

# Note

## Tissue Specificity of *Caenorhabditis elegans* Enhanced RNA Interference Mutants

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### ABSTRACT

Gene knockdown by RNA interference (RNAi) in *Caenorhabditis elegans* is readily achieved by feeding bacteria expressing double-stranded RNA (dsRNA). Enhanced RNAi (Eri) mutants facilitate RNAi due to their hypersensitivity to dsRNA. Here, we compare eight Eri mutants for sensitivity to ingested dsRNA, targeting a variety of tissue-specific genes.

THE effectiveness of double-strand RNA (dsRNA) delivery in *Caenorhabditis elegans* has made high-throughput RNA interference (RNAi) screens an essential research tool (MITANI 2009). For RNAi screens, dsRNA is usually administered via feeding RNAi, whereby worms ingest bacteria expressing gene-specific dsRNA (referred to as RNAi food). This is a less potent procedure than microinjecting dsRNAs, perhaps due to the lower amounts of internalized dsRNA (TIMMONS and FIRE 1998). The discovery of enhanced RNAi (Eri) mutants, which increases the sensitivity of worms to dsRNA, increases the discovery of RNAi phenotypes in large-scale screens. Nine Eri loci have been discovered thus far (SIMMER *et al.* 2002; KENNEDY *et al.* 2004; DUCHAINE *et al.* 2006; FISCHER *et al.* 2008; PAVELEC *et al.* 2009).

Although a variety of Eri mutants are used in RNAi screens, their selection has been *ad hoc*, as no systematic comparative analysis of the Eri strains has been reported. Such an analysis would provide a logical basis for selecting the most sensitive Eri mutant for general and tissue-specific screens. Here, we comprehensively characterize the tissue-specific RNAi sensitivities of eight Eri mutants. To characterize phenotypic differences among Eri mutants, we compared the relative penetrance of RNAi sensitivity at varying doses of dsRNA-expressing bacteria (REA *et al.* 2007). For each bacterial strain that expresses dsRNA targeting a *C. elegans* gene, we scored only one defined knockdown phenotype (supporting information, Table S1, Supporting Citations). A representative

dilution series is shown in Figure S1 (Table S2). We sought to use this dose-response data to compare the enhanced silencing for each Eri mutant. For all strains, the variability in penetrance is greatest at intermediate dsRNA doses, suggesting a threshold effect. This variability, best observed via coefficient of variations (Table S3), strongly interferes with determining the onset of silencing. In contrast, the trend toward reduced variability at higher dsRNA doses provides a means to discriminate among Eri mutants. On the basis of this analysis, we developed a criterion for selecting the “most effective” Eri’s: one(s) that causes near complete (upper bound of 95% confidence interval at least 100% penetrant) and robust (<10% standard deviation) silencing at the lowest dsRNA dose.

We used the methods and criterion described above (File S1) to evaluate eight Eri mutants on 24 RNAi foods in either tissues (Table S1, Supporting Citations). The results of this analysis are presented in Figure 1 (Tables S4–S27). The majority of Eri mutants enhanced RNAi for nearly all tested tissues, but all showed relative differences in RNAi hypersensitivity for some foods. Our comprehensive phenotypic analysis of the Eri mutants indicates that they are not equivalent, consistent with the reported nonoverlapping expression profiles of *eri-1* and *mf-3* mutants (LEE *et al.* 2006).

In all experiments, we observed a sigmoidal curve for silencing penetrance *vs.* RNAi concentration; at intermediate concentrations, the variance was highest. Therefore, to minimize variability associated with dose, all feeding RNAi assays should be preceded by a dilution series control to ensure that the RNAi food is not used at an “inflection point” concentration. When dsRNA doses cannot be controlled, using the most appropriate Eri mutant maximizes robustness and sensitivity.

Supporting information is available online at <http://www.genetics.org/cgi/content/full/genetics.111.127209/DC1>.

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	T.S. sterile	Epidermis			Gonad			Intestine			Muscle			Neuron			Pharynx			Ubiquitous			Germline		
		<i>bli</i> -1	<i>dpy</i> -11	<i>dpy</i> -13	<i>fkh</i> -6	<i>gon</i> -1	<i>gon</i> -4	<i>act</i> -5	<i>gtl</i> -1	<i>lfc</i> -2	<i>act</i> -3	<i>myo</i> -3	<i>unc</i> -22	<i>hbl</i> -1	<i>hmr</i> -1	<i>unc</i> -73	<i>div</i> -1	<i>pbs</i> -6	<i>pha</i> -4	<i>cdk</i> -1	<i>lml</i> -3	<i>vha</i> -15	<i>gfp</i> -1	<i>par</i> -1	<i>pos</i> -1
Wild type (N2)	No																								
<i>eri-1</i> (mg366)	Yes																								
<i>rrf-3</i> (pk1426)	Yes																								
<i>eri-3</i> (tm1361)	Yes																								
<i>eri-5</i> (tm1705)	No																								
<i>eri-6/7</i> (tm1917)	No																								
<i>ergo-1/eri-8</i> (gg100)	No																								
<i>eri-9</i> (gg106)	No																								
<i>eri-11</i> (gg99)	No																								

FIGURE 1.—Summary metric of tissue-specific Eri efficacy for the eight Eri strains tested on 24 RNAi foods representing eight tissues. A strain exhibiting significantly higher ( $t$  test,  $P < 0.05$ ) penetrance than the N2 wild-type strain's penetrance (green), at any tested bacterial RNAi food concentration, is marked as Eri (yellow or red). Strains exhibiting an Eri phenotype that have an upper bound of 95% confidence interval at least 100% penetrant with a  $<10\%$  standard deviation are marked as the "best" Eri (red). "T.S. sterile" indicates strains that exhibit temperature-sensitive sterility at 25°.

