Supporting Information

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SI Materials and Methods

***C. elegans* RNAi Screen.** The RNAi screen of the genes on Chromosome 1 was initially carried out once; RNAi clones that affected *clect-85*::*gfp* expression were then retested in duplicate. RNAi clones that had an effect 3/3 times were considered positive. The 192 gene RNAi candidate gene library was initially screened in triplicate. Genes that affected *clec-85*::*gfp* expression were then reassayed at least three more times. Any RNAi treatment that inhibited *clec-85*::*gfp* expression in at least half of the experiments determined by manually examining overlay plots was considered a candidate positive; this was verified by automated mean fluorescence measurements in all replicates. The negative control RNAi clone used in the library was from (1). Positive RNAi clones were sequenced to verify the identity of the dsRNA plasmid; clone sequences that differed from the predicted sequence are noted in Tables S1and S3.

RNAi clones that induced lethality or arrested nematode development were not included as positives in the analysis. These RNAi treatments were recognized because they decreased both fluorescence and nematode size. RNAi was also repeated on solid media to verify that candidate positive clones did not affect viability and did not induce other obvious visible morphological defects (in these RNAi experiments, inhibition of *mat-1* and *vab-10* on solid media did induce lethality; data not shown). Twenty ribosomal genes on Chromosome 1 were inhibited by RNAi in our assay; all these genes are reported to induce growth defects or lethality (www.wormbase.org.). None of these twenty genes passed our viability screening, consistent with the view that we are successfully censoring genes that are required for viability. Two ribosomal proteins, *rps-27* and *rpl-22* (orthologs of *Drosophila* genes that regulate the fly innate immune response), were recovered in our candidate gene RNAi screen (Table S3). These genes could affect antimicrobial production either indirectly, because they are generally required for translation, or directly, because they are direct stress response regulators. Expression of *rpl-22* and *rps-27* is increased in the stress resistant *daf-2* mutant background, suggesting that these genes could have a specific stress response function and an essential ribosomal function (2).

1. Dillin A, Crawford DK, Kenyon C (2002) Timing requirements for insulin/IGF-1 signaling in *C. elegans*. *Science* 298:830–834.
2. Halaschek-Wiener J, *et al.* (2005) Analysis of long-lived *C. elegans* daf-2 mutants using serial analysis of gene expression. *Genome Res* 15:603–615.

