Supplementary materials and methods

Strains

The following strains were used in this work: N2 Bristol (wild type), *rpl-43(bp399), atg-3(bp412), lgg-1(bp407), epg-8(bp251), sma-3(wk20), dbl-1(wk70), sma-2(e502), lin-35(n745), lin-15B(n744), lin-15A(n767), lin-9(n112), lon-1(e185), xbp-1(zc12), atf-6(ok551), daf-2(e1370), daf-16(mu86), egl-46(n1126), pep-2(lg1601), gfi-1(ok2669), atfs-1(gk3094), adIs2122(gfp::lgg-1; rol-6(su1006)), bpIs151(Psqst-1::sqst-1::gfp, unc-76(+)), zcIs4(Phsp-4::GFP)* and *zcIs9(Phsp-60::GFP).*

RNAi injection experiments

For RNAi injection experiments, single-stranded RNA was transcribed from T7- and SP6-flanked PCR templates. ssRNAs were then annealed and injected into wild-type or *rpl-43* animals carrying various reporters. F1 progeny were examined for the corresponding phenotype.

RNA isolation and real-time RT-PCR

Animals were collected and total RNA was extracted from about 500 animals using Trizol reagent (Sigma) according to the manufacturer's protocol. Total RNA was reverse transcribed using an Invitrogen Superscript III kit. Quantitative PCR reactions were carried out using a SYBR RT-PCR kit (TaKaRa) and an Applied Biosystems (ABI) 7500 Fast Dx. Real-Time PCR Instrument. *act-1* was used as an internal control. The mRNA level in mutant animals was normalized to the level in

wild-type worms, which was set to 1. Error bars indicate the standard deviation (s.d.) of three independent experiments.

Immunoblotting assays

For immunoblotting assays in *C. elegans*, lysates from 200 worms were used and diluted primary antibody and HRP-conjugated secondary antibody were used. As a gel loading control, anti-actin monoclonal antibody (A3853, Sigma) was used.

Bioinformatic analysis

Interactions used for generating protein networks were from the WormBase, found at ftp://ftp.wormbase.org/pub/wormbase/releases/WS235/species/C_elegans/anotation/ (dataset includes predicted interactions) and ftp://ftp.wormbase.org/pub/wormbase/species/c_elegans/annotation/gene_interactions / (dataset includes more physical interactions) [1-3]. The first dataset was also divided into two groups, containing predicted and non-predicted interactions, and corresponding networks were examined. Cytoscape (www.cytoscape.org) was used to illustrate the nodes and edges in the interaction networks. Four sets of controls were generated by randomly selected genes from the *C. elegans* genome (ftp://ftp.wormbase.org/pub/wormbase/species/c_elegans/annotation/), and results were compared with the *rpl-43* suppressor dataset.

Supplemental References:

1. Lee I, Lehner B, Crombie C, Wong W, Fraser AG, Marcotte EM (2008) A single gene network accurately predicts phenotypic effects of gene perturbation in *Caenorhabditis elegans*. *Nat Genet* **40:** 181-8.

2. Li S *et al* (2004) A map of the interactome network of the metazoan *C. elegans*. *Science* **303:** 540-3.

3. Zhong W, Sternberg PW (2006) Genome-wide prediction of C. elegans genetic interactions. *Science* **311:** 1481-4.