We selected RNAi targets on the basis of tissue-specific gene expression and/or phenotypes and interpreted the data based on these differences, but it is important to consider that the differences in responses might relate to unknown relationships between the genes. Consistent with our goal, most sets of tissue-specific genes show consistent phenotypes within Eri mutant classes. For *rrf-3* and *ergo-1/eri-8*, we analyzed a second independent allele, finding similar tissue specificity (Figure S2). Therefore, the observed tissue specificity is likely a property of the *eri* genes rather than a consequence of unique alleles.

To further document tissue-specific Eri phenotypes, we crossed all the Eri mutants into a *sur-5::gfp* strain that ubiquitously expresses GFP in all cells (GU *et al.* 1998). All the *eri(-);sur-5::gfp* doubles exhibited spontaneous transgene silencing (Figure S3), which interfered with the effect of *gfp* dsRNA. However, consistent with the tissue-specific effects described above, the relative differences in spontaneous *gfp* silencing in the intestinal nuclei among *eri-1;sur-5::gfp*, *rrf-3;sur-5::gfp* and *ergo-1/eri-8;sur-5::gfp* strains corresponded with their relative differences in RNAi efficacy against endogenous intestinal targets (Table S28).

A limited comparison of the Eri phenotypes of the retinoblastoma pathway mutants *lin-15b(n744)* and *lin-35(n745)* (WANG *et al.* 2005) with *eri-1* and *rrf-3* showed that their sensitivity and robustness were less than that of the Eri mutants (Figure S4).

We also found that all the Eri mutants show strong maternal rescue (Figure S5 and Figure S6 and Table S29, Table S30, Table S31, and Table S32). However, there is no maternal rescue for the temperature-sensitive (T.S.) sterility phenotype of T.S. Eri mutants (Table S33). This is not due to a perdurance problem in which the maternally loaded products are depleted before *eri*-related spermatogenesis begins because we utilized *bli-1* RNAi—whose target is expressed only during the fourth larval stage (PAGE and JOHNSTONE 1997) when spermatogenesis begins—and found penetrant maternal rescue of the Eri phenotype (Table S34). Eri maternal rescue could suggest that part of the maternal

contribution to the embryo includes small RNAs or their associates.

The described tissue-specific RNAi sensitivities, T.S. sterility data, maternal rescue penetrance, brood size (Table S27), and effect on transgenes provide a practical guide to the selection of Eri mutants (File S2, Figure S7). There are other weaker enhanced RNAi mutants, including *dcr-1/eri-4(mg375)* (PAVELEC *et al.* 2009), tissue-specific *sid-1* overexpressers (CALIXTO *et al.* 2010), and transgene-specific silencers (KNIGHT and BASS 2002). Although these may not be versatile genetic tools, their future phenotypic analysis is equally important because understanding the interactions among all *eri* genes provides insights about small RNA pathways.

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# GENETICS

## Supporting Information

<http://www.genetics.org/cgi/content/full/genetics.111.127209/DC1>

## Tissue Specificity of *Caenorhabditis elegans* Enhanced RNA Interference Mutants

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## FILE S1

## Materials and Methods

## Strains used

Strain	Allele	Reference
N2 Bristol	Wild type	
GR1373	<i>eri-1(mg366)</i>	Kennedy <i>et al.</i> 2004
NL2099	<i>rjf-3(pk1426)</i>	Simmer <i>et al.</i> 2002
YY13	<i>rjf-3(mg373)</i>	Pavelec <i>et al.</i> 2009
WM172	<i>eri-3(tm1361)</i>	Duchaine <i>et al.</i> 2006
WM171	<i>eri-5(tm1705)</i>	Duchaine <i>et al.</i> 2006
FX01917	<i>eri-6/7(tm1917)</i>	Fischer <i>et al.</i> 2008
YY168	<i>eri-8(gg100)</i>	Pavelec <i>et al.</i> 2009
WM158	<i>eri-8(tm1860)</i>	Pavelec <i>et al.</i> 2009
YY216	<i>eri-9(gg106)</i>	Pavelec <i>et al.</i> 2009
YY209	<i>eri-11 (gg99)</i>	Unpublished. S. Kennedy
MT2495	<i>lin-15b(n744)</i>	Wang <i>et al.</i> 2005
MT10430	<i>lin-35(n745)</i>	Wang <i>et al.</i> 2005
HC195	<i>nrIs20[sur-5::gfp]</i>	Jose <i>et al.</i> 2009
HC745	<i>eri-1(mg366); nrIs20 [sur-5::gfp]</i>	
HC746	<i>rjf-3(pk1426); nrIs20 [sur-5::gfp]</i>	
HC747	<i>eri-3(tm1316); nrIs20 [sur-5::gfp]</i>	
HC748	<i>eri-6/7(tm1917); nrIs20 [sur-5::gfp]</i>	
HC749	<i>ergo-1/eri-8(gg100); nrIs20 [sur-5::gfp]</i>	
HC750	<i>eri-9(gg106); nrIs20 [sur-5::gfp]</i>	
HC751	<i>eri-11(gg99); nrIs20 [sur-5::gfp]</i>	