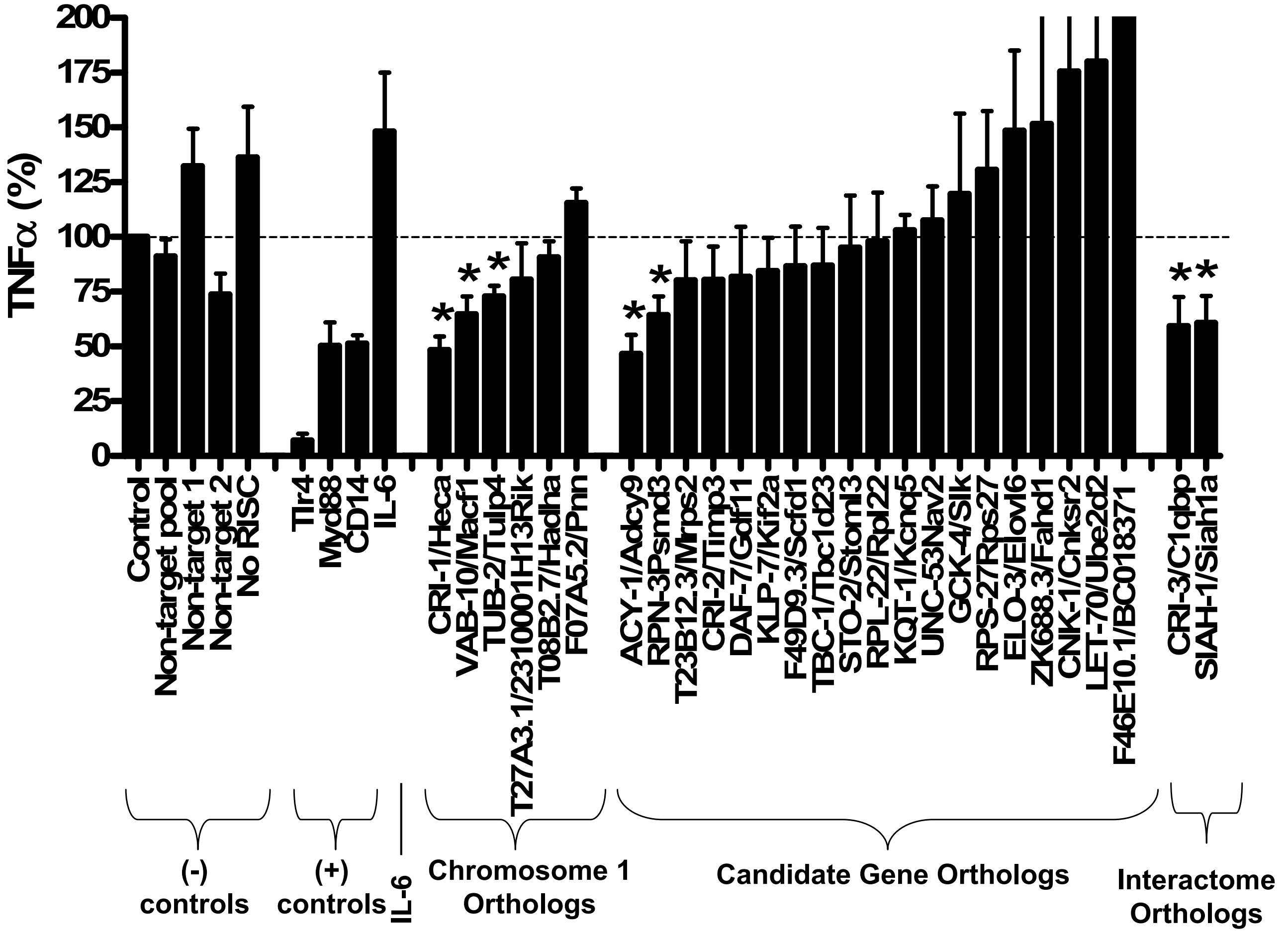

Fig. S1. Orthologs of *C. elegans* candidate innate immunity genes regulate TNF-α production in mammals. The indicated siRNA pools were transfected into a mouse macrophage cell line, the cells were induced with *E. coli* LPS, and TNF-α production was measured. Cytokine production was normalized relative to a negative control siRNA and cell number as described in *Materials and Methods*, and is graphed as percentage of control TNF-α production. Depicted from left to right are five negative controls, three positive controls (Tlr4, Myd88, and CD14), IL-6 siRNA (which should not affect TNF-α), and 27 test genes orthologous to genes that affect antimicrobial production in *C. elegans*. TNF-α values that were significantly less than wild type in the test siRNAs ($P < 0.05$, *t* test) are indicated with an asterisk.

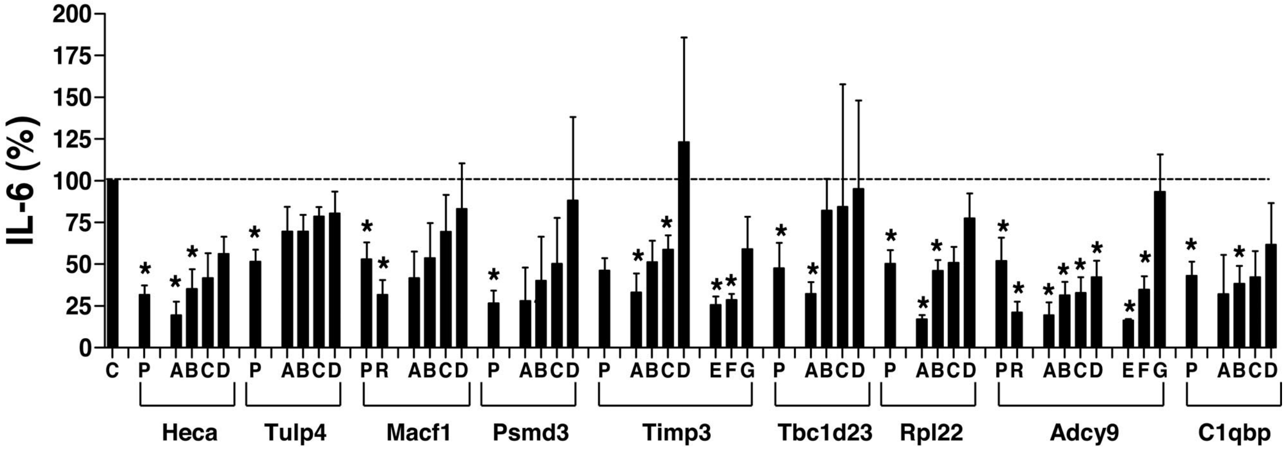

Fig. S2. Use of multiple siRNAs to verify the specificity of the induced cytokine phenotypes. The mouse macrophage cell line J77A4.1 was treated with the indicated siRNAs and subsequent LPS-induced IL-6 production was measured and normalized as described in *Materials and Methods* and is graphed as percentage of control IL-6 production. To verify that the siRNA-induced phenotypes described in Fig. 3 were due to specific gene inhibition and not an ''off target'' siRNA effect, we subsequently transfected multiple individual siRNAs for each candidate positive gene. P refers to the original test Dharmacon siRNA pool of four siRNA duplexess/gene. A–D are the four individual siRNAs present in those pools; R refers to an independently generated pool of four siRNAs that targets a particular gene; and E–G refer to 27-mer siRNAs [Kim DH, *et al.* (2005) Synthetic dsRNA Dicer substrates enhance RNAi potency and efficacy. *Nat Biotechnol* 23:222–226] designed to target two of the genes. Because at least two, and usually many, individual siRNAs that target these genes induce a similar IL-6 phenotype, we conclude that the siRNA effect is specific and these genes are regulating cytokine production. IL-6 values that were significantly different from wild type in the test siRNAs ($P < 0.05$, *t* test) are indicated with an asterisk.

