Supplemental Figures and Tables

Figure S1, relates to Figure 1.

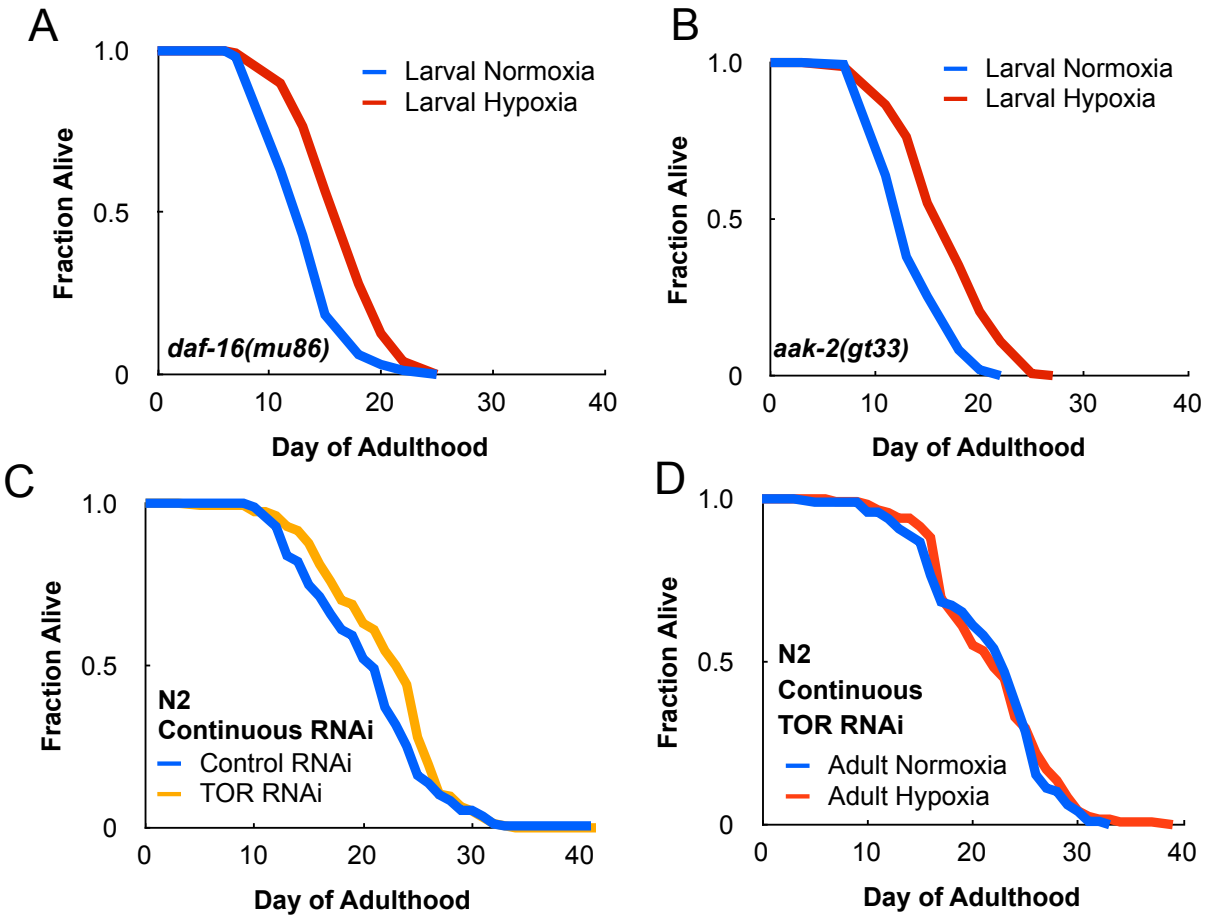

Figure S2, relates to Figure 2.

