine nucleotide exchange factor (GEF) 2	2.74	6.695E-09	2.56	2.427E-26
ENSG00000114796	KLHL24	kelch-like family member 24	2.73	1.183E-06	2.26	1.772E-19
ENSG00000166900	STX3	syntaxin 3	2.66	3.505E-10	2.28	2.233E-20
ENSG00000115902	SLC1A4	solute carrier family 1, member 4	2.65	2.972E-09	2.78	2.634E-19
ENSG00000172432	GTPBP2	GTP binding protein 2	2.64	9.597E-05	2.34	1.162E-19
ENSG00000111266	DUSP16	dual specificity phosphatase 16	2.63	4.695E-10	2.20	3.336E-19
ENSG00000165507	C10orf10	chromosome 10 open reading frame 10	2.58	8.202E-08	2.31	9.509E-13
ENSG00000164463	**CREBRF**	**CREB3 regulatory factor**	**2.58**	**8.088E-09**	**2.04**	**1.495E-12**
ENSG00000108244	KRT23	keratin 23 (histone deacetylase inducible)	2.56	5.738E-08	2.59	2.241E-07
ENSG00000152409	JMY	junction mediating and regulatory protein, p53 cofactor	2.55	8.524E-09	2.34	1.102E-18
ENSG00000172216	CEBPB	CCAAT/enhancer binding protein (C/EBP), beta	2.55	1.809E-06	2.30	1.052E-14
ENSG00000178607	ERN1	endoplasmic reticulum to nucleus signaling 1	2.51	1.285E-08	2.31	2.588E-16
ENSG00000158186	MRAS	muscle RAS oncogene homolog	2.49	1.815E-07	2.46	5.630E-13
ENSG00000163993	S100P	S100 calcium binding protein P	2.44	1.258E-07	3.96	2.806E-32

ENSG00000164949	GEM	GTP binding protein overexpressed in skeletal muscle	2.39	8.888E-06	2.38	1.614E-08
ENSG00000171471	MAP1LC3B2	microtubule-associated protein 1 light chain 3 beta 2	2.39	1.941E-05	2.05	1.542E-04
ENSG00000089876	DHX32	DEAH box polypeptide 32	2.39	1.956E-07	2.06	8.874E-12
ENSG00000185950	IRS2	insulin receptor substrate 2	2.38	1.195E-04	2.25	1.970E-08
ENSG00000148426	**PROSER2**	**proline and serine-rich protein 2**	**2.29**	**5.899E-07**	**2.13**	**5.053E-12**
ENSG00000188295	**ZNF669**	**zinc finger protein 669**	**2.29**	**1.626E-06**	**2.04**	**5.892E-10**
ENSG00000113739	STC2	stanniocalcin 2	2.29	1.873E-07	2.72	8.598E-29
ENSG00000107485	**GATA3**	**GATA binding protein 3**	**2.26**	**2.027E-04**	**2.15**	**1.180E-04**
ENSG00000111252	SH2B3	SH2B adaptor protein 3	2.25	5.904E-07	2.23	3.138E-16
ENSG00000204386	NEU1	sialidase 1	2.22	1.792E-05	2.67	1.372E-29
ENSG00000095739	BAMBI	BMP and activin membrane-bound inhibitor	2.21	8.567E-07	2.18	6.796E-16
ENSG00000049323	LTBP1	latent transforming growth factor beta binding protein 1	2.16	9.841E-05	2.24	6.931E-07
ENSG00000126947	ARMCX1	armadillo repeat containing, X-linked 1	2.09	8.628E-05	2.02	2.620E-09
ENSG00000115295	CLIP4	CAP-GLY domain containing linker protein family, member 4	2.08	1.805E-04	2.06	9.928E-09
ENSG00000173812	EIF1	eukaryotic translation initiation factor 1	2.06	7.195E-06	2.39	9.800E-26

Supplementary Table 1.B. The list of the significantly down-regulated genes (FC ≤ -2, P adj. value < 0.001; 72 and 96 hpi) upon HCV infection in the Huh-7.5 cells. Fold change is shown for two time points post inoculation (72 h and 96 h). Genes are presented in ascending order of fold change of gene expression in HCV infected cells relative to non-infected cells at 72 h post inoculation. Newly identified differentially genes are shown in bold.

Ensembl Gene ID	Gene Name	Gene Description	Fold Change 72 h	P adj. value	Fold Change 96 h	P adj. value
ENSG00000185745	IFIT1	interferon-induced protein with tetratricopeptide repeats 1	-3.48	8.651E-09	-2.16	3.623E-06
ENSG00000197991	PCDH20	protocadherin 20	-3.41	3.592E-11	-2.14	1.120E-08
ENSG00000187867	**PALM3**	**paralemmin 3**	**-3.14**	**2.860E-09**	**-2.30**	**7.414E-08**
ENSG00000248746	ACTN3	actinin, alpha 3	-3.09	8.017E-07	-2.47	5.638E-13
ENSG00000183508	**FAM46C**	**family with sequence similarity 46, member C**	**-2.87**	**2.163E-06**	**-2.28**	**1.437E-07**
ENSG00000087303	NID2	nidogen 2	-2.85	1.891E-05	-2.30	3.700E-07
ENSG00000134240	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2	-2.56	1.160E-07	-2.16	4.540E-14
ENSG00000139209	SLC38A4	solute carrier family 38, member 4	-2.48	7.452E-08	-2.35	7.228E-18
ENSG00000152760	TCTEX1D1	Tctex1 domain containing 1	-2.42	2.276E-05	-2.55	3.560E-10
ENSG00000196177	ACADSB	acyl-CoA dehydrogenase, short/branched chain	-2.19	6.639E-07	-2.00	7.146E-14
ENSG00000188175	**HEPACAM2**	**HEPACAM family member 2**	**-2.10**	**9.931E-05**	**-2.10**	**1.132E-05**

Supplementary Table 2. Enriched biological processes for the up-regulated genes (FC ≥ 2, P adj. value ≤ 0.001; 72 and 96 hpi)

GO biological process	Genes in the process	DEGs	P-value	Up-regulated genes that overlap the process
negative regulation of phosphorylation (GO:0042326)	325	21	5.972E-12	DUSP4; PRNP; JUN; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; IRS2; KLF4; DUSP8; PPM1E; DUSP16; DUSP10; PIK3IP1; DDIT4; INPP5J; TRIB3; TRIB1; AJUBA; BIRC3
response to endoplasmic reticulum stress (GO:0034976)	145	14	2.011E-10	PPP1R15A; JUN; CEBPB; ASNS; THBS1; HERPUD1; ERN1; STC2; CTH; DDIT3; CREBRF; TRIB3; CHAC1; ATF3
negative regulation of kinase activity (GO:0033673)	202	15	1.321E-09	DUSP4; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; IRS2; DUSP8; PPM1E; DUSP16; DUSP10; PIK3IP1; TRIB3; TRIB1; AJUBA
negative regulation of phosphate metabolic process (GO:0045936)	458	21	2.414E-09	DUSP4; PRNP; JUN; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; IRS2; KLF4; DUSP8; PPM1E; DUSP16; DUSP10; PIK3IP1; DDIT4; INPP5J; TRIB3; TRIB1; AJUBA; BIRC3
negative regulation of phosphorus metabolic process (GO:0010563)	458	21	2.414E-09	DUSP4; PRNP; JUN; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; IRS2; KLF4; DUSP8; PPM1E; DUSP16; DUSP10; PIK3IP1; DDIT4; INPP5J; TRIB3; TRIB1; AJUBA; BIRC3
negative regulation of protein phosphorylation (GO:0001933)	260	16	4.639E-09	DUSP4; PRNP; JUN; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; DUSP8; PPM1E; DUSP16; DUSP10; DDIT4; INPP5J; TRIB3; TRIB1
cell cycle arrest (GO:0007050)	140	12	1.459E-08	ERN1; PPP1R15A; PRNP; CDKN2B; GADD45A; DUSP1; IRF1; DDIT3; JMY; TP53INP1; THBS1; SKIL
regulation of protein serine/threonine kinase activity (GO:0071900)	416	18	8.676E-08	DUSP4; CDKN2B; GADD45B; GADD45A; ACSL1; DUSP1; TNFAIP3; DUSP8; DUSP16; THBS1; BMP2; ZEB2; DAB2; DUSP10; SESN2; TRIB3; TRIB1; AJUBA
response to unfolded protein (GO:0006986)	135	11	9.691E-08	ERN1; PPP1R15A; DDIT3; STC2; CTH; CREBRF; ASNS; CHAC1; THBS1; ATF3; HERPUD1
negative regulation of transferase activity (GO:0051348)	284	15	9.866E-08	DUSP4; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; IRS2; DUSP8; PPM1E; DUSP16; DUSP10; PIK3IP1; TRIB3; TRIB1; AJUBA
response to topologically incorrect protein	143	11	1.672E-07	ERN1; PPP1R15A; DDIT3; STC2; CTH; CREBRF; ASNS; CHAC1; THBS1; ATF3; HERPUD1

(GO:0035966)				
negative regulation of intracellular signal transduction (GO:1902532)	345	16	1.966E-07	DUSP4; PRNP; DUSP1; TNFAIP3; RORA; KLF4; DUSP8; DUSP16; THBS1; SOCS2; NFKBIA; DUSP10; PIK3IP1; DDIT4; ARHGEF2; AJUBA
negative regulation of protein kinase activity (GO:0006469)	189	12	3.187E-07	DUSP4; CDKN2B; DUSP10; GADD45B; GADD45A; DUSP1; TNFAIP3; TRIB3; TRIB1; DUSP8; PPM1E; DUSP16
negative regulation of protein modification process (GO:0031400)	407	16	1.618E-06	DUSP4; PRNP; JUN; CDKN2B; GADD45B; GADD45A; DUSP1; TNFAIP3; DUSP8; PPM1E; DUSP16; DUSP10; DDIT4; INPP5J; TRIB3; TRIB1
endoplasmic reticulum unfolded protein response (GO:0030968)	83	8	1.812E-06	ERN1; PPP1R15A; DDIT3; CTH; STC2; ASNS; ATF3; HERPUD1
cellular response to unfolded protein (GO:0034620)	86	8	2.319E-06	ERN1; PPP1R15A; CTH; DDIT3; STC2; ASNS; ATF3; HERPUD1
response to alcohol (GO:0097305)	274	13	2.320E-06	SLC34A2; ANXA1; DUSP1; RORA; GATA3; FBXO32; THBS1; AREG; ICAM1; FOSL2; SOCS2; STC2; TP53INP1
cellular response to topologically incorrect protein (GO:0035967)	92	8	3.703E-06	ERN1; PPP1R15A; DDIT3; STC2; CTH; ASNS; ATF3; HERPUD1
response to peptide (GO:1901652)	384	15	3.777E-06	KLF10; KLF11; ANXA1; TNFAIP3; IRS2; KLF4; HDAC9; AREG; EREG; SOCS2; NFKBIA; STC2; SESN2; TRIB3; ARHGEF2
regulation of sequence-specific DNA binding transcription factor activity (GO:0051090)	338	14	4.258E-06	PRNP; JUN; ANXA3; TNFAIP3; KLF4; ICAM1; NFKBIA; CTH; DDIT3; BHLHE40; JMY; ARHGEF2; TRIB1; PPARGC1A
ER-nucleus signaling pathway (GO:0006984)	94	8	4.298E-06	ERN1; PPP1R15A; DDIT3; STC2; CTH; ASNS; ATF3; HERPUD1
regulation of extrinsic apoptotic signaling pathway via death domain receptors (GO:1902041)	45	6	6.808E-06	PMAIP1; TNFAIP3; ARHGEF2; THBS1; SKIL; ICAM1
regulation of MAP kinase activity (GO:0043405)	273	12	1.213E-05	DUSP4; ZEB2; DAB2; BMP2; DUSP10; DUSP1; TRIB3; TRIB1; DUSP8; AJUBA; DUSP16; THBS1
cellular response to external stimulus (GO:0071496)	185	10	1.231E-05	KLF10; CDKN2B; JUN; NUAK2; GADD45A; IRF1; ANKRD1; PMAIP1; ASNS; ICAM1
negative regulation of cell cycle (GO:0045786)	430	15	1.397E-05	PPP1R15A; PRNP; CDKN2B; GADD45A; DUSP1; TNFAIP3; GATA3; THBS1; ERN1; BMP2; IRF1; DDIT3; TP53INP1; JMY; SKIL