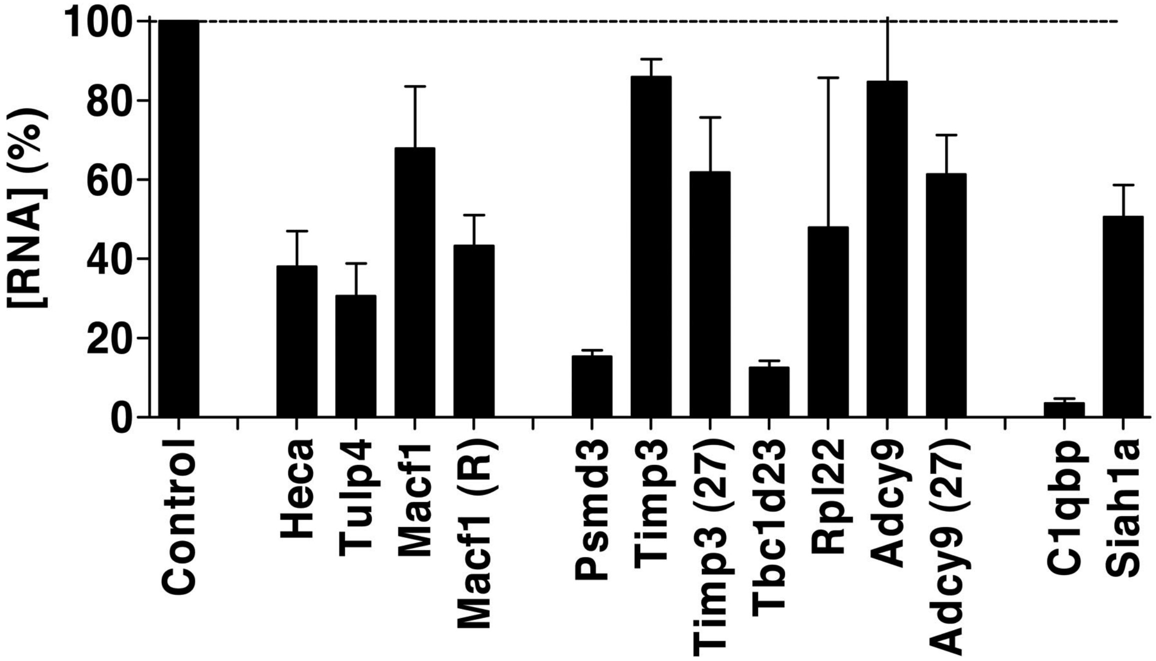

Fig. S3. RNA knockdown in siRNA experiments. Cells were treated with the indicated siRNAs, and expression of the corresponding cellular mRNAs was monitored by qPCR, using actin RNA as a normalization control. R refers to a second siRNA pool tested for that gene; 27 indicates a 27mer siRNA directed against that gene. The data are from three independent biological replicates.

Table S1. Genes on chromosome 1 that affect expression of clec-85::gfp

Clone	Gene	Gene description	GFP, %	*P*
C07F11.2			36	0.05
C27A12.6		Predicted E3 ubiquitin ligase	49	<0.05
C36B1.10	*gska-3*	Glycogen synthase kinase-3	68	0.24
C41D11.7*		DNA helicase	18	<0.05
C46H11.7		Secreted surface protein; conatins Metridin-like ShK toxin domain	52	<0.05
F07A5.2		none	65	<0.05
F14D2.9*		Alternative splicing factor	47	<0.05
F15H9.2*	*sri-15*	predicted olfactory GPCR34	48	<0.05
F23C8.11		Small secreted protein with conserved cysteines	29	<0.05
F25D7.2	*tag-353*	Membrane-associated ER protein involved in stress response (contains ubiquitin-like domain)	43	<0.05
F30F8.4		transposon	48	<0.05
F32B5.6			34	0.07
F56C11.2	*ptr-11*	Predicted membrane protein (patched superfamily)	37	0.05
F56C11.6		Carboxylesterase and related proteins	44	<0.05
K07A1.7	*cri-1*	Cell differentiation regulator of the Headcase family	62	0.11
K09H9.3	*col-49*	Collagens (type IV and type XIII), and related proteins	43	<0.05
M01A12.2		former gene	45	<0.05
M01D7.5	*nlp-12*	encodes two predicted neuropeptide-like proteins	46	<0.05
M04C9.4		Small secreted protein with conserved cysteines	40	<0.05
T08B2.7		Hydroxyacyl-CoA dehydrogenase/enoyl-CoA hydratase	46	<0.05
T23G11.3	*gld-1*	RNA-binding protein Sam68 and related KH domain proteins	48	<0.05
T27A3.1		Uncharacterized coiled coil protein	48	<0.05
T27A3.3	*ssp-16*	Uncharacterized protein, contains major sperm protein (MSP) domain	50	<0.05
T27A3.5		tyr phosphatase domain/dual specificity phosphatase	48	<0.05
Y106G6E.1		Glycogen synthase kinase-3	45	<0.05
Y106G6E.2			49	<0.05
Y110A7A.17	*mat-1*	DNA-binding cell division cycle control protein	39	<0.05
Y48G1C.1		contains similarity to Saccharomyces cerevisiae B-type cyclin	58	<0.05
Y71G12A.3	*tub-2/tag-305*	Tubby superfamily protein TULP4	43	<0.05
ZK1151.1	*vab-10*	Dystonin, GAS (Growth-arrest-specific protein), and related proteins	47	<0.05
ZK1248.9*		translation initiation factor 2C	37	<0.05
ZK484.1		Ornithine decarboxylase antizyme	42	<0.05

