

Supplementary Materials for

**MON-2, a Golgi protein, mediates autophagy-dependent longevity in
*Caenorhabditis elegans***

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Figure S1

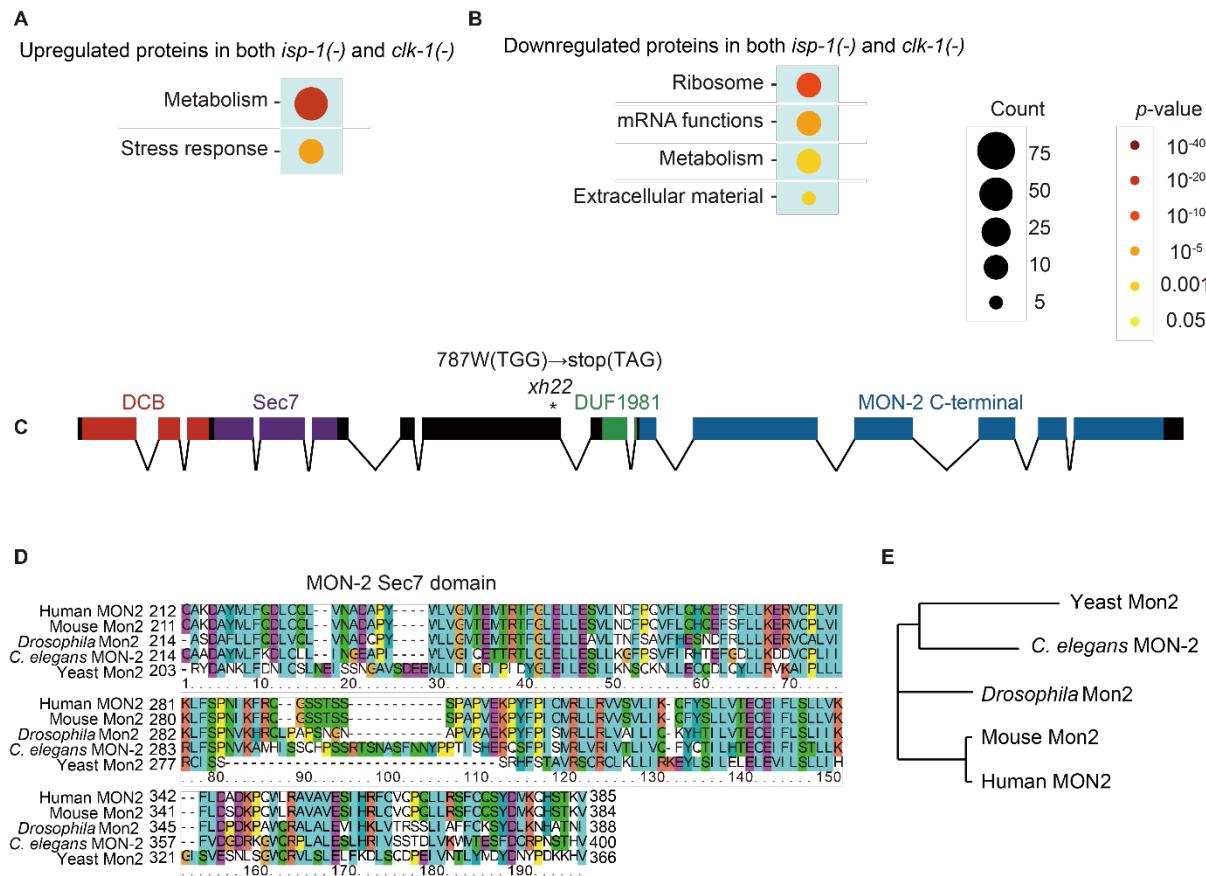


Fig. S1. The Sec 7 domain of MON-2 is highly conserved across phyla. **A-B.** WormCAT gene set enrichment analysis (73) of proteins whose levels increased (A) or decreased (B) ≥ 1.5 -fold in both *isp-1(qm150)* [*isp-1(-)*] and *clk-1(qm30)* [*clk-1(-)*] animals compared with those in wild-type (WT) animals. WormCAT analysis indicates that metabolism and stress response were enriched among proteins upregulated in *isp-1(-)* and *clk-1(-)* mutants. Ribosome, mRNA functions, metabolism and extracellular material were enriched among proteins downregulated in *isp-1(-)* and *clk-1(-)* mutants. The sizes of circles indicate gene counts, and the colors of circles indicate *p*-values obtained by using Fisher's exact test. The number of hit RNAi clones from our RNAi screen that significantly affected lifespan using *isp-1(qm150)*; *ctb-1(qm189)* [*isp-1(-); ctb-1(-)*] mutants was substantially decreased after confirmation using *isp-1(-)* single mutants. First, it is possible that *ctb-1(-)* mutation may have altered the effect of RNAi clones on the lifespan of *isp-1(-)* mutants. A previous study reported that the expression level of *gst-4p::gfp*, a reporter of SKN-1/NRF activity, is increased by genetic inhibition of *isp-1* but decreased by *ctb-1(-)* mutation (74). Decreased activity of complex I by *isp-1(-)* is also suppressed by *ctb-1(-)*, which does not cause additive effects on the activity of complex III downregulated by *isp-1(-)* (75). Therefore, we speculate that *ctb-1(-)* may modulate the effects of some RNAi clones on the lifespan of *isp-1(-)* single mutants. Second, narrowing down to a small number of candidates by performing a secondary screen from a large-scale primary RNAi screen is not rare. For example,

a previous study that used *isp-1(-); ctb-1(-)* mutants for an RNAi screen targeting 387 transcription factor-encoding genes identified 17 genes whose knockdown significantly decreases the lifespan of *isp-1(-); ctb-1(-)* double mutants (39). After further experiments and confirmation using *isp-1(-)* mutants, they narrowed down candidates to three RNAi clones. Our group also reported that lifespan data obtained by using RNAi-mediated knockdown are not always recapitulated with the loss of function mutations (76, 23). In this study, we actually obtained very consistent lifespan results with all three tested mutants, *mon-2(xh22)*, *hrpu-2(tm1474)*, and *patr-1(gk155841)*, and with the RNAi-based screen (Figure 2 and Table S2), further validating our RNAi screen. **C.** Structure of the *C. elegans* *mon-2* gene. Red: dimerization and cyclophilin-binding (DCB) domain; purple: Sec7 domain involved in guanine nucleotide exchange; *xh22* is a G-to-A base change that generates a premature termination codon; green: domain of unknown function 1981 (DUF1981); blue: MON-2 C-terminal domain. **D.** The Sec7 domain of MON-2 is conserved from yeast to humans. **E.** Phylogenetic tree showing sequence similarities among MON-2/MON2 proteins in humans, mice, *Drosophila*, *C. elegans*, and yeast.

Figure S2

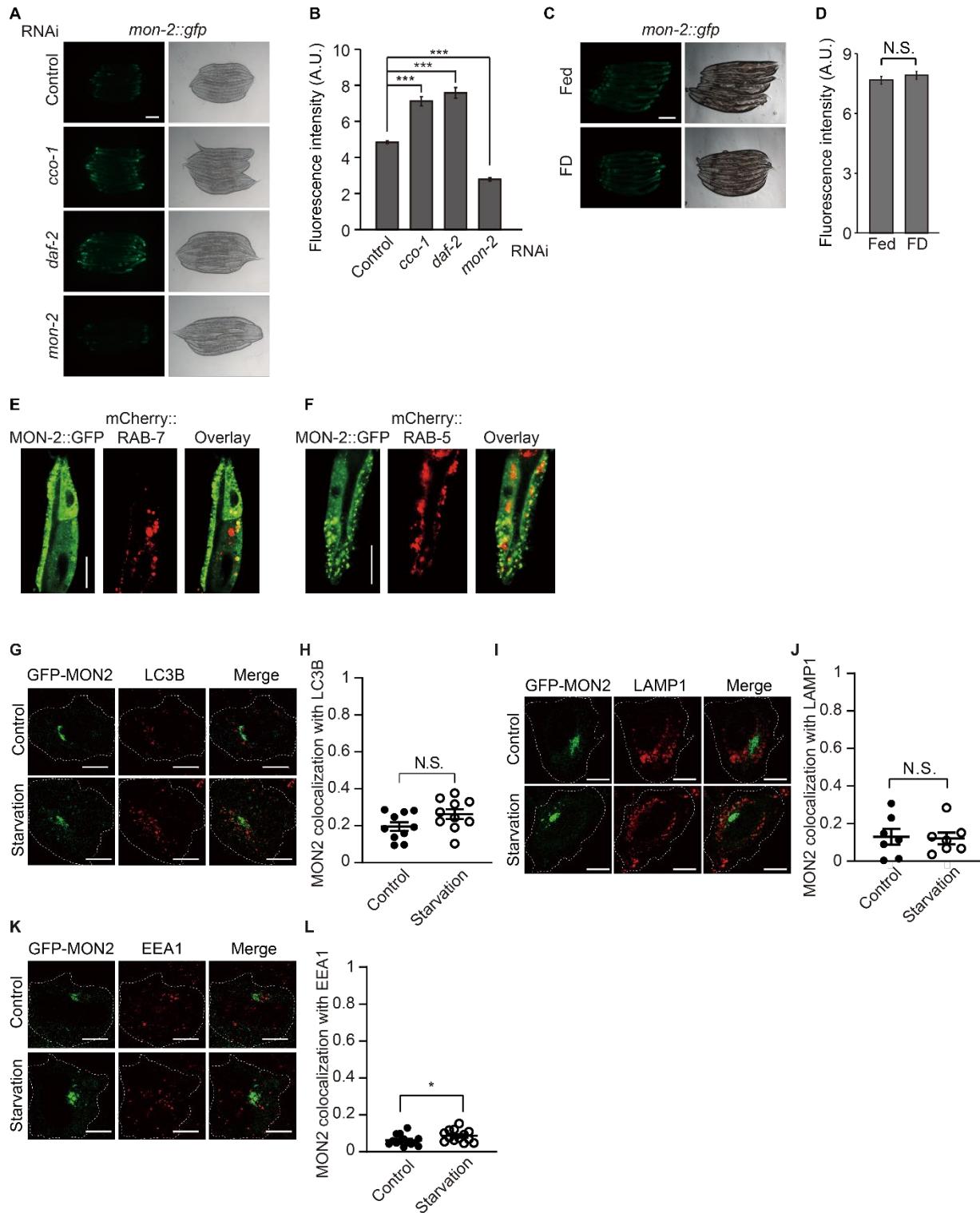


Fig. S2. Changes in MON-2 levels caused by various longevity interventions and colocalization of MON-2/MON2 with markers of various subcellular organelles. A. *daf-2*

RNAi or *cco-1* RNAi increased the levels of MON-2::GFP. *mon-2* RNAi significantly decreased the GFP level, validating the efficiency of RNAi. L2 or L3 larvae were used for imaging. Scale bar: 100 μ m. **B.** Quantification of fluorescence images in panel A (n = 3, > 54 animals). **C.** Food deprivation (FD) for 6 h did not alter the level of MON-2::GFP. Day 2 adult animals were used for retaining consistency with lifespan assays with FD. Scale bar: 200 μ m. **D.** Quantification of fluorescence images in panel C (n = 3, > 48 animals). **E.** Fluorescence microscope images of intestinal cells in transgenic animals expressing *mon-2::gfp*, the lysosome-specific marker *mCherry::rab-7*, and the overlay of the two images. Scale bar: 20 μ m. **F.** Fluorescence microscope images of intestinal cells in transgenic animals expressing *mon-2::gfp*, the endosome-specific marker *mCherry::rab-5*, and the overlay of the two images. Scale bar: 20 μ m. **G-L.** Colocalization of MON2 with LC3B, an autophagy marker (N = 8, 8) (**G-H**), LAMP1, a lysosome marker (N = 7, 7) (**I-J**), and EEA1, an early endosome marker (N = 14, 13) (**K-L**) in HeLa cells. Scale bars: 10 μ m. For all the panels, error bars represent the s.e.m. (* p < 0.05, *** p < 0.001, N.S.: not significant; two-tailed Student's *t*-test). For all the graphs, each dot represents a result from a single cell.