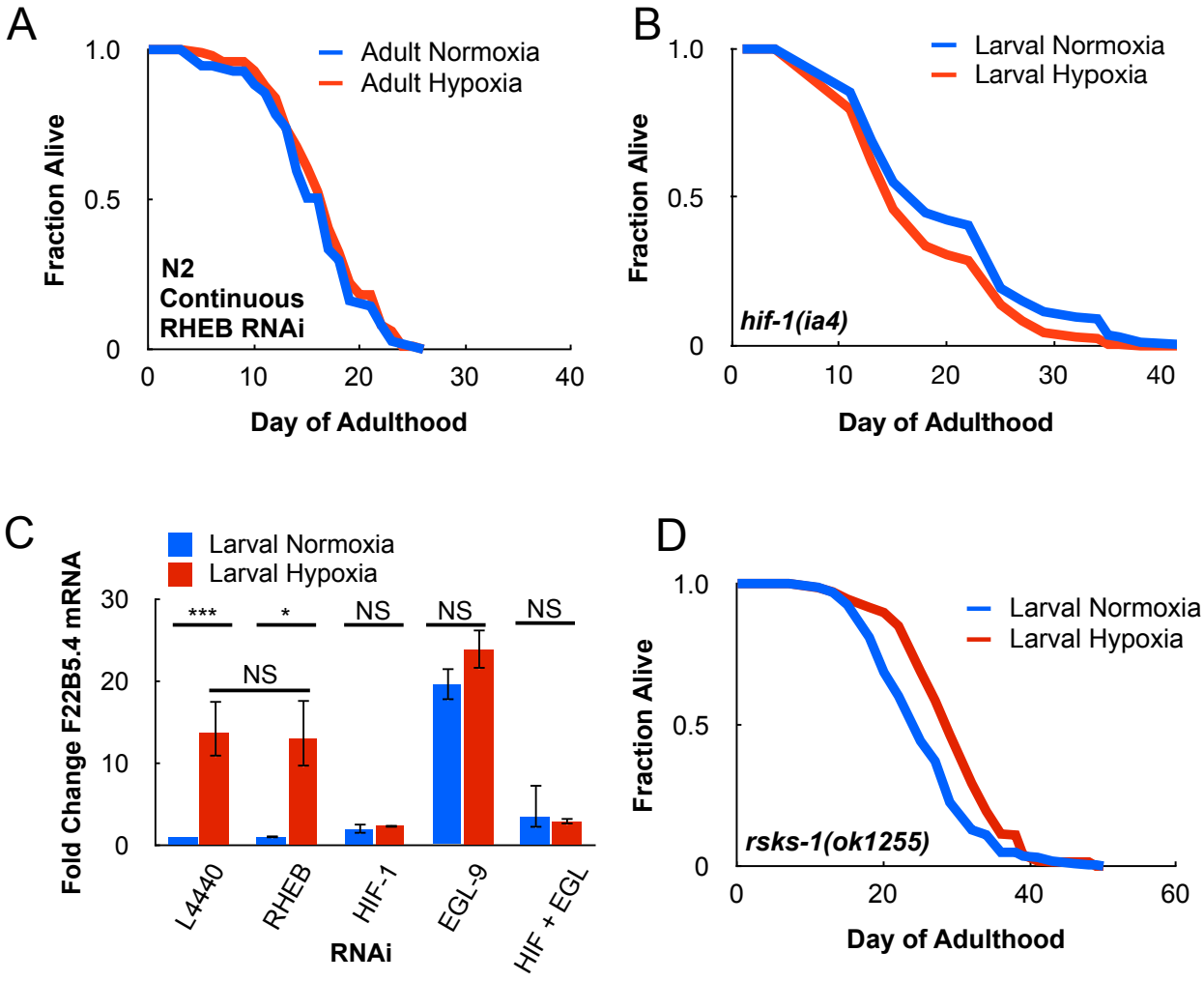

Figure S3, relates to Figure 3.