All strains and their assays were maintained and performed at 20°C, except heat shift experiments for temperature-sensitive alleles, which were performed at 25°C.

## Dilution series procedure

Single colonies from the Ahringer library (Kamath and Ahringer 2003) were inoculated and grown using previously described methods (Timmons *et al.* 2001). The final optical density (OD) of bacteria was determined by spectrometry at 600 nm. For dilution series, the bacteria were diluted in either LB media for final OD of 1.0 or greater, or in neutral carrier bacteria (*E.coli* HT115(DE3) containing an empty L4440 vector) to maintain a minimal total bacteria concentration of 1.0 OD. This minimal bacterial concentration was found necessary to maintain worm growth. In each case 20  $\mu$ L of RNAi food (which is enough to support the progeny from one worm) at the desired concentrations were seeded onto and grown overnight at room temperature onto 1mM isopropyl- $\beta$ -D-thiogalactopyranoside (GoldBio), 1mM carbenicillin (EMD Biosciences) NG plates (Brenner 1974) in 30mm petri dishes (Greiner Bio-One) to induce dsRNA production. Non-starved third-larval stage single *C. elegans* worms of the desired strain were placed onto each seeded plate at 20°C, with the exception of *fkh-6*, *gon-1*, and *gon-4* RNAi foods, which required first-larval stage single worms to be placed to ensure the elimination of the gonad.

Observed knockdown phenotypes were similar to previously observed RNAi experiments with the same gene targets, as reported in WormBase Release WS217. A single scored phenotype, as listed in Table S1, was scored for penetrance in the progeny generation of each plate's single worm four days later. HC196:*sid-1(qt9)* was used as a negative control and, as expected,

did not show any RNAi knockdown phenotypes across all foods tested (Winston *et al.* 2002). Each Eri strain on each concentration of RNAi food was replicated between five to 12 times, as indicated in Tables S2 & S4-S26.

Means and standard deviations were calculated for each Eri strain on each RNAi food concentration for nonlethal/non-growth-defective phenotypes. Normalized mean and standard errors of the mean were calculated for each Eri strain on each RNAi food concentration for lethal/growth-defective phenotypes, with brood sizes of each Eri strain feeding on vector RNAi food (Table S27) – which agreed very well with previously published data (Duchaine *et al.* 2006; Pavelec *et al.* 2009) – used for normalization. A *t* test analysis of the N2 wild-type response on each RNAi food concentration is the basis for determining an Eri phenotype on that RNAi food concentration, with a two-tailed *p* value less than 0.05 indicating significant difference. Coefficients of variation were tabulated by dividing the standard deviation by the mean.

#### **Maternal rescue analysis:**

Genetic cross analysis for an Eri phenotype on *dpy-13* RNAi food was tested at OD<sub>600nm</sub> 1.5, on *hmr-1* RNAi food at OD<sub>600nm</sub> 0.5, and on *unc-73* RNAi food at OD<sub>600nm</sub> 3.0, using the same aforementioned setup for inoculating, growing, and seeding the RNAi plates. The shift to 25°C to test for maternal rescue of temperature-sensitive sterility was made at the third-larval stage to ensure that spermatogenesis occurred at 25°C.

#### **Imaging:**

All images were initially analyzed on an Olympus dissecting scope, with Illumatool Tunable Lighting System, attached to an EXFO X-Cite Fluorescence Illumination System for fluorescent detection assays. All presented images were captured on a Zeiss Axiophot, attached to a Zeiss AttoArc for fluorescent detection assays, using a Hamamatsu Digital Camera, with Openlab software. Scale bar was measured using a 0.01 mm stage micrometer (Olympus). After initial image capture, all subsequent analysis of images was performed using ImageJ software (National Institutes of Health, USA).

#### **Laser ablation:**

The *eri-8; sur-5::gfp* strain underwent germline removal via laser ablation as described in Bargmann and Avery 1995.

**FILE S2****Supporting Results and Discussion**

As listed in Table S1, some RNAi foods had relatively extreme loss-of-function phenotypes scored for the sake of more explicit precision. For example, *unc-22* RNAi is usually scored just for the mere presence of twitching (Fire *et al.* 1991). However, *unc-22* RNAi still causes twitching down to a 1/200,000 dilution of bacterial RNAi food in both N2 and *eri-1* (data not shown), at which point, errors from dilution is probably more variable than the phenotypic penetrance. Therefore, the more extreme phenotype of twitching to the point of paralysis is more appropriate for our dilution series' scoring purposes. Knockdown assays in general should therefore similarly consider the relationship between expressivity and penetrance at the concentrations of RNAi foods used. Although expressivity is another factor usually considered for RNAi efficacy, it is much harder to quantify objectively. Penetrance of one very specific phenotype was therefore used as the sole measure of knockdown efficacy.