Figure S3

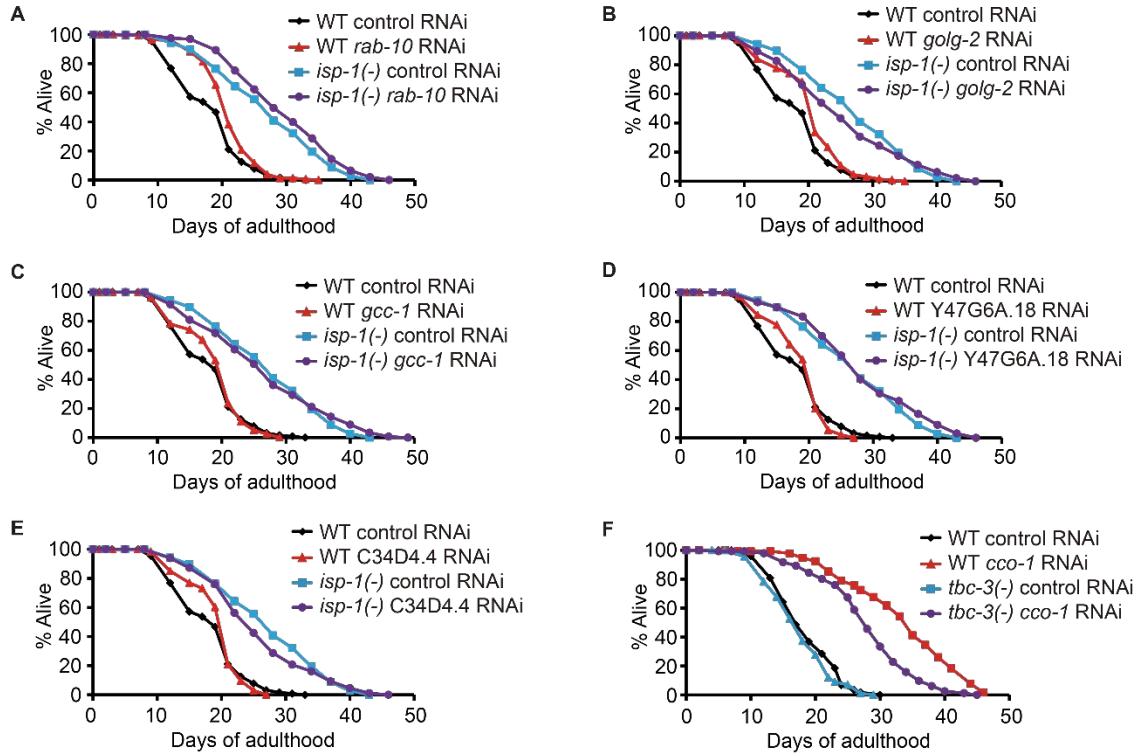


Fig. S3. Effects of knocking down genes encoding various Golgi components on the long lifespan of mitochondrial respiration mutants. A-E. RNAi-mediated knockdown of *rab-10*/Rab-like GTPase (A), *golg-2*/Golgin family member (B), *gcc-1*/coiled coil protein predicted to function in transport between early endosomes and the trans-Golgi network (C), Y47G6A.18/ortholog of human Golgi phosphoprotein 3 (D), or C34D4.4/trans-Golgi network vesicle protein (E) did not shorten the lifespan of wild-type (WT) or *isp-1(qm150)* [*isp-1(-)*] animals. F. *tbc-3(xh23)* [*tbc-3(-)*] mutations decreased longevity conferred by *cco-1* RNAi. See Table S5 for values and statistical analyses of the lifespan data.

Figure S4

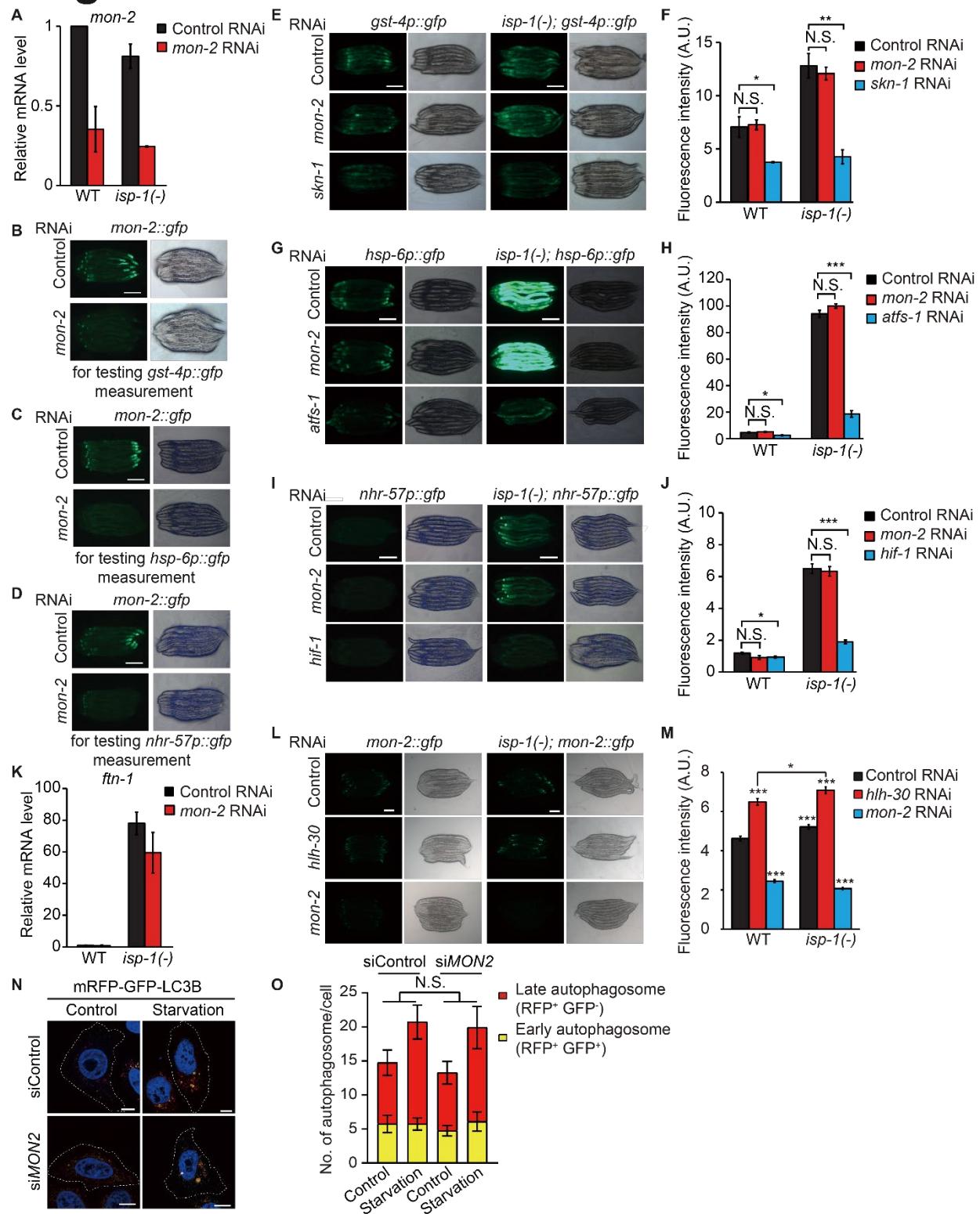


Fig. S4. *mon-2* RNAi in *C. elegans* has minor or no effects on SKN-1, UPR^{mt}, HIF-1, or CEP-1 activity, and knockdown of mammalian *MON2* does not affect the pattern of mRFP-

GFP-LC3B. **A.** *mon-2* RNAi effectively reduced the mRNA level of *mon-2* in both wild-type (WT) and *isp-1(qm150)* [*isp-1(-)*] animals (n = 2). **B-D.** *mon-2* RNAi decreased GFP levels in *mon-2::gfp* transgenic animals. The assay was used to test the efficiency of *mon-2* RNAi for measurement of *gst-4p::gfp* (**B**), *hsp-6p::gfp* (**C**), and *nhr-57p::gfp* (**D**) levels. **E-F.** *mon-2* RNAi did not affect the expression level of *gst-4p::gfp*, a SKN-1 activity reporter, in WT or *isp-1(-)* animals (**E**); quantification of panel E (**F**) (n = 3, > 60 animals). Scale bar: 200 μm . *skn-1* RNAi was used as a positive control. **G-H.** *mon-2* RNAi did not change the expression of *hsp-6p::gfp*, a mitochondrial unfolded protein response (UPR^{mt}) reporter, in WT or *isp-1(-)* animals (**G**); quantification of panel G (**H**) (n = 3, > 60 animals). Scale bar: 200 μm . Error bars represent the standard error of the mean (s.e.m.) (*p < 0.05 and ***p < 0.001; two-tailed Student's t-test). *atfs-1* RNAi was used as a positive control. **I-J.** *mon-2* RNAi did not alter the expression of *nhr-57p::gfp*, a HIF-1 activity reporter, in WT or *isp-1(-)* animals (**I**); quantification of panel I (**J**) (n = 3, > 60 animals). Scale bar: 200 μm . Error bars represent s.e.m. (*p < 0.05 and ***p < 0.001; two-tailed Student's t-test). *hif-1* RNAi was used as a positive control. **K.** *mon-2* RNAi did not alter the mRNA level of *ftn-1*, a putative CEP-1 transcriptional target, in WT or *isp-1(-)* animals (n = 2). **L-M.** *hlh-30* RNAi increased the fluorescence intensity of MON-2::GFP in WT and *isp-1(-)* animals (**L**); quantification of panel L (**M**) (n = 3, > 49 animals). Here, the degree of increased MON-2::GFP levels by *isp-1(-)* was relatively low compared to that in Figure 3H-I and 3K. We speculate that the difference between Figure S4L-M and Figures 3H-I and 3K was caused by different food sources; *E. coli* HT115 strain, which is used for RNAi-mediated knockdown, was used for the food source for Figure S4L-M experiments, whereas *E. coli* OP50 strain was used for Figure 3H-I and 3K experiments. Scale bar: 100 μm . Error bars represent s.e.m. (*p < 0.05 and ***p < 0.001; two-tailed Student's t-test). **N.** Knockdown of *MON2* (si*MON2*) did not alter the flux of mRFP-GFP-LC3B in stable HeLa cells under basal or starvation conditions. We tested changes in LC3B, which is a widely and commonly used autophagy marker (77). Scale bars: 10 μm . **O.** The numbers of RFP⁺GFP⁺ puncta and RFP⁺GFP⁻ puncta in HeLa cells were counted for each cell and analyzed for statistical differences (N = 19, 20, 17, and 19). Error bars represent s.e.m. (N.S.: not significant, Mann-Whitney test).

Table S1B. GO analysis of proteins whose levels are at least 1.5-fold increased or decreased in both *clk-1(qm30)* and *isp-1(qm150)* animalsGO terms that are enriched in proteins whose levels are increased in both *clk-1(qm30)* and *isp-1(qm150)* animals

GO terms with a Benjamini p-value <0.05 are shaded in grey.

