Supplementary Material

Suppressor of Cytokine Signaling 1 is Involved in Gene Regulation Which Controls the Survival of Ly6C^{low} Monocytes in Mice

Jutta Schuett[a] Julian Kreutz[a] Karsten Grote[a] Ann-Kathrin Vlacil[a]
Harald Schuett[a] Raghav Oberoi[a] Andreas Schmid[b] Anika Witten[c]
Monika Stoll[c,d] Bernhard Schieffer[a] Frank Rühle[c]

[a]Department of Cardiology and Angiology, Philipps-University Marburg, Marburg, Germany, [b]Department of Internal Medicine III, Giessen University Hospital, Giessen, Germany, [c]Department of Genetic Epidemiology, Institute of Human Genetics, University of Münster, Münster, Germany, [d]Department of Biochemistry, Genetic Epidemiology and Statistical Genetics, CARIM School for Cardiovascular Diseases, Maastricht Center for Systems Biology (MaCSBio), Maastricht University, Maastricht, The Netherlands

1 Supplementary Tables

Supplemental Table 1. Identification of 26 genes differentially expressed in Ly6C^{high} and Ly6C^{low} monocytes of RL$^{-/-}$ vs. L$^{-/-}$ mice.

Symbol	**FC**	**Regulation**	**p-value (adj)**	**Description**
Atp10d	0.44	-2.27	$3.8 * 10^{-32}$	ATPase, Class V, type 10D (Atp10d)
BC018473	0.48	-2.07	$2.7 * 10^{-6}$	
BC056474	2.12	2.12	$4.3 * 10^{-7}$	
Cap1	8.28	8.28	$1.7 * 10^{-34}$	adenylate cyclase-associated protein 1
E430014K09 Rik	0.32	-3.15	$1.5 * 10^{-4}$	
Faim3	0.41	-2.45	$2.7 * 10^{-4}$	Fas apoptotic inhibitory molecule 3
Fcer1g	0.43	-2.35	$9.3 * 10^{-3}$	
Fgr	0.43	-2.34	$1.0 * 10^{-3}$	
Gpr114	0.16	-6.10	$8.9 * 10^{-10}$	G protein-coupled receptor 114
H28	0.48	-2.09	$1.0 * 10^{-15}$	histocompatibility 28
Hsp105	0.41	-2.42	$1.6 * 10^{-7}$	
Igh-VJ558	0.03	-31.66	$4.5 * 10^{-2}$	immunoglobulin heavy chain (J558 family)
Igk-C	0.04	-27.48	$1.4 * 10^{-2}$	
IGLC2_J00595_Ig_lambda_constant_2_14	0.40	-2.50	$1.3 * 10^{-2}$	
Igl-V1	0.05	-21.97	$3.0 * 10^{-2}$	
Lgals3bp	2.07	2.07	$1.8 * 10^{-10}$	lectin, galactoside-binding, soluble, 3 binding protein
LOC675899	0.46	-2.17	$7.5 * 10^{-9}$	similar to H2A histone family, member Z
Lrrc57	0.33	-3.03	$2.6 * 10^{-34}$	leucine rich repeat containing 57
Ly6a	2.52	2.52	$2.2 * 10^{-2}$	lymphocyte antigen 6 complex, locus A
Mela	2.45	2.45	$2.3 * 10^{-3}$	
Myl4	0.38	-2.62	$2.8 * 10^{-5}$	myosin, light polypeptide 4
Plcb2	0.41	-2.46	$1.3 * 10^{-2}$	
Prdx2	2.06	2.06	$1.5 * 10^{-24}$	peroxiredoxin 2
Tmem87a	3.29	3.29	$1.7 * 10^{-34}$	transmembrane protein 87A
Xdh	2.45	2.45	$1.7 * 10^{-34}$	xanthine dehydrogenase
Zfp330	2.51	2.51	$5.2 * 10^{-18}$	zinc finger protein 330

Supplemental Table 2. Identification of 166 genes differentially expressed in Ly6C^{high} and Ly6C^{low} monocytes of SRL$^{-/-}$ vs. L$^{-/-}$ mice.