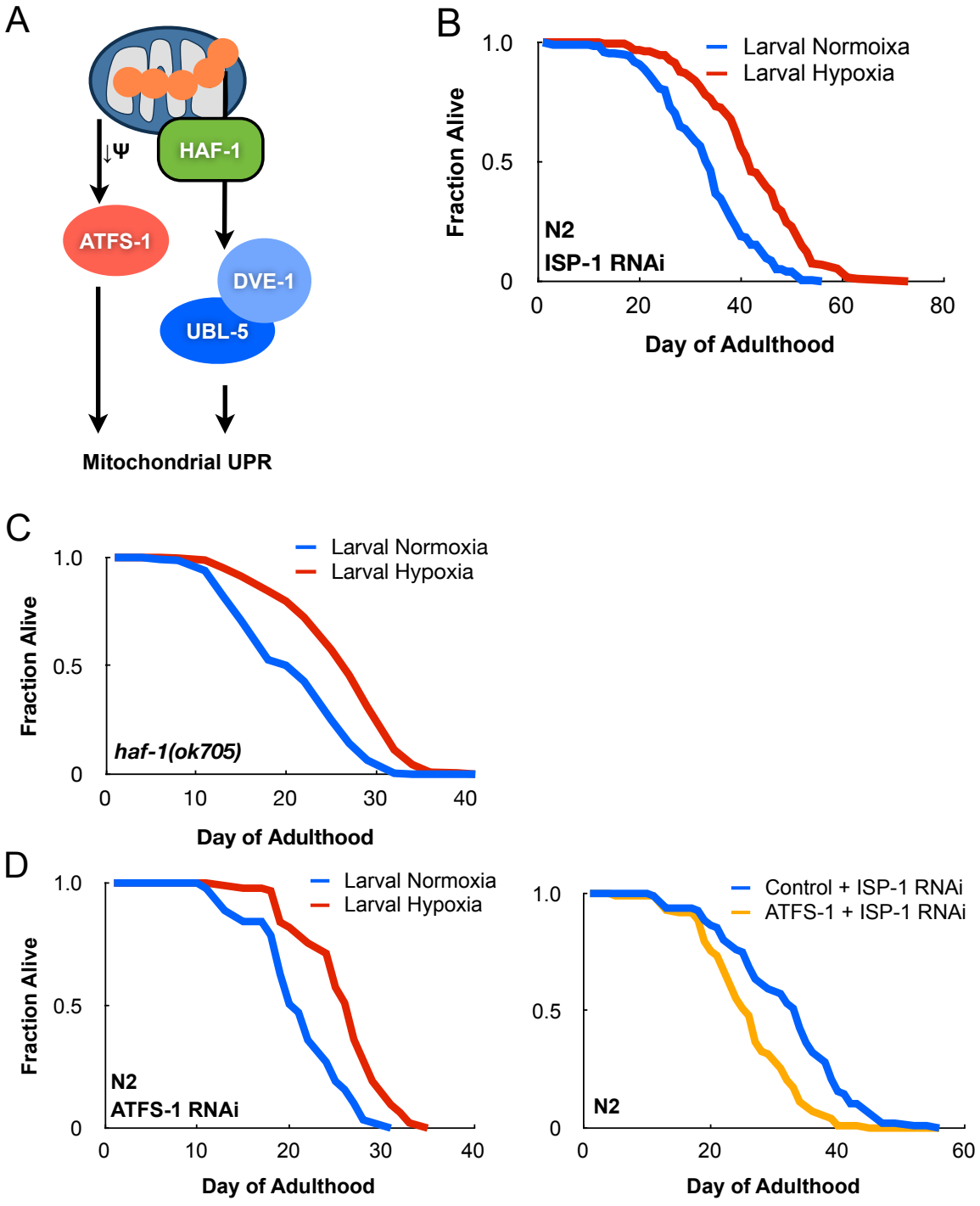

Figure S4, relates to figure 4.