Term	Count	%	p-value	Fold Enrich	Benjamini	FDR
oxidation-reduction process	22	15.90	0.000000013	4.5	2.30E-06	2.20E-06
glycolytic process	6	4.30	0.0000024	26.4	2.20E-04	2.20E-04
metabolic process	25	18.10	0.000038	2.5	1.70E-03	1.70E-03
gluconeogenesis	4	2.90	0.000027	60.4	1.70E-03	1.60E-03
tricarboxylic acid cycle	4	2.90	0.0016	16.9	4.80E-02	4.70E-02
nucleobase-containing compound metabolic process	4	2.90	0.0016	16.9	4.80E-02	4.70E-02
determination of adult lifespan	19	13.80	0.0041	2.1	8.20E-02	8.00E-02
cell redox homeostasis	5	3.60	0.0036	7.9	8.20E-02	8.00E-02
glucose metabolic process	3	2.20	0.0045	28.8	8.20E-02	8.00E-02
nucleotide phosphorylation	3	2.20	0.0037	31.7	8.20E-02	8.00E-02
carboxylic acid metabolic process	3	2.20	0.0063	24.4	1.10E-01	1.00E-01
fatty acid metabolic process	4	2.90	0.0096	9	1.50E-01	1.40E-01
striated muscle myosin thick filament assembly	6	4.30	0.012	4.3	1.70E-01	1.60E-01
carbohydrate metabolic process	6	4.30	0.016	4	2.10E-01	2.00E-01
cysteine biosynthetic process	2	1.40	0.046	42.3	5.60E-01	5.40E-01
cysteine biosynthetic process from serine	2	1.40	0.064	30.2	7.30E-01	7.10E-01
stress response to cadmium ion	2	1.40	0.09	21.1	9.60E-01	9.40E-01

GO terms that are enriched in proteins whose levels are decreased in both *clk-1(qm30)* and *isp-1(qm150)* animals

Term	Count	%	p-value	Fold Enrich	Benjamini	FDR
ribosome biogenesis	5	4.20	0.00041	14.1	1.20E-02	1.20E-02
rRNA processing	5	4.20	0.001	11	2.60E-02	2.60E-02
gamete generation	7	5.90	0.0002	8.2	6.90E-03	6.70E-03
RNA interference	8	6.70	0.00019	6.6	6.90E-03	6.70E-03
translation	13	10.90	0.000001	6.2	2.00E-04	1.90E-04
reproduction	35	29.40	0.000049	2	3.40E-03	3.30E-03
nematode larval development	32	26.90	0.00011	2	5.50E-03	5.40E-03
embryo development ending in birth or egg hatching	47	39.50	0.0000019	1.9	2.00E-04	1.90E-04
hermaphrodite genitalia development	14	11.80	0.0057	2.3	1.30E-01	1.30E-01
flavonoid glucuronidation	4	3.40	0.019	7	3.50E-01	3.40E-01
flavonoid biosynthetic process	4	3.40	0.019	7	3.50E-01	3.40E-01
mature ribosome assembly	2	1.70	0.024	82.5	3.50E-01	3.40E-01
regulation of translation	3	2.50	0.024	12.4	3.50E-01	3.40E-01
maturity of SSU-rRNA from tricistronic rRNA transcript (SSU-rRNA, 5.8S rRNA, LSU-rRNA)	3	2.50	0.024	12.4	3.50E-01	3.40E-01
receptor-mediated endocytosis	12	10.10	0.032	2	4.30E-01	4.20E-01
RNA secondary structure unwinding	3	2.50	0.033	10.3	4.30E-01	4.20E-01
tryptophan catabolic process	2	1.70	0.039	49.5	4.80E-01	4.70E-01
translational initiation	3	2.50	0.048	8.4	5.50E-01	5.40E-01
ribosomal small subunit biogenesis	2	1.70	0.055	35.3	5.90E-01	5.80E-01
germ cell development	5	4.20	0.058	3.4	6.00E-01	5.80E-01
collagen and cuticulin-based cuticle development	4	3.40	0.062	4.4	6.10E-01	5.90E-01
nuclear-transcribed mRNA catabolic process, exonucleolytic, 3'-5'	2	1.70	0.07	27.5	6.50E-01	6.40E-01
determination of adult lifespan	13	10.90	0.088	1.6	7.90E-01	7.70E-01

Table S1C. WormCAT analysis of proteins whose levels are at least 1.5-fold increased or decreased in both *clk-1(qm30)* and *isp-1(qm150)* animals
Gene set enrichment analysis among proteins whose levels are increased in both *clk-1(qm30)* and *isp-1(qm150)* animals

Category	RGS	AC	PValue	Bonferroni
Metabolism	53	1577	1.46E-25	2.34E-24
Stress response	19	810	2.28E-08	3.65E-07

Gene set enrichment analysis among proteins whose levels are decreased in both *clk-1(qm30)* and *isp-1(qm150)* animals

Category	RGS	AC	PValue	Bonferroni
Ribosome	17	244	1.54E-15	2.61E-14
mRNA functions	12	390	1.08E-07	1.84E-06
Metabolism	22	1577	1.11E-06	1.89E-05
Extracellular material	9	485	0.00017	0.002892695

Table S2A. Result of lifespan screen with *isp-1(qm150)*; *ctb-1(qm189)* double mutants treated with 61 RNAi clones targeting genes that encode proteins whose levels were influenced by both *clk-1(qm30)* and *isp-1(qm150)* mutations (related to Figure 2A and Table S1)

Strain/treatment	Mean lifespan \pm SEM (days)	75th percentile	% change ^A	Number of animals that died/total	p-value vs. control
Wild-type control RNAi	18.6 \pm 0.54	22	0	98/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	27.33 \pm 0.64	32	+47	87/120	<0.0001
Wild-type <i>sodh-1</i> RNAi	15.27 \pm 0.53	18	-18	64/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) sodh-1</i> RNAi	26.91 \pm 0.69	32	-2	86/120	0.9745
Wild-type <i>cul-5</i> RNAi	14.43 \pm 0.56	16	-22	55/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) cul-5</i> RNAi	25.36 \pm 0.72	30	-7	87/120	0.1751
Wild-type <i>thn-1</i> RNAi	17.36 \pm 0.62	20	-7	65/120	0.15
<i>isp-1(qm150); ctb-1(qm189) thn-1</i> RNAi	23.23 \pm 0.6	26	-15	92/120	<0.0001
Wild-type <i>cyp-33C8</i> RNAi	17.93 \pm 0.55	20	-4	69/120	0.2294
<i>isp-1(qm150); ctb-1(qm189) cyp-33C8</i> RNAi	24.39 \pm 0.61	26	-11	77/120	0.0015
Wild-type control RNAi	17.98 \pm 0.32	22	0	99/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	23.67 \pm 0.48	27	+32	90/120	<0.0001
Wild-type <i>sodh-1</i> RNAi	17.34 \pm 0.4	20	-4	85/120	0.4397
<i>isp-1(qm150); ctb-1(qm189) sodh-1</i> RNAi	24.69 \pm 0.56	27	+4	77/120	0.1555
Wild-type <i>cul-5</i> RNAi	16.63 \pm 0.32	20	-8	76/120	0.0033
<i>isp-1(qm150); ctb-1(qm189) cul-5</i> RNAi	22.91 \pm 0.55	25	-3	78/120	0.3976
Wild-type <i>thn-1</i> RNAi	16.75 \pm 0.41	20	-7	63/90	0.0354

<i>isp-1(qm150); ctb-1(qm189) thn-1</i> RNAi	23.16±0.48	25	-2	70/90	0.2506
Wild-type <i>cyp-33C8</i> RNAi	16.16±0.43	20	-10	77/120	0.0052
<i>isp-1(qm150); ctb-1(qm189) cyp-33C8</i> RNAi	21.51±0.47	25	-9	72/120	0.0009
Wild-type <i>gfp</i> RNAi	17.32±0.49	20		78/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	29.20±0.86	34	+69	84/120	<0.0001
Wild-type <i>acs-2</i> RNAi	15.53±0.55	18	-10	86/120	0.0605
<i>isp-1(qm150); ctb-1(qm189) acs-2</i> RNAi	29.07±0.89	36	0	88/120	0.9644
Wild-type <i>aldo-1</i> RNAi	15.9±0.4	18	-8	91/120	0.0286
<i>isp-1(qm150); ctb-1(qm189) aldo1</i> RNAi	25.6±0.83	30	-12	102/120	0.0126
Wild-type <i>mce-1</i> RNAi	17.21±0.58	20	-1	75/120	0.9414
<i>isp-1(qm150); ctb-1(qm189) mce-1</i> RNAi	27.84±0.86	34	-5	86/120	0.4647
Wild-type <i>sdz-8</i> RNAi	17.25±0.67	22	0	74/120	0.6626
<i>isp-1(qm150); ctb-1(qm189) sdz-8</i> RNAi	27.17±0.93	32	-7	80/120	0.158
Wild-type <i>gfp</i> RNAi	16.12±0.39	17		91/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	26.04±0.71	32	+62	55/120	<0.0001
Wild-type <i>acs-2</i> RNAi	16.52±0.34	19	+2	98/120	0.545
<i>isp-1(qm150); ctb-1(qm189) acs-2</i> RNAi	26.55±0.45	29	+2	103/120	0.8568
Wild-type <i>aldo-1</i> RNAi	17.64±0.5	21	+9	99/120	0.0198
<i>isp-1(qm150); ctb-1(qm189) aldo1</i> RNAi	25.02±0.47	29	-4	96/120	0.1095
Wild-type <i>mce-1</i> RNAi	16.79±0.41	19	+4	91/120	0.3195
<i>isp-1(qm150); ctb-1(qm189) mce-1</i> RNAi	26.33±0.52	29	+1	74/90	0.9172
Wild-type <i>sdz-8</i> RNAi	15.89±0.44	19	-1	91/120	0.7507

<i>isp-1(qm150); ctb-1(qm189) sdz-8</i> RNAi	25.97±0.63	29	0	62/90	0.8623
Wild-type control RNAi	19.41±0.48	22		68/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	27.64±0.73	34	+42	87/120	<0.0001
Wild-type <i>nit-1</i> RNAi	19.5±0.57	22	0	67/120	0.644
<i>isp-1(qm150); ctb-1(qm189) nit-1</i> RNAi	25.34±0.7	30	-8	62/90	0.0101
Wild-type <i>cdr-4</i> RNAi	17.65±0.51	20	-9	53/120	0.0269
<i>isp-1(qm150); ctb-1(qm189) cdr-4</i> RNAi	27.74±0.63	32	+1	70/90	0.3322
Wild-type <i>pck-1</i> RNAi	17.80±0.63	22	-8	57/90	0.6574
<i>isp-1(qm150); ctb-1(qm189) pck-1</i> RNAi	27.12±0.67	32	-2	62/120	0.2007
Wild-type <i>R08E5.3</i> RNAi	19.04±0.58	22	-2	66/120	0.9963
<i>isp-1(qm150); ctb-1(qm189) R08E5.3</i> RNAi	27.33±0.92	35	-1	77/120	0.4162
Wild-type control RNAi	21.71±0.56	28		89/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	29.29±0.74	34	+35	78/120	<0.0001
Wild-type <i>nit-1</i> RNAi	23.05±0.53	28	+6	106/120	0.1037
<i>isp-1(qm150); ctb-1(qm189) nit-1</i> RNAi	29.31±0.58	34	0	105/120	0.6905
Wild-type <i>cdr-4</i> RNAi	21.57±0.52	25	-1	85/120	0.8427
<i>isp-1(qm150); ctb-1(qm189) cdr-4</i> RNAi	30.21±0.62	34	+3	83/120	0.5305
Wild-type <i>pck-1</i> RNAi	20.86±0.53	25	-4	74/120	0.1717
<i>isp-1(qm150); ctb-1(qm189) pck-1</i> RNAi	28.64±0.63	34	-2	70/120	0.2733
Wild-type <i>R08E5.3</i> RNAi	20.93±0.59	28	-4	101/120	0.4159
<i>isp-1(qm150); ctb-1(qm189) R08E5.3</i> RNAi	27.87±0.49	30	-5	103/120	0.0024

Wild-type <i>gfp</i> RNAi	20.68±0.67	24		40/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	31.25±0.98	39	+51	84/120	<0.0001
Wild-type <i>tbb-6</i> RNAi	19.08±0.62	22	-8	47/120	0.0601
<i>isp-1(qm150); ctb-1(qm189) tbb-6</i> RNAi	31.91±1.06	39	+2	70/120	0.7561
Wild-type <i>gpd-2/gpd-3</i> RNAi	19.24±0.6	22	-7	55/120	0.1672
<i>isp-1(qm150); ctb-1(qm189) gpd-2/gpd-3</i> RNAi	26.21±0.98	33	-16	77/120	0.0006
Wild-type <i>har-1</i> RNAi	22.59±0.87	26	+9	39/120	0.0283
<i>isp-1(qm150); ctb-1(qm189) har-1</i> RNAi	32.06±1.00	37	+3	65/120	0.859
Wild-type <i>mon-2</i> RNAi	19.61±0.64	22	-5	31/90	0.1805
<i>isp-1(qm150); ctb-1(qm189) mon-2</i> RNAi	27.18±0.74	33	-13	80/120	0.0001
Wild-type <i>gfp</i> RNAi	17.74±0.39	21		70/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	30.21±0.86	38	+70	73/120	<0.0001
Wild-type <i>tbb-6</i> RNAi	19.3±0.44	21	+9	64/120	0.0081
<i>isp-1(qm150); ctb-1(qm189) tbb-6</i> RNAi	30.34±1.18	38	0	53/120	0.5876
Wild-type <i>gpd-2/gpd-3</i> RNAi	19.29±0.37	23	+9	80/120	0.0036
<i>isp-1(qm150); ctb-1(qm189) gpd-2/gpd-3</i> RNAi	25.97±0.85	32	-14	94/120	0.0013
Wild-type <i>har-1</i> RNAi	18.57±0.43	21	+5	78/120	0.1394
<i>isp-1(qm150); ctb-1(qm189) har-1</i> RNAi	30.04±0.84	38	-1	81/120	0.9328
Wild-type <i>mon-2</i> RNAi	17.72±0.38	21	0	76/120	0.9898
<i>isp-1(qm150); ctb-1(qm189) mon-2</i> RNAi	25.8±0.79	32	-15	63/120	<0.0001
Wild-type control RNAi	20.52±0.64	26		83/120	