Symbol	**FC**	**Regulation**	**p-value (adj)**	**Description**
0610037M15Rik	2.26	2.26	$1.0 * 10^{-2}$	
1200016G03Rik	0.46	-2.17	$1.0 * 10^{-2}$	
1810009N02Rik	0.49	-2.02	$2.5 * 10^{-4}$	RIKEN cDNA 1810009N02 gene
2010001M09Rik	0.46	-2.18	$3.0 * 10^{-4}$	RIKEN cDNA 2010001M09 gene
2610024M03Rik	2.47	2.47	$2.7 * 10^{-4}$	
5033414K04Rik	0.36	-2.77	$3.6 * 10^{-20}$	RIKEN cDNA 5033414K04 gene
5830411K21Rik	0.47	-2.12	$1.8 * 10^{-5}$	
Abca9	0.33	-3.06	$6.8 * 10^{-18}$	ATP-binding cassette transporter sub-family A member 9
Abi3	0.33	-3.04	$3.7 * 10^{-2}$	
Acss1	0.28	-3.55	$5.5 * 10^{-4}$	acyl-CoA synthetase short-chain family member 1
Agpat4	0.28	-3.60	$1.6 * 10^{-2}$	1-acylglycerol-3-phosphate O-acyltransferase 4 (lysophosphatidic acid acyltransferase, delta)
AI451557	2.90	2.90	$8.0 * 10^{-5}$	Mus musculus expressed sequence AI451557
Apoe	0.11	-9.05	$6.6 * 10^{-4}$	apolipoprotein E
Arrdc3	0.46	-2.15	$8.0 * 10^{-4}$	
Atp10d	0.32	-3.10	$1.5 * 10^{-34}$	ATPase, Class V, type 10D
Axl	0.46	-2.16	$1.6 * 10^{-2}$	
Bach2	0.43	-2.33	$9.7 * 10^{-4}$	BTB and CNC homology 2
Batf2	2.72	2.72	$2.4 * 10^{-2}$	basic leucine zipper transcription factor, ATF-like 2
BC018473	0.33	-3.05	$4.7 * 10^{-20}$	Mus musculus cDNA sequence BC018473
BC031353	0.42	-2.40	$1.1 * 10^{-2}$	Mus musculus cDNA sequence BC031353
BC056474	2.14	2.14	$7.4 * 10^{-5}$	Mus musculus cDNA sequence BC056474
Bcl2a1b	0.25	-3.93	$4.9 * 10^{-2}$	B-cell leukemia/lymphoma 2 related protein A1b
Bcl2a1d	0.28	-3.59	$4.8 * 10^{-2}$	
Bcl6	0.48	-2.07	$3.0 * 10^{-2}$	B-cell leukemia/lymphoma 6
Cap1	8.26	8.26	$9.3 * 10^{-35}$	adenylate cyclase-associated protein 1
Ccdc86	2.37	2.37	$2.3 * 10^{-11}$	coiled-coil domain containing 86
Cd209a	0.32	-3.09	$2.1 * 10^{-2}$	CD209a antigen
Cd300lf	2.28	2.28	$9.8 * 10^{-3}$	CD300 antigen like family member F
Cd72	0.42	-2.40	$1.2 * 10^{-2}$	CD72 antigen
Cd79b	0.43	-2.33	$1.3 * 10^{-10}$	CD79B antigen
Cd83	0.28	-3.60	$3.0 * 10^{-2}$	CD83 antigen