inactivation of MAPK activity (GO:0000188)	31	5	1.802E-05	DUSP4; DUSP10; DUSP1; DUSP8; DUSP16
response to oxidative stress (GO:0006979)	290	12	2.160E-05	PRNP; JUN; ANXA1; DUSP1; STC2; RCAN2; TP53INP1; TNFAIP3; SLC7A11; KLF4; PPARGC1A; AREG
response to nutrient levels (GO:0031667)	291	12	2.231E-05	KLF10; JUN; CDKN2B; NUAK2; ACSL1; DDIT3; STC2; PMAIP1; ASNS; PPARGC1A; SLC25A25; ICAM1
positive regulation of protein kinase activity (GO:0045860)	456	15	2.713E-05	GADD45B; CSF1; GADD45A; ACSL1; ASNS; THBS1; HERPUD1; EREG; ERN1; ZEB2; DAB2; BMP2; DDIT3; AJUBA; ATF3
regulation of cellular response to stress (GO:0080135)	404	14	2.951E-05	GADD45B; GADD45A; SH3RF1; ERN1; ZEB2; DAB2; BMP2; DUSP10; CREBRF; ANKRD1; PMAIP1; ARHGEF2; AJUBA; SKIL
response to transforming growth factor beta (GO:0071559)	166	9	3.326E-05	PPP1R15A; KLF10; DAB2; CDKN2B; JUN; BAMBI; GDF15; ANKRD1; SKIL
cellular response to transforming growth factor beta stimulus (GO:0071560)	166	9	3.326E-05	PPP1R15A; KLF10; DAB2; CDKN2B; JUN; BAMBI; GDF15; ANKRD1; SKIL
transcription from RNA polymerase II promoter (GO:0006366)	470	15	3.802E-05	KLF11; CEBPB; JUN; CEBPD; BHLHE41; GATA3; AHR; KLF4; FOSL2; ELF3; IRF1; DDIT3; BHLHE40; MAFF; CREB5
response to extracellular stimulus (GO:0009991)	313	12	4.430E-05	KLF10; JUN; CDKN2B; NUAK2; ACSL1; DDIT3; STC2; PMAIP1; ASNS; PPARGC1A; SLC25A25; ICAM1
positive regulation of kinase activity (GO:0033674)	480	15	4.800E-05	CSF1; GADD45B; GADD45A; ACSL1; ASNS; THBS1; HERPUD1; EREG; ERN1; ZEB2; DAB2; BMP2; DDIT3; AJUBA; ATF3
cellular response to nutrient levels (GO:0031669)	99	7	5.328E-05	KLF10; CDKN2B; JUN; NUAK2; PMAIP1; ASNS; ICAM1
regulation of transcription involved in cell fate commitment (GO:0060850)	20	4	6.224E-05	CEBPB; BMP2; DLX2; RORA
peptidyl-tyrosine dephosphorylation (GO:0035335)	102	7	6.368E-05	DUSP4; DUSP10; DUSP1; DUSP8; PTPRH; DUSP16; CDC14A
regulation of transforming growth factor beta receptor signaling pathway (GO:0017015)	103	7	6.749E-05	PPP1R15A; DAB2; CDKN2B; BAMBI; THBS1; LTBP1; SKIL
response to starvation (GO:0042594)	106	7	8.007E-05	KLF10; JUN; NUAK2; DDIT3; PMAIP1; ASNS; PPARGC1A
response to hypoxia (GO:0001666)	241	10	1.052E-04	BMP2; STC2; DDIT4; ANKRD1; PMAIP1; RORA; PPARGC1A;

				AJUBA; THBS1; ICAM1
regulation of smooth muscle cell proliferation (GO:0048660)	77	6	1.123E-04	JUN; TNFAIP3; TRIB1; KLF4; PPARGC1A; EREG
transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0007178)	196	9	1.132E-04	PPP1R15A; KLF10; JUN; CDKN2B; BMP2; GDF15; BAMBI; LTBP1; SKIL
positive regulation of p38MAPK cascade (GO:1900745)	8	3	1.178E-04	BMP2; GADD45B; GADD45A
response to decreased oxygen levels (GO:0036293)	245	10	1.198E-04	BMP2; STC2; DDIT4; ANKRD1; PMAIP1; RORA; PPARGC1A; THBS1; AJUBA; ICAM1
intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress (GO:0070059)	25	4	1.343E-04	ERN1; DDIT3; TRIB3; CHAC1
regulation of apoptotic signaling pathway (GO:2001233)	356	12	1.445E-04	HRK; DAB2; CTH; TP53INP1; PMAIP1; TNFAIP3; BMF; ARHGEF2; THBS1; SKIL; SH3RF1; ICAM1
negative regulation of protein serine/threonine kinase activity (GO:0071901)	118	7	1.510E-04	DUSP4; CDKN2B; DUSP10; DUSP1; TNFAIP3; DUSP8; DUSP16
circadian regulation of gene expression (GO:0032922)	51	5	1.577E-04	BHLHE40; BHLHE41; RORA; AHR; PPARGC1A
cellular response to extracellular stimulus (GO:0031668)	119	7	1.587E-04	KLF10; CDKN2B; JUN; NUAK2; PMAIP1; ASNS; ICAM1
regulation of extrinsic apoptotic signaling pathway (GO:2001236)	161	8	1.638E-04	DAB2; PMAIP1; TNFAIP3; ARHGEF2; THBS1; SKIL; SH3RF1; ICAM1
protein dephosphorylation (GO:0006470)	161	8	1.638E-04	DUSP4; DUSP10; DUSP1; DUSP8; PTPRH; PPM1E; DUSP16; CDC14A
positive regulation of protein complex assembly (GO:0031334)	122	7	1.836E-04	HRK; JMY; PMAIP1; BMF; AHR; AJUBA; ICAM1
response to oxygen levels (GO:0070482)	259	10	1.852E-04	BMP2; STC2; DDIT4; ANKRD1; PMAIP1; RORA; PPARGC1A; AJUBA; THBS1; ICAM1
negative regulation of sequence-specific DNA binding transcription factor activity (GO:0043433)	126	7	2.217E-04	NFKBIA; PRNP; DDIT3; BHLHE40; TNFAIP3; TRIB1; KLF4
intrinsic apoptotic	170	8	2.336E-04	ERN1; DDIT3; JMY; DDIT4;

signaling pathway (GO:0097193)				PMAIP1; TRIB3; BMF; CHAC1
cellular response to tumor necrosis factor (GO:0071356)	89	6	2.364E-04	ANKRD1; ARHGEF2; GATA3; PPARGC1A; THBS1; ICAM1
negative regulation of inflammatory response (GO:0050728)	89	6	2.364E-04	ANXA1; DUSP10; TNFAIP3; RORA; GATA3; KLF4
regulation of endothelial cell apoptotic process (GO:2000351)	31	4	2.837E-04	TNFAIP3; GATA3; THBS1; ICAM1
regulation of cellular response to growth factor stimulus (GO:0090287)	176	8	2.924E-04	PPP1R15A; DAB2; CDKN2B; BAMBI; GATA3; LTBP1; THBS1; SKIL
regulation of cytokine biosynthetic process (GO:0042035)	93	6	2.958E-04	CEBPB; IRF1; GATA3; KLF4; THBS1; EREG
regulation of p38MAPK cascade (GO:1900744)	12	3	3.163E-04	BMP2; GADD45B; GADD45A
response to muramyl dipeptide (GO:0032495)	12	3	3.163E-04	NFKBIA; TNFAIP3; ARHGEF2
transforming growth factor beta receptor signaling pathway (GO:0007179)	134	7	3.170E-04	PPP1R15A; KLF10; CDKN2B; JUN; BAMBI; GDF15; SKIL
response to hydrogen peroxide (GO:0042542)	95	6	3.296E-04	JUN; ANXA1; DUSP1; TNFAIP3; KLF4; AREG
negative regulation of extrinsic apoptotic signaling pathway (GO:2001237)	97	6	3.664E-04	DAB2; TNFAIP3; ARHGEF2; THBS1; SH3RF1; ICAM1
alpha-beta T cell differentiation (GO:0046632)	34	4	3.915E-04	ANXA1; IRF1; RORA; GATA3
cellular response to hypoxia (GO:0071456)	99	6	4.063E-04	STC2; ANKRD1; PMAIP1; RORA; PPARGC1A; ICAM1
regulation of transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0090092)	186	8	4.171E-04	PPP1R15A; DAB2; CDKN2B; BMP2; BAMBI; THBS1; LTBP1; SKIL
cellular response to hormone stimulus (GO:0032870)	462	13	4.214E-04	ANXA1; DUSP1; ACSL1; ASNS; IRS2; NR1D2; RORA; FBXO32; HDAC9; FOSL2; SOCS2; TRIB3; PPARGC1A
activation of signaling protein activity involved in unfolded protein response	64	5	4.220E-04	ERN1; DDIT3; ASNS; ATF3; HERPUD1