RNAi phenotypes were scored in the next generation for of three reasons. One, this practice is more common in the field for reverse genetics applications, so our method would serve as a more fitting guideline. Two, putting L3s on RNAi food and scoring the next generation versus putting embryos on RNAi food and scoring the same generation results in almost identical phenotypic penetrance (data not shown; Vastenhouw *et al.* 2006). Three, scoring in the next generation allows for a more consistent method across all the to-be tested RNAi foods, including those with germline phenotypes that cannot be assayed in the same generation.

The data in Figure 1 and Tables S2-S26 should not be construed as an absolute scale (that feeding a particular Eri mutant on a particular RNAi food concentration will result in the listed penetrance), due to differences between protocols. Rather, the relative differences between conditions (that one particular Eri mutant has different penetrance on different concentrations of an RNAi food) are the trends that should be robust.

Previous reports showed that a portion of the spontaneous transgene silencing is due to mobile silencing signals (Jose *et al.* 2009) and the silenced cells in the gut correspond to the position of the developing gonad, suggestive that silencing signals emanate from the germline. We tested this by ablating the gonad of L1 animals and found that the extent of silencing was unchanged (Figure S7). Thus the silencing is either entirely of somatic origin or is initiated in the embryo.

The strong germline-specific *eri-5(tm1705)* phenotype was unexpected. This may reflect the incomplete penetrance *eri-5* has on small RNA metabolism; *eri-5* mutants show reduced but not eliminated endo-siRNA processing (Duchaine *et al.* 2006). To date, no screens have been performed for germline-specific Eri mutants; such a screen could reveal the different requirements for endogenous small RNA pathways.

Duchaine *et al.* 2006 reported a rather weak Eri phenotype for *eri-5(mg392)* for some somatic targets, whereas we generally did not see a somatic Eri phenotype for *eri-5(tm1705)*. This difference could be due to the fact that we systemically enumerated the RNAi food concentrations at which we scored our animals, whereas Duchaine *et al.* did not; it is quite likely that

when they scored their animals, they were at a concentration of food that may have produced a weak Eri phenotype. Furthermore, we scored only penetrance of a strict phenotype, whereas Duchaine *et al.* scored a combination of expressivity and penetrance, also possibly accounting for our differences.