Cdc20	2.04	2.04	$5.2 * 10^{-7}$	cell division cycle 20 homolog
Cdkn3	2.08	2.08	$3.8 * 10^{-5}$	cyclin-dependent kinase inhibitor 3
Cfl1	2.32	2.32	$2.7 * 10^{-5}$	cofilin 1
Ckb	0.24	-4.25	$4.7 * 10^{-7}$	creatine kinase
Clec2i	0.43	-2.30	$6.2 * 10^{-14}$	C-type lectin domain family 2, member i
Clec4a1	0.46	-2.19	$1.0 * 10^{-4}$	C-type lectin domain family 4, member a1
Clec4a3	0.40	-2.49	$3.2 * 10^{-5}$	C-type lectin domain family 4, member a3
Csf1r	0.39	-2.57	$8.0 * 10^{-4}$	colony stimulating factor 1 receptor
Csprs	2.22	2.22	$9.5 * 10^{-13}$	component of Sp100-rs
Cx3cr1	0.11	-8.73	$2.5 * 10^{-18}$	
Cyp27a1	0.45	-2.23	$5.8 * 10^{-15}$	cytochrome P450, family 27, subfamily a, polypeptide 1
D12Ertd553e	0.47	-2.11	$1.5 * 10^{-4}$	DNA segment, Chr 12, ERATO Doi 553, expressed
D15Wsu169e	0.46	-2.19	$5.2 * 10^{-6}$	DNA segment, Chr 15, Wayne State University 169, expressed
D230048P18Rik	0.44	-2.30	$1.6 * 10^{-4}$	
D930028F11Rik	0.30	-3.29	$4.7 * 10^{-11}$	RIKEN cDNA D930028F11 gene
Dgat2	3.19	3.19	$4.5 * 10^{-2}$	diacylglycerol O-acyltransferase 2
Dleu2	0.38	-2.61	$1.2 * 10^{-14}$	
Dusp1	0.48	-2.07	$2.0 * 10^{-3}$	dual specificity phosphatase 1
Dusp6	0.50	-2.00	$1.7 * 10^{-5}$	dual specificity phosphatase 6
E030027L17	0.48	-2.10	$1.9 * 10^{-5}$	
E430014K09Rik	0.04	-23.70	$1.4 * 10^{-30}$	
Ear10	0.30	-3.36	$3.5 * 10^{-2}$	eosinophil-associated, ribonuclease A family, member 10
Ear12	0.30	-3.39	$3.4 * 10^{-2}$	eosinophil-associated, ribonuclease A family, member 12
Edg8	0.24	-4.12	$1.5 * 10^{-2}$	endothelial differentiation, sphingolipid G-protein-coupled receptor, 8
EG328314	0.44	-2.25	$1.8 * 10^{-3}$	Mus musculus predicted gene, EG328314
EG622339	2.01	2.01	$1.5 * 10^{-13}$	Mus musculus predicted gene, EG622339
Ehd4	0.38	-2.62	$6.1 * 10^{-11}$	
Eif2ak2	2.19	2.19	$1.0 * 10^{-6}$	eukaryotic translation initiation factor 2-alpha kinase 2
Emr1	0.35	-2.85	$4.7 * 10^{-5}$	EGF-like module containing, mucin-like, hormone receptor-like sequence 1
Eno3	0.14	-7.36	$4.9 * 10^{-2}$	enolase 3
Faim3	0.39	-2.55	$2.5 * 10^{-5}$	Fas apoptotic inhibitory molecule 3
Fcer1g	0.36	-2.81	$1.5 * 10^{-4}$	
Fcgr1	2.82	2.82	$3.8 * 10^{-2}$	Fc receptor, IgG, high affinity I
Fcgrt	0.27	-3.72	$9.7 * 10^{-5}$	Fc receptor, IgG, alpha chain transporter