(GO:0006987)				
negative regulation of apoptotic signaling pathway (GO:2001234)	187	8	4.317E-04	DAB2; CTH; TNFAIP3; BMF; ARHGEF2; THBS1; SH3RF1; ICAM1
cellular response to decreased oxygen levels (GO:0036294)	101	6	4.495E-04	STC2; ANKRD1; PMAIP1; RORA; PPARGC1A; ICAM1
positive regulation of nuclease activity (GO:0032075)	66	5	4.817E-04	ERN1; DDIT3; ASNS; ATF3; HERPUD1
negative regulation of cellular response to growth factor stimulus (GO:0090288)	104	6	5.209E-04	PPP1R15A; BAMBI; GATA3; THBS1; LTBP1; SKIL
response to molecule of bacterial origin (GO:0002237)	243	9	5.229E-04	NFKBIA; JUN; CEBPB; DUSP10; ANKRD1; TNFAIP3; TRIB1; CXCL2; ICAM1
response to drug (GO:0042493)	354	11	5.360E-04	JUN; ANXA1; ACSL1; GAD1; ANKRD1; GATA3; PPARGC1A; THBS1; PPM1E; ICAM1; FOSL2
regulation of lipid metabolic process (GO:0019216)	245	9	5.535E-04	BMP2; ANXA1; PIK3IP1; TRIB3; IRS2; NR1D2; RORA; KLF4; PPARGC1A
negative regulation of interleukin-2 production (GO:0032703)	15	3	5.559E-04	PRNP; TNFAIP3; GATA3
epithelial cell differentiation (GO:0030855)	303	10	6.148E-04	JUN; DAB2; BMP2; CEBPB; ANXA1; ELF3; SLC7A11; KLF4; SKIL; EREG
regulation of cytokine production (GO:0001817)	482	13	6.210E-04	PRNP; CEBPB; ANXA1; TNFAIP3; RORA; GATA3; KLF4; THBS1; EREG; NFKBIA; DDIT3; IRF1; ARHGEF2
positive regulation of extrinsic apoptotic signaling pathway via death domain receptors (GO:1902043)	16	3	6.558E-04	PMAIP1; THBS1; SKIL
cellular response to oxygen levels (GO:0071453)	109	6	6.593E-04	STC2; ANKRD1; PMAIP1; RORA; PPARGC1A; ICAM1
rhythmic process (GO:0048511)	252	9	6.726E-04	JUN; BHLHE40; BHLHE41; RORA; NR1D2; AHR; PPARGC1A; EREG; ICAM1
alpha-beta T cell activation (GO:0046631)	40	4	6.901E-04	ANXA1; IRF1; RORA; GATA3
regulation of nuclease activity (GO:0032069)	72	5	6.997E-04	ERN1; DDIT3; ASNS; ATF3; HERPUD1
response to tumor necrosis factor (GO:0034612)	111	6	7.221E-04	ANKRD1; ARHGEF2; GATA3; PPARGC1A; THBS1; ICAM1
response to steroid hormone (GO:0048545)	369	11	7.479E-04	SOCS2; SLC34A2; ANXA1; DUSP1; NR1D2; RORA; GATA3; FBXO32; AREG; THBS1; FOSL2

negative regulation of muscle cell differentiation (GO:0051148)	41	4	7.521E-04	BMP2; DDIT3; BHLHE41; EREG
cellular response to glucose starvation (GO:0042149)	17	3	7.663E-04	NUAK2; ASNS; PMAIP1
cellular response to starvation (GO:0009267)	74	5	7.866E-04	KLF10; JUN; NUAK2; PMAIP1; ASNS
negative regulation of MAP kinase activity (GO:0043407)	74	5	7.866E-04	DUSP4; DUSP10; DUSP1; DUSP8; DUSP16
leukocyte activation (GO:0045321)	373	11	8.149E-04	KLF6; JUN; ANXA1; CSF1; ANXA3; IRF1; RORA; GATA3; HDAC9; ULBP1; ICAM1
inflammatory response (GO:0006954)	376	11	8.684E-04	BMP2; CEBPB; ANXA1; CSF1; ELF3; PLA2G4C; TNFAIP3; GATA3; CXCL2; THBS1; HDAC9
regulation of circadian rhythm (GO:0042752)	76	5	8.813E-04	KLF10; BHLHE40; RORA; NR1D2; PPARGC1A
positive regulation of protein oligomerization (GO:0032461)	18	3	8.881E-04	HRK; PMAIP1; BMF
response to radiation (GO:0009314)	442	12	9.549E-04	JUN; ANXA1; GADD45A; DUSP1; BHLHE40; TP53INP1; PMAIP1; ASNS; HOXA1; GATA3; ICAM1; BEST1
connective tissue development (GO:0061448)	44	4	9.616E-04	CSF1; THBS1; SLC25A25; CREB5
negative regulation of defense response (GO:0031348)	120	6	1.063E-03	ANXA1; DUSP10; TNFAIP3; RORA; GATA3; KLF4
regulation of muscle cell differentiation (GO:0051147)	122	6	1.154E-03	BMP2; DDIT3; BHLHE41; HDAC9; RBM24; EREG
negative regulation of endothelial cell apoptotic process (GO:2000352)	20	3	1.167E-03	TNFAIP3; GATA3; ICAM1
regulation of stress-activated MAPK cascade (GO:0032872)	170	7	1.225E-03	DAB2; BMP2; ZEB2; DUSP10; GADD45B; GADD45A; SH3RF1
regulation of stress-activated protein kinase signaling cascade (GO:0070302)	171	7	1.265E-03	DAB2; BMP2; ZEB2; DUSP10; GADD45B; GADD45A; SH3RF1
dephosphorylation (GO:0016311)	278	9	1.312E-03	DUSP4; DUSP10; DUSP1; INPP5J; DUSP8; PTPRH; DUSP16; PPM1E; CDC14A
positive regulation of cell migration (GO:0030335)	280	9	1.377E-03	DAB2; BMP2; CSF1; ANXA3; IRS2; GATA3; THBS1; HDAC9; ICAM1
cellular glucose	49	4	1.397E-03	HKDC1; IRS2; PPARGC1A; ICAM1

homeostasis (GO:0001678)				
circadian rhythm (GO:0007623)	127	6	1.406E-03	JUN; BHLHE40; BHLHE41; RORA; AHR; PPARGC1A
regulation of striated muscle cell differentiation (GO:0051153)	85	5	1.416E-03	BMP2; DDIT3; BHLHE41; HDAC9; RBM24
positive regulation of organelle organization (GO:0010638)	340	10	1.436E-03	HRK; ANXA1; JMY; PMAIP1; BMF; WHAMM; PPM1E; PPARGC1A; ICAM1; EREG
response to mechanical stimulus (GO:0009612)	176	7	1.484E-03	JUN; GADD45A; IRF1; ANKRD1; ASNS; THBS1; FOSL2
response to lipopolysaccharide (GO:0032496)	228	8	1.492E-03	NFKBIA; JUN; CEBPB; DUSP10; ANKRD1; TNFAIP3; TRIB1; ICAM1
negative regulation of Notch signaling pathway (GO:0045746)	22	3	1.495E-03	NFKBIA; DLX2; CHAC1
regulation of fat cell differentiation (GO:0045598)	87	5	1.561E-03	BMP2; CEBPB; RORA; TRIB3; GATA3
negative regulation of MAPK cascade (GO:0043409)	130	6	1.575E-03	DUSP4; DUSP10; DUSP1; DUSP8; KLF4; DUSP16
regulation of cellular ketone metabolic process (GO:0010565)	178	7	1.579E-03	BMP2; ANXA1; SESN2; TRIB3; IRS2; GATA3; PPARGC1A
leukocyte homeostasis (GO:0001776)	51	4	1.604E-03	ANXA1; PMAIP1; TNFAIP3; SKIL
positive regulation of cell motility (GO:2000147)	287	9	1.624E-03	DAB2; BMP2; CSF1; ANXA3; IRS2; GATA3; THBS1; HDAC9; ICAM1
positive regulation of transforming growth factor beta receptor signaling pathway (GO:0030511)	23	3	1.679E-03	CDKN2B; DAB2; THBS1
stress-activated MAPK cascade (GO:0051403)	89	5	1.718E-03	DUSP4; JUN; DUSP10; SH2D3C; TRIB1
stress-activated protein kinase signaling cascade (GO:0031098)	91	5	1.885E-03	DUSP4; JUN; DUSP10; SH2D3C; TRIB1
regulation of endothelial cell migration (GO:0010594)	92	5	1.973E-03	ANXA3; GATA3; KLF4; THBS1; HDAC9
positive regulation of cellular component movement (GO:0051272)	296	9	1.992E-03	DAB2; BMP2; CSF1; ANXA3; IRS2; GATA3; THBS1; HDAC9; ICAM1
regulation of cellular carbohydrate	137	6	2.033E-03	DDIT4; SESN2; PMAIP1; RORA; IRS2; PPARGC1A

metabolic process (GO:0010675)				
positive regulation of endothelial cell migration (GO:0010595)	55	4	2.081E-03	ANXA3; GATA3; HDAC9; THBS1
positive regulation of neuron death (GO:1901216)	55	4	2.081E-03	JUN; DDIT3; DDIT4; PMAIP1
negative regulation of response to wounding (GO:1903035)	138	6	2.105E-03	ANXA1; DUSP10; TNFAIP3; RORA; GATA3; KLF4
regulation of glucose metabolic process (GO:0010906)	94	5	2.158E-03	SESN2; PMAIP1; RORA; IRS2; PPARGC1A
regulation of protein complex assembly (GO:0043254)	244	8	2.250E-03	HRK; JMY; INPP5J; PMAIP1; BMF; AHR; AJUBA; ICAM1
negative regulation of extrinsic apoptotic signaling pathway via death domain receptors (GO:1902042)	26	3	2.313E-03	TNFAIP3; ARHGEF2; ICAM1
positive regulation of release of cytochrome c from mitochondria (GO:0090200)	26	3	2.313E-03	HRK; PMAIP1; BMF
positive regulation of epithelial to mesenchymal transition (GO:0010718)	26	3	2.313E-03	DAB2; BMP2; BAMBI
response to reactive oxygen species (GO:0000302)	141	6	2.335E-03	JUN; ANXA1; DUSP1; TNFAIP3; KLF4; AREG
regulation of myotube differentiation (GO:0010830)	57	4	2.353E-03	DDIT3; BHLHE41; HDAC9; RBM24
homeostasis of number of cells (GO:0048872)	96	5	2.356E-03	ANXA1; CSF1; PMAIP1; TNFAIP3; SKIL
positive regulation of locomotion (GO:0040017)	304	9	2.373E-03	DAB2; BMP2; CSF1; ANXA3; IRS2; GATA3; THBS1; HDAC9; ICAM1
regulation of inflammatory response (GO:0050727)	247	8	2.421E-03	ANXA1; DUSP10; TNFAIP3; RORA; NR1D2; GATA3; KLF4; BIRC3
positive regulation of cellular component biogenesis (GO:0044089)	249	8	2.541E-03	HRK; JMY; PMAIP1; BMF; AHR; PPM1E; AJUBA; ICAM1
response to inorganic substance (GO:0010035)	370	10	2.622E-03	PRNP; JUN; ANXA1; DUSP1; TNFAIP3; KLF4; PPARGC1A; THBS1; AREG; ICAM1
leukocyte	251	8	2.665E-03	JUN; KLF6; ANXA1; CSF1; IRF1;