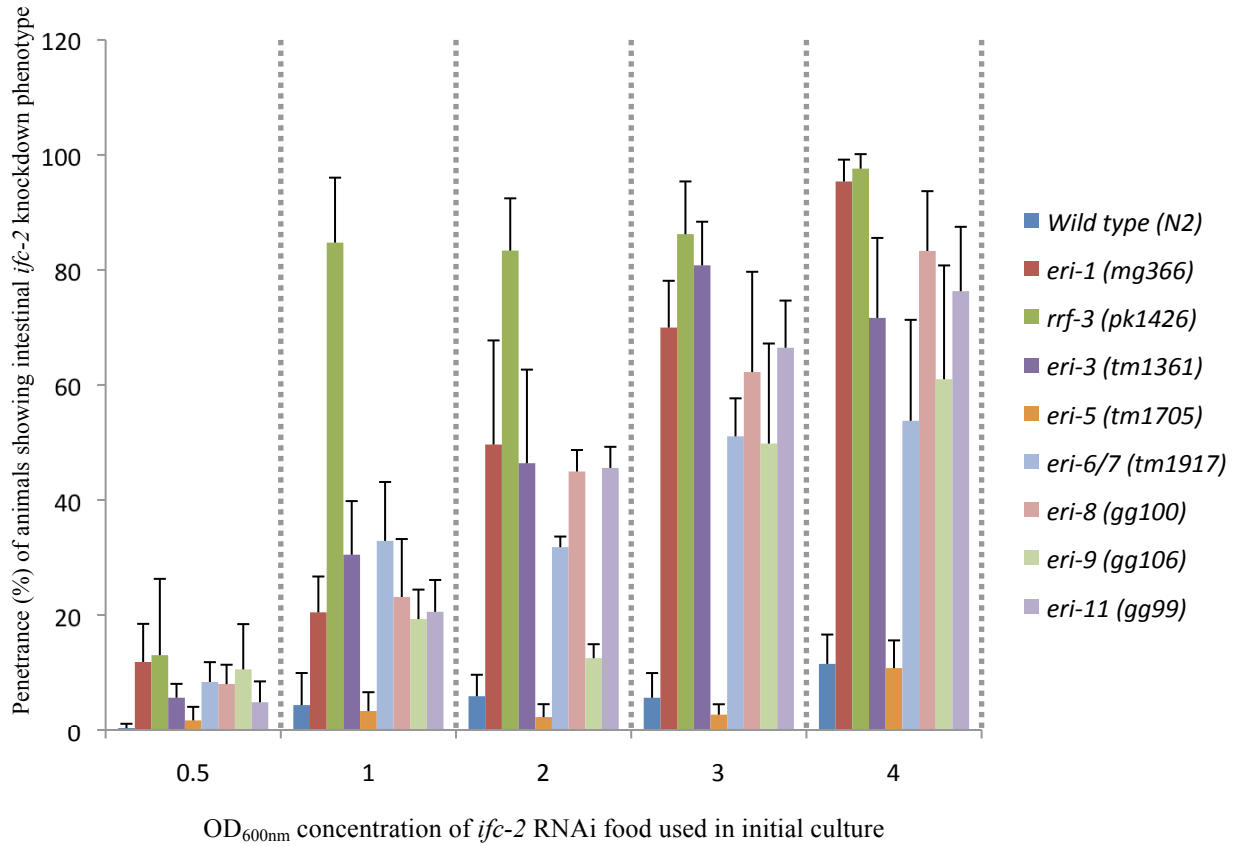


FIGURE S1.—Dilution series of Eri responses by RNAi feeding against *ifc-2*. Single L3-stage larvae were placed on RNAi food targeting *ifc-2*; 4 days later, the percent of progeny showing the expected bent posterior and accompanying paralysis at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.1, 0.25, and 0.75), which produced similar Eri penetrances as adjacent concentrations, are not included. Error bars represent standard deviation.

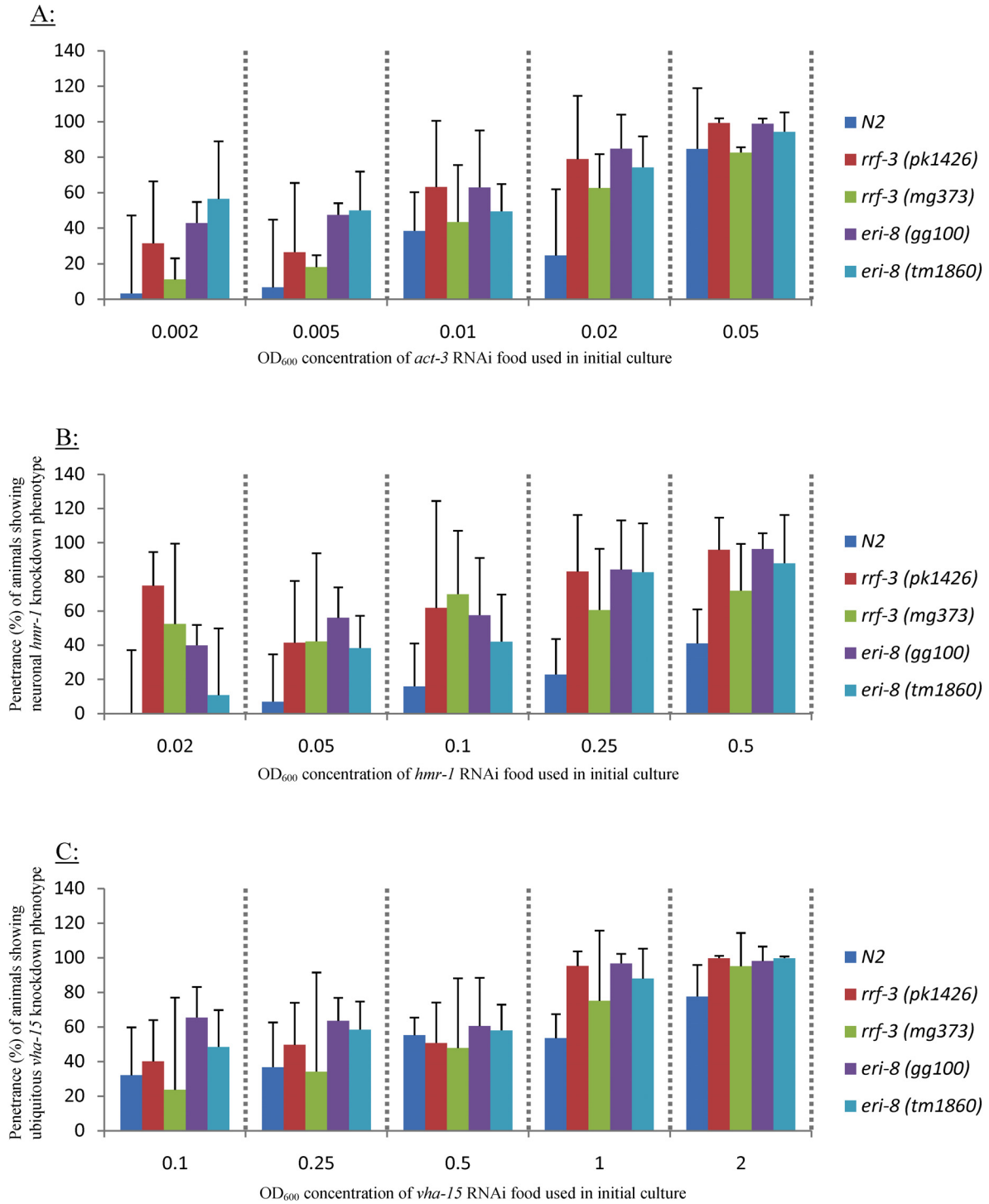


FIGURE S2.—Dilution series of Eri responses of different *rrf-3* and *eri-8* alleles by RNAi feeding against *act-3*, *hmr-1*, and *vha-15*. Single L3-stage larvae were placed on RNAi food targeting *act-3* (A), *hmr-1* (B), and *vha-15* (C); 4 days later, the percent of progeny showing the expected knockdown phenotypes, as listed in Table S1, at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. Error bars represent 95% confidence intervals.