Fcrla	0.47	-2.13	$1.8 * 10^{-5}$	Fc receptor-like A
Fkbp5	2.49	2.49	$2.0 * 10^{-5}$	FK506 binding protein 5
Flot2	2.05	2.05	$3.3 * 10^{-6}$	flotillin 2
Fosb	0.42	-2.35	$8.1 * 10^{-3}$	FBJ osteosarcoma oncogene B
G6pdx	2.13	2.13	$2.9 * 10^{-2}$	glucose-6-phosphate dehydrogenase X-linked
Gbp2	6.96	6.96	$3.3 * 10-^{2}$	guanylate binding protein 2
Gbp3	2.43	2.43	$4.7 * 10^{-2}$	guanylate nucleotide binding protein 3
Gbp6	2.27	2.27	$4.6 * 10^{-4}$	guanylate binding protein 6
Gngt2	0.33	-3.00	$1.4 * 10^{-2}$	guanine nucleotide binding protein, gamma transducing activity polypeptide
Gpr114	0.48	-2.08	$5.7 * 10^{-3}$	G protein-coupled receptor 114
Gpr18	0.42	-2.37	$4.9 * 10^{-5}$	G protein-coupled receptor 18
H28	0.48	-2.07	$9.5 * 10^{-16}$	histocompatibility 28
H2-Q6	2.05	2.05	$3.1 * 10^{-2}$	histocompatibility 2, Q region locus 6
H2-Q8	2.50	2.50	$1.6 * 10^{-3}$	
H2-T10	2.22	2.22	$3.3 * 10^{-18}$	histocompatibility 2, T region locus 10
Hfe	0.23	-4.32	$5.0 * 10^{-3}$	hemochromatosis
HIP-1	0.41	-2.46	$9.1 * 10^{-4}$	
Hsp105	0.32	-3.08	$9.2 * 10^{-10}$	
Hspa1a	0.23	-4.33	$1.9 * 10^{-3}$	
Hspa1b	0.29	-3.47	$5.9 * 10^{-3}$	heat shock protein 1B
Ifi202b	2.08	2.08	$4.7 * 10^{-2}$	interferon activated gene 202B
Ifi47	2.70	2.70	$2.9 * 10^{-2}$	interferon gamma inducible protein 47
Igh-6	0.40	-2.49	$8.2 * 10^{-3}$	
Igh-VJ558	0.02	-42.33	$9.8 * 10^{-3}$	immunoglobulin heavy chain (J558 family)
Igk-C	0.02	-48.96	$2.1 * 10^{-3}$	
IGLC2_J00595_Ig_lambda_constant_2_14	0.39	-2.55	$1.9 * 10^{-3}$	
Igl-V1	0.04	-24.23	$6.0 * 10^{-3}$	
Igtp	4.30	4.30	$8.1 * 10^{-4}$	interferon gamma induced GTPase
Iigp2	3.23	3.23	$1.1 * 10^{-4}$	interferon inducible GTPase 2
Il10ra	0.39	-2.58	$6.7 * 10^{-4}$	interleukin 10 receptor, alpha
Il1r2	3.90	3.90	$1.0 * 10^{-4}$	interleukin 1 receptor, type II
Il31ra	0.45	-2.22	$1.8 * 10^{-2}$	interleukin 31 receptor A
Il4i1	0.38	-2.65	$1.1 * 10^{-2}$	interleukin 4 induced 1
Inppl1	0.49	-2.04	$1.6 * 10^{-6}$	inositol polyphosphate phosphatase-like 1
Irf4	0.46	-2.18	$2.7 * 10^{-5}$	interferon regulatory factor 4
Irgb10	2.55	2.55	$3.9 * 10^{-3}$	interferon-gamma-inducible p47 GTPase
Itgb5	0.30	-3.33	$2.8 * 10^{-4}$	integrin beta 5
Lbp	2.53	2.53	$4.3 * 10^{-2}$	lipopolysaccharide binding protein
Lgals3bp	2.04	2.04	$3.8 * 10^{-4}$	lectin, galactoside-binding, soluble, 3 binding