<i>isp-1(qm150); ctb-1(qm189) control RNAi</i>	29.07±0.88	35	+42	87/120	<0.0001
Wild-type <i>rde-4</i> RNAi	21.93±0.67	26	+7	83/120	0.1169
<i>isp-1(qm150); ctb-1(qm189) rde-4 RNAi</i>	30.49±1.06	39	+5	74/120	<0.0001
Wild-type <i>ugt-26</i> RNAi	21.36±0.65	26	+4	81/120	0.4103
<i>isp-1(qm150); ctb-1(qm189) ugt-26 RNAi</i>	25.32±0.88	31	-13	72/120	<0.0001
Wild-type <i>C46C2.2</i> RNAi	21.73±0.67	26	+6	70/120	0.2551
<i>isp-1(qm150); ctb-1(qm189) C46C2.2 RNAi</i>	28.72±0.93	35	-1	83/120	<0.0001
Wild-type <i>C50F4.1</i> RNAi	20.33±0.66	24	-1	71/120	0.8316
<i>isp-1(qm150); ctb-1(qm189) C50F4.1 RNAi</i>	27.76±0.95	35	-5	78/120	<0.0001
Wild-type control RNAi	20.17±0.6	23		64/120	
<i>isp-1(qm150); ctb-1(qm189) control RNAi</i>	35.03±1.17	41	+74	62/90	<0.0001
Wild-type <i>rde-4</i> RNAi	21.42±0.7	26	+6	66/120	0.1278
<i>isp-1(qm150); ctb-1(qm189) rde-4 RNAi</i>	35.61±0.94	41	+2	77/120	0.8821
Wild-type <i>ugt-26</i> RNAi	20.2±0.74	26	0	56/120	0.8235
<i>isp-1(qm150); ctb-1(qm189) ugt-26 RNAi</i>	30.22±1.09	35	-14	54/90	0.0046
Wild-type <i>C46C2.2</i> RNAi	20.03±0.67	23	-1	50/120	0.8793
<i>isp-1(qm150); ctb-1(qm189) C46C2.2 RNAi</i>	33.27±1.01	39	-5	59/90	0.2273
Wild-type <i>C50F4.1</i> RNAi	19.87±0.72	23	-1	49/120	0.8501

<i>isp-1(qm150); ctb-1(qm189) C50F4.1</i> RNAi	31.28±0.96	37	-11	85/120	0.0249
Wild-type <i>gfp</i> RNAi	19.08±0.46	22		82/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	29.7±0.84	36	+56	102/120	<0.0001
Wild-type <i>pud-1.2</i> RNAi	20.68±0.44	24	+8	98/120	0.0083
<i>isp-1(qm150); ctb-1(qm189) pud-1.2</i> RNAi	29.83±1.01	40	0	96/120	0.3181
Wild-type <i>csr-1</i> RNAi	17.72±0.49	20	-7	78/120	0.061
<i>isp-1(qm150); ctb-1(qm189) csr-1</i> RNAi	26.79±0.85	32	-10	92/120	0.0184
Wild-type <i>gfp</i> RNAi	20.62±0.48	23		86/120	
<i>isp-1(qm150); ctb-1(qm189) gfp</i> RNAi	27.96±0.81	33	+36	75/120	<0.0001
Wild-type <i>pud-1.2</i> RNAi	21.66±0.43	25	+5	94/120	0.1644
<i>isp-1(qm150); ctb-1(qm189) pud-1.2</i> RNAi	28.84±0.79	35	+3	102/120	0.3956
Wild-type <i>csr-1</i> RNAi	17.06±0.56	19	-17	57/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) csr-1</i> RNAi	27.16±0.77	31	-3	85/120	0.4779
Wild-type control RNAi	20.31±0.56	23		81/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	31.78±1.06	40	+56	82/120	<0.0001
Wild-type <i>F22E5.1</i> RNAi	20.83±0.55	25	+3	78/120	0.5946
<i>isp-1(qm150); ctb-1(qm189) F22E5.1</i> RNAi	30.84±0.95	36	-3	87/120	0.4458
Wild-type <i>F42A10.7</i> RNAi	22.57±0.52	27	+11	95/120	0.0115
<i>isp-1(qm150); ctb-1(qm189) F42A10.7</i> RNAi	35.92±0.92	42	+13	85/120	0.0223
Wild-type <i>cey-2</i> RNAi	22.12±0.53	27	+9	88/120	0.0527
<i>isp-1(qm150); ctb-1(qm189) cey-2</i> RNAi	34.16±1.12	44	+7	97/120	0.0796

Wild-type <i>K01D12.15</i> RNAi	21.17±0.52	25	+4	67/120	0.3589
<i>isp-1(qm150); ctb-1(qm189) K01D12.15</i> RNAi	31.77±0.88	38	0	82/120	0.4865
Wild-type <i>T05E12.6</i> RNAi	23.04±0.61	29	+13	90/120	0.0009
<i>isp-1(qm150); ctb-1(qm189) T05E12.6</i> RNAi	36.13±1.14	45	+14	91/120	0.002
Wild-type <i>T17H7.1</i> RNAi	21.42±0.6	24	+5	71/120	0.1746
<i>isp-1(qm150); ctb-1(qm189) T17H7.1</i> RNAi	32.57±1.24	40	+2	80/120	0.4036
Wild-type <i>ant-1.2</i> RNAi	20.65±0.59	24	+2	81/120	0.5593
<i>isp-1(qm150); ctb-1(qm189) ant-1.2</i> RNAi	32.38±1.31	43	+2	71/120	0.4805
Wild-type <i>Y38C1AB.3</i> RNAi	24.31±0.54	29	+20	77/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) Y38C1AB.3</i> RNAi	34.4±1.46	47	+8	80/120	0.0701
Wild-type control RNAi	17.42±0.37	19		76/175	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	30.97±0.69	36	+78	91/140	<0.0001
Wild-type <i>F22E5.1</i> RNAi	17.47±0.4	19	0	83/175	0.7148
<i>isp-1(qm150); ctb-1(qm189) F22E5.1</i> RNAi	30.1±0.96	33	-3	69/140	0.7992
Wild-type <i>F42A10.7</i> RNAi	17.03±0.55	19	-2	50/105	0.8114
<i>isp-1(qm150); ctb-1(qm189) F42A10.7</i> RNAi	27.77±0.77	30	-10	75/140	0.0045
Wild-type <i>cey-2</i> RNAi	17.93±0.4	21	+3	85/175	0.2392
<i>isp-1(qm150); ctb-1(qm189) cey-2</i> RNAi	29.81±0.64	33	-4	113/140	0.2969

Wild-type <i>K01D12.15</i> RNAi	19.2±0.51	23	+10	91/175	0.0018
<i>isp-1(qm150); ctb-1(qm189) K01D12.15</i> RNAi	28.51±0.69	33	-8	59/140	0.008
Wild-type <i>T05E12.6</i> RNAi	19.07±0.47	22	+9	61/140	0.005
<i>isp-1(qm150); ctb-1(qm189) T05E12.6</i> RNAi	32.45±0.87	38	+5	87/140	0.0926
Wild-type <i>T17H7.1</i> RNAi	19.74±0.66	24	+13	48/105	0.0009
<i>isp-1(qm150); ctb-1(qm189) T17H7.1</i> RNAi	31.72±1.12	38	+2	60/140	0.2411
Wild-type <i>ant-1.2</i> RNAi	18.28±0.72	22	+5	28/140	0.3233
<i>isp-1(qm150); ctb-1(qm189) ant-1.2</i> RNAi	32.74±0.86	38	+6	57/140	0.1872
Wild-type <i>Y38C1AB.3</i> RNAi	19.07±0.78	22	+9	36/140	0.0186
<i>isp-1(qm150); ctb-1(qm189) Y38C1AB.3</i> RNAi	34.26±0.88	41	+11	61/125	0.0153
Wild-type control RNAi	21.21±0.51	25		98/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	30.03±0.91	36	+42	96/120	<0.0001
Wild-type <i>dhs-4</i> RNAi	19.99±0.47	23	-6	105/121	0.0554
<i>isp-1(qm150); ctb-1(qm189) dhs-4</i> RNAi	29.41±0.84	34	-2	97/120	0.4159
Wild-type <i>pgp-6</i> RNAi	19.58±0.55	23	-8	84/120	0.0259
<i>isp-1(qm150); ctb-1(qm189) pgp-6</i> RNAi	26.85±1.07	30	-11	57/90	0.0247
Wild-type <i>gld-1</i> RNAi	14.27±0.2	18	-33	105/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) gld-1</i> RNAi	20.8±0.26	23	-31	113/122	<0.0001
Wild-type <i>ssp-9</i> RNAi	20.53±0.47	25	-3	92/120	0.2935

<i>isp-1(qm150); ctb-1(qm189) ssp-9</i> RNAi	25.27±0.78	31	-16	121/180	0.0004
Wild-type control RNAi	18.92±0.53	24		92/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	30.79±0.98	39	+63	82/120	<0.0001
Wild-type <i>dhs-4</i> RNAi	20.79±0.53	24	+10	84/120	0.0278
<i>isp-1(qm150); ctb-1(qm189) dhs-4</i> RNAi	29.99±0.87	34	-3	69/90	0.1239
Wild-type <i>pgp-6</i> RNAi	20.53±0.51	24	+9	72/120	0.1407
<i>isp-1(qm150); ctb-1(qm189) pgp-6</i> RNAi	28.01±1.25	34	-11	30/120	0.0137
Wild-type <i>gld-1</i> RNAi	12.56±0.24	16	-34	102/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) gld-1</i> RNAi	19.18±0.21	22	-38	106/120	<0.0001
Wild-type <i>ssp-9</i> RNAi	21.1±0.5	24	+12	94/120	0.0081
<i>isp-1(qm150); ctb-1(qm189) ssp-9</i> RNAi	33.05±0.96	39	+7	79/120	0.1261
Wild-type control RNAi	20.37±0.49	25		118/140	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	27.3±1.04	34	+34	83/120	<0.0001
Wild-type <i>cyp-14A1</i> RNAi	21.01±0.44	25	+3	106/140	0.8647
<i>isp-1(qm150); ctb-1(qm189) cyp-14A1</i> RNAi	27.73±0.9	34	+2	84/120	0.9717
Wild-type <i>F48D6.4</i> RNAi	20.77±0.5	25	+2	109/140	0.5233
<i>isp-1(qm150); ctb-1(qm189) F48D6.4</i> RNAi	23.75±1.06	29	-13	66/120	0.0362
Wild-type <i>ugt-61</i> RNAi	20.49±0.51	25	+1	113/140	0.6781
<i>isp-1(qm150); ctb-1(qm189) ugt-61</i> RNAi	24.51±0.94	29	-10	82/120	0.0846
Wild-type control RNAi	19.62±0.35	23		99/120	

<i>isp-1(qm150); ctb-1(qm189) control RNAi</i>	29.84±1.1	38	+52	66/120	<0.0001
Wild-type <i>cyp-14A1</i> RNAi	19.99±0.3	23	+2	121/160	0.6069
<i>isp-1(qm150); ctb-1(qm189) cyp-14A1</i> RNAi	26.5±1.12	34	-11	59/120	0.0127
Wild-type <i>F48D6.4</i> RNAi	21.77±0.3	25	+11	116/160	<0.0001
<i>isp-1(qm150); ctb-1(qm189) F48D6.4</i> RNAi	27.89±0.8	34	-7	77/120	0.0148
Wild-type <i>ugt-61</i> RNAi	21.17±0.39	23	+8	95/120	0.0005
<i>isp-1(qm150); ctb-1(qm189) ugt-61</i> RNAi	25.9±0.92	34	-13	68/120	0.001
Wild-type control RNAi	18.75±0.38	21		89/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	24.96±0.74	28	+33	63/110	<0.0001
Wild-type <i>col-175</i> RNAi	16.92±0.4	19	-10	88/120	0.0015
<i>isp-1(qm150); ctb-1(qm189) col-175</i> RNAi	26.52±0.54	30	+6	71/120	0.2395
Wild-type <i>bam-2</i> RNAi	15.83±0.38	19	-16	85/120	<0.0001
<i>isp-1(qm150); ctb-1(qm189) bam-2</i> RNAi	23.63±0.82	28	-5	66/120	0.1103
Wild-type <i>C09B9.3</i> RNAi	17.84±0.39	21	-5	85/120	0.145
<i>isp-1(qm150); ctb-1(qm189) C09B9.3</i> RNAi	27.27±0.62	33	+9	73/120	0.0177
Wild-type <i>E04D5.1</i> RNAi	18.55±0.39	21	-1	82/120	0.6835
<i>isp-1(qm150); ctb-1(qm189) E04D5.1</i> RNAi	24.31±0.78	28	-3	83/120	0.7164