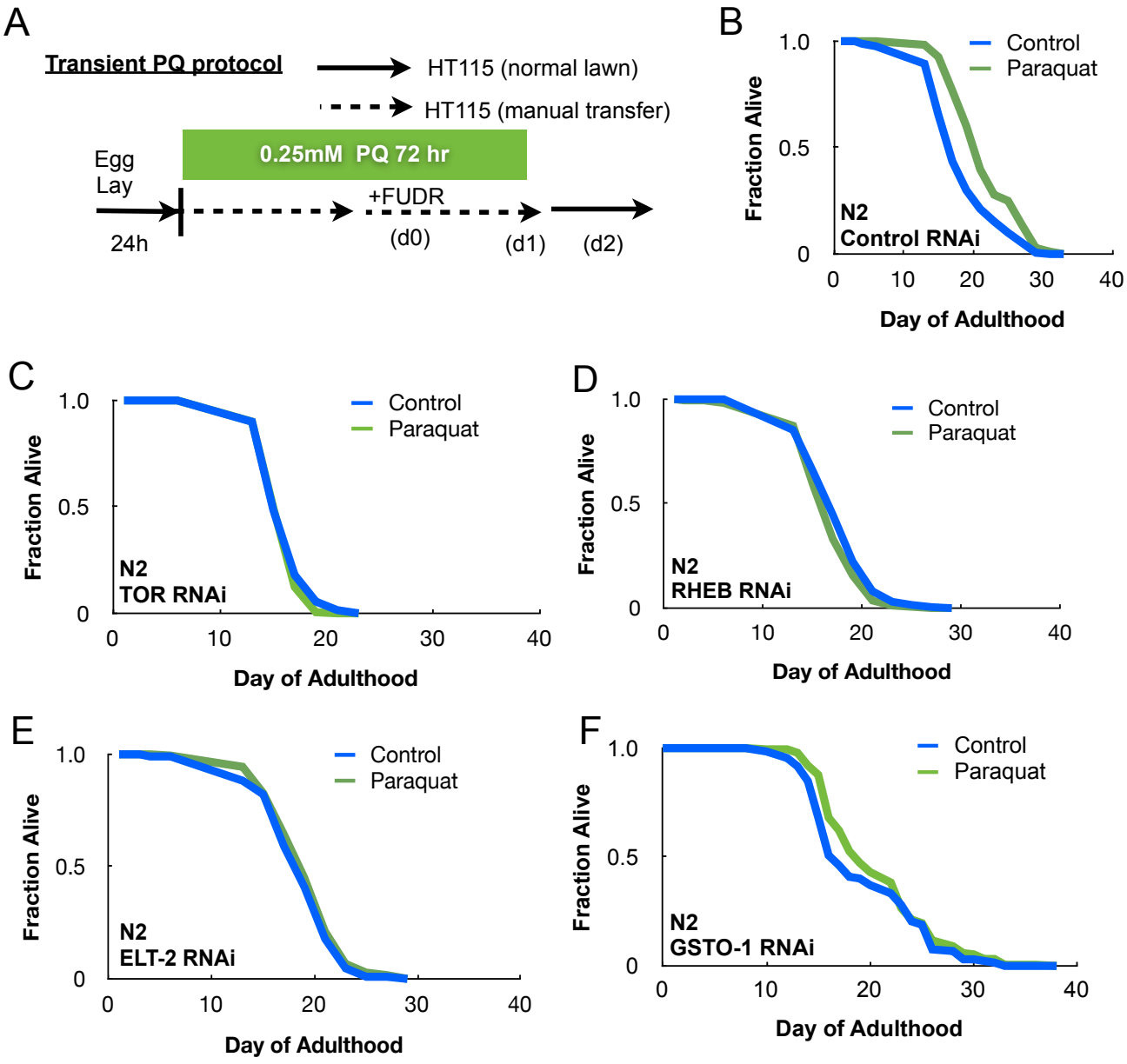

Table S1, relates to all figures.

This table has been uploaded in a separate excel file due to its length. Each spreadsheet tab refers to the individual figures in this manuscript.

Table S2, relates to Figure 4.

GENES AND CATEGORIES	Normoxia	Hypoxia	Normoxia + ELT-2 RNAi	Hypoxia + ELT-2 RNAi	Notes
Fatty Acid and Lipid Metabolism					
acs-2	1	9.58	0.72	1.53	acyl-CoA synthetase. Converts fatty acid to acetyl CoA for beta-oxidation. Mitochondrial localization
fat-4	1	4.56	0.88	1.91	delta 5 fatty acid desaturase. converts linolenic acid to aracadonic acid. required for delta-5 unsaturated fatty acid synthesis
fat-6	1	5.13	0.60	2.33	delta 9 fatty acid desaturase. predicted mitochondrial localization
acdh-1	1	0.25	0.54	0.04	short chain acyl CoA dehydrogenase. Catalyzes the first step in B-oxidation of fatty acids
T10B5.7	1	2.83	0.44	0.67	Predicted Lipase
Carbohydrate Metabolism					
sodh-1	1	5.31	0.29	0.46	Sorbitol dehdrogenase. Converts glucose to fructose.
ROS Homeostasis					
gsto-1	1	8.63	0.02	0.18	Omega class glutathione transferase. Knockdown induces sensitivity to paraquat
fmo-2	1	19.03	0.26	2.25	Flavin-containing monooxygenase. Participates in oxygenation of atoms and disulfide bond formation
Neurotransmission					
comt-4	1	33.59	0.45	1.79	Degradation of catecholamines
Other or Unknown					
spp-3	1	3.23	0.51	0.78	Pore forming saposin-like protein
dod-3	1	17.03	1.41	4.11	Downstream of DAF-16; unknown function. Contains DNA helicase and ELAV domain.
scl-2	1	4.20	1.17	0.48	Cysteine rich extracellular glycoprotein
K06A4.7	1	2.81	0.85	0.72	Unknown. Predicted domains: MAPKKK, MDR-associated-protein, gammaglutamyltranspeptidase