				protein
LOC100038882	2.64	2.64	$1.3 * 10^{-4}$	hypothetical protein LOC100038882
LOC100043257	2.26	2.26	$4.0 * 10^{-13}$	similar to RNA binding motif protein 3
LOC100044190	2.14	2.14	$1.0 * 10^{-3}$	hypothetical protein LOC100044190
LOC100044376	0.43	-2.32	$1.2 * 10^{-10}$	similar to Dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2
LOC100045280	2.14	2.14	$1.6 * 10^{-4}$	similar to mKIAA1021 protein
LOC100045780	0.50	-2.00	$1.4 * 10^{-5}$	similar to metalloprotease-disintegrin meltrin beta
LOC100046741	2.65	2.65	$9.3 * 10^{-35}$	similar to red-1
LOC100047628	0.05	-22.11	$4.3 * 10^{-2}$	similar to Chain L, Structural Basis Of Antigen Mimicry In A Clinically Relevant Melanoma Antigen System
LOC435565	2.02	2.02	$4.3 * 10^{-2}$	similar to interferon-inducible GTPase
LOC624610	0.42	-2.40	$1.3 * 10^{-2}$	hypothetical protein LOC624610
LOC630729	2.66	2.66	$7.3 * 10^{-6}$	similar to glutathione reductase 1
LOC638935	0.38	-2.66	$9.4 * 10^{-13}$	similar to peptidylarginine deiminase, type II
LOC669658	2.36	2.36	$2.4 *10^{-2}$	similar to melanoma antigen
LOC676389	0.46	-2.20	$5.8 * 10^{-4}$	similar to Baculoviral IAP repeat-containing protein 1e (Neuronal apoptosis inhibitory protein 5)
Lrrc57	0.32	-3.12	$1.5 * 10^{-34}$	leucine rich repeat containing 57
Ly6c1	2.02	2.02	$1.1 * 10^{-2}$	lymphocyte antigen 6 complex, locus C1
Lyz1	0.44	-2.30	$1.1 * 10^{-5}$	lysozyme 1
Mfng	0.50	-2.01	$1.2 * 10^{-5}$	MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
Mgst2	2.98	2.98	$2.0 * 10^{-2}$	microsomal glutathione S-transferase 2
Mrc1	0.38	-2.65	$8.8 * 10^{-3}$	mannose receptor, C type 1
Mt1	2.15	2.15	$1.0 * 10^{-2}$	metallothionein 1
Myl4	0.37	-2.71	$2.6 * 10^{-6}$	myosin, light polypeptide 4
Naip5	0.49	-2.06	$5.3 * 10^{-3}$	NLR family, apoptosis inhibitory protein 5
Nav1	0.26	-3.88	$3.5 * 10^{-10}$	neuron navigator 1
Oas1g	2.17	2.17	$2.0 * 10^{-4}$	2'-5' oligoadenylate synthetase 1G
Oas2	3.08	3.08	$3.3 * 10^{-3}$	2'-5' oligoadenylate synthetase 2
Oas3	2.18	2.18	$7.9 * 10^{-3}$	2'-5' oligoadenylate synthetase 3
Oasl2	3.54	3.54	$7.8 * 10^{-4}$	2'-5' oligoadenylate synthetase-like 2
P2ry13	2.04	2.04	$1.9 * 10^{-8}$	purinergic receptor P2Y, G-protein coupled 13
P2ry6	0.33	-3.02	$1.8 * 10^{-25}$	pyrimidinergic receptor P2Y, G-protein coupled, 6
Parp12	2.10	2.10	$8.3 * 10^{-9}$	poly (ADP-ribose) polymerase family, member 12