*Based on *E. coli* RNAi clone sequencing; gene differs from predicted gene in library.

Table S2. One hundred ninety-two RNAi clones in the *C. elegans* RNAi library

Clone	Gene	*C. elegans* gene description	Fly locus ID	Fly gene	Fly description
Orthologs of *Drosophila* genes					
B0025.1	*vps-34*	Phosphatidylinositol 3-kinase VPS34, involved in signal transduction	37733	Pi3K59F	Phosphotidylinositol 3 kinase 59F
B0495.8		Spliceosome subunit	39956	CG7564	
C04A11.3	*gck-4*	Ste20-like serine/threonine protein kinase	37893	slik	Sterile20-like kinase
C06H2.1	*atp-5*	Mitochondrial F1F0-ATP synthase, subunit d/ATP7	42291	ATPsyn-d	ATP synthase, subunit d
C07H6.4		Predicted splicing regulator, contains RRM, SWAP and RPR domains	37381	CG9346	
C16E9.2		Uncharacterized conserved protein	36918	CG9646	
C25B8.1	*kqt-1*	Voltage-gated K^+ channel KCNQ	36071	KCNQ	KCNQ potassium channel
C27A2.2	*rpl-22*	60S ribosomal protein L22	31022	RpL22	Ribosomal protein L22
C30C11.2	*rpn-3*	26S proteasome regulatory complex, subunit RPN3/PSMD3	35176	Dox-A2	Diphenol oxidase A2
C48D1.3	*cho-1*	Choline transporter	42245	CG7708	
D1043.1		Uncharacterized conserved protein	39141	defl	deflated
F08C6.2		Phosphorylcholine transferase/cholinephosphate cytidylyltransferase	117353	Cct1	CTP:phosphocholine cytidylyltransferase 1
F10B5.4	*tub-1*	Tub family proteins	37400	king-tubby	
F17C8.1	*acy-1*	Adenylyl cyclase	32485	Ac13E	Adenylyl cyclase 35C
F32A6.5	*sto-2*	Prohibitins and stomatins of the PID superfamily	2768889	CG7633	
F32F2.1	*uig-1*	Putative guanine nucleotide exchange factor	37134	CG5503	
F41E6.3			41675	CG9351	
F43H9.1	*ech-3*	Enoyl-CoA hydratase	41533	CG5844	
F45E10.1	*unc-53*	Nuclear pore membrane and/or filament interacting like (POMFIL) protein	35278	sick	sickie
F46E10.1		Long chain fatty acid acyl-CoA ligase	33766	CG12512	
F56E10.4	*rps-27*	40S ribosomal protein S27	43039	RpS27	Ribosomal protein S27
F59A3.4		Zinc transporter and related ZIP domain-containing proteins	36273	CG13189	
K01C8.1		Threonine/serine dehydratases	41117	CG8129	
K09H9.6	*lpd-6*	RNA-binding protein required for 60S ribosomal subunit biogenesis	298699	ppan	peter pan
K11D9.1	*klp-7*	Kinesin-like protein	32049	Klp10A	
M7.1	*let-70*	Ubiquitin-protein ligase	41785	eff	effete
R01H10.8	*cnk-1*	protein that contains a SAM domain, a PDZ domain, and a PH domain	36952	cnk	connector enhancer of ksr
R06C1.3	*wve-1*	Wiskott Aldrich syndrome proteins	34519	SCAR	SCAR
T01C1.3	*mbr-1*	honeybee MBlk-related	44936	Eip93F	
T10E9.7	*nuo-2*	vigilin; NADH-ubiquinone oxidoreductase, NDUFS3/30-kDa subunit	38378	CG12079	
T10G3.6	*gut-2*	Predicted snRNP core protein	39408	CG10418	
T23B12.3		Mitochondrial/chloroplast ribosomal protein S2	33688	mRpS2	mitochondrial ribosomal protein S2
W02A11.2		Uncharacterized conserved protein	35847	Vps25	Vacuolar protein sorting 25
W04A4.5		Uncharacterized conserved protein	31793	l(1)G0095	lethal (1) G0095
Y38F1A.5	*cyd-1*	G1/S-specific cyclin D	32551	CycD	Cyclin D
Y45F10A.4		Selenophosphate synthetase	36587	SelD	selenide, water dikinase
ZK1098.1		Spliceosomal protein FBP11/Splicing factor PRP40	33513	CG3542	
ZK688.3		Predicted fumarylacetoacetate hydralase	42505	CG5793	
ZK792.6	*let-60*	Ras-related GTPase	41140	Ras85D	Ras oncogene at 85D