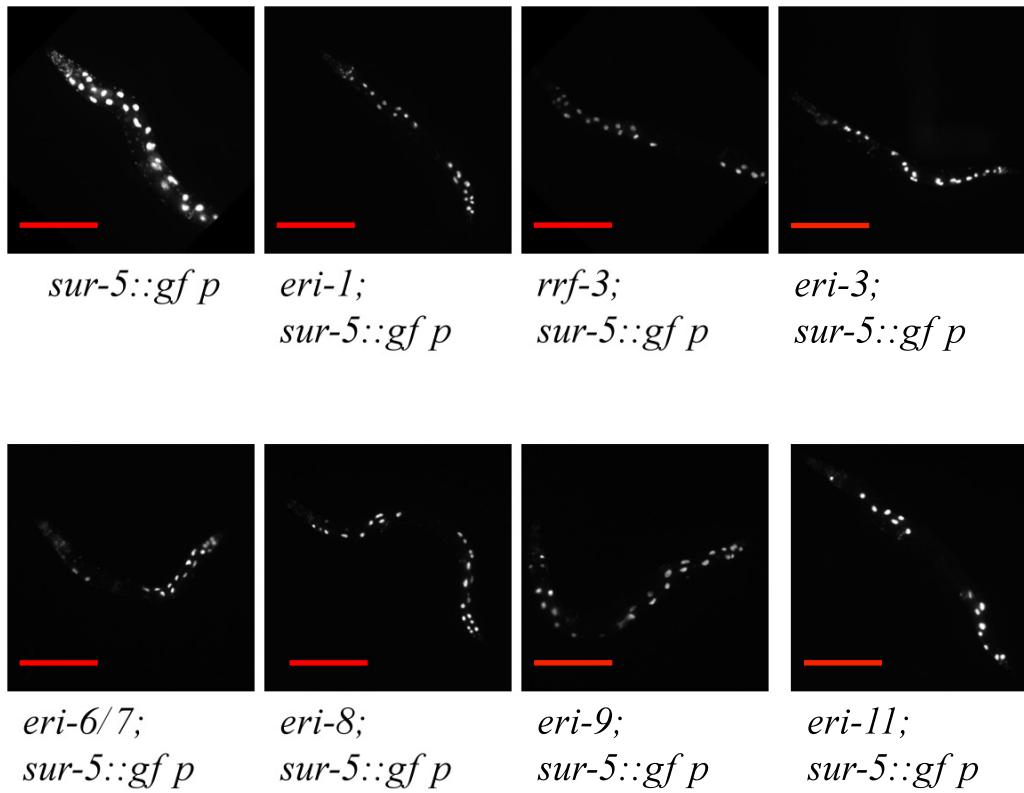


FIGURE S3.—All Eri mutants enhance transgene silencing. Eri mutants enhance transgene silencing in a *sur-5::gf p* background. GFP images were exposed for 100 milliseconds. Red scale bar indicates 0.2 mm.