Parvg	2.44	2.44	$7.2 * 10^{-3}$	parvin, gamma
Plcb2	0.37	-2.69	$3.7 * 10^{-3}$	
Plscr1	3.00	3.00	$1.7 * 10^{-2}$	phospholipid scramblase 1
Pou2af1	0.39	-2.59	$5.3 * 10^{-9}$	POU domain, class 2, associating factor 1
Pou2f2	0.40	-2.48	$4.1 * 10^{-3}$	POU domain, class 2, transcription factor
Ppp2cb	2.45	2.45	$1.4 * 10^{-8}$	protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform
Prnp	2.33	2.33	$8.9 * 10^{-5}$	prion protein
Psmb9	2.17	2.17	$4.5 * 10^{-10}$	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional peptidase 2)
Rbpms	0.42	-2.36	$7.2 * 10^{-4}$	RNA binding protein gene with multiple splicing
Rgs2	0.50	-2.01	$3.7 * 10^{-6}$	
Rras	0.43	-2.30	$1.2 * 10^{-12}$	Harvey rat sarcoma oncogene, subgroup R
Sh2d1b1	0.33	-3.00	$8.9 * 10^{-3}$	SH2 domain protein 1B1
Slc46a3	0.23	-4.34	$1.1 * 10^{-6}$	solute carrier family 46, member 3
Slfn1	2.23	2.23	$1.4 * 10^{-4}$	schlafen 1
St6galnac2	0.31	-3.25	$3.1 * 10^{-5}$	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1, 3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2
Tap1	3.27	3.27	$4.3 * 10^{-12}$	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
Tbc1d2	2.02	2.02	$5.2 * 10^{-3}$	TBC1 domain family, member 2
Thbd	0.42	-2.36	$4.8 * 10^{-4}$	thrombomodulin
Tmem176b	0.42	-2.40	$3.9 * 10^{-4}$	transmembrane protein 176B
Tmem51	0.34	-2.91	$4.3 * 10^{-6}$	transmembrane protein 51
Tmem68	0.48	-2.07	$4.4 * 10^{-27}$	transmembrane protein 68
Tmem87a	3.50	3.50	$9.3 * 10^{-35}$	transmembrane protein 87A
Trf	0.31	-3.28	$1.6 * 10^{-13}$	transferrin
Tubb6	0.41	-2.45	$5.2 * 10^{-3}$	tubulin, beta 6
Tyki	2.50	2.50	$3.3 * 10^{-3}$	
Upp1	2.71	2.71	$3.8 * 10^{-2}$	uridine phosphorylase 1
Usp18	2.00	2.00	$3.9 * 10^{-3}$	ubiquitin specific peptidase 18
Vpreb3	0.37	-2.72	$2.4 * 10^{-5}$	pre-B lymphocyte gene 3
Xdh	2.76	2.76	$8.5 * 10^{-6}$	xanthine dehydrogenase
Zeb2	0.48	-2.09	$1.4 * 10^{-2}$	zinc finger E-box binding homeobox 2
Zfp330	2.36	2.36	$9.9 * 10^{-7}$	zinc finger protein 330

Supplemental Table 3. Gene enrichment analysis of genes differentially expressed in SRL$^{-/-}$ vs. RL$^{-/-}$ mice.