Table S2. Continued

Clone	Gene	*C. elegans* gene description	Mouse locus ID	Mouse gene	Mouse description
		Orthologs of mouse genes			
B0414.7	*mtk-1*	MEKK and related serine/threonine protein kinases	26406	Map3k3	mitogen activated protein kinase kinase kinase 3
C07H6.5	*cgh-1*	ATP-dependent RNA helicase	13209	Ddx6	DEAD (Asp-Glu-Ala-Asp) box polypeptide 6
C15H11.8		RNA polymerase I transcription factor TFIIS, subunit A12.2/RPA12	66136	Znrd1	zinc ribbon domain containing, 1
C15H11.9		Regulator of ribosome synthesis	59014	Rrs1	RRS1 ribosome biogenesis regulator homolog
C25A1.10	*dao-5*	Nucleolar GTPase/ATPase p130	70769	Nolc1	nucleolar and coiled-body phosphoprotein 1
C34C6.5	*tag-274*	Sphingosine kinase, involved in sphingolipid metabolism	20698	Sphk1	sphingosine kinase 1
C41G7.5	*ahr-1*	Aryl-hydrocarbon receptor	11622	Ahr	aryl-hydrocarbon receptor
C47E12.4	*pyp-1*	Inorganic pyrophosphatase/ Nucleosome remodeling factor, subunit NURF38	67895	Ppa1	pyrophosphatase (inorganic) 1
C50D2.5		contains similarity to Pfam domain PF00076 RNA recognition motif	66055	0610009D07Rik	riken cDNA
C54H2.5	*sft-4*	Putative cargo transport protein ERV29	20932	Surf4	surfeit gene 4
D2024.3	*elo-3*	Long chain fatty acid elongase	170439	Elovl6	ELOVL family member 6, elongation of long chain fatty acids
F14B4.3		RNA polymerase I, second largest subunit	20017	Rpo 1–2	RNA polymerase 1–2
F20D1.2		Uncharacterized conserved protein, contains TBC and Rhodanese domains	67581	Tbc1d23	TBC1 domain family, member 23
F23C8.6	*phi-24*	Vacuolar assembly/sorting protein DID2	67028	2610002M06Rik	riken cDNA
F32B5.8	*cpz-1*	Cysteine proteinase Cathepsin L	64138	Ctsz	cathepsin Z
F37B12.2	*gcs-1*	Gamma-glutamylcysteine synthetase	14629	Gclc	glutamate-cysteine ligase, catalytic subunit
F43D9.3		Vesicle trafficking protein Sly1	76983	Scfd1	sec1 family domain containing 1
F45H7.4	*prk-2*	Serine/threonine protein kinase	18712	Pim1	proviral integration site 1
F53E10.6		Uncharacterized conserved protein	67223	2810430M08Rik	riken cDNA
F55A11.4		possible pseudogene?	66972	Slc25a23	solute carrier family 25; member 23
F56E10.2	*fhod-2*	Rho GTPase effector BNI1 and related formins	208846	Daam1	dishevelled associated activator of morphogenesis 1
K01A2.5		Predicted hydrolase	68021	Bph1	biphenyl hydrolase-like (serine hydrolase, breast epithelial mucin-associated antigen)
K02F2.3	*tag-203*	Splicing factor 3b, subunit 3	101943	Sf3b3	splicing factor 3b, subunit 3
K07C11.5	*cri-2/tag-225*	Metalloproteinase inhibitor TIMP and related proteins	21858	Timp2	tissue inhibitor of metalloproteinase 2
K07H8.10			17975	Ncl	nucleolin
K08B4.1	*lag-1*	Recombination signal binding protein-J kappa(CBF1, Su(H), HS2NF5)	19664	Rbpsuh	recombining binding protein suppressor of hairless
M110.5	*dab-1*	Adaptor protein Disabled	13132	Dab2	disabled homolog 2
R04B5.5		Sorbitol dehydrogenase	20322	Sord	sorbitol dehydrogenase
T10H10.3		contains similarity to Pfam domain PF00397 WW domain	64010	Sav1	salvador homolog 1
T11B7.4	*alp-1*	Adaptor protein Enigma and related PDZ-LIM proteins	24131	Ldb3	LIM domain binding 3
T22H2.5		Phospholipid scramblase	22038	Plscr1	phospholipid scramblase 1
T26E3.3	*par-6*	Cell polarity protein PAR6	93737	Pardg6	par-6 partitioning defective 6 homolog gamma
W01B11.3		Ribosome biogenesis protein - Nop58p/Nop5p	55989	Nol5	nucleolar protein 5
W02B12.10		Methyltransferase-like protein	17299	Mettl1	methyltransferase-like 1
W06H3.2	*pus-1*	Pseudouridylate synthase	56361	Pus1	pseudouridine synthase 1