Wild-type control RNAi	19.48±0.44	21		91/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	27.7±0.88	32	+42	56/120	<0.0001
Wild-type <i>col-175</i> RNAi	18.98±0.48	21	-3	94/120	0.7309
<i>isp-1(qm150); ctb-1(qm189) col-175</i> RNAi	27.51±0.73	32	-1	72/120	0.6742
Wild-type <i>bam-2</i> RNAi	19.7±0.42	21	+1	74/90	0.9542
<i>isp-1(qm150); ctb-1(qm189) bam-2</i> RNAi	24.34±0.82	30	-12	62/120	0.0048
Wild-type <i>C09B9.3</i> RNAi	19.14±0.45	21	-2	94/120	0.7075
<i>isp-1(qm150); ctb-1(qm189) C09B9.3</i> RNAi	25.1±0.76	30	-9	71/120	0.0259
Wild-type <i>E04D5.1</i> RNAi	18.73±0.57	21	-4	89/120	0.767
<i>isp-1(qm150); ctb-1(qm189) E04D5.1</i> RNAi	23.52±0.81	28	-15	67/120	0.0009
Wild-type control RNAi	19.83±0.39	23		81/120	
<i>isp-1(qm150); ctb-1(qm189) control</i> RNAi	22.68±0.75	26	+14	88/118	0.0002
Wild-type <i>C01B4.6</i> RNAi	18.88±0.46	23	-5	79/120	0.2318
<i>isp-1(qm150); ctb-1(qm189) C01B4.6</i> RNAi	24.73±0.9	32	+9	67/120	0.103
Wild-type <i>gei-7</i> RNAi	18.01±0.28	19	-9	89/120	0.0001
<i>isp-1(qm150); ctb-1(qm189) gei-7</i> RNAi	22.67±0.54	26	0	95/120	0.6092
Wild-type <i>Y57G11A.2</i> RNAi	20.67±0.44	25	+4	85/120	0.0863
<i>isp-1(qm150); ctb-1(qm189) Y57G11A.2</i> RNAi	26.53±0.83	32	+17	75/120	0.0013
Wild-type <i>cdr-2</i> RNAi	18.16±0.36	21	-8	83/120	0.002

<i>isp-1(qm150); ctb-1(qm189) cdr-2</i> RNAi	22.4±0.8	26	-1	79/120	0.9302
Wild-type control RNAi	19.12±0.59	22		67/90	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	25.9±0.78	32	+35	71/120	<0.0001
Wild-type <i>C01B4.6</i> RNAi	20.05±0.6	27	+5	90/120	0.0941
<i>isp-1(qm150); ctb-1(qm189) C01B4.6</i> RNAi	24.99±0.82	30	-4	68/120	0.4949
Wild-type <i>gei-7</i> RNAi	19.18±0.56	22	0	73/90	0.8648
<i>isp-1(qm150); ctb-1(qm189) gei-7</i> RNAi	25.94±0.71	30	0	84/120	0.9752
Wild-type <i>Y57G11A.2</i> RNAi	20.04±0.54	24	+5	90/120	0.2041
<i>isp-1(qm150); ctb-1(qm189) Y57G11A.2</i> RNAi	24.34±0.69	30	-6	75/120	0.0814
Wild-type <i>cdr-2</i> RNAi	20.01±0.5	24	+5	103/120	0.2044
<i>isp-1(qm150); ctb-1(qm189) cdr-2</i> RNAi	24.8±0.9	30	-4	52/120	0.3253
Wild-type control RNAi	21.02±0.52	26		99/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	28.92±0.84	34	+38	94/120	<0.0001
Wild-type <i>col-88</i> RNAi	20.6±0.55	24	-2	84/120	0.5456
<i>isp-1(qm150); ctb-1(qm189) col-88</i> RNAi	29.47±1.02	36	+2	78/120	0.4705
Wild-type <i>F57H12.6</i> RNAi	21.79±0.57	26	+4	85/120	0.3007
<i>isp-1(qm150); ctb-1(qm189) F57H12.6</i> RNAi	31.24±0.76	38	+8	96/120	0.1263
Wild-type <i>Y38H8A.3</i> RNAi	20.77±0.6	26	-1	96/120	0.9855
<i>isp-1(qm150); ctb-1(qm189) Y38H8A.3</i> RNAi	26.81±0.91	34	-7	75/120	0.0528

Wild-type control RNAi	22.01±0.6	26		76/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	30.73±1.24	37	+40	52/90	<0.0001
Wild-type <i>col-88</i> RNAi	22.01±0.56	26	0	82/120	0.9224
<i>isp-1(qm150); ctb-1(qm189) col-88</i> RNAi	32.19±0.92	37	+5	83/120	0.5245
Wild-type <i>F57H12.6</i> RNAi	21.26±0.58	26	-3	66/120	0.3443
<i>isp-1(qm150); ctb-1(qm189) F57H12.6</i> RNAi	34.37±1.09	45	+12	80/120	0.0327
Wild-type <i>Y38H8A.3</i> RNAi	22.66±0.53	26	+3	88/120	0.4666
<i>isp-1(qm150); ctb-1(qm189) Y38H8A.3</i> RNAi	28.76±0.99	35	-6	92/120	0.3232
Wild-type control RNAi	21.87±0.53	26		98/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	28.17±0.96	36	+29	90/120	<0.0001
Wild-type <i>C35B1.5</i> RNAi	21.61±0.52	26	-1	86/120	0.4338
<i>isp-1(qm150); ctb-1(qm189) C35B1.5</i> RNAi	29.11±0.84	36	+3	103/120	0.9565
Wild-type <i>C44B7.10</i> RNAi	19.35±0.46	22	-12	100/120	0.0001
<i>isp-1(qm150); ctb-1(qm189) C44B7.10</i> RNAi	22.75±0.91	28	-19	84/120	0.0002
Wild-type <i>ugt-29</i> RNAi	21.27±0.5	26	-3	94/120	0.3054
<i>isp-1(qm150); ctb-1(qm189) ugt-29</i> RNAi	27.84±0.9	36	-1	110/120	0.8317
Wild-type control RNAi	21.39±0.55	25		73/120	

<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	29.04±0.9	36	+36	101/120	<0.0001
Wild-type <i>C35B1.5</i> RNAi	19.69±0.58	25	-8	50/90	0.0345
<i>isp-1(qm150); ctb-1(qm189) C35B1.5</i> RNAi	33.88±0.9	42	+17	103/120	0.0001
Wild-type <i>C44B7.10</i> RNAi	20.19±0.55	25	-6	63/120	0.0995
<i>isp-1(qm150); ctb-1(qm189) C44B7.10</i> RNAi	26.09±0.81	33	-10	91/120	0.0063
Wild-type <i>ugt-29</i> RNAi	21.03±0.6	25	-2	90/120	0.8898
<i>isp-1(qm150); ctb-1(qm189) ugt-29</i> RNAi	28.65±0.92	36	-1	108/120	0.9932
Wild-type control RNAi	21.37±0.6	27		87/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	32.15±1.2	41	+50	57/90	<0.0001
Wild-type <i>alh-4/alh-5</i> RNAi	23.76±0.58	27	+11	90/120	0.0066
<i>isp-1(qm150); ctb-1(qm189) alh-4/alh-5</i> RNAi	28.21±0.89	32	-12	57/90	0.0007
Wild-type <i>ddo-2</i> RNAi	21.9±0.63	27	+2	79/120	0.5151
<i>isp-1(qm150); ctb-1(qm189) ddo-2</i> RNAi	31.8±0.97	39	-1	72/120	0.6098
Wild-type <i>F08A8.2</i> RNAi	22.05±0.68	27	+3	83/120	0.3365
<i>isp-1(qm150); ctb-1(qm189) F08A8.2</i> RNAi	31.45±0.87	39	-2	95/120	0.4786
Wild-type <i>T22B3.2</i> RNAi	21.65±0.63	27	+1	82/120	0.7008
<i>isp-1(qm150); ctb-1(qm189) T22B3.2</i> RNAi	30.03±1.19	39	-7	64/90	0.3168

Wild-type control RNAi	22.66±0.4	27		80/140	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	33.17±0.9	40	+46	89/140	<0.0001
Wild-type <i>alh-4/alh-5</i> RNAi	23.44±0.48	27	+3	83/140	0.095
<i>isp-1(qm150); ctb-1(qm189) alh-4/alh-5</i> RNAi	29.07±0.89	34	-12	61/140	0.0008
Wild-type <i>ddo-2</i> RNAi	21.71±0.56	24	-4	49/105	0.2703
<i>isp-1(qm150); ctb-1(qm189) ddo-2</i> RNAi	31.75±0.93	37	-4	75/140	0.2078
Wild-type <i>F08A8.2</i> RNAi	20.94±0.56	24	-8	72/140	0.0459
<i>isp-1(qm150); ctb-1(qm189) F08A8.2</i> RNAi	33.61±1.09	40	+1	71/105	0.5814
Wild-type <i>T22B3.2</i> RNAi	22.67±0.49	24	0	76/140	0.7494
<i>isp-1(qm150); ctb-1(qm189) T22B3.2</i> RNAi	31.81±1.02	40	-4	68/105	0.2407
Wild-type control RNAi	21.28±0.64	27		93/120	
<i>isp-1(qm150); ctb-1(qm189)</i> control RNAi	32.94±1.34	40	+55	82/120	<0.0001
Wild-type <i>haf-3</i> RNAi	18.72±0.52	23	-12	111/90	0.0002
<i>isp-1(qm150); ctb-1(qm189) haf-3</i> RNAi	35.23±1.45	44	+7	99/120	0.2056
Wild-type <i>patr-1</i> RNAi	20.73±0.54	25	-3	87/120	0.2395
<i>isp-1(qm150); ctb-1(qm189) patr-1</i> RNAi	24.2±0.79	30	-27	74/120	<0.0001
Wild-type <i>ugt-62</i> RNAi	24.24±0.56	27	+14	67/120	0.0068
<i>isp-1(qm150); ctb-1(qm189) ugt-62</i> RNAi	30.52±1.06	36	-7	101/120	0.0885
Wild-type <i>hrpu-2</i> RNAi	24.23±0.67	27	+14	77/120	0.0038

<i>isp-1(qm150); ctb-1(qm189) hrpu-2 RNAi</i>	29.59±0.93	34	-10	89/120	0.0099
Wild-type control RNAi	21.66±0.61	26		96/140	
<i>isp-1(qm150); ctb-1(qm189) cont RNAi</i>	34.99±1.14	45	+62	88/140	<0.0001
Wild-type <i>haf-3</i> RNAi	19.74±0.39	23	-9	108/140	0.0013
<i>isp-1(qm150); ctb-1(qm189) haf-3 RNAi</i>	34.85±1.08	45	0	81/140	0.7295
Wild-type <i>patr-1</i> RNAi	18.71±0.38	23	-14	119/140	<0.0001
<i>isp-1(qm150); ctb-1(qm189) patr-1 RNAi</i>	25.6±0.60	30	-27	113/140	<0.0001
Wild-type <i>ugt-62</i> RNAi	24.53±0.50	29	+13	115/140	0.0026
<i>isp-1(qm150); ctb-1(qm189) ugt-62 RNAi</i>	32.47±1.16	42	-7	92/140	0.4323
Wild-type <i>hrpu-2</i> RNAi	24.13±0.51	29	+11	113/140	0.0148
<i>isp-1(qm150); ctb-1(qm189) hrpu-2 RNAi</i>	30.9±1.27	42	-12	62/140	0.0157
Wild-type control RNAi	21±0.44	26	0	120/150	
<i>isp-1(qm150); ctb-1(qm189) control RNAi</i>	29.45±0.82	35	+40	113/150	<0.0001
Wild-type <i>asp-8</i> RNAi	20.97±0.47	24	0	111/150	0.9335
<i>isp-1(qm150); ctb-1(qm189) asp-8 RNAi</i>	29.31±0.73	35	0	107/140	0.4523
Wild-type <i>hmt-1</i> RNAi	19.94±0.41	24	-5	115/150	0.0224
<i>isp-1(qm150); ctb-1(qm189) hmt-1 RNAi</i>	28.99±0.67	35	-2	124/150	0.271
Wild-type control RNAi	18.64±0.37	22	0	121/150	
<i>isp-1(qm150); ctb-1(qm189) control RNAi</i>	27.57±0.65	32	+48	125/150	<0.0001

Wild-type <i>asp-8</i> RNAi	19.45±0.37	22	+4	105/150	0.1692
<i>isp-1(qm150); ctb-1(qm189) asp-8</i> RNAi	31.3±0.85	37	+14	109/140	0.0001
Wild-type <i>hmt-1</i> RNAi	19.06±0.49	22	+2	86/120	0.2896
<i>isp-1(qm150); ctb-1(qm189) hmt-1</i> RNAi	27.78±0.72	32	+1	108/150	0.9423

In this table, the lifespan data sets within thick solid lines were performed in parallel.

Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. Both control RNAi (L4440 empty vector) and *gfp* RNAi were used as control conditions. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type or *isp-1(qm150); ctb-1(qm189)* mutant animals treated with control or *gfp* RNAi].

^Δ: % change in lifespan was calculated against the same control data [wild-type or *isp-1(qm150); ctb-1(qm189)* mutant animals treated with control or *gfp* RNAi]. Increased (+) or decreased (-) mean lifespan was indicated.

Treatment with *pmt-1* RNAi starting from egg hatching caused developmental arrest. Thus, we were not able to perform lifespan assays for *pmt-1* RNAi.

Table S2B. Fourteen candidate RNAi clones that suppressed the longevity of *isp-1(qm150)* mutants (related to Figure 2B-D)

Strain/treatment	Mean lifespan ±SEM (days)	75th percentile	% changeΔ	Number of animals that died/total	p-value vs. control	Figure in text
Wild-type control RNAi	19.95±0.47	23		147/150		
<i>isp-1(qm150)</i> control RNAi	28.74±1.03	36	44	86/90	<0.0001	
Wild-type <i>gpd-2/gpd-3</i> RNAi	20.99±0.44	26	5	139/150	0.2909	
<i>isp-1(qm150) gpd-2/gpd-3</i> RNAi	26.36±0.94	33	-8	87/151	0.0915	
Wild-type <i>mon-2</i> RNAi	17.95±0.3	21	-11	181/240	<0.0001	
<i>isp-1(qm150) mon-2</i> RNAi	22.88±0.88	29	-20	115/121	0.0003	
Wild-type <i>ugt-26</i> RNAi	20.05±0.39	23	0	136/150	0.416	
<i>isp-1(qm150) ugt-26</i> RNAi	26.10±0.84	33	-9	137/150	0.1071	
Wild-type control RNAi	16.00±0.3	20		144/150		Fig. 2B
<i>isp-1(qm150)</i> control RNAi	26.61±0.79	33	66	104/120	<0.0001	Fig. 2B
Wild-type <i>gpd-2/gpd-3</i> RNAi	16.39±0.28	20	2	135/150	0.5452	
<i>isp-1(qm150) gpd-2/gpd-3</i> RNAi	24.31±0.88	29	-9	71/120	0.0322	
Wild-type <i>mon-2</i> RNAi	17.16±0.29	21	7	64/120	0.1349	Fig. 2B
<i>isp-1(qm150) mon-2</i> RNAi	20.31±0.77	27	-24	105/120	<0.0001	Fig. 2B
Wild-type <i>ugt-26</i> RNAi	16.08±0.28	20	0	120/120	0.7963	
<i>isp-1(qm150) ugt-26</i> RNAi	22.85±0.82	29	-14	104/120	0.0054	
Wild-type control RNAi	17.39±0.49	20		65/120		Fig. 2C
<i>isp-1(qm150)</i> control RNAi	26.70±0.74	34	54	100/120	<0.0001	Fig. 2C
Wild-type <i>hrpu-2</i> RNAi	16.73±0.51	20	-4	75/120	0.5808	Fig. 2C
<i>isp-1(qm150) hrpu-2</i> RNAi	20.65±0.68	25	-23	106/120	<0.0001	Fig. 2C
Wild-type <i>patr-1</i> RNAi	17.92±0.37	20	3	91/120	0.6495	
<i>isp-1(qm150) patr-1</i> RNAi	18.80±0.59	24	-30	103/120	<0.0001	
Wild-type <i>haf-3</i> RNAi	17.23±0.58	22	-1	54/120	0.9787	

<i>isp-1(qm150) haf-3</i> RNAi	24.00±0.79	30	-10	106/120	0.0442	
Wild-type <i>alh-4/alh-5</i> RNAi	18.67±0.52	22	7	53/120	0.0932	
<i>isp-1(qm150) alh-4/alh-5</i> RNAi	24.48±0.62	31	-8	107/120	0.0003	
Wild-type <i>ugt-62</i> RNAi	18.60±0.47	20	7	57/120	0.1382	
<i>isp-1(qm150) ugt-62</i> RNAi	24.91±0.98	34	-7	85/120	0.7427	
Wild-type control RNAi	21.38±0.57	26		90/120		Fig. 2D
<i>isp-1(qm150)</i> control RNAi	28.24±0.86	36	32	114/120	<0.0001	Fig. 2D
Wild-type <i>hrpu-2</i> RNAi	18.36±0.54	23	-14	96/120	0.0005	
<i>isp-1(qm150) hrpu-2</i> RNAi	24.05±0.82	31	-15	112/120	0.0032	
Wild-type <i>patr-1</i> RNAi	19.55±0.5	23	-9	108/121	0.0166	Fig. 2D
<i>isp-1(qm150) patr-1</i> RNAi	20.59±0.66	23	-27	107/120	<0.0001	Fig. 2D
Wild-type <i>haf-3</i> RNAi	19.97±0.58	26	-7	92/120	0.1643	
<i>isp-1(qm150) haf-3</i> RNAi	24.44±0.86	31	-13	102/120	0.0095	
Wild-type <i>alh-4/alh-5</i> RNAi	21.07±0.54	26	-1	96/120	0.5272	
<i>isp-1(qm150) alh-4/alh-5</i> RNAi	26.34±0.97	34	-7	105/120	0.3783	
Wild-type <i>ugt-62</i> RNAi	20.57±0.54	26	-4	86/120	0.2533	
<i>isp-1(qm150) ugt-62</i> RNAi	26.28±0.97	34	-7	106/120	0.38	
Wild-type control RNAi	20.86±0.53	24		65/115		
<i>isp-1(qm150)</i> control RNAi	29.88±0.74	38	43	126/151	<0.0001	
Wild-type <i>C35B1.5</i> RNAi	19.81±0.49	22	-5	98/150	0.2105	
<i>isp-1(qm150) C35B1.5</i> RNAi	31.45±0.78	40	5	105/150	0.0977	
Wild-type <i>F48D6.4</i> RNAi	20.09±0.51	24	-4	108/150	0.5783	
<i>isp-1(qm150) F48D6.4</i> RNAi	28.70±0.83	38	-4	122/150	0.7083	
Wild-type <i>K01D12.15</i> RNAi	20.64±0.41	24	-1	98/150	0.641	
<i>isp-1(qm150) K01D12.15</i> RNAi	31.29±0.78	37	5	116/150	0.2206	
Wild-type <i>pgp-6</i> RNAi	20.97±0.51	24	1	88/144	0.7566	

<i>isp-1(qm150) pgp-6</i> RNAi	28.75±0.69	35	-4	117/150	0.1767	
Wild-type <i>sodh-1</i> RNAi	21.05±0.54	24	1	84/150	0.6269	
<i>isp-1(qm150) sodh-1</i> RNAi	29.02±0.62	35	-3	123/150	0.1032	
Wild-type <i>ugt-61</i> RNAi	21.17±0.45	24	1	111/150	0.5751	
<i>isp-1(qm150) ugt-61</i> RNAi	30.53±0.87	39	2	113/130	0.4158	
<hr/>						
Wild-type control RNAi	17.40±0.35	20		108/150		
<i>isp-1(qm150)</i> control RNAi	27.19±0.69	33	56	131/150	<0.0001	
Wild-type <i>C35B1.5</i> RNAi	18.98±0.61	22	9	73/150	0.0068	
<i>isp-1(qm150) C35B1.5</i> RNAi	26.39±0.73	33	-3	128/150	0.6464	
Wild-type <i>F48D6.4</i> RNAi	16.54±0.42	20	-5	92/150	0.196	
<i>isp-1(qm150) F48D6.4</i> RNAi	25.23±0.73	30	-7	132/150	0.1421	
Wild-type <i>K01D12.15</i> RNAi	18.59±0.50	22	7	96/120	0.013	
<i>isp-1(qm150) K01D12.15</i> RNAi	27.22±0.73	32	0	132/150	0.8836	
Wild-type <i>pgp-6</i> RNAi	17.20±0.41	20	-1	92/140	0.8605	
<i>isp-1(qm150) pgp-6</i> RNAi	25.24±0.73	30	-7	135/150	0.1427	
Wild-type <i>sodh-1</i> RNAi	17.05±0.49	20	-2	96/120	0.9844	
<i>isp-1(qm150) sodh-1</i> RNAi	24.59±0.70	30	-10	130/150	0.0117	
Wild-type <i>ugt-61</i> RNAi	17.25±0.36	20	-1	108/150	0.7694	
<i>isp-1(qm150) ugt-61</i> RNAi	24.96±0.73	32	-8	143/150	0.0324	

In this table, the lifespan data sets within thick solid lines were performed in parallel.

Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type or *isp-1(qm150)* mutant animals treated with control RNAi].

Δ: % change in lifespan was calculated against the same control data [wild-type or *isp-1(qm150)* mutant animals treated with control RNAi].

Table S2C. Lifespan measurements of *isp-1* and *clk-1* mutants with *mon-2*, *hrpu-2*, *patr-1* mutations (related to Figure 2E-K)

Strain/treatment	Mean survival ±SEM (days)	75th percentile	% change Δ	Number of animals that died/total	p-value vs. control	Figure in text
Wild-type	19.01±0.51	23		129/150		
<i>mon-2(xh22)</i>	16.73±0.34	20	-12	115/150	<0.0001	
<i>isp-1(qm150)</i>	25.01±0.8	33	32	136/150	<0.0001	
<i>isp-1(qm150) mon-2(xh22)</i>	18.81±0.52	23	-25	140/150	<0.0001	
<i>clk-1(qm30)</i>	20.91±0.68	25	10	126/150	0.0152	
<i>clk-1(qm30); mon-2(xh22)</i>	16.37±0.42	19	-22	117/150	<0.0001	
Wild-type	16.32±0.39	20		137/150		Fig. 2E-F
<i>mon-2(xh22)</i>	14.31±0.33	16	-12	113/150	<0.0001	Fig. 2E-F
<i>isp-1(qm150)</i>	21±0.64	26	29	114/150	<0.0001	Fig. 2E
<i>isp-1(qm150) mon-2(xh22)</i>	15.72±0.36	20	-25	137/150	<0.0001	Fig. 2E
<i>clk-1(qm30)</i>	19.29±0.55	24	18	119/150	<0.0001	Fig. 2F
<i>clk-1(qm30); mon-2(xh22)</i>	13.86±0.31	16	-28	144/150	<0.0001	Fig. 2F
Wild-type	24.57±0.31	28		139/150		
<i>hrpu-2(tm1474)</i>	21.04±0.26	23	-14	126/150	<0.0001	
<i>isp-1(qm150)</i>	29.49±0.65	36	20	129/150	<0.0001	
<i>hrpu-2(tm1474) isp-1(qm150)</i>	26.58±0.83	30	-10	106/150	0.1418	
<i>clk-1(qm30)</i>	30.37±0.59	37	24	99/120	<0.0001	
<i>clk-1(qm30); hrpu-2(tm1474)</i>	23.23±0.23	26	-24	127/150	<0.0001	
Wild-type	21.34±0.3	24		114/120		
<i>hrpu-2(tm1474)</i>	21.5±0.3	24	1	127/150	0.5088	
<i>isp-1(qm150)</i>	27.67±0.5	31	30	136/150	<0.0001	
<i>hrpu-2(tm1474) isp-1(qm150)</i>	24.76±0.64	30	-11	108/150	0.0055	
<i>clk-1(qm30)</i>	22.66±0.39	26	6	136/150	0.0001	
<i>clk-1(qm30); hrpu-2(tm1474)</i>	24.19±0.42	28	7	132/150	0.0043	
Wild-type	17.54±0.49	21		120/150		Fig. 2G-H
<i>hrpu-2(tm1474)</i>	16.05±0.37	19	-8	123/150	0.0027	Fig. 2G-H
<i>isp-1(qm150)</i>	30.28±0.91	39	73	124/150	<0.0001	Fig. 2G
<i>hrpu-2(tm1474) isp-1(qm150)</i>	25.56±0.81	33	-16	141/152	<0.0001	Fig. 2G
<i>clk-1(qm30)</i>	20.41±0.7	28	16	99/150	0.0001	Fig. 2H