Supplemental Figure and Table Legends

Figure S1. TOR is required for longevity following transient hypoxia. (A) Transient larval hypoxia extends the lifespan of a *C. elegans* strain harboring a null mutation in the FOXO homolog DAF-16. (B) Loss of the AMP-Kinase homolog AAK-2 does not effect lifespan following hypoxia treatment. (C) Continuous knockdown of TOR during adulthood extends lifespan of wildtype *C. elegans*, as previously reported. (D) Continuous TOR knockdown during adulthood prevents lifespan following transient hypoxia treatment.

Figure S2. Mitochondrial ROS activate TORC1 to extend lifespan under transient hypoxia. (A) Continuous RHEB-1 knockdown by RNAi prevents lifespan extension following transient hypoxia. (B) HIF-1 is required for lifespan under transient hypoxia. (C) F22B5.4 is a hypoxia-inducible and HIF-1-dependent gene. Knockdown of RHEB-1 does not effect induction of F22B5.4 in contrast to HIF-1 RNAi. Additionally, RNAi knockdown of the HIF-1 inhibitor and PHD2 homolog EGL-9 is sufficient to upregulate F22B5.4 under normoxia in a HIF-1-dependent manner (*** = $p < 0.01$, * = $p < 0.05$, NS = not significant). (D) *C. elegans* bearing a mutation in the P70/S6-Kinase homolog, RSKS-1, are long-lived following transient hypoxia, suggesting inhibition of translation is not the primary mechanism for longevity under hypoxia.

Figure S3. Intestinal TORC1\ELT-2 signaling is required for lifespan under hypoxia. (A) A scheme depicting the two arms of the mitochondrial UPR^{mt}. Misfolded proteins within the mitochondria are hydrolyzed and the resulting peptides are exported through the HAF-1 transporter to activate the transcription factors, UBL-5 and DVE-1. Alternatively, a decrease in mitochondrial membrane potential (ψ) results in cytosolic accumulation of the ATFS-1 transcription factor, which translocates into the nucleus to stimulate stress response genes. (B) *C. elegans* fed ISP-1 RNAi, to induce the UPR^{mt}, have increased lifespan following transient hypoxia treatment. (C) Animals deficient for the HAF-1 transporter, *haf-1(ok705)*, are long-lived following transient hypoxia. (D) ATFS-1 knockdown via RNAi feeding does not affect transient hypoxia-induced lifespan. Alternatively, ISP-1 RNAi requires ATFS-1 for longevity, suggesting the UPR^{mt} increases lifespan by a genetically distinct mechanism than transient hypoxia.

Figure S4. GSTO-1 is required for lifespan following transient hypoxia. Paraquat (PQ) is a mitochondrial ROS generator. (A) Methods for treatment of *C. elegans* with 0.25 mM PQ for 72 hours during development and young adulthood. (B) Transient PQ treatment is sufficient to extend lifespan in wildtype *C. elegans*, as previously described. Mitochondrial ROS extends lifespan in *C. elegans* through (C) TOR, (D) RHEB-1, and (E) ELT-2. (F) Additionally, GSTO-1 is partially required for lifespan following transient PQ treatment.

Table S1. Longevity Supplement. This table summarizes all longevity experiments presented in this manuscript organized by each numbered figure. Independent experiments are depicted with a continuous gray background. The strain, food source, and all other treatment conditions are also described. Standard error of the mean (SEM) was calculated based on the mean lifespan of the total number of worms that died. Percent increase/decrease refers to the cell immediately above the calculated number. p-values were calculated using the Logrank\Mantel-Cox method (Prism 6). Independent replicates refer to the number of individual experiments scored with the given controls listed. We have indicated in the text where survival curves may be found, but have chosen not to graph the controls of select experiments to minimize redundancies in the presentation of data.

Table S2. Summary of RNA-Seq Candidates. RNA-Seq was performed on adult *C. elegans* fed ELT-2 RNAi following transient hypoxia treatment. A summary of the most significant candidates is presented here with a brief description of function provided from annotated information on Wormbase. Twelve genes (in red) showed a significant upregulation following hypoxia in an ELT-2-dependent manner. One gene was downregulated under hypoxia (in green, ACDH-1) and showed a further decrease following ELT-2 RNAi. We note multiple genes involved in fat metabolism and ROS homeostasis were identified in this analysis.