Clone	Gene	*C. elegans* gene description	Mouse locus ID	Mouse gene	Mouse description
Y53C12B.2		Predicted RNA-binding protein Pno1p interacting with Nob1p and involved in 26S proteasome assembly	66249	1810003N24Rik	riken cDNA
ZK1290.4	*nfi-1*	Nuclear factor I	18029	Nfic	nuclear factor I/C
ZK688.3		Predicted fumarylacetoacetate hydralase	68636	Fahd1	fumarylacetoacetate hydrolase domain containing 1

Table S2. Continued

Clone	Gene	*C. elegans* gene description
		C. elegans candidates and controls
B0218.8	*clec-52*	C-type lectin
B0285.4		Carboxymethyl transferase
B0334.8	*age-1*	Phosphatidylinositol 3-kinase catalytic subunit (p110)
B0412.2	*daf-7*	Transforming growth factor beta, bone morphogenetic protein and related proteins
C02A12.4	*lys-7*	*N*-acetylmuraminidase/lysozyme
C02H7.3	*aex-3*	MAPK-activating protein DENN
C04F12.3	*ikb-1*	Ankyrin repeat; ortholog of human BCL3
C04F12.8		Dual specificity phosphatase
C05B10.1	*lip-1*	Dual specificity phosphatase
C05D2.1	*daf-4*	Transforming growth factor beta/activin receptor subfamily of serine/threonine kinases
C09G5.6	*bli-1*	Collagens (type IV and type XIII), and related proteins
C12D8.10	*akt-1*	Serine/threonine protein kinase
C16A3.2		Dual specificity phosphatase
C17G10.5	*lys-8*	*N*-acetylmuraminidase/lysozyme
C24F3.2		Dual specificity phosphatase
C28C12.5	*spp-8*	Prosaposin
C28C12.7	*spp-10*	Prosaposin
C32D5.2	*sma-6*	Activin A type IB receptor, serine/threonine protein kinase
C35D10.9	*ced-4*	Apoptotic ATPase
C39F7.4	*rab-1*	GTPase Rab1/YPT1, small G protein superfamily, and related GTP-binding proteins
C47C12.3	*ref-2*	orthologous to the human gene ZINC FINGER PROTEIN OF CEREBELLUM ZIC2
C53D6.2	*unc-129*	Transforming growth factor beta, bone morphogenetic protein and related proteins
F01G10.8	*daf-14*	TGFbeta receptor signaling protein SMAD and related proteins
F08B1.1	*vhp-1*	Dual specificity phosphatase
F08F1.6	*spp-13*	saposin-like protein family
F10D11.6		BPI/LBP/CETP family protein
F11A1.3	*daf-12*	member of the steroid hormone receptor superfamily
F13B10.1	*tir-1*	SARM protein (with sterile alpha and armadillo motifs)
F13D11.3		Dual specificity phosphatase
F16F9.2	*dpy-6*	Unnamed protein
F17E9.11	*lys-10*	*N*-acetylmuraminidase/lysozyme
F20D12.2		Nuclear protein export factor
F25E2.5	*daf-3*	TGFbeta receptor signaling protein SMAD and related proteins
F25H2.1	*tli-1*	Toll-interacting protein
F26A3.4		Dual specificity phosphatase
F27C8.4	*spp-18*	saposin-like protein family
F28C6.8		Dual specificity phosphatase
F28D1.3	*thn-1*	Thaumatin family; Pathogenesis related proteins, group 5, and related proteins
F28D1.4	*thn-3*	Thaumatin family; Pathogenesis related proteins, group 5, and related proteins