differentiation (GO:0002521)				RORA; GATA3; HDAC9
regulation of carbohydrate metabolic process (GO:0006109)	145	6	2.671E-03	DDIT4; SESN2; PMAIP1; RORA; IRS2; PPARGC1A
response to estradiol (GO:0032355)	100	5	2.790E-03	SOCS2; SLC34A2; ANXA1; DUSP1; AREG
positive regulation of fatty acid metabolic process (GO:0045923)	28	3	2.807E-03	ANXA1; IRS2; PPARGC1A
negative regulation of smooth muscle cell proliferation (GO:0048662)	28	3	2.807E-03	TNFAIP3; TRIB1; KLF4
cellular response to nitrogen compound (GO:1901699)	438	11	2.815E-03	KLF10; SOCS2; KLF11; CEBPB; TRIB3; IRS2; ARHGEF2; KLF4; PPARGC1A; HDAC9; ICAM1
regulation of innate immune response (GO:0045088)	254	8	2.860E-03	NFKBIA; DUSP4; JUN; DUSP10; IRF1; TNFAIP3; EREG; BIRC3
regulation of JNK cascade (GO:0046328)	148	6	2.945E-03	DAB2; ZEB2; DUSP10; GADD45B; GADD45A; SH3RF1
cellular response to lipid (GO:0071396)	315	9	2.989E-03	NFKBIA; ANXA1; ANKRD1; TNFAIP3; RORA; NR1D2; FBXO32; PPARGC1A; ICAM1
positive regulation of protein serine/threonine kinase activity (GO:0071902)	257	8	3.066E-03	ZEB2; DAB2; BMP2; GADD45B; GADD45A; ACSL1; AJUBA; THBS1
regulation of protein oligomerization (GO:0032459)	29	3	3.077E-03	HRK; PMAIP1; BMF
regulation of hormone metabolic process (GO:0032350)	30	3	3.363E-03	BMP2; STC2; GATA3
adipose tissue development (GO:0060612)	30	3	3.363E-03	CSF1; SLC25A25; CREB5
positive regulation of mitochondrion organization (GO:0010822)	64	4	3.496E-03	HRK; PMAIP1; BMF; PPARGC1A
negative regulation of fatty acid transport (GO:2000192)	8	2	3.578E-03	IRS2; THBS1
apoptotic signaling pathway (GO:0097190)	327	9	3.798E-03	ERN1; DDIT3; DDIT4; JMY; PMAIP1; TRIB3; BMF; CHAC1; ARHGEF2
positive regulation of glucose metabolic process (GO:0010907)	32	3	3.980E-03	PMAIP1; IRS2; PPARGC1A
positive regulation of	214	7	4.264E-03	NFKBIA; ANXA3; CTH; JMY;

sequence-specific DNA binding transcription factor activity (GO:0051091)				ARHGEF2; PPARGC1A; ICAM1
response to hexose (GO:0009746)	111	5	4.279E-03	SLC34A2; SESN2; IRS2; THBS1; ICAM1
lamellipodium assembly (GO:0030032)	33	3	4.313E-03	ABLIM3; WHAMM; AJUBA
activation of MAPKKK activity (GO:0000185)	9	2	4.347E-03	GADD45B; GADD45A
negative regulation of necroptotic process (GO:0060546)	9	2	4.347E-03	ARHGEF2; BIRC3
negative regulation of lipopolysaccharide-mediated signaling pathway (GO:0031665)	9	2	4.347E-03	TNFAIP3; TRIB1
peptidyl-threonine dephosphorylation (GO:0035970)	9	2	4.347E-03	DUSP1; PPM1E
positive regulation of protein homooligomerization (GO:0032464)	9	2	4.347E-03	HRK; BMF
regulation of RIG-I signaling pathway (GO:0039535)	9	2	4.347E-03	DDX60; BIRC3
cellular response to peptide (GO:1901653)	273	8	4.368E-03	KLF10; SOCS2; KLF11; TRIB3; IRS2; ARHGEF2; KLF4; HDAC9
negative regulation of response to external stimulus (GO:0032102)	215	7	4.370E-03	ANXA1; DUSP10; TNFAIP3; RORA; GATA3; KLF4; TRIB1
negative regulation of cysteine-type endopeptidase activity involved in apoptotic process (GO:0043154)	69	4	4.511E-03	KLF4; THBS1; SH3RF1; HERPUD1
regulation of muscle tissue development (GO:1901861)	113	5	4.600E-03	BMP2; DDIT3; NR1D2; HDAC9; PPARGC1A
regulation of binding (GO:0051098)	218	7	4.700E-03	NFKBIA; DAB2; JUN; BAMBI; TRIB3; GATA3; HERPUD1
negative regulation of cysteine-type endopeptidase activity (GO:2000117)	71	4	4.967E-03	KLF4; THBS1; SH3RF1; HERPUD1
response to estrogen (GO:0043627)	166	6	5.057E-03	SOCS2; SLC34A2; ANXA1; DUSP1; GATA3; AREG
response to	116	5	5.115E-03	SLC34A2; SESN2; IRS2; THBS1;

monosaccharide (GO:0034284)				ICAM1
positive regulation of odontogenesis (GO:0042482)	10	2	5.186E-03	BMP2; CSF1
regulation of viral-induced cytoplasmic pattern recognition receptor signaling pathway (GO:0039531)	10	2	5.186E-03	DDX60; BIRC3
parturition (GO:0007567)	10	2	5.186E-03	PLA2G4C; MAFF
regulation of fatty acid metabolic process (GO:0019217)	72	4	5.207E-03	ANXA1; IRS2; TRIB3; PPARGC1A
positive regulation of apoptotic signaling pathway (GO:2001235)	168	6	5.346E-03	HRK; TP53INP1; PMAIP1; BMF; THBS1; SKIL
cellular response to organonitrogen compound (GO:0071417)	411	10	5.395E-03	KLF10; SOCS2; KLF11; CEBPB; TRIB3; IRS2; ARHGEF2; KLF4; HDAC9; ICAM1
lamellipodium organization (GO:0097581)	36	3	5.412E-03	ABLIM3; WHAMM; AJUBA
negative regulation of transforming growth factor beta receptor signaling pathway (GO:0030512)	73	4	5.453E-03	PPP1R15A; BAMBI; LTBP1; SKIL
positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0090100)	73	4	5.453E-03	DAB2; BMP2; CDKN2B; THBS1
positive regulation of stress-activated MAPK cascade (GO:0032874)	118	5	5.479E-03	DAB2; BMP2; ZEB2; GADD45B; GADD45A
regulation of response to wounding (GO:1903034)	347	9	5.521E-03	ANXA1; DUSP10; TNFAIP3; RORA; NR1D2; GATA3; KLF4; THBS1; BIRC3
regulation of neuron death (GO:1901214)	225	7	5.543E-03	JUN; CEBPB; DDIT3; DDIT4; PMAIP1; GATA3; PPARGC1A
positive regulation of stress-activated protein kinase signaling cascade (GO:0070304)	119	5	5.668E-03	DAB2; BMP2; ZEB2; GADD45B; GADD45A
regulation of toll-like receptor signaling pathway (GO:0034121)	37	3	5.812E-03	IRF1; TNFAIP3; BIRC3

lymphocyte differentiation (GO:0030098)	172	6	5.961E-03	KLF6; ANXA1; IRF1; RORA; GATA3; HDAC9
regulation of fibroblast proliferation (GO:0048145)	75	4	5.971E-03	JUN; PMAIP1; FOSL2; EREG
negative regulation of phosphatidylinositol 3-kinase signaling (GO:0014067)	11	2	6.092E-03	PIK3IP1; KLF4
negative regulation of necrotic cell death (GO:0060547)	11	2	6.092E-03	ARHGEF2; BIRC3
regulation of energy homeostasis (GO:2000505)	11	2	6.092E-03	NR1D2; PPARGC1A
TRIF-dependent toll-like receptor signaling pathway (GO:0035666)	76	4	6.241E-03	NFKBIA; DUSP4; JUN; BIRC3
regulation of leukocyte proliferation (GO:0070663)	176	6	6.626E-03	PRNP; CSF1; IRF1; TNFAIP3; IRS2; AHR
negative regulation of fat cell differentiation (GO:0045599)	39	3	6.664E-03	TRIB3; RORA; GATA3
positive regulation of stem cell differentiation (GO:2000738)	39	3	6.664E-03	DAB2; BMP2; BAMBI
regulation of monocyte differentiation (GO:0045655)	12	2	7.065E-03	JUN; CSF1
lens fiber cell differentiation (GO:0070306)	12	2	7.065E-03	SLC7A11; SKIL
regulation of necroptotic process (GO:0060544)	12	2	7.065E-03	ARHGEF2; BIRC3
regulation of odontogenesis of dentin-containing tooth (GO:0042487)	12	2	7.065E-03	BMP2; CSF1
protein-cofactor linkage (GO:0018065)	12	2	7.065E-03	CTH; GAD1
positive regulation of epithelial cell migration (GO:0010634)	79	4	7.101E-03	ANXA3; GATA3; THBS1; HDAC9
MyD88-independent toll-like receptor signaling pathway (GO:0002756)	79	4	7.101E-03	NFKBIA; DUSP4; JUN; BIRC3
response to ionizing	127	5	7.350E-03	ANXA1; GADD45A; PMAIP1;

radiation (GO:0010212)				GATA3; ICAM1
toll-like receptor 3 signaling pathway (GO:0034138)	80	4	7.404E-03	NFKBIA; DUSP4; JUN; BIRC3
response to peptide hormone (GO:0043434)	364	9	7.415E-03	SOCS2; ANXA1; STC2; SESN2; TRIB3; IRS2; HDAC9; AREG; EREG
regulation of release of cytochrome c from mitochondria (GO:0090199)	41	3	7.587E-03	HRK; PMAIP1; BMF
regulation of epithelial cell migration (GO:0010632)	129	5	7.820E-03	ANXA3; GATA3; KLF4; THBS1; HDAC9
response to glucocorticoid (GO:0051384)	130	5	8.062E-03	ANXA1; DUSP1; FBXO32; AREG; FOSL2
lymphocyte activation (GO:0046649)	304	8	8.063E-03	KLF6; ANXA1; IRF1; RORA; GATA3; ULBP1; HDAC9; ICAM1
positive regulation of fatty acid oxidation (GO:0046321)	13	2	8.103E-03	IRS2; PPARGC1A
positive regulation of DNA damage response, signal transduction by p53 class mediator (GO:0043517)	13	2	8.103E-03	ANKRD1; PMAIP1
negative regulation of cytokine production (GO:0001818)	185	6	8.316E-03	PRNP; ANXA1; TNFAIP3; GATA3; KLF4; THBS1
intracellular receptor signaling pathway (GO:0030522)	186	6	8.522E-03	NFKBIA; TNFAIP3; RORA; NR1D2; AHR; PPARGC1A
cellular response to biotic stimulus (GO:0071216)	132	5	8.563E-03	NFKBIA; DDIT3; ANKRD1; TNFAIP3; ICAM1
regulation of interleukin-6 production (GO:0032675)	84	4	8.701E-03	CEBPB; TNFAIP3; ARHGEF2; EREG
regulation of neuron apoptotic process (GO:0043523)	188	6	8.943E-03	JUN; CEBPB; DDIT3; PMAIP1; GATA3; PPARGC1A
negative regulation of I-kappaB kinase/NF-kappaB signaling (GO:0043124)	44	3	9.106E-03	NFKBIA; TNFAIP3; RORA
lymphocyte homeostasis (GO:0002260)	44	3	9.106E-03	PMAIP1; TNFAIP3; SKIL
negative regulation of fibroblast growth factor receptor signaling pathway	14	2	9.205E-03	GATA3; THBS1