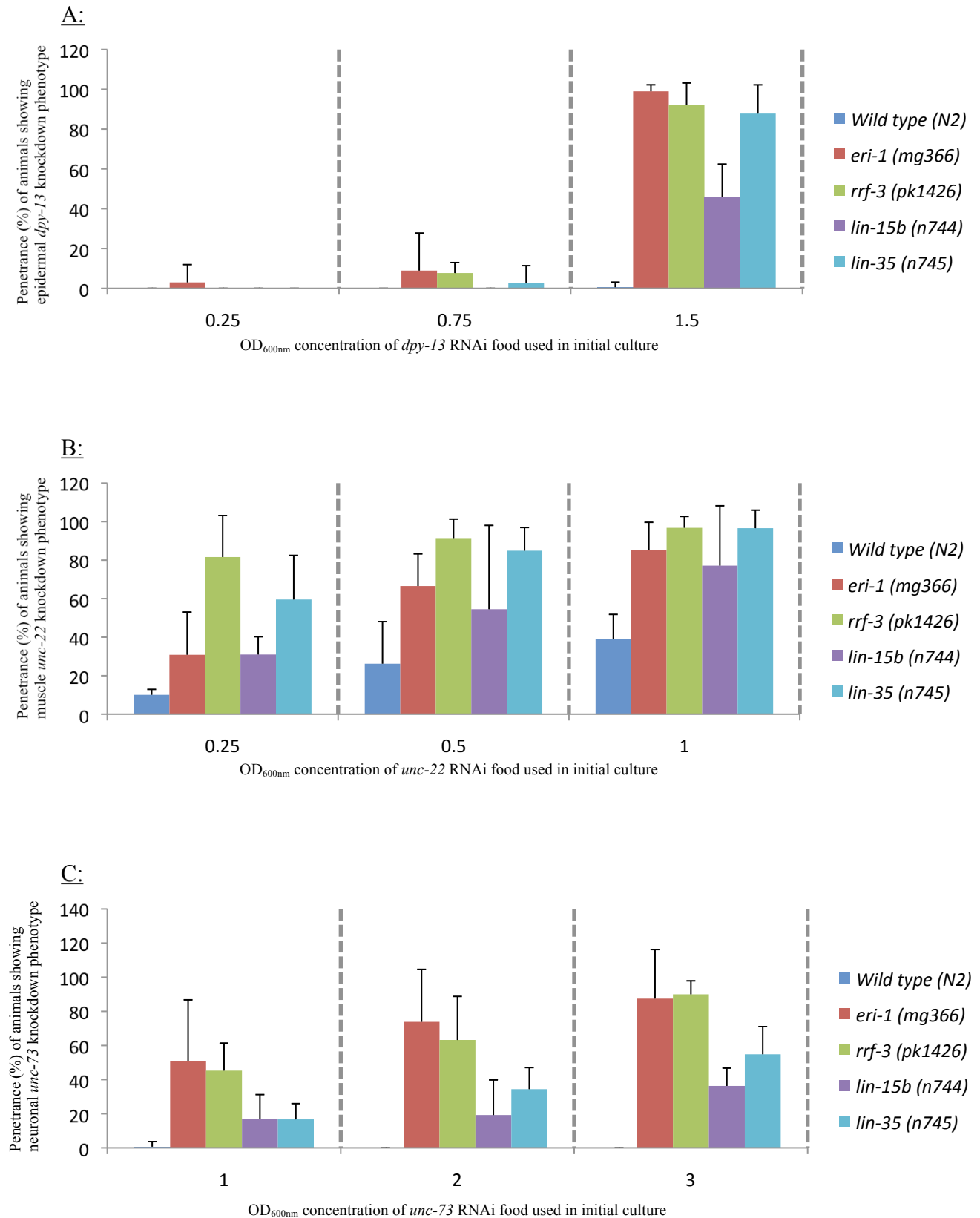


FIGURE S4.—Dilution series of Eri responses of *eri-1* and *rrf-3* versus *lin-15b* and *lin-35* by RNAi feeding against *dpy-13*, *unc-22*, and *unc-73*. Single L3-stage larvae were placed on RNAi food targeting *dpy-13* (A), *unc-22* (B), and *unc-73* (C); 4 days later, the percent of progeny showing the expected knockdown phenotypes, as listed in Table S1, at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. Error bars represent 95% confidence intervals.