Clone	Gene	*C. elegans* gene description
F28D1.5	*thn-2*	Thaumatin family; Pathogenesis related proteins, group 5, and related proteins
F29C4.1	*daf-1*	Activin A type IB receptor, serine/threonine protein kinase
F32D8.9	*spp-16*	saposin-like protein family
F33E2.2	*dlk-1*	Serine/threonine protein kinase, contains leucine zipper domain
F35C5.6	*clec-63*	Lectin C-type domain/CUB domain
F35C5.8	*clec-65*	Lectin C-type domain/CUB domain
F35C5.9	*clec-66*	Lectin C-type domain/CUB domain
F35C8.1		Serine/threonine protein kinase
F35C8.2		Serine/threonine protein kinase
F38A1.5		C-type lectin
F39G3.8	*tig-2*	Transforming growth factor beta, bone morphogenetic protein and related proteins
F42G10.2	*mkk-4*	Mitogen-activated protein kinase (MAPK) kinase MKK4
F42G8.3	*pmk-2*	Mitogen-activated protein kinase
F42G8.4	*pmk-3*	Mitogen-activated protein kinase
F52F12.3	*mom-4*	Tyrosine kinase specific for activated (GTP-bound) p21cdc42Hs
F53A2.8	*mtm-6*	Myotubularin-related phosphatidylinositol 3-phosphate 3-phosphatase MTM6
F53H8.2	*arr-1*	beta-arrestin ortholog
F54B11.11		contains similarity to Pfam domain PF02408 CUB-like domain
F54B8.5	*abf-3*	antibacterial factor related
F55G11.5	*dod-22*	contains similarity to Pfam domain PF02408 CUB-like domain
F56D12.4	*jip-1*	Mitogen-activated protein kinase scaffold protein JIP
F58B3.1	*lys-4*	*N*-acetylmuraminidase/lysozyme
F58B3.2	*lys-5*	*N*-acetylmuraminidase/lysozyme
F59A6.1	*nsy-1*	Serine/threonine protein kinase
F59E12.12	*bli-2*	Collagens (type IV and type XIII), and related proteins
H16D19.1	*clec-13*	C-type lectin
H24G06.1		WD40 repeat protein
K04A8.9	*spp-19*	saposin-like protein family
K08A8.1	*mek-1*	Mitogen-activated protein kinase (MAPK) kinase MKK7/JNKK2
K08D8.5		contains similarity to Pfam domain PF02408 CUB-like domain
K09B11.1	*pik-1*	Serine/threonine protein kinase; pelle/IRAK kinase
K09F5.3	*spp-14*	saposin-like protein family
K11E8.1	*unc-43*	Ca^{2+}/calmodulin-dependent protein kinase, EF-Hand protein superfamily
M04C9.5	*dyf-5*	MAPK related serine/threonine protein kinase
R03G5.2	*sek-1*	Mitogen-activated protein kinase (MAPK) kinase MKK3/MKK6
R03G5.2	*sek-1*	Mitogen-activated protein kinase (MAPK) kinase MKK3/MKK6
R07B1.10	*lec-8*	Galectin, galactose-binding lectin
R09B5.3	*cnc-2*	Unnamed protein
R12B2.1	*sma-4*	TGFbeta receptor signaling protein SMAD and related proteins
R13A5.1	*cup-5*	Mucolipidin and related proteins
R13F6.6	*zak-1*	mitogen-activated protein kinase kinase kinase

Clone	Gene	*C. elegans* gene description
R13F6.9	*sma-3*	TGFbeta receptor signaling protein SMAD and related proteins
R13H8.1	*daf-16*	Transcription factor of the Forkhead/HNF3 family
R53.4		Mitochondrial F1F0-ATP synthase, subunit f
T01E8.2	*ref-1*	protein with two basic helix-loop-helix (bHLH) domains
T07A9.3	*kgb-1*	Jun-N-terminal kinase (JNK)
T07C4.4	*spp-1*	saposin-like protein family
T07D10.4	*clec-15*	C-type lectin
T08A9.10	*spp-6*	saposin-like protein family
T08A9.8	*spp-4*	Prosaposin
T08A9.9	*spp-5*	saposin-like protein family
T17E9.1	*kin-18*	Serine/threonine protein kinase
T19E7.2	*skn-1*	bZIP transcription factor NRF1
T22G5.7	*spp-12*	saposin-like protein family
T22H6.5	*abf-5*	antibacterial factor related
T24B8.3		
T25C12.2	*spp-9*	saposin-like protein family
T25D10.3	*spp-11*	saposin-like protein family
T25F10.2	*dlb-1*	Transforming growth factor beta, bone morphogenetic protein and related proteins
VZC374L.1		Mitogen-activated protein kinase (MAPK) kinase MKK4
W05E7.1	*grd-3*	hedgehog-like family
W10D5.1	*mef-2*	MADS box transcription factor
Y22F5A.4	*lys-1*	*N*-acetylmuraminidase/lysozyme
Y22F5A.5	*lys-2*	*N*-acetylmuraminidase/lysozyme
Y22F5A.6	*lys-3*	*N*-acetylmuraminidase/lysozyme
Y38H6C.22	*abf-4*	antibacterial factor related
Y47H9C.4	*ced-1*	Proteins containing Ca^{2+}-binding EGF-like domains
Y53C10A.12	*hsf-1*	Heat shock transcription factor
Y55D5A.5	*daf-2*	Insulin/growth factor receptor
ZC416.4	*kgb-2*	Jun-N-terminal kinase (JNK)
ZC449.3		Mitogen-activated protein kinase (MAPK) kinase MKK4
ZK1098.10	*unc-16*	JNK/SAPK-associated protein-1
ZK370.2	*sma-2*	TGFbeta receptor signaling protein SMAD and related proteins
ZK6.7		Triglyceride lipase-cholesterol esterase
ZK757.2		Dual specificity phosphatase
ZK792.6	*let-60*	Ras-related GTPase