(GO:0040037)				
endoderm formation (GO:0001706)	14	2	9.205E-03	DUSP4; DUSP1
negative regulation of interleukin-8 production (GO:0032717)	14	2	9.205E-03	ANXA1; KLF4
positive regulation of innate immune response (GO:0045089)	190	6	9.379E-03	NFKBIA; DUSP4; JUN; TNFAIP3; EREG; BIRC3
positive regulation of Wnt signaling pathway (GO:0030177)	86	4	9.402E-03	DAB2; BMP2; ZEB2; BAMBI
response to amino acid (GO:0043200)	86	4	9.402E-03	CEBPB; ASNS; PPARGC1A; ICAM1
regulation of interleukin-2 production (GO:0032663)	45	3	9.649E-03	PRNP; TNFAIP3; GATA3
regulation of blood vessel endothelial cell migration (GO:0043535)	45	3	9.649E-03	KLF4; HDAC9; THBS1
inner ear development (GO:0048839)	46	3	1.021E-02	BMP2; HOXA1; GATA3
positive regulation of smooth muscle cell proliferation (GO:0048661)	46	3	1.021E-02	JUN; PPARGC1A; EREG
regulation of cell migration involved in sprouting angiogenesis (GO:0090049)	15	2	1.037E-02	KLF4; HDAC9
CD4-positive, alpha-beta T cell differentiation involved in immune response (GO:0002294)	15	2	1.037E-02	RORA; GATA3
T-helper cell differentiation (GO:0042093)	15	2	1.037E-02	RORA; GATA3
mammary gland epithelial cell proliferation (GO:0033598)	15	2	1.037E-02	CEBPB; AREG
regulation of protein homooligomerization (GO:0032462)	15	2	1.037E-02	HRK; BMF
response to carbohydrate (GO:0009743)	139	5	1.048E-02	SLC34A2; SESN2; IRS2; THBS1; ICAM1
response to corticosteroid (GO:0031960)	140	5	1.078E-02	ANXA1; DUSP1; FBXO32; AREG; FOSL2
positive regulation of	47	3	1.079E-02	JUN; DDIT3; PMAIP1

neuron apoptotic process (GO:0043525)				
positive regulation of myeloid leukocyte differentiation (GO:0002763)	47	3	1.079E-02	KLF10; JUN; CSF1
skeletal muscle cell differentiation (GO:0035914)	47	3	1.079E-02	MAFF; ANKRD1; ATF3
response to cAMP (GO:0051591)	90	4	1.091E-02	JUN; DUSP1; AREG; FOSL2
regulation of cysteine-type endopeptidase activity (GO:2000116)	197	6	1.103E-02	PMAIP1; KLF4; THBS1; SH3RF1; BIRC3; HERPUD1
regulation of epithelial cell proliferation (GO:0050678)	258	7	1.112E-02	JUN; CDKN2B; BMP2; TNFAIP3; GATA3; THBS1; EREG
intrinsic apoptotic signaling pathway by p53 class mediator (GO:0072332)	48	3	1.139E-02	JMY; DDIT4; PMAIP1
positive regulation of intrinsic apoptotic signaling pathway (GO:2001244)	48	3	1.139E-02	PMAIP1; BMF; SKIL
T cell activation involved in immune response (GO:0002286)	48	3	1.139E-02	RORA; GATA3; ICAM1
pattern recognition receptor signaling pathway (GO:0002221)	142	5	1.139E-02	NFKBIA; DUSP4; JUN; TNFAIP3; BIRC3
mRNA transcription (GO:0009299)	16	2	1.160E-02	DDIT3; EREG
SMAD protein signal transduction (GO:0060395)	16	2	1.160E-02	BMP2; JUN
regulation of interleukin-6 biosynthetic process (GO:0045408)	16	2	1.160E-02	CEBPB; EREG
positive regulation of signal transduction by p53 class mediator (GO:1901798)	16	2	1.160E-02	ANKRD1; PMAIP1
positive regulation of fibroblast proliferation (GO:0048146)	49	3	1.201E-02	JUN; FOSL2; EREG
response to dsRNA (GO:0043331)	49	3	1.201E-02	NFKBIA; PMAIP1; SLC3A2
innate immune response-activating	144	5	1.202E-02	NFKBIA; DUSP4; JUN; TNFAIP3; BIRC3

signal transduction (GO:0002758)				
positive regulation of cytokine production (GO:0001819)	327	8	1.205E-02	NFKBIA; DDIT3; IRF1; RORA; GATA3; ARHGEF2; THBS1; EREG
positive regulation of binding (GO:0051099)	93	4	1.214E-02	BAMBI; TRIB3; GATA3; HERPUD1
negative regulation of organic acid transport (GO:0032891)	17	2	1.288E-02	IRS2; THBS1
negative regulation of peptidyl-serine phosphorylation (GO:0033137)	17	2	1.288E-02	DDIT4; INPP5J
alpha-beta T cell activation involved in immune response (GO:0002287)	17	2	1.288E-02	RORA; GATA3
T cell differentiation involved in immune response (GO:0002292)	17	2	1.288E-02	RORA; GATA3
alpha-beta T cell differentiation involved in immune response (GO:0002293)	17	2	1.288E-02	RORA; GATA3
hemopoiesis (GO:0030097)	95	4	1.301E-02	CSF1; GATA3; KLF4; SH2B3
cellular response to cytokine stimulus (GO:0071345)	471	10	1.309E-02	KLF6; ACSL1; IRF1; ANKRD1; GATA3; ARHGEF2; PPARGC1A; THBS1; ICAM1; EREG
cellular response to oxidative stress (GO:0034599)	148	5	1.336E-02	ANXA1; TP53INP1; TNFAIP3; KLF4; PPARGC1A
lipid homeostasis (GO:0055088)	96	4	1.346E-02	SESN2; RORA; IRS2; NR1D2
fat cell differentiation (GO:0045444)	96	4	1.346E-02	CEBPB; KLF4; PPARGC1A; CREB5
regulation of mitochondrion organization (GO:0010821)	97	4	1.392E-02	HRK; PMAIP1; BMF; PPARGC1A
T cell differentiation (GO:0030217)	97	4	1.392E-02	ANXA1; IRF1; RORA; GATA3
toll-like receptor 4 signaling pathway (GO:0034142)	97	4	1.392E-02	NFKBIA; DUSP4; JUN; BIRC3
regulation of epithelial to mesenchymal transition (GO:0010717)	52	3	1.397E-02	DAB2; BMP2; BAMBI
regulation of interleukin-8 production (GO:0032677)	52	3	1.397E-02	ANXA1; DDIT3; KLF4
regulation of	18	2	1.423E-02	ARHGEF2; BIRC3

necrotic cell death (GO:0010939)				
positive regulation of defense response (GO:0031349)	272	7	1.442E-02	NFKBIA; DUSP4; JUN; TNFAIP3; DDX60; BIRC3; EREG
activation of innate immune response (GO:0002218)	151	5	1.443E-02	NFKBIA; DUSP4; JUN; TNFAIP3; BIRC3
regulation of Notch signaling pathway (GO:0008593)	53	3	1.467E-02	NFKBIA; DLX2; CHAC1
positive regulation of protein binding (GO:0032092)	53	3	1.467E-02	BAMBI; TRIB3; HERPUD1
neurotrophin TRK receptor signaling pathway (GO:0048011)	274	7	1.494E-02	NFKBIA; DUSP4; DDIT4; IRS2; TRIB3; ARHGEF2; EREG
response to acid chemical (GO:0001101)	275	7	1.521E-02	CEBPB; ACSL1; DUSP1; ASNS; KLF4; PPARGC1A; ICAM1
regulation of I-kappaB kinase/NF-kappaB signaling (GO:0043122)	213	6	1.554E-02	NFKBIA; CTH; TNFAIP3; RORA; AJUBA; BIRC3
myeloid cell differentiation (GO:0030099)	154	5	1.555E-02	DAB2; CDKN2B; JUN; CSF1; GATA3
regulation of lipopolysaccharide-mediated signaling pathway (GO:0031664)	19	2	1.563E-02	TNFAIP3; TRIB1
neurotrophin signaling pathway (GO:0038179)	278	7	1.603E-02	NFKBIA; DUSP4; DDIT4; TRIB3; IRS2; ARHGEF2; EREG
JNK cascade (GO:0007254)	55	3	1.611E-02	DUSP10; SH2D3C; TRIB1
autophagy (GO:0006914)	102	4	1.635E-02	MAP1LC3B; SESN2; TP53INP1; MAP1LC3B2
positive regulation of cellular carbohydrate metabolic process (GO:0010676)	56	3	1.686E-02	PMAIP1; IRS2; PPARGC1A
sensory organ development (GO:0007423)	103	4	1.687E-02	RCN1; GATA3; KLF4; SLC25A25
response to copper ion (GO:0046688)	20	2	1.710E-02	PRNP; ICAM1
negative regulation of striated muscle cell differentiation (GO:0051154)	20	2	1.710E-02	BMP2; BHLHE41
negative regulation of blood vessel endothelial cell migration (GO:0043537)	20	2	1.710E-02	KLF4; THBS1
positive regulation of	57	3	1.764E-02	PMAIP1; THBS1; SKIL

extrinsic apoptotic signaling pathway (GO:2001238)				
positive regulation of response to DNA damage stimulus (GO:2001022)	57	3	1.764E-02	ANKRD1; PMAIP1; SKIL
gland development (GO:0048732)	220	6	1.787E-02	JUN; CDKN2B; ASNS; IRS2; GATA3; AHR
response to ketone (GO:1901654)	105	4	1.794E-02	DUSP1; FBXO32; THBS1; FOSL2
camera-type eye development (GO:0043010)	58	3	1.843E-02	RCN1; KLF4; SLC25A25
response to glucose (GO:0009749)	106	4	1.848E-02	SESN2; IRS2; THBS1; ICAM1
cellular amino acid biosynthetic process (GO:0008652)	106	4	1.848E-02	MTHFD2; CTH; GAD1; ASNS
in utero embryonic development (GO:0001701)	222	6	1.858E-02	SLC34A2; DAB2; BMP2; RCN1; MAFF; GATA3
negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0090101)	107	4	1.904E-02	PPP1R15A; BAMBI; LTBP1; SKIL
positive regulation of JNK cascade (GO:0046330)	107	4	1.904E-02	DAB2; ZEB2; GADD45B; GADD45A
regulation of response to biotic stimulus (GO:0002831)	107	4	1.904E-02	TNFAIP3; TRIB1; DDX60; BIRC3
positive regulation of cytokine biosynthetic process (GO:0042108)	59	3	1.924E-02	IRF1; THBS1; EREG
cellular response to organic cyclic compound (GO:0071407)	291	7	1.995E-02	BMP2; ANXA1; ANKRD1; RORA; NR1D2; FBXO32; KLF4
chordate embryonic development (GO:0043009)	226	6	2.005E-02	SLC34A2; DAB2; BMP2; RCN1; MAFF; GATA3
positive regulation of DNA replication (GO:0045740)	60	3	2.007E-02	JUN; AREG; EREG
response to BMP (GO:0071772)	22	2	2.019E-02	BMP2; GATA3
cellular response to BMP stimulus (GO:0071773)	22	2	2.019E-02	BMP2; GATA3
regulation of hormone biosynthetic process (GO:0046885)	22	2	2.019E-02	BMP2; STC2
positive regulation of	22	2	2.019E-02	KLF10; CSF1