<i>clk-1(qm30); hrpu-2(tm1474)</i>	15.58±0.52	19	-24	130/150	<0.0001	Fig. 2H
Wild-type	14.43±0.41	17		92/150		
<i>hrpu-2(tm1474)</i>	15.03±0.42	19	4	119/150	0.1994	
<i>isp-1(qm150)</i>	23.93±1.04	32	66	73/90	<0.0001	
<i>hrpu-2(tm1474) isp-1(qm150)</i>	22.17±0.56	27	-7	132/150	0.01	
<i>clk-1(qm30)</i>	16.8±0.58	21	16	86/150	0.0008	
<i>clk-1(qm30); hrpu-2(tm1474)</i>	12.84±0.31	15	-24	129/150	<0.0001	
Wild-type	16.18±0.43	22		141/153		
<i>patr-1(gk155841)</i>	21.07±0.4	25	30	126/150	<0.0001	
<i>isp-1(qm150)</i>	24.97±0.84	31	54	131/152	<0.0001	
<i>patr-1(gk155841); isp-1(qm150)</i>	21.16±0.78	26	-15	112/120	0.0009	
<i>clk-1(qm30)</i>	21.13±0.51	25	31	124/150	<0.0001	
<i>patr-1(gk155841); clk-1(qm30)</i>	16.3±0.48	17	-23	127/150	<0.0001	
Wild-type	13.28±0.25	15		135/150		Fig. 2I-J
<i>patr-1(gk155841)</i>	15.82±0.33	17	19	130/150	<0.0001	Fig. 2I-J
<i>isp-1(qm150)</i>	22.94±0.66	29	73	127/150	<0.0001	Fig. 2I
<i>patr-1(gk155841); isp-1(qm150)</i>	16.86±0.64	20	-27	131/150	<0.0001	Fig. 2I
<i>clk-1(qm30)</i>	17.13±0.55	21	29	119/150	<0.0001	Fig. 2J
<i>patr-1(gk155841); clk-1(qm30)</i>	11.59±0.34	13	-32	122/150	<0.0001	Fig. 2J
Wild-type [#]	16.66±0.46	20		84/120		Fig. 2K
<i>mon-2(xh22)</i> [#]	18.45±0.65	23	11	77/150	0.0204	Fig. 2K
<i>isp-1(qm150)</i> [#]	24.72±1.01	31	48	71/150	<0.0001	Fig. 2K
<i>isp-1(qm150) mon-2(xh22)</i> [#]	19.39±0.68	24	-22	113/150	<0.0001	Fig. 2K
Wild-type [#]	21.89±0.46	26		92/150		
<i>mon-2(xh22)</i> [#]	20.2±0.63	24	-8	59/120	0.0294	
<i>isp-1(qm150)</i> [#]	24.21±0.77	31	11	106/150	0.006	
<i>isp-1(qm150) mon-2(xh22)</i> [#]	20.03±0.47	23	-17	146/200	<0.0001	
Wild-type [#]	16.16±0.42	19		59/150		
<i>mon-2(xh22)</i> [#]	16.79±0.42	18	4	64/390	0.2917	
Wild-type [#]	15.26±0.46	17		69/150		
<i>mon-2(xh22)</i> [#]	14.76±0.43	17	-3	68/390	0.1196	

In this table, the lifespan data sets within thick solid lines were performed in parallel. Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type, *isp-1(qm150)* or *clk-1(qm30)* mutant animals].

Δ: % change in lifespan was calculated against the same control data [wild-type, *isp-1(qm150)* or *clk-1(qm30)* mutant animals].

indicates lifespan assay without 5-fluoro-2'-deoxyuridine (FUDR) treatment.

Table S3. The effect of *mon-2* mutation on the lifespan of various long-living mutants or *cco-1* RNAi-treated animals (related to Figure 3A-D)

Strain/treatment	Mean survival ±SEM (days)	75th percentile	% change Δ	Number of animals that died/total	p-value vs. control	Figure in text
Wild-type control RNAi	18.45±0.42	23		121/151		Fig. 3A
Wild-type <i>cco-1</i> RNAi	33.58±0.77	41	82	111/150	<0.0001	Fig. 3A
<i>mon-2(xh22)</i> control RNAi	17.82±0.34	21	-3	121/150	0.0206	Fig. 3A
<i>mon-2(xh22) cco-1</i> RNAi	30.03±0.5	33	-11 ^{WT} <i>cco-1</i> RNAi	113/150	<0.0001 WT <i>cco-1</i> RNAi	Fig. 3A
Wild-type control RNAi	18.57±0.36	22		114/150		
Wild-type <i>cco-1</i> RNAi	28.77±0.72	37	55	137/150	<0.0001	
<i>mon-2(xh22)</i> control RNAi	17.66±0.29	22	-5	122/150	0.0003	
<i>mon-2(xh22) cco-1</i> RNAi	26.88±0.41	31	-7 ^{WT} <i>cco-1</i> RNAi	135/150	<0.0001 WT <i>cco-1</i> RNAi	
Wild-type	20.01±0.39	23		125/150		Fig. 3B-C
<i>mon-2(xh22)</i>	18.93±0.41	21	-5	131/155	0.5247	Fig. 3B-C
<i>eat-2(ad1116)</i>	26.04±0.48	30	30	111/175	<0.0001	Fig. 3C
<i>eat-2(ad1116); mon-2(xh22)</i>	19.34±0.5	23	-26 ^{eat-2(ad1116)}	117/150	<0.0001 <i>eat-2(ad1116)</i>	Fig. 3C
<i>daf-2(e1370)</i>	37.63±0.82	42	88	100/120	<0.0001	Fig. 3B
<i>daf-2(e1370); mon-2(xh22)</i>	25.35±0.67	32	-33 ^{daf-2(e1370)}	133/150	<0.0001 <i>daf-2(e1370)</i>	Fig. 3B
Wild-type	16.39±0.25	18		121/150		
<i>mon-2(xh22)</i>	17.3±0.28	20	6	127/150	0.0117	
<i>eat-2(ad1116)</i>	21.47±0.46	24	31	111/150	<0.0001	
<i>eat-2(ad1116); mon-2(xh22)</i>	15.35±0.38	20	-29 ^{eat-2(ad1116)}	135/150	<0.0001 <i>eat-2(ad1116)</i>	
<i>daf-2(e1370)</i>	34.31±1.08	43	109	101/120	<0.0001	
<i>daf-2(e1370); mon-2(xh22)</i>	25.12±0.87	34	-27 ^{daf-2(e1370)}	126/150	<0.0001 <i>daf-2(e1370)</i>	
Wild-type fed	14.48±0.54	17		115/120		Fig. 3D
Wild-type FD	25.15±0.73	31	74	142/160	<0.0001	Fig. 3D
<i>mon-2(xh22)</i> fed	14.73±0.5	19	2	111/120	0.9156	Fig. 3D
<i>mon-2(xh22)</i> FD	20.43±0.46	25	-19 ^{WT} FD	212/240	<0.0001 WT FD	Fig. 3D

Wild-type fed	19.02±0.68	23		105/120		
Wild-type FD	23.88±0.43	28	26	165/240	<0.0001	
<i>mon-2(xh22)</i> fed	17.27±0.41	19	-9	92/120	0.0142	
<i>mon-2(xh22)</i> FD	21.1±0.37	26	-12 ^{WT} FD	172/240	<0.0001 WT FD	
Wild-type fed	18.78±0.6	22		104/120		
Wild-type FD	24.46±0.54	27	30	74/199	<0.0001	
<i>mon-2(xh22)</i> fed	19.02±0.44	22	1	89/120	0.6818	
<i>mon-2(xh22)</i> FD	20.37±0.33	24	-17 ^{WT} FD	173/240	<0.0001 WT FD	

In this table, the lifespan data sets within thick solid lines were performed in parallel.

Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type control RNAi, wild-type or wild-type fed conditions] or against indicated condition as superscript.

^Δ: % change in lifespan was calculated against the same control data [wild-type control RNAi, wild-type or wild-type fed conditions] or against indicated condition as superscript. FD indicates food deprived conditions.

mon-2(-) mutations did not affect lifespan in the WT background in five out of 11 trials, slightly decreased that in four out of 11 trials, and slightly increased that in two out of 11 trials. Overall, the effects of *mon-2(-)* on the lifespan of WT animals are variable but do not seem to be significant (*p* = 0.3156, one sample *t*-test using % change of lifespan caused by *mon-2(-)*).

Table S4. Lifespan measurement with animals expressing *mon-2::gfp* (related to Fig. 3E-G)

Strain/treatment	Mean survival ±SEM (days)	75th percentile	% change Δ	Number of animals that died/total	p-value vs. control	Figure in text
<i>isp-1(qm150) mon-2(xh22)</i>	20.89±0.77	24		101/120		Fig. 3E
<i>isp-1(qm150)</i>	27.80±0.77	36	33	145/151	<0.0001	Fig. 3E
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #1</i>	27.75±0.73	33	33	107/122	<0.0001	Fig. 3E
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #2</i>	26.90±0.79	35	29	120/150	<0.0001	Fig. 3E
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #3</i>	27.38±0.72	35	31	123/150	<0.0001	Fig. 3E
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<i>isp-1(qm150) mon-2(xh22)</i>	17.78±0.57	22		129/150		
<i>isp-1(qm150)</i>	26.11±0.72	32	47	98/118	<0.0001	
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #1</i>	25.09±0.61	31	41	115/150	<0.0001	
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #2</i>	24.42±0.62	28	37	114/150	<0.0001	
<i>isp-1(qm150) mon-2(xh22); mon-2::gfp #3</i>	25.10±0.72	31	41	82/120	<0.0001	
Wild-type	15.95±0.53	19		112/120		Fig. 3F
<i>mon-2::gfp #1</i>	16.43±0.48	21	3	111/120	0.6991	Fig. 3F
<i>mon-2::gfp #2</i>	16.2±0.47	19	2	101/120	0.7825	Fig. 3F
<i>mon-2::gfp #3</i>	15.65±0.44	19	-2	112/121	0.5968	Fig. 3F
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Wild-type	14.3±0.34	16		115/120		
<i>mon-2::gfp #1</i>	15.28±0.39	19	7	117/120	0.0514	
<i>mon-2::gfp #2</i>	14.09±0.37	16	-1	113/125	0.7732	
<i>mon-2::gfp #3</i>	13.36±0.33	16	-7	106/120	0.0735	
Wild-type	18.23±0.52	24		103/120		
<i>mon-2::gfp #1</i>	20.24±0.53	24	11	101/120	0.0081	
<i>mon-2::gfp #2</i>	21.45±0.47	24	18	110/150	<0.0001	
<i>mon-2::gfp #3</i>	21.49±0.49	27	18	137/150	<0.0001	
Wild-type control RNAi	21.47±0.48	26		93/120		Fig. 3G
<i>mon-2::gfp #1</i> control RNAi	21.05±0.59	26	-2	92/120	0.6259	Fig. 3G
Wild-type <i>cco-1</i> RNAi	34.29±0.88	42	60	106/120	<0.0001	Fig. 3G
<i>mon-2::gfp #1 cco-1</i> RNAi	39.13±0.88	45	14 ^{WT} <i>cco-1</i> RNAi	104/120	0.0001 ^{WT} <i>cco-1</i> RNAi	Fig. 3G
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Wild-type control RNAi	18.96±0.47	22		95/120		
<i>mon-2::gfp #1</i> control RNAi	19.76±0.48	22	4	96/119	0.2382	

Wild-type <i>cco-1</i> RNAi	30.75±0.63	36	62	111/120	<0.0001	
<i>mon-2::gfp</i> #1 <i>cco-1</i> RNAi	34.28±0.54	39	11 ^{WT} <i>cco-1</i> RNAi	114/120	<0.0001 WT <i>cco-1</i> RNAi	

In this table, the lifespan data sets within thick solid lines were performed in parallel.

Experimental repeats were divided by bold dashed lines.

Statistical analysis was done within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type or *isp-1(qm150)* *mon-2(xh22)* mutant animals].

^Δ: % change in lifespan was calculated against the same control data [wild-type or *isp-1(qm150)* *mon-2(xh22)* mutant animals] or against indicated condition as superscript.

[#] indicates lifespan assay without FUDR treatment.