Supplemental Experimental Procedures

RNAi Cloning Primer Sequences and Methods. Primers were designed against *C. elegans* cDNA sequences publicly available through Wormbase. All clones were designed with *Pst*I and *XhoI* restriction sites for cloning into the L4440 vector. A 'GATTA' leader sequence was placed at the 5'-end of the primer to increase restriction enzyme efficiency.

Primer Name	Sequence
let-363 5993F (XhoI)	GAT TA CTC GAG ACC CTG TTC CAC CAC CAC
let-363 6431R (PstI)	GAT TA CTG CAG GCT TGT GGT CTA TGC CTG G
rheb-1 191F (XhoI)	GAT TA CTC GAG GAG TCA CTG ACA CAG CAG G
rheb-1 614R (PstI)	GAT TA CTG CAG CTA CAC GGC TTT CCA TCA TCC
isp-1 444F (PstI)	GAT TAC TGC AGT GCC TTG GCT TCG AT
isp-1 831 (XhoI)	GAT TAC TCG AGT TAG CTC GAT CCA AT
atfs-1 706F (XhoI)	GAT TA CTC GAG CAC TAC TTG GAG AGC GAC GAC
atfs-1 1106R (PstI)	GAT TA CTG CAG CTT CTG GCT TCA GAT GCT GG
elt-2 34F (XhoI)	GAT TA CTC GAG TGG GCC GAA ATG GAA CC
elt-2 453R (PstI)	GAT TA CTG CAG GTA AGT TGG AGC CAC AGT TGG
hif-1 1F (PstI)	GAT TAC TGC AGA TGG AAG ACA ATC GG
hif-1 400R (XhoI)	GAT TAC TCG AGG AAA GTC TCG AAG GG
egl-9 1F (PstI)	GAT TAC TGC AGA TGA GCA GTC CCC CA
egl-9 440R (XhoI)	GAT TAC TCG AGT CGG TCT TCG ATG TG
gsto-1 87F (XhoI)	GAT TA CTC GAG CAT GAG ATT CTG TCC ATG GGC
gsto-1 512R (PstI)	GAT TA CTG CAG GGA TAA CCT GGT TGA GAT CCA G

RT-PCR Methods and Primer Sequences. Primers for RT-PCR were designed against *C. elegans* cDNA sequences publicly available through Wormbase. At least one primer per set was exon bridging to ensure amplification of spliced messenger RNA.

RT-PCR Primer (exon)	Sequence
act-3 963F (exon 2/3)	TGC CCC ATC AAC CAT GAA GAT
act-3 1102R (exon 3)	GGC CGG ACT CGT CGT ATT CTT
F22B5.4 (exon 1/2)	CTC CTT ATC AAT TCC TTG TCC GC
F22B5.4 (exon 2)	CCA TGG TGC TTT GGA ATT GC
acs-2 526F (exon 2/3)	ACA ATG CTT GAG GCA ATG CC
acs-2 666R (exon 3)	GTC AGA GTA GAC CCA GGC TC
fat-4 126F (exon 2/3)	GGA TGC CAC TAC CGT ATT CC
fat-4 252R (exon 3/4)	GAT TGG GTC ATC CTT AAT ATC TGG G
fat-6 728F (exon 5/6)	GCG CTG CTC ACT ATT TCG G
fat-6 837R (exon 6)	GTG ATG GAA GTT GTG ACC TCC
T10B5.7 68F (exon 1/2)	GCG ACG ATA ACG CAT CCT C
T10B5.7 210R (exon 2/3)	CAC GTT TAC ATG TCT TTT TAG CTC
gsto-1 133F (exon 1/2)	GCT AAA GGA ATT GAA GCG GAG G
gsto-1 239R (exon 2)	CCA TTG TGC TCT ACT GCT GG
fmo-2 49F (exon 1/2)	CCG TCG ATT CGA CAT GGT C
fmo-2 160R (exon 2/3)	CTG ACG ACT CAT TCG TTT CGT G
comt-4 50F (exon1/2)	CTT ATT GCG CGG AGC AC
comt-4 167R (exon 2/3)	CCA AAT GTA AGA ACT TCA GGA GCT