osteoclast differentiation (GO:0045672)				
regulation of epithelial cell differentiation (GO:0030856)	109	4	2.019E-02	CDKN2B; ZEB2; MAFF; GATA3
cellular response to lipopolysaccharide (GO:0071222)	110	4	2.078E-02	NFKBIA; ANKRD1; TNFAIP3; ICAM1
negative regulation of epithelial cell proliferation (GO:0050680)	110	4	2.078E-02	CDKN2B; GATA3; THBS1; EREG
regulation of skeletal muscle tissue development (GO:0048641)	61	3	2.091E-02	DDIT3; NR1D2; HDAC9
embryo development ending in birth or egg hatching (GO:0009792)	230	6	2.160E-02	SLC34A2; DAB2; BMP2; RCN1; MAFF; GATA3
cellular response to hydrogen peroxide (GO:0070301)	62	3	2.178E-02	ANXA1; TNFAIP3; KLF4
regulation of fatty acid transport (GO:2000191)	23	2	2.181E-02	IRS2; THBS1
CD4-positive, alpha-beta T cell differentiation (GO:0043367)	23	2	2.181E-02	RORA; GATA3
regulation of macrophage activation (GO:0043030)	23	2	2.181E-02	RORA; THBS1
positive regulation of blood vessel endothelial cell migration (GO:0043536)	23	2	2.181E-02	THBS1; HDAC9
cell-substrate adherens junction assembly (GO:0007045)	23	2	2.181E-02	WHAMM; AJUBA
focal adhesion assembly (GO:0048041)	23	2	2.181E-02	WHAMM; AJUBA
JAK-STAT cascade involved in growth hormone signaling pathway (GO:0060397)	23	2	2.181E-02	SOCS2; IRS2
posttranscriptional regulation of gene expression (GO:0010608)	438	9	2.191E-02	PPP1R15A; BMP2; SAMD4A; PPARGC1A; RBM24; AJUBA; THBS1; LARP6; EIF1
regulation of adaptive immune	112	4	2.199E-02	DUSP10; IRF1; TNFAIP3; MR1

response (GO:0002819)				
regulation of striated muscle tissue development (GO:0016202)	112	4	2.199E-02	BMP2; DDIT3; NR1D2; HDAC9
leukocyte activation involved in immune response (GO:0002366)	112	4	2.199E-02	ANXA3; RORA; GATA3; ICAM1
cell activation involved in immune response (GO:0002263)	112	4	2.199E-02	ANXA3; RORA; GATA3; ICAM1
negative regulation of cell motility (GO:2000146)	170	5	2.253E-02	TP53INP1; GATA3; TRIB1; KLF4; THBS1
MAPK cascade (GO:0000165)	170	5	2.253E-02	DUSP4; JUN; DUSP10; SH2D3C; TRIB1
positive regulation of carbohydrate metabolic process (GO:0045913)	63	3	2.267E-02	PMAIP1; IRS2; PPARGC1A
regulation of mononuclear cell proliferation (GO:0032944)	171	5	2.302E-02	PRNP; CSF1; IRF1; IRS2; AHR
regulation of establishment of protein localization (GO:0070201)	442	9	2.305E-02	NFKBIA; DAB2; ANXA1; BAMBI; CREBRF; ANKRD1; PMAIP1; BMF; GATA3
regulation of muscle organ development (GO:0048634)	114	4	2.324E-02	BMP2; DDIT3; NR1D2; HDAC9
heart valve morphogenesis (GO:0003179)	24	2	2.349E-02	BMP2; GATA3
regulation of fatty acid oxidation (GO:0046320)	24	2	2.349E-02	IRS2; PPARGC1A
embryonic hemopoiesis (GO:0035162)	24	2	2.349E-02	GATA3; SH2B3
branching involved in mammary gland duct morphogenesis (GO:0060444)	24	2	2.349E-02	CSF1; AREG
response to X-ray (GO:0010165)	24	2	2.349E-02	ANXA1; PMAIP1
anatomical structure maturation (GO:0071695)	24	2	2.349E-02	DDIT3; GATA3
negative regulation of lipid metabolic process (GO:0045833)	65	3	2.450E-02	BMP2; PIK3IP1; TRIB3
negative regulation of NF-kappaB transcription factor activity	65	3	2.450E-02	NFKBIA; TNFAIP3; KLF4

(GO:0032088)				
toll-like receptor 10 signaling pathway (GO:0034166)	65	3	2.450E-02	NFKBIA; DUSP4; JUN
toll-like receptor 5 signaling pathway (GO:0034146)	65	3	2.450E-02	NFKBIA; DUSP4; JUN
cellular response to molecule of bacterial origin (GO:0071219)	116	4	2.454E-02	NFKBIA; ANKRD1; TNFAIP3; ICAM1
hematopoietic or lymphoid organ development (GO:0048534)	175	5	2.507E-02	CDKN2B; CSF1; GATA3; KLF4; SH2B3
release of cytochrome c from mitochondria (GO:0001836)	25	2	2.522E-02	JUN; PMAIP1
CD4-positive, alpha-beta T cell activation (GO:0035710)	25	2	2.522E-02	RORA; GATA3
response to testosterone (GO:0033574)	25	2	2.522E-02	DUSP1; THBS1
response to organophosphorus (GO:0046683)	118	4	2.588E-02	JUN; DUSP1; AREG; FOSL2
positive regulation of leukocyte differentiation (GO:1902107)	118	4	2.588E-02	KLF10; JUN; CSF1; GATA3
cellular chemical homeostasis (GO:0055082)	452	9	2.607E-02	PRNP; SLC34A2; HKDC1; DDIT3; STC2; IRS2; PPARGC1A; HERPUD1; ICAM1
cellular response to mechanical stimulus (GO:0071260)	67	3	2.642E-02	GADD45A; IRF1; ANKRD1
regulation of odontogenesis (GO:0042481)	26	2	2.700E-02	BMP2; CSF1
positive regulation of pathway-restricted SMAD protein phosphorylation (GO:0010862)	26	2	2.700E-02	DAB2; BMP2
negative regulation of response to biotic stimulus (GO:0002832)	26	2	2.700E-02	TNFAIP3; TRIB1
regulation of glycolytic process (GO:0006110)	26	2	2.700E-02	DDIT4; PPARGC1A
regulation of angiogenesis (GO:0045765)	179	5	2.723E-02	ANXA3; TNFAIP3; KLF4; THBS1; HDAC9
alpha-amino acid biosynthetic process (GO:1901607)	69	3	2.841E-02	MTHFD2; CTH; ASNS
response to temperature	122	4	2.869E-02	NFKBIA; TP53INP1; THBS1; PPARGC1A

stimulus (GO:0009266)				
toll-like receptor signaling pathway (GO:0002224)	122	4	2.869E-02	NFKBIA; DUSP4; JUN; BIRC3
negative regulation of interferon-gamma production (GO:0032689)	27	2	2.882E-02	PRNP; GATA3
negative regulation of lipid transport (GO:0032369)	27	2	2.882E-02	IRS2; THBS1
response to gonadotropin (GO:0034698)	27	2	2.882E-02	ASNS; ICAM1
regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900739)	27	2	2.882E-02	PMAIP1; BMF
positive regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900740)	27	2	2.882E-02	PMAIP1; BMF
cellular response to steroid hormone stimulus (GO:0071383)	123	4	2.942E-02	ANXA1; RORA; NR1D2; FBXO32
positive regulation of cell morphogenesis involved in differentiation (GO:0010770)	123	4	2.942E-02	DAB2; BMP2; BAMBI; SKIL
cellular response to alcohol (GO:0097306)	70	3	2.943E-02	TP53INP1; RORA; FBXO32
negative regulation of cellular component movement (GO:0051271)	183	5	2.950E-02	TP53INP1; GATA3; KLF4; TRIB1; THBS1
positive regulation of DNA metabolic process (GO:0051054)	124	4	3.016E-02	JUN; PPARGC1A; AREG; EREG
regulation of leukocyte activation (GO:0002694)	390	8	3.021E-02	PRNP; IRF1; TNFAIP3; RORA; IRS2; GATA3; AHR; THBS1
response to interleukin-1 (GO:0070555)	71	3	3.047E-02	ANXA1; ANKRD1; ICAM1
toll-like receptor TLR1:TLR2 signaling pathway (GO:0038123)	71	3	3.047E-02	NFKBIA; DUSP4; JUN

toll-like receptor TLR6:TLR2 signaling pathway (GO:0038124)	71	3	3.047E-02	NFKBIA; DUSP4; JUN
response to virus (GO:0009615)	250	6	3.057E-02	IRF1; DDIT4; PMAIP1; GATA3; DDX60; ICAM1
nucleotide-binding oligomerization domain containing signaling pathway (GO:0070423)	28	2	3.070E-02	NFKBIA; TNFAIP3
regulation of DNA damage response, signal transduction by p53 class mediator (GO:0043516)	28	2	3.070E-02	ANKRD1; PMAIP1
regulation of macrophage derived foam cell differentiation (GO:0010743)	28	2	3.070E-02	NFKBIA; CSF1
triglyceride homeostasis (GO:0070328)	28	2	3.070E-02	SESN2; RORA
negative regulation of innate immune response (GO:0045824)	28	2	3.070E-02	DUSP10; TNFAIP3
acylglycerol homeostasis (GO:0055090)	28	2	3.070E-02	SESN2; RORA
neutral amino acid transport (GO:0015804)	28	2	3.070E-02	SLC3A2; SLC1A4
regulation of cysteine-type endopeptidase activity involved in apoptotic process (GO:0043281)	186	5	3.128E-02	PMAIP1; KLF4; THBS1; SH3RF1; HERPUD1
regulation of intrinsic apoptotic signaling pathway (GO:2001242)	126	4	3.167E-02	PMAIP1; BMF; ARHGEF2; SKIL
positive regulation of NF-kappaB transcription factor activity (GO:0051092)	126	4	3.167E-02	NFKBIA; CTH; ARHGEF2; ICAM1
hexose metabolic process (GO:0019318)	187	5	3.189E-02	HKDC1; IRS2; PPARGC1A; FUT1; ATF3
transcription initiation from RNA polymerase II promoter (GO:0006367)	187	5	3.189E-02	CDKN2B; RORA; NR1D2; PPARGC1A; SKIL
response to light stimulus	322	7	3.192E-02	DUSP1; TP53INP1; BHLHE40; PMAIP1; ASNS; HOXA1; BEST1

(GO:0009416)				
positive regulation of MAPK cascade (GO:0043410)	395	8	3.218E-02	ZEB2; DAB2; BMP2; GADD45B; GADD45A; AJUBA; THBS1; ICAM1
epithelial cell proliferation (GO:0050673)	73	3	3.262E-02	CEBPB; AREG; EREG
toll-like receptor 9 signaling pathway (GO:0034162)	73	3	3.262E-02	NFKBIA; DUSP4; JUN
toll-like receptor 2 signaling pathway (GO:0034134)	73	3	3.262E-02	NFKBIA; DUSP4; JUN
regulation of fibroblast growth factor receptor signaling pathway (GO:0040036)	29	2	3.262E-02	GATA3; THBS1
regulation of fatty acid biosynthetic process (GO:0042304)	29	2	3.262E-02	ANXA1; TRIB3
regulation of protein binding (GO:0043393)	128	4	3.323E-02	DAB2; BAMBI; TRIB3; HERPUD1
regulation of generation of precursor metabolites and energy (GO:0043467)	74	3	3.372E-02	DDIT4; IRS2; PPARGC1A
positive regulation of myeloid cell differentiation (GO:0045639)	74	3	3.372E-02	KLF10; JUN; CSF1
intrinsic apoptotic signaling pathway in response to DNA damage by p53 class mediator (GO:0042771)	30	2	3.459E-02	DDIT4; PMAIP1
positive regulation of protein catabolic process (GO:0045732)	130	4	3.483E-02	DAB2; CREBRF; TNFAIP3; TRIB1
regulation of JUN kinase activity (GO:0043506)	75	3	3.484E-02	DAB2; ZEB2; DUSP10
epidermal cell differentiation (GO:0009913)	76	3	3.598E-02	ANXA1; KLF4; EREG
response to purine-containing compound (GO:0014074)	132	4	3.648E-02	JUN; DUSP1; AREG; FOSL2
cellular response to glucocorticoid stimulus (GO:0071385)	31	2	3.661E-02	ANXA1; FBXO32
negative regulation	31	2	3.661E-02	KLF4; THBS1

of endothelial cell migration (GO:0010596)				
adherens junction assembly (GO:0034333)	31	2	3.661E-02	WHAMM; AJUBA
peptide cross-linking (GO:0018149)	31	2	3.661E-02	ANXA1; THBS1
regulation of DNA binding (GO:0051101)	77	3	3.714E-02	NFKBIA; JUN; GATA3
lymphocyte activation involved in immune response (GO:0002285)	77	3	3.714E-02	RORA; GATA3; ICAM1
regulation of defense response to virus (GO:0050688)	77	3	3.714E-02	TNFAIP3; DDX60; BIRC3
regulation of immune effector process (GO:0002697)	264	6	3.812E-02	DUSP10; TNFAIP3; DDX60; MR1; ICAM1; BIRC3
regulation of tumor necrosis factor production (GO:0032680)	78	3	3.832E-02	TNFAIP3; ARHGEF2; THBS1
regulation of vasculature development (GO:1901342)	197	5	3.838E-02	ANXA3; TNFAIP3; KLF4; THBS1; HDAC9
positive regulation of MAP kinase activity (GO:0043406)	197	5	3.838E-02	BMP2; ZEB2; DAB2; AJUBA; THBS1
positive regulation of nitric oxide biosynthetic process (GO:0045429)	32	2	3.867E-02	KLF4; ICAM1
negative regulation of microtubule polymerization or depolymerization (GO:0031111)	32	2	3.867E-02	INPP5J; ARHGEF2
brown fat cell differentiation (GO:0050873)	32	2	3.867E-02	CEBPB; PPARGC1A
T cell activation (GO:0042110)	198	5	3.907E-02	ANXA1; IRF1; RORA; GATA3; ICAM1
eye development (GO:0001654)	79	3	3.951E-02	RCN1; KLF4; SLC25A25
regulation of carbohydrate biosynthetic process (GO:0043255)	79	3	3.951E-02	SESN2; IRS2; PPARGC1A
inositol lipid-mediated signaling (GO:0048017)	136	4	3.990E-02	TRIB3; IRS2; GATA3; EREG
phosphatidylinositol-mediated signaling (GO:0048015)	136	4	3.990E-02	IRS2; TRIB3; GATA3; EREG
regulation of tumor	80	3	4.073E-02	TNFAIP3; ARHGEF2; THBS1

necrosis factor superfamily cytokine production (GO:1903555)				
cellular response to corticosteroid stimulus (GO:0071384)	33	2	4.077E-02	ANXA1; FBXO32
response to progesterone (GO:0032570)	33	2	4.077E-02	THBS1; FOSL2
regulation of cellular carbohydrate catabolic process (GO:0043471)	33	2	4.077E-02	DDIT4; PPARGC1A
regulation of carbohydrate catabolic process (GO:0043470)	33	2	4.077E-02	DDIT4; PPARGC1A
signal transduction by phosphorylation (GO:0023014)	202	5	4.191E-02	DUSP4; JUN; DUSP10; SH2D3C; TRIB1
regulation of reactive oxygen species metabolic process (GO:2000377)	81	3	4.196E-02	GADD45A; THBS1; BIRC3
cytoplasmic pattern recognition receptor signaling pathway (GO:0002753)	34	2	4.292E-02	NFKBIA; TNFAIP3
positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway (GO:1901030)	34	2	4.292E-02	PMAIP1; BMF
MyD88-dependent toll-like receptor signaling pathway (GO:0002755)	82	3	4.322E-02	NFKBIA; DUSP4; JUN
aging (GO:0007568)	204	5	4.338E-02	SOCS2; SLC34A2; CDKN2B; JUN; ICAM1
negative regulation of locomotion (GO:0040013)	204	5	4.338E-02	TP53INP1; GATA3; KLF4; TRIB1; THBS1
regulation of cell activation (GO:0050865)	420	8	4.339E-02	PRNP; IRF1; TNFAIP3; RORA; IRS2; GATA3; AHR; THBS1
regulation of lipid transport (GO:0032368)	83	3	4.449E-02	NFKBIA; IRS2; THBS1
myeloid leukocyte differentiation (GO:0002573)	83	3	4.449E-02	JUN; CSF1; GATA3
regulation of skeletal muscle fiber development (GO:0048742)	35	2	4.510E-02	DDIT3; HDAC9

response to toxic substance (GO:0009636)	142	4	4.537E-02	ASNS; AHR; SLC7A11; SKIL
positive regulation of cytoskeleton organization (GO:0051495)	142	4	4.537E-02	JMY; WHAMM; PPM1E; ICAM1
embryo development (GO:0009790)	276	6	4.547E-02	SLC34A2; DAB2; BMP2; RCN1; MAFF; GATA3
glucose homeostasis (GO:0042593)	143	4	4.632E-02	HKDC1; IRS2; PPARGC1A; ICAM1
carbohydrate homeostasis (GO:0033500)	143	4	4.632E-02	HKDC1; IRS2; PPARGC1A; ICAM1
regulation of phosphatidylinositol 3-kinase activity (GO:0043551)	36	2	4.733E-02	PIK3IP1; KLF4
negative regulation of cellular carbohydrate metabolic process (GO:0010677)	36	2	4.733E-02	DDIT4; PPARGC1A
regulation of gluconeogenesis (GO:0006111)	36	2	4.733E-02	SESN2; PPARGC1A
response to cold (GO:0009409)	36	2	4.733E-02	NFKBIA; PPARGC1A
regulation of leukocyte differentiation (GO:1902105)	210	5	4.796E-02	KLF10; JUN; CSF1; IRF1; GATA3
liver development (GO:0001889)	86	3	4.841E-02	CDKN2B; JUN; ASNS
myeloid leukocyte activation (GO:0002274)	86	3	4.841E-02	JUN; CSF1; ANXA3
central nervous system neuron differentiation (GO:0021953)	87	3	4.976E-02	RORA; HOXA1; PHLDA1

Supplementary Table 3. Enriched biological processes for the down-regulated genes (FC ≤ -2, P adj. value ≤ 0.001; 72 and 96 hpi)

GO biological process	Genes in the process	DEGs	P-value	Down-regulated genes that overlap the process
cellular ketone body metabolic process (GO:0046950)	8	1	5.662E-03	HMGCS2
cellular response to exogenous dsRNA (GO:0071360)	8	1	5.662E-03	IFIT1
ketone body metabolic process (GO:1902224)	9	1	6.290E-03	HMGCS2
regulation of helicase activity (GO:0051095)	9	1	6.290E-03	IFIT1
basement membrane organization (GO:0071711)	11	1	7.543E-03	NID2
cellular response to dsRNA (GO:0071359)	15	1	1.005E-02	IFIT1
negative regulation of defense response to virus (GO:0050687)	16	1	1.067E-02	IFIT1
positive regulation of viral genome replication (GO:0045070)	18	1	1.192E-02	IFIT1
branched-chain amino acid catabolic process (GO:0009083)	19	1	1.254E-02	ACADSB
isoprenoid biosynthetic process (GO:0008299)	23	1	1.504E-02	HMGCS2
branched-chain amino acid metabolic process (GO:0009081)	23	1	1.504E-02	ACADSB
cell-substrate adherens	23	1	1.504E-02	ACTN3

junction assembly (GO:0007045)				
focal adhesion assembly (GO:0048041)	23	1	1.504E-02	ACTN3
negative regulation of response to biotic stimulus (GO:0002832)	26	1	1.690E-02	IFIT1
regulation of defense response to virus by host (GO:0050691)	26	1	1.690E-02	IFIT1
adherens junction assembly (GO:0034333)	31	1	2.000E-02	ACTN3
negative regulation of cytokine-mediated signaling pathway (GO:0001960)	32	1	2.062E-02	PALM3
transport of virus (GO:0046794)	32	1	2.062E-02	IFIT1
intracellular transport of virus (GO:0075733)	32	1	2.062E-02	IFIT1
multi-organism transport (GO:0044766)	32	1	2.062E-02	IFIT1
multi-organism localization (GO:1902579)	32	1	2.062E-02	IFIT1
multi-organism intracellular transport (GO:1902583)	32	1	2.062E-02	IFIT1
cholesterol biosynthetic process (GO:0006695)	34	1	2.186E-02	HMGCS2
negative regulation of response to cytokine stimulus (GO:0060761)	36	1	2.310E-02	PALM3
muscle filament sliding (GO:0030049)	38	1	2.433E-02	ACTN3
actin-myosin filament sliding (GO:0033275)	38	1	2.433E-02	ACTN3

sterol biosynthetic process (GO:0016126)	39	1	2.495E-02	HMGCS2
negative regulation of viral genome replication (GO:0045071)	40	1	2.557E-02	IFIT1
response to exogenous dsRNA (GO:0043330)	41	1	2.618E-02	IFIT1
cell-substrate junction assembly (GO:0007044)	41	1	2.618E-02	ACTN3
actin-mediated cell contraction (GO:0070252)	46	1	2.926E-02	ACTN3
amino acid transmembrane transport (GO:0003333)	46	1	2.926E-02	SLC38A4
response to dsRNA (GO:0043331)	49	1	3.110E-02	IFIT1
negative regulation of protein binding (GO:0032091)	50	1	3.171E-02	IFIT1
regulation of viral genome replication (GO:0045069)	57	1	3.599E-02	IFIT1
actin filament-based movement (GO:0030048)	61	1	3.843E-02	ACTN3
centrosome organization (GO:0051297)	64	1	4.026E-02	HEPACAM2
cellular response to type I interferon (GO:0071357)	65	1	4.087E-02	IFIT1
type I interferon signaling pathway (GO:0060337)	65	1	4.087E-02	IFIT1
response to type I interferon (GO:0034340)	66	1	4.147E-02	IFIT1
adherens junction organization (GO:0034332)	69	1	4.330E-02	ACTN3
microtubule organizing center	70	1	4.390E-02	HEPACAM2

organization (GO:0031023)				
negative regulation of viral process (GO:0048525)	75	1	4.693E-02	IFIT1
regulation of defense response to virus (GO:0050688)	77	1	4.814E-02	IFIT1

Supplementary Table 4. Enriched molecular functions for the up-regulated genes (FC ≥ 2, P adj. value ≤ 0.001; 72 and 96 hpi)