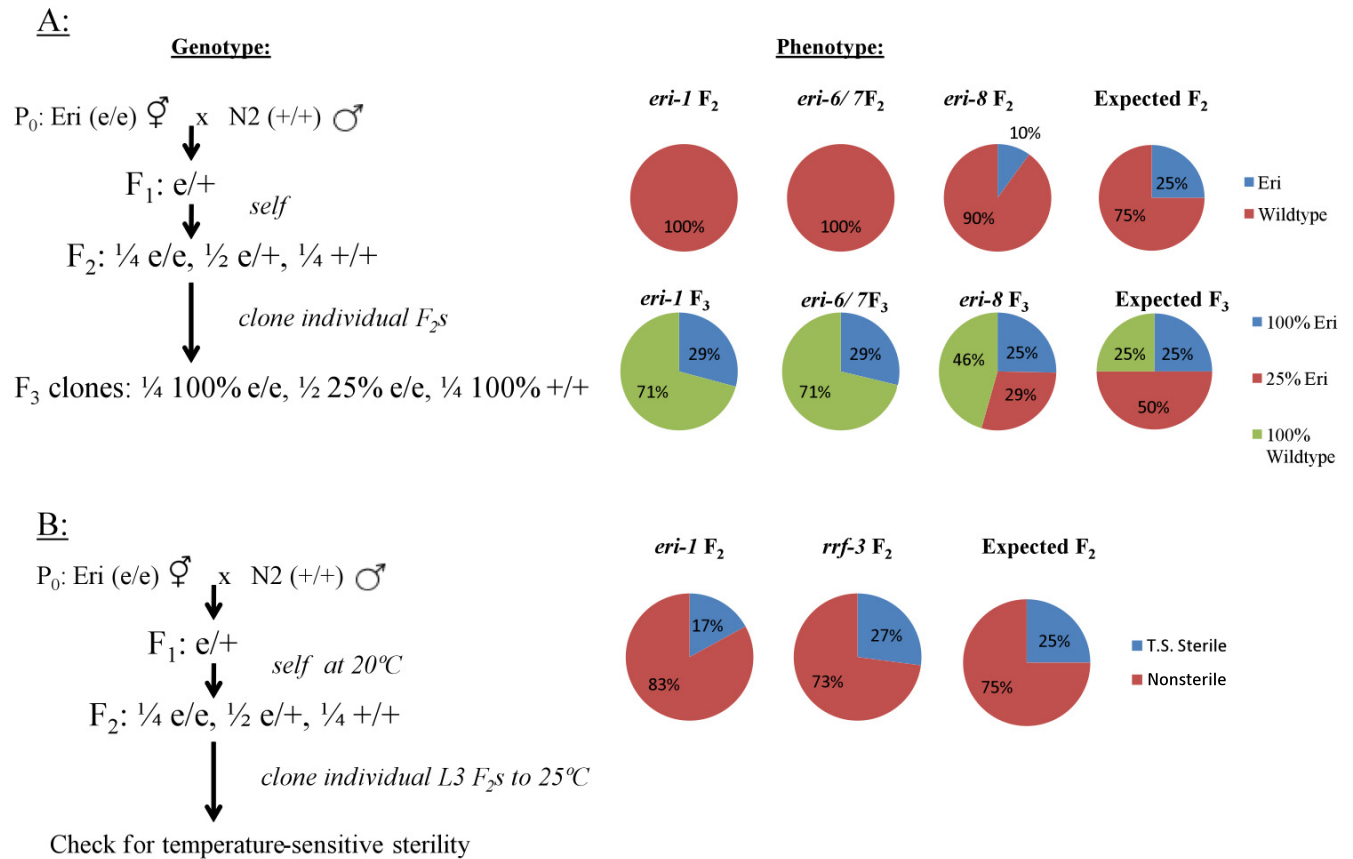


FIGURE S5.—Somatic maternal rescue of the Eri phenotype. An outcross between an Eri (e/e) hermaphrodite and a N2 wild type (+/+) male begets a 1:2:1 (e/e):(e/+):(+/+) genotypic ratio at the F<sub>2</sub>. Assuming a single-locus recessive trait, the expectation is that one quarter of the F<sub>2</sub> progeny should be Eri. (A) Out-crossed *eri-1* (which is sterile at 25°C), *eri-6/7*, and *eri-8* (which are not sterile at 25°C) show significantly lower than expected levels ( $p < 10^{-9}$ ) of the Eri phenotype at the F<sub>2</sub>. Similarly, the F<sub>3</sub> progeny of the F<sub>2</sub> show significantly higher than expected levels ( $p < 10^{-5}$ ) of wild-type progeny. (B) Out-crossed *eri-1* and *rrf-3* (which are both sterile at 25°C) show expected levels ( $p > 0.18$ ) of the temperature-sensitive sterile progeny at the F<sub>2</sub>. Figure S6 eliminates other possible parental rescue/effect mechanisms. Tables S29 and S32 show data used for  $p$  values.

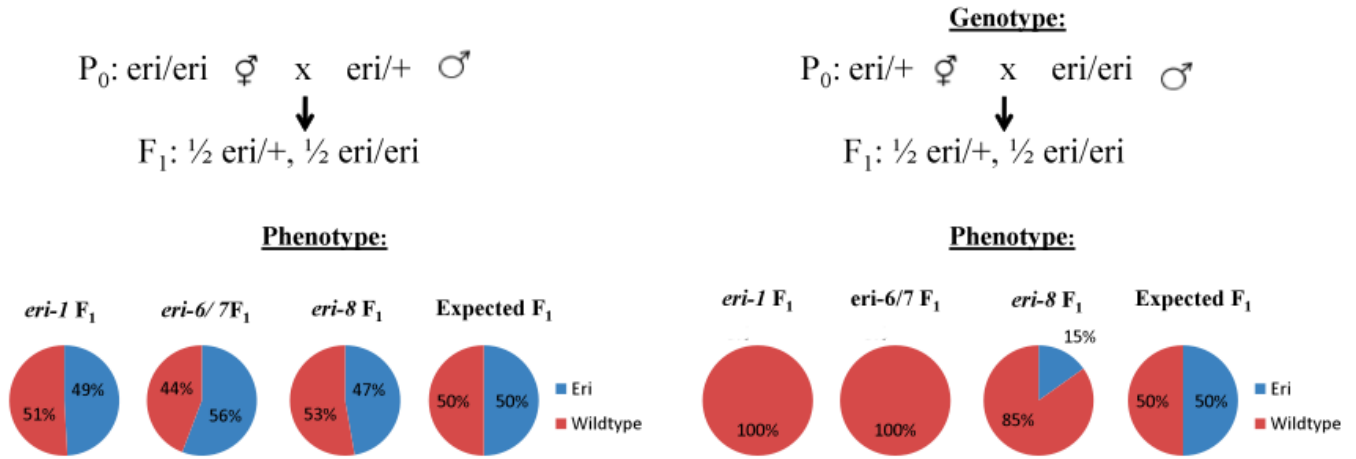


FIGURE S6.—Somatic maternal rescue of the Eri phenotype. The progeny of a heterozygous Eri male crossed to homozygous Eri hermaphrodite versus a homozygous Eri male crossed to a heterozