Supplemental Experimental Procedures

Induction of ER stress
Synchronized L4 stage animals were treated with 25ng/µl solution of tunicamycin in M9 buffer for 4 hours. Control animals were treated in an equivalent solution of DMSO in M9 buffer.

Analysis of the fluorescence intensity in whole worm with COPAS biosort
For fluorescence image, animals were anesthetized with 50mM sodium azide, and a Leica S6E dissecting microscope and a Zeiss Axio Observer Z1 were used. A COPAS Biosort (Union Biometrica) was also used to measure GFP fluorescence for quantification. Fluorescence was normalized to worm size to compare between genotypes.

Immunofluorescence
Immunofluorescence (IF) was carried out by freeze-cracking method. Worms were cut open on a poly-lysine coated slide. The slide was fixed in methanol for 15 minutes followed by acetone for 15 minutes at -20°C. H3K9me2 antibody was incubated at 4°C overnight and worms were mounted with Vectashield mounting solution plus DAPI.

Dissection and fixation for intestinal nuclei analysis
Modified from (Phillips et al., 2009) Animals were dissected in M9 buffer containing sodium azide and 0.1% Tween 20, fixed for 4 minutes in 1% PFA by addition of paraformaldehyde in M9/PBS , and frozen on dry ice between a coverslip and Histobond slide. The coverslips were removed, the slides were placed in PBS, and washed 3X with fresh PBS for 10 minutes. Slides were mounted with Vectashield with DAPI.

Volume and fluorescence intensity analysis of intestinal nuclei
Intestinal cells were imaged at 63x using a Zeiss LSM 710, AxioObserver 34-channel spectral laser scanning confocal microscope. Z-stacks of the intestine were analyzed using Bitplane Imaris 8.1. Contours of individual nuclei, according to EMR-1::GFP fluorescence, were manually defined and used to render nuclei surfaces. Nuclear volumes, H3K9me2 and DAPI intensity sums of each nuclear surface were acquired from the surface tool statistics. The analysis of DAPI distribution was performed using a custom Python script. At least 20 nuclei were measured per strain.

Chromatin quantification
Voxels within each nucleus were ranked by DAPI intensity and divided into 10 equal-volume bins. Percentage of total DAPI intensity in each of the bins was measured; the distribution of the fractions from the top four bins, which correspond to the most DNA-rich regions within the nucleus, were shown.

DVE-1::GFP intensity analysis
DVE1::GFP gut cells were imaged on a Leica TCS SP8 microscope using a 63×, 1.4 NA objective lense. The scanning settings for SP8 were: 1,024 × 1,024 pixels frame size, 51.5 nm pixel size, 3.5 zoom factor, 400 Hz scanning speed and 83.9 nm step size for *z* sections. The image stacks were deconvolved using Huygens Professional Software. Background subtraction was performed using automatically chosen threshold values and the distribution of DVE-1::GFP and DAPI was analyzed using a custom Python script. Image voxels were ranked by DAPI staining intensity and divided into 3 bins with equal number of voxels. Percentage of total DAPI and DVE-1::GFP intensity in each of the equal-volume bin were then measured. The analyses were performed in more than 30 nuclei.

qPCR
Total RNA was isolated from harvested worms at L4 stage using Qiazol reagent (QIAGEN), after freezing and thaw three times. RNA pellets were purified on RNeasy mini columns (QIAGEN) and cDNA was synthesized using QuantiTect Reverse Transcription kit (QIAGEN). SybrGreen quantitative RT-PCR experiments were performed as described in the manual using Bio-Rad 96 well qPCR machine. Internal controls utilized a geometric mean of *cdc-42*, *pmp-3* and *Y45F10D.4*. Experiments were repeated three times. Primers used for qPCR are listed below.

hsp-6 forward 5'-CAAACTCCTGTGTCAGTATCATGGAAGG-3'

hsp-6 reverse 5'- -GCTGGCTTTGACAATCTTGTATGGAACG -3'

dve-1 forward 5'-TAGCAGCTCTTGGACATTCGAGCA-3'

dve-1 reverse 5'- CGAATGGCAAGGGTTTCCAGTTGT-3'

lin-65 forward 5'-GGAGATAACTGAGCAGAAAGACG-3'

lin-65 reverse 5'- TCCGGAGTGTCGTCATCAT-3'

timm-23 forward 5'-AGTGCCGGAATGAACTTCTC-3'

timm-23 reverse 5'- GTTGATCCAAGGCGAGGAC-3'

cdc-42 forward 5'- AGGAACGTCTTCCTTGTCTCC -3'

cdc-42 reverse 5'- GGACATAGAAAGAAAAACACAGTCAC -3'

pmp-3 forward 5'- CGGTGTTAAAACTCACTGGAGA -3'

pmp-3 reverse 5'- TCGTGAAGTTCCATAACACGA -3'

Y45F10D.4 forward 5'- AAGCGTCGGAACAGGAATC -3'

Y45F10D.4 reverse 5'- TTTTTCCGTTATCGTCGACTC -3'

RNA-seq

N2, *lin-65(n3441)* and *met-2(ok2307)* animals were grown from hatch at 20ºC on either empty vector (EV) or EV+*cco-1* RNAi bacteria and collected by washing with M9 at the L4 stage, then snap frozen in liquid nitrogen. Pellets were grinded with mortar and pestle on dry ice and the resulting powder was thawed in the presence of lysis buffer (50mM Tris-HCl, 50mM NaCl, 10mM $MgCl_2$, 5mM $CaCl_2$, 200µg/ml cycloheximide, 200µg/ml heparin, 1% Triton X-100, 0.1% NaDOC) and incubated on ice for 10 minutes prior to centrifugation at 4ºC, 16,000 x g for 10 minutes. Total RNA was purified from clarified lysate using Trizol-LS (Life Technologies and poly-A RNA was was extracted with oligo-dT(25) Dynabeads (Ambion), each according to manufacturer's instructions. Sequencing libraries were prepared using the Epicentre ScriptSeq v2 according to manufacturer's instructions. Illumina HiSeq 2500 reads were pre-processed and mapped to a set of noncoding RNAs before mapping the remaining reads to an index containing the longest single isoform ± 30nt for each gene in the *C. elegans* WS230 genome using Bowtie version 0.12.7 (Langmead et al., 2009) with the following settings: -m 1 -v 2 -a --norc --best --strata. In-house Python scripts were used to count reads mapping to each transcript and the count data were used for statistical analysis by DESeq (Anders and Huber, 2010), where changes in empty vector to EV+*cco-1* RNAi conditions were evaluated for each genotype by the negative binomial method. Statistical significance was defined by a Benjamini-Hochberg adjusted p-value of less than 0.05.

Table S1. Lifespan analyses, Related to Figure S5 and 6

Related Figures	Strains	Median lifespan (Days)	Mean lifespan ± Std error (Days)	Total Animals	Censored Animals	P-value
Figure S5B	wild type; *empty vector (ev)*	21	19.93 ± 0.49	134	25	
	set-25(n5021); ev	21	20.94 ± 0.48	120	28	0.3135 (ns)
	wild type; *cco-1* RNAi	33	33.09 ± 0.94	116	39	
	set-25(n5021); cco-1 RNAi	35	35.02 ± 0.92	103	28	0.1641 (ns)
Figure 6C	wild type; *empty vector (ev)*	17	18.36 ±0.45	140	11	
	lin-65(n3441); *empty vector*	13	14.52 ± 0.36	139	13	***< 0.0001
	wild type; *ev+cco-1* RNAi	33	31.40 ± 0.93	150	19	
	lin-65(n3441); *ev+cco-1* RNAi	23	23.05 ± 0.55	158	13	***< 0.0001
Figure 6D	wild type; *empty vector (ev)*	22	20.76 ± 0.43	126	15	
	wild type; *atfs-1* RNAi	22	20.86 ± 0.42	112	18	0.8 (ns)
	met-2(ok2307); ev	17	18.33 ± 0.39	84	25	
	met-2(ok2307); atfs-1 RNAi	19	17.98 ± 0.38	99	19	0.6 (ns)
Figure 6E	wild type; *ev+cco-1* RNAi	34	34.60 ± 0.85	98	35	
	wild type; *cco-1+atfs-1* RNAi	26	26.43 ± 0.78	110	28	***< 0.0001
	met-2(ok2307); *ev+cco-1* RNAi	25	25.41 ± 0.73	80	30	***< 0.0001
	met-2(ok2307);*cco-1+atfs-1* RNAi	21	21.74 ± 0.52	113	19	0.0794 (ns)

Reference:
Anders, S., and Huber, W. (2010). Differential expression analysis for sequence count data. Genome Biol. *11*, R106.

Langmead, B., Trapnell, C., Pop, M., and Salzberg, S.L. (2009). Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. Genome Biol. *10*, R25.

Phillips, C.M., McDonald, K.L., and Dernburg, A.F. (2009). Cytological analysis of meiosis in Caenorhabditis elegans. Methods Mol. Biol. Clifton NJ *558*, 171–195.