ID	**Pathway / GO term**	**p-value**	**p(adj)**	**Input genes**
GO:0016020	membrane	$2.3*10^{-3}$	0.184	Tmem176b, Edg8, Fkbp5, Agpat4, Iigp2, Apoe, Fcgrt, Abca9, Itgb5, Cfl1, P2ry6, Tmem51, Il1r2, Emr1, Cx3cr1, Slc46a3, Abi3, Gngt2, Cyp27a1, Csf1r, Hfe, Il10ra, Igtp, Mrc1, Trf
GO:0003924	GTPase activity	0.009	0.642	Iigp2, Gngt2, Igtp, Tubb6
GO:1990712	HFE-transferrin receptor complex	0.012	0.431	Hfe, Trf
GO:0071281	cellular response to iron ion	0.014	0.988	Hfe, Trf
GO:0044794	positive regulation by host of viral process	0.014	0.988	Apoe, Cfl1
GO:1990459	transferrin receptor binding	0.016	0.607	Hfe, Trf
GO:0031232	extrinsic component of external side of plasma membrane	0.017	0.394	Apoe, Trf
GO:0070062	extracellular exosome	0.018	0.340	Nxpe4, Ppp2cb, Fkbp5, Ckb, Apoe, Slc46a3, Hpgd, Igl-5, Tubb6, Itgb5, Cfl1, Trf
GO:0003823	antigen binding	0.018	0.503	Fcgrt, Igl-5, Hfe
GO:0030881	beta-2-microglobulin binding	0.027	0.532	Fcgrt, Hfe
GO:0007263	nitric oxide mediated signal transduction	0.029	0.991	Mt1, Apoe
GO:0072562	blood microparticle	0.031	0.436	Apoe, Igl-5, Trf
GO:2000147	positive regulation of cell motility	0.033	0.972	Csf1r, Trf
GO:0045178	basal part of cell	0.035	0.413	Hfe, Trf
mmu04060	Cytokine-cytokine receptor interaction	0.039	0.931	Il1r2, Cx3cr1, Csf1r, Il10ra
GO:0009986	cell surface	0.041	0.419	Apoe, Csf1r, Mrc1, Itgb5, Trf
GO:0048260	positive regulation of receptor-mediated endocytosis	0.043	0.969	Hfe, Trf
GO:0004871	signal transducer activity	0.043	0.633	Emr1, Edg8, Cx3cr1, Gngt2, P2ry6

Supplemental Table 4. Gene enrichment analysis of genes belonging to the yellow co-expression module obtained from WGCNA (top 25 terms).

ID	**Pathway / GO term**	**p-value**	**p-value (adj)**
GO:0005737	cytoplasm	3.1E-14	1.9E-11
GO:0006355	regulation of transcription, DNA-templated	3.8E-13	1.5E-09
GO:0005515	protein binding	4.8E-12	5.4E-09
GO:0006351	transcription, DNA-templated	1.3E-10	2.6E-07
GO:0005634	nucleus	3.6E-09	1.1E-06
GO:0016020	membrane	5.9E-07	1.2E-04
GO:0043065	positive regulation of apoptotic process	1.5E-07	1.5E-04
GO:0045893	positive regulation of transcription, DNA-templated	1.3E-07	1.7E-04
GO:0000166	nucleotide binding	4.3E-07	2.4E-04
GO:0005654	nucleoplasm	3.0E-06	4.6E-04
GO:0005524	ATP binding	2.1E-06	8.0E-04
GO:0000122	negative regulation of transcription from RNA polymerase II promoter	1.0E-06	8.2E-04
GO:0016740	transferase activity	4.1E-06	9.3E-04
GO:0046872	metal ion binding	5.3E-06	1.0E-03
GO:0016301	kinase activity	3.6E-06	1.0E-03
GO:0004672	protein kinase activity	6.4E-06	1.0E-03
GO:0003700	transcription factor activity, sequence-specific DNA binding	1.2E-05	1.7E-03
GO:0006915	apoptotic process	3.4E-06	2.3E-03
GO:0016310	phosphorylation	4.9E-06	2.8E-03
GO:0005829	cytosol	2.9E-05	3.6E-03
mmu04380	Osteoclast differentiation	1.5E-05	3.8E-03
mmu04010	MAPK signaling pathway	3.1E-05	4.0E-03
GO:0003677	DNA binding	3.5E-05	4.4E-03
GO:0006468	protein phosphorylation	9.7E-06	4.8E-03
GO:0007264	small GTPase mediated signal transduction	1.1E-05	5.0E-03

Supplemental Table 5. Gene enrichment analysis of genes belonging to the black co-expression module obtained from WGCNA (top 25 terms).