Table S5. The effect of genetic inhibition of factors that mediate membrane trafficking on the lifespan of *isp-1(qm150)* mutants or *cco-1* RNAi-treated animals (related to Figure 4 and Figure S3)

Strain/treatment	Mean survival ±SEM (days)	75th percentile	% change ^Δ	Number of animals that died/total	p-value vs. control	Figure in text
Wild-type control RNAi	18.26±0.43	21		140/180		Fig. 4H and Fig. S3A-E
Wild-type <i>mon-2</i> RNAi	17±0.42	21	-7	108/180	0.0097	
Wild-type <i>rab-10</i> RNAi	21±0.35	23	15	157/180	0.0002	Fig. S3A
Wild-type <i>pad-1</i> RNAi	16.83±0.29	19	-8	155/180	<0.0001	Fig. 4H
Wild-type <i>golg-2</i> RNAi	20.39±0.44	23	12	135/180	0.0015	Fig. S3B
Wild-type <i>gcc-1</i> RNAi	18.96±0.43	21	4	122/150	0.5837	Fig. S3C
Wild-type <i>Y47G6A.18</i> RNAi	18.92±0.4	21	4	98/180	0.8977	Fig. S3D
Wild-type <i>C34D4.4</i> RNAi	19.38±0.38	21	6	109/150	0.3857	Fig. S3E
<i>isp-1(qm150)</i> control RNAi	27.42±0.66	34	50	150/180	<0.0001	Fig. 4H and Fig. S3A-E
<i>isp-1(qm150)</i> <i>mon-2</i> RNAi	24.15±0.55	28	-12 <i>isp-1</i> ctrl RNAi	144/180	<0.0001 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>rab-10</i> RNAi	29.83±0.62	37	9 <i>isp-1</i> ctrl RNAi	155/180	0.0132 <i>isp-1</i> ctrl RNAi	Fig. S3A
<i>isp-1(qm150)</i> <i>pad-1</i> RNAi	22.21±0.51	28	-19 <i>isp-1</i> ctrl RNAi	151/180	<0.0001 <i>isp-1</i> ctrl RNAi	Fig. 4H
<i>isp-1(qm150)</i> <i>golg-2</i> RNAi	25.65±0.75	31	-6 <i>isp-1</i> ctrl RNAi	146/180	0.4018 <i>isp-1</i> ctrl RNAi	Fig. S3B
<i>isp-1(qm150)</i> <i>gcc-1</i> RNAi	26.87±0.76	34	-2 <i>isp-1</i> ctrl RNAi	152/180	0.6296 <i>isp-1</i> ctrl RNAi	Fig. S3C
<i>isp-1(qm150)</i> <i>Y47G6A.18</i> RNAi	28.39±0.74	37	4 <i>isp-1</i> ctrl RNAi	137/180	0.1151 <i>isp-1</i> ctrl RNAi	Fig. S3D
<i>isp-1(qm150)</i> <i>C34D4.4</i> RNAi	25.96±0.86	31	-5 <i>isp-1</i> ctrl RNAi	88/120	0.3304 <i>isp-1</i> ctrl RNAi	Fig. S3E
Wild-type control RNAi	21.48±0.47	25		109/150		
Wild-type <i>mon-2</i> RNAi	20.23±0.46	25	-6 <i>isp-1</i> ctrl RNAi	81/120	0.0165	
Wild-type <i>rab-10</i> RNAi	23.24±0.49	27	8	97/120	0.0021	
Wild-type <i>pad-1</i> RNAi	19.21±0.31	21	-11	123/150	<0.0001	
Wild-type <i>golg-2</i> RNAi	23.16±0.35	25	8	119/150	0.0341	
Wild-type <i>gcc-1</i> RNAi	23.29±0.43	27	8	115/150	0.0024	

Wild-type <i>Y47G6A.18</i> RNAi	20.87±0.44	25	-3	98/150	0.1462	
Wild-type <i>C34D4.4</i> RNAi	21.5±0.41	25	0	110/150	0.7471	
<i>isp-1(qm150)</i> control RNAi	27.18±0.6	30	27	92/120	<0.0001	
<i>isp-1(qm150)</i> <i>mon-2</i> RNAi	25.7±0.53	30	-5 <i>isp-1</i> ctrl RNAi	124/150	0.0786 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>rab-10</i> RNAi	28.29±0.76	34	4 <i>isp-1</i> ctrl RNAi	81/150	0.116 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>pad-1</i> RNAi	25.2±0.49	30	-7 <i>isp-1</i> ctrl RNAi	124/150	0.0062 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>golg-2</i> RNAi	27.56±0.59	30	1 <i>isp-1</i> ctrl RNAi	95/120	0.6306 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>gcc-1</i> RNAi	26.86±0.62	34	-1 <i>isp-1</i> ctrl RNAi	112/150	0.9434 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>Y47G6A.18</i> RNAi	26.87±0.63	30	-1 <i>isp-1</i> ctrl RNAi	87/150	0.861 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>C34D4.4</i> RNAi	25.19±0.51	30	-7 <i>isp-1</i> ctrl RNAi	121/150	0.0152 <i>isp-1</i> ctrl RNAi	
Wild-type control RNAi [#]	18.45±0.42	23		121/151		Fig. S3F
Wild-type <i>cco-1</i> RNAi [#]	33.58±0.77	41	82	111/150	<0.0001	Fig. S3F
<i>tbc-3(xh23)</i> control RNAi	17.59±0.46	22	-5	105/150	0.1705	Fig. S3F
<i>tbc-3(xh23)</i> <i>cco-1</i> RNAi	27.93±0.65	32	-17 ^{WT} <i>cco-1</i> RNAi	115/150	<0.0001 WT <i>cco-1</i> RNAi	Fig. S3F
Wild-type control RNAi [#]	18.57±0.36	22		114/150		
Wild-type <i>cco-1</i> RNAi [#]	28.77±0.72	37	55	137/150	<0.0001	
<i>tbc-3(xh23)</i> control RNAi	16±0.42	21	-14	131/150	0.0004	
<i>tbc-3(xh23)</i> <i>cco-1</i> RNAi	27.96±0.35	32	-3 ^{WT} <i>cco-1</i> RNAi	139/150	0.0001 ^{WT} <i>cco-1</i> RNAi	
Wild-type control RNAi	16±0.3	18		144/150		Fig. 4J
Wild-type <i>mon-2</i> RNAi	17.16±0.29	18	7	64/120	0.1349	
Wild-type <i>tbc-3</i> RNAi	16.15±0.21	18	1	147/150	0.5612	Fig. 4J
<i>isp-1(qm150)</i> control RNAi	26.61±0.79	33	66	104/150	<0.0001	Fig. 4J
<i>isp-1(qm150)</i> <i>mon-2</i> RNAi	20.31±0.77	27	-24 <i>isp-1</i> ctrl RNAi	105/120	<0.0001 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150)</i> <i>tbc-3</i> RNAi	20.67±0.82	27	-22 <i>isp-1</i> ctrl RNAi	94/150	<0.0001 <i>isp-1</i> ctrl RNAi	Fig. 4J
Wild-type control RNAi	19.95±0.47	23		147/150		
Wild-type <i>mon-2</i> RNAi	17.59±0.35	23	-12	137/150	<0.0001	
Wild-type <i>tbc-3</i> RNAi	20.19±0.39	23	1	143/152	0.5715	

<i>isp-1(qm150)</i> control RNAi	28.74±1.03	36	44	86/90	<0.0001	
<i>isp-1(qm150) mon-2</i> RNAi	22.88±0.88	38	-20 ^{isp-1} ctrl RNAi	115/121	0.0003 ^{isp-1} ctrl RNAi	
<i>isp-1(qm150) tbc-3</i> RNAi	23.6±0.76	29	-18 ^{isp-1} ctrl RNAi	120/145	<0.0001 <i>isp-1</i> ctrl RNAi	
Wild-type control RNAi*	21.46±0.41	23		103/120		Fig. 4I
Wild-type <i>mon-2</i> RNAi*	19.26±0.3	21	-10	107/120	<0.0001	
Wild-type <i>tbc-3</i> RNAi*	20.59±0.33	23	-4	105/120	0.0723	
Wild-type <i>snx-3</i> RNAi*	21.94±0.35	25	2	109/120	0.5442	Fig. 4I
<i>isp-1(qm150)</i> control RNAi*	26.53±0.71	30	24	100/120	<0.0001	Fig. 4I
<i>isp-1(qm150) mon-2</i> RNAi*	22.62±0.56	26	-15 ^{isp-1} ctrl RNAi	99/120	<0.0001 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150) tbc-3</i> RNAi*	23.18±0.57	26	-13 ^{isp-1} ctrl RNAi	112/120	0.0003 ^{isp-1} ctrl RNAi	
<i>isp-1(qm150) snx-3</i> RNAi*	21.94±0.62	26	-17 ^{isp-1} ctrl RNAi	96/119	<0.0001 <i>isp-1</i> ctrl RNAi	Fig. 4I
Wild-type control RNAi*	21.15±0.37	28		114/120		
Wild-type <i>mon-2</i> RNAi*	19.61±0.3	25	-7	104/120	0.0005	
Wild-type <i>tbc-3</i> RNAi*	21.09±0.4	28	0	101/120	0.9746	
Wild-type <i>snx-3</i> RNAi*	22.41±0.47	27	6	75/90	0.0829	
<i>isp-1(qm150)</i> control RNAi*	28.27±0.72	39	34	112/120	<0.0001	
<i>isp-1(qm150) mon-2</i> RNAi*	23.59±0.47	30	-17 ^{isp-1} ctrl RNAi	94/120	<0.0001 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150) tbc-3</i> RNAi*	24.15±0.55	30	-15 ^{isp-1} ctrl RNAi	106/119	<0.0001 <i>isp-1</i> ctrl RNAi	
<i>isp-1(qm150) snx-3</i> RNAi*	24.43±0.44	30	-14 ^{isp-1} ctrl RNAi	99/120	<0.0001 <i>isp-1</i> ctrl RNAi	

In this table, the lifespan data sets within the thick solid lines were performed in parallel. Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type control RNAi or wild-type] or against indicated condition as superscript.

* indicates lifespan assay using 10 μM FUDR.

indicates lifespan assay, which is the same experimental set with Fig. 3K and a repeat (Table S4).

Table S6. The effect of *TFEB/hlh-30* RNAi or *Atg6/bec-1* RNAi on the lifespan of *isp-1(qm150)* mutants (related to Figure 5)

Strain/treatment	Mean survival ±SEM (days)	75th percentile	% change ^Δ	Number of animals that died/total	p-value vs. control	Figure in text
<i>isp-1(qm150)</i> control RNAi	26.98±0.88	33		109/120		Fig. 5D
<i>isp-1(qm150) hlh-30</i> RNAi	21.29±0.69	25	-21	73/90	<0.0001	Fig. 5D
<i>isp-1(qm150) bec-1</i> RNAi	19.61±0.28	22	-27	102/120	<0.0001	
<i>isp-1(qm150) mon-2(xh22)</i> control RNAi	18.47±0.46	22	-32	108/121	<0.0001	Fig. 5D
<i>isp-1(qm150) mon-2(xh22) hlh-30</i> RNAi	19.41±0.53	22	-28	78/120	<0.0001	Fig. 5D
<i>isp-1(qm150) mon-2(xh22) bec-1</i> RNAi	16.44±0.29	19	-39	107/117	<0.0001	
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<i>isp-1(qm150)</i> control RNAi	25.69±0.91	33	0	81/90		Fig. 5E
<i>isp-1(qm150) hlh-30</i> RNAi	21.68±0.6	26	-16	106/120	0.0001	
<i>isp-1(qm150) bec-1</i> RNAi	20.93±0.4	22	-19	116/120	<0.0001	Fig. 5E
<i>isp-1(qm150) mon-2(xh22)</i> control RNAi	18.94±0.49	22	-26	105/120	<0.0001	Fig. 5E
<i>isp-1(qm150) mon-2(xh22) hlh-30</i> RNAi	20.22±0.47	22	-21	97/120	<0.0001	
<i>isp-1(qm150) mon-2(xh22) bec-1</i> RNAi	18.23±0.31	19	-29	115/120	<0.0001	Fig. 5E

In this table, the lifespan data sets within the thick solid lines were performed in parallel. Experimental repeats were divided by bold dashed lines.

Statistical analysis was performed within the same data set. *p*-values were calculated using the log-rank (Mantel-Cox) method and calculated against the same control data [wild-type or *isp-1(qm150)* control RNAi].

^Δ: % change in lifespan was calculated against the same control data [wild-type or *isp-1(qm150)* control RNAi].

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