Table S3. Genes in RNAi library that regulate clec-85 expression

Clone	Gene	Gene description	GFP, %	*P*
B0412.2	*daf-7*	Transforming growth factor beta, bone morphogenetic protein and related proteins	66	0.16
C03G6.11	*srh-231**	Predicted olfactory G-protein coupled receptor	71	<0.05
C04A11.3	*gck-4*	Ste20-like serine/threonine protein kinase	59	<0.05
C25B8.1	*kqt-1*	Voltage-gated K^+ channel KCNQ	53	<0.05
C27A2.2	*rpl-22*	60S ribosomal protein L22	60	<0.05
C30C11.2	*rpn-3*	26S proteasome regulatory complex, subunit RPN3/PSMD3	43	<0.05
C54H2.5	*sft-4*	Putative cargo transport protein ERV29	88	0.21
D2024.3	*elo-3*	Long chain fatty acid elongase	74	0.05
F13B10.1	*tir-1*	SARM protein (with sterile alpha and armadillo motifs)	33	<0.05
F13B10.1	*tir-1*[†]	SARM protein (with sterile alpha and armadillo motifs)	52	<0.05
F17C8.1	*acy-1*	Adenylyl cyclase	78	0.05
F20D1.2	*tbc-1*	Uncharacterized conserved protein, contains TBC and Rhodanese domains	62	<0.05
F20D12.2		Nuclear protein export factor	82	0.13
F32A6.5	*sto-2*	Prohibitins and stomatins of the PID superfamily	72	<0.05
F35C5.8	*clec-65*	Lectin C-type domain/CUB domain	55	<0.05
F43D9.3		Vesicle trafficking protein Sly1	88	0.19
F45E10.1	*unc-53*	Nuclear pore membrane and/or filament interacting like (POMFIL) protein	66	<0.05
F46E10.1		Long chain fatty acid acyl-CoA ligase	50	<0.05
F56E10.4	*rps-27*	40 s ribosomal protein S27	47	<0.05
F59A6.1	*nsy-1*	Serine/threonine protein kinase	31	<0.05
F59A6.1	*nsy-1*[†]	Serine/threonine protein kinase	73	<0.05
K07C11.5	*cri-2/tag-225*	Metalloproteinase inhibitor TIMP and related proteins	68	<0.05
K11D9.1	*klp-7*	Kinesin-like protein	77	<0.05
M7.1	*let-70*	Ubiquitin-protein ligase	49	<0.05
R01H10.8	*cnk-1*	protein that contains a SAM domain, a PDZ domain, and a PH domain	89	0.16
T23B12.3		Mitochondrial/chloroplast ribosomal protein S2	85	0.15
ZK688.3		Predicted fumarylacetoacetate hydralase	56	<0.05

*Based on E. coli RNAi clone sequencing, gene differs from predicted gene in library.

[†] The control genes *tir-1* and *nsy-1* were present in the library in duplicate.

Table S4. qPCR Primers used for monitoring siRNA-mediated gene inhibition

Mouse gene	Primer 1	Primer 2
Actin	CTG AAC CCT AAG GCC AAC CGT G	CCG TCT CCG GAG TCC ATC ACA ATG
Heca	CGCTAAGAATGGAGCTCCTTGTGCC	CAGGTGCTGCAGGGACAGTGC
Tulp4	CCACAACAGTGAGGTTGTGCTGGTGAG	CTGAGCCCCACGGTCATTGAC
Macf1	GAAGAGATGCAGATGAAACTGGAGCG	CACTGGTATGGATATGCTGCTGTGTTTC
Psmd3	GCTACAAAGAGGCACAGAAAATCTCTGATGACC	GGGCATGCAAGAAGCTGCGCACCAC
Timp3	CTC CGA CAT CGT GAT CCG GGC CAA AG	CA TCT GCT TAA TAG TGT AGA CCA GAG TGC CAA AGG
Tbc1d23	CTC CTG TGG ACC GGC ACG TGA GCA GC	GTC ATA TTC CTC TTC ATC GCC GAT GCT G
Rpl22	GCT GCC AAT TTT GAG CAG TTC CTC CAG G	GCG TTC GAT GGT CAC GAC TCC TCC GCC
Adcy9	CCA GCT ACC AGG AAG AGG TCA TAA AGA	CAC CAA AGA CGG CCA GGG CAG CCG GT
C1qbp	TGC ACA CGG AAG GAG ACA AGG CCT TC	CGG CAA CTT TGC GCA ATA ATT TAG CC
Siah1a	GAG GGT ACC TGC CTT GAC CGG	AGA TGG CCA CTC TGA CAC TGA AGA ATA