GO molecular function	Genes in the function category	DEGs	P-value	Up-regulated genes that overlap the function category
MAP kinase tyrosine/serine/threonine phosphatase activity (GO:0017017)	15	5	9.348E-07	DUSP4; DUSP10; DUSP1; DUSP8; DUSP16
MAP kinase phosphatase activity (GO:0033549)	16	5	1.218E-06	DUSP4; DUSP10; DUSP1; DUSP8; DUSP16
sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981)	397	15	7.143E-06	KLF11; JUN; CEBPB; BHLHE41; RORA; NR1D2; GATA3; AHR; KLF4; BACH2; ELF3; BHLHE40; MXD1; ATF3; CREB5
protein tyrosine/serine/threonine phosphatase activity (GO:0008138)	46	6	8.704E-06	DUSP4; DUSP10; DUSP1; DUSP8; DUSP16; CDC14A
transcription regulatory region sequence-specific DNA binding (GO:0000976)	340	13	2.697E-05	KLF10; JUN; BHLHE41; RORA; NR1D2; GATA3; KLF4; BACH2; FOSL2; ELF3; IRF1; MXD1; ATF3
RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity (GO:0000982)	204	10	3.314E-05	JUN; CEBPB; ELF3; BHLHE40; BHLHE41; GATA3; MXD1; KLF4; ATF3; CREB5
transcription corepressor activity (GO:0003714)	208	10	3.880E-05	DDIT3; BHLHE40; BHLHE41; ANKRD1; TRIB3; MXD1; HDAC9; AJUBA; SKIL; ATF3
transcription factor binding (GO:0008134)	464	15	4.189E-05	CEBPB; JUN; BHLHE41; RORA; GATA3; AHR; KLF4; HDAC9; NFKBIA; DDIT3; BHLHE40; ANKRD1; ARHGEF2; TRIB1; PPARGC1A
SMAD binding (GO:0046332)	68	6	6.694E-05	DAB2; JUN; ZEB2; BMP2; ANKRD1; SKIL
protein tyrosine phosphatase activity (GO:0004725)	103	7	7.783E-05	DUSP4; DUSP10; DUSP1; DUSP8; PTPRH; DUSP16; CDC14A
RNA polymerase II distal enhancer sequence-specific DNA binding transcription factor activity (GO:0003705)	84	6	1.991E-04	CEBPB; JUN; BHLHE40; BHLHE41; AHR; BACH2
RNA polymerase II transcription regulatory	88	6	2.526E-04	BHLHE40; BHLHE41; GATA3; MXD1; ATF3;

region sequence-specific DNA binding transcription factor activity involved in negative regulation of transcription (GO:0001227)				BACH2
phosphoprotein phosphatase activity (GO:0004721)	172	8	2.934E-04	DUSP4; DUSP10; DUSP1; DUSP8; PTPRH; PPM1E; DUSP16; CDC14A
phosphate ion binding (GO:0042301)	13	3	4.148E-04	SLC34A2; MTHFD2; SH2B3
E-box binding (GO:0070888)	34	4	4.281E-04	BHLHE40; BHLHE41; GATA3; AHR
RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity involved in negative regulation of transcription (GO:0001078)	63	5	4.386E-04	BHLHE40; BHLHE41; GATA3; MXD1; ATF3
RNA polymerase II transcription factor binding transcription factor activity (GO:0001076)	112	6	8.517E-04	JUN; BHLHE40; BHLHE41; ANKRD1; KLF4; PPARGC1A
phosphatase activity (GO:0016791)	266	9	1.140E-03	DUSP4; DUSP10; DUSP1; INPP5J; DUSP8; PTPRH; PPM1E; DUSP16; CDC14A
R-SMAD binding (GO:0070412)	22	3	1.602E-03	JUN; ZEB2; ANKRD1
core promoter proximal region sequence-specific DNA binding (GO:0000987)	176	7	1.692E-03	ELF3; IRF1; BHLHE41; GATA3; KLF4; MXD1; ATF3
RNA polymerase II regulatory region sequence-specific DNA binding (GO:0000977)	284	9	1.768E-03	JUN; ELF3; IRF1; BHLHE41; GATA3; MXD1; BACH2; ATF3; FOSL2
core promoter proximal region DNA binding (GO:0001159)	178	7	1.800E-03	ELF3; IRF1; BHLHE41; GATA3; KLF4; MXD1; ATF3
RNA polymerase II regulatory region DNA binding (GO:0001012)	288	9	1.939E-03	JUN; ELF3; IRF1; BHLHE41; GATA3; MXD1; ATF3; BACH2; FOSL2
RNA polymerase II transcription factor binding (GO:0001085)	90	5	1.994E-03	JUN; BHLHE40; ANKRD1; BHLHE41; KLF4
neutral amino acid transmembrane transporter activity (GO:0015175)	24	3	2.009E-03	SLC3A2; SLC1A4; SLC7A11
RNA polymerase II transcription regulatory region sequence-	202	7	3.565E-03	JUN; CEBPB; ELF3; GATA3; KLF4; ATF3; CREB5

specific DNA binding transcription factor activity involved in positive regulation of transcription (GO:0001228)				
RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity involved in positive regulation of transcription (GO:0001077)	151	6	3.632E-03	JUN; CEBPB; ELF3; GATA3; KLF4; CREB5
ligase regulator activity (GO:0055103)	8	2	3.753E-03	TRIB3; TRIB1
cytokine activity (GO:0005125)	213	7	4.716E-03	IL32; BMP2; CSF1; GDF15; CXCL2; AREG; CXCL5
core promoter binding (GO:0001047)	111	5	4.724E-03	KLF10; GADD45A; RORA; NR1D2; GATA3
growth factor activity (GO:0008083)	163	6	5.197E-03	BMP2; CSF1; GDF15; AREG; INHBE; EREG
core promoter sequence-specific DNA binding (GO:0001046)	71	4	5.400E-03	KLF10; RORA; NR1D2; GATA3
modified amino acid transmembrane transporter activity (GO:0072349)	10	2	5.437E-03	SLC1A4; SLC7A11
calcium-dependent phospholipid binding (GO:0005544)	36	3	5.785E-03	ANXA1; SYT11; ANXA3
RNA polymerase II activating transcription factor binding (GO:0001102)	36	3	5.785E-03	JUN; BHLHE40; BHLHE41
RNA polymerase II transcription factor binding transcription factor activity involved in positive regulation of transcription (GO:0001190)	40	3	7.602E-03	JUN; ANKRD1; KLF4
phosphoric ester hydrolase activity (GO:0042578)	360	9	7.999E-03	DUSP4; DUSP10; DUSP1; INPP5J; DUSP8; PTPRH; PPM1E; DUSP16; CDC14A
phospholipase inhibitor activity (GO:0004859)	13	2	8.492E-03	ANXA1; ANXA3
enhancer binding (GO:0035326)	83	4	9.076E-03	JUN; GATA3; AHR; BACH2
protein binding, bridging (GO:0030674)	134	5	9.995E-03	SOCS2; DAB2; ANXA1; SH3BP2; SH2D3C
transforming growth factor beta binding (GO:0050431)	16	2	1.215E-02	LTBP1; THBS1
direct ligand regulated sequence-specific DNA	50	3	1.349E-02	NR1D2; RORA; AHR

binding transcription factor activity (GO:0098531)				
SH3/SH2 adaptor activity (GO:0005070)	50	3	1.349E-02	SOCS2; SH3BP2; SH2D3C
ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879)	50	3	1.349E-02	NR1D2; RORA; AHR
binding, bridging (GO:0060090)	146	5	1.393E-02	SOCS2; DAB2; ANXA1; SH3BP2; SH2D3C
HMG box domain binding (GO:0071837)	18	2	1.490E-02	JUN; GATA3
14-3-3 protein binding (GO:0071889)	18	2	1.490E-02	DDIT4; IRS2
lipase inhibitor activity (GO:0055102)	18	2	1.490E-02	ANXA1; ANXA3
activating transcription factor binding (GO:0033613)	53	3	1.564E-02	JUN; BHLHE40; BHLHE41
protein kinase inhibitor activity (GO:0004860)	54	3	1.640E-02	CDKN2B; TRIB3; TRIB1
calcium-dependent protein binding (GO:0048306)	56	3	1.797E-02	ANXA1; ANXA3; S100P
kinase inhibitor activity (GO:0019210)	57	3	1.879E-02	CDKN2B; TRIB3; TRIB1
phosphatidylinositol 3-kinase binding (GO:0043548)	22	2	2.113E-02	PIK3IP1; IRS2
double-stranded DNA binding (GO:0003690)	109	4	2.182E-02	JUN; DDX60; KLF4; FOSL2
cytokine receptor binding (GO:0005126)	228	6	2.306E-02	SOCS2; CSF1; BAMBI; GATA3; CXCL2; CXCL5
RNA polymerase II core promoter proximal region sequence-specific DNA binding (GO:0000978)	167	5	2.309E-02	ELF3; IRF1; BHLHE41; MXD1; ATF3
dicarboxylic acid transmembrane transporter activity (GO:0005310)	24	2	2.458E-02	SLC1A4; SLC7A11
amino acid transmembrane transporter activity (GO:0015171)	66	3	2.708E-02	SLC3A2; SLC1A4; SLC7A11
signaling adaptor activity (GO:0035591)	67	3	2.811E-02	SOCS2; SH3BP2; SH2D3C
sulfur compound transmembrane transporter activity (GO:1901682)	26	2	2.824E-02	SLC1A4; SLC7A11
epidermal growth factor receptor binding (GO:0005154)	27	2	3.015E-02	AREG; EREG
bHLH transcription	27	2	3.015E-02	BHLHE40; BHLHE41

factor binding (GO:0043425)				
enhancer sequence-specific DNA binding (GO:0001158)	70	3	3.130E-02	JUN; GATA3; BACH2
magnesium ion binding (GO:0000287)	190	5	3.682E-02	ERN1; NUAK2; MTHFD2; S100P; GEM
histone deacetylase binding (GO:0042826)	75	3	3.702E-02	BHLHE41; ANKRD1; HDAC9
RNA polymerase II transcription factor binding transcription factor activity involved in negative regulation of transcription (GO:0001191)	33	2	4.261E-02	BHLHE40; BHLHE41
kinase regulator activity (GO:0019207)	141	4	4.779E-02	CDKN2B; TRIB3; KLF4; TRIB1

Supplementary Table 5. Enriched molecular functions for the down-regulated genes (FC ≤ - 2, P adj. value ≤ 0.001; 72 and 96 hpi)

GO molecular function	Genes in the function category	DEGs	P-value	Down-regulated genes that overlap the function category
calcium ion binding (GO:0005509)	698	3	4.891E-03	ACTN3; PCDH20; NID2
acyl-CoA dehydrogenase activity (GO:0003995)	15	1	8.747E-03	ACADSB
structural constituent of muscle (GO:0008307)	41	1	2.282E-02	ACTN3
oxidoreductase activity, acting on the CH-CH group of donors (GO:0016627)	56	1	3.086E-02	ACADSB
collagen binding (GO:0005518)	62	1	3.406E-02	NID2
amino acid transmembrane transporter activity (GO:0015171)	66	1	3.619E-02	SLC38A4
flavin adenine dinucleotide binding (GO:0050660)	74	1	4.044E-02	ACADSB