ID	**Pathway / GO term**	**p-value**	**p-value (adj)**
GO:0009897	external side of plasma membrane	1.7E-10	5.0E-08
mmu04064	NF-kappa B signaling pathway	4.9E-08	1.0E-05
GO:0042102	positive regulation of T cell proliferation	6.2E-08	1.3E-04
mmu05152	Tuberculosis	1.8E-06	1.9E-04
mmu04650	Natural killer cell mediated cytotoxicity	6.5E-06	3.4E-04
mmu04662	B cell receptor signaling pathway	8.6E-06	3.6E-04
mmu04660	T cell receptor signaling pathway	5.9E-06	4.1E-04
GO:0030246	carbohydrate binding	1.1E-06	5.8E-04
mmu05020	Prion diseases	3.3E-05	1.1E-03
mmu05212	Pancreatic cancer	3.8E-05	1.1E-03
GO:0050852	T cell receptor signaling pathway	1.3E-06	1.4E-03
mmu04510	Focal adhesion	5.7E-05	1.5E-03
mmu05202	Transcriptional misregulation in cancer	1.1E-04	2.4E-03
GO:0009986	cell surface	1.7E-05	2.5E-03
mmu05142	Chagas disease (American trypanosomiasis)	1.9E-04	3.6E-03
mmu04380	Osteoclast differentiation	1.9E-04	3.9E-03
mmu05210	Colorectal cancer	2.5E-04	4.4E-03
mmu05200	Pathways in cancer	3.0E-04	4.8E-03
mmu04060	Cytokine-cytokine receptor interaction	3.4E-04	5.1E-03
mmu05166	HTLV-I infection	3.9E-04	5.4E-03
mmu04062	Chemokine signaling pathway	4.9E-04	6.4E-03
GO:0050728	negative regulation of inflammatory response	9.8E-06	7.1E-03
mmu04014	Ras signaling pathway	5.9E-04	7.3E-03
GO:0031234	extrinsic component of cytoplasmic side of plasma membrane	8.5E-05	8.3E-03
GO:0070062	extracellular exosome	2.1E-04	1.5E-02

Supplemental Table 6. Gene enrichment analysis of genes belonging to the blue co-expression module obtained from WGCNA (top 25 terms).

ID	**Pathway / GO term**	**p-value**	**p-value (adj)**
GO:0016020	membrane	5.47E-26	3.54E-23
GO:0005737	cytoplasm	8.92E-18	2.89E-15
GO:0005515	protein binding	3.22E-13	4.15E-10
GO:0016301	kinase activity	5.19E-11	3.34E-08
GO:0005794	Golgi apparatus	5.86E-10	1.27E-07
GO:0035556	intracellular signal transduction	1.43E-10	3.06E-07
GO:0016310	phosphorylation	1.42E-10	6.06E-07
GO:0006468	protein phosphorylation	2.03E-09	2.89E-06
GO:0046872	metal ion binding	9.01E-09	2.90E-06
GO:0016740	transferase activity	6.78E-09	2.91E-06
GO:0004672	protein kinase activity	1.63E-08	4.20E-06
GO:0009897	external side of plasma membrane	2.84E-08	4.60E-06
GO:0002376	immune system process	7.00E-09	7.48E-06
GO:0004674	protein serine/threonine kinase activity	4.34E-08	9.32E-06
mmu05140	Leishmaniasis	4.33E-07	3.84E-05
GO:0006915	apoptotic process	6.09E-08	5.20E-05
mmu04010	MAPK signaling pathway	3.98E-07	5.29E-05
GO:0005829	cytosol	7.21E-07	6.68E-05
GO:0005886	plasma membrane	6.54E-07	7.06E-05
mmu04670	Leukocyte transendothelial migration	3.06E-07	8.13E-05
GO:0031410	cytoplasmic vesicle	6.37E-07	8.26E-05
GO:0008270	zinc ion binding	5.15E-07	9.47E-05
GO:0005096	GTPase activator activity	1.44E-06	2.32E-04
GO:0070062	extracellular exosome	3.36E-06	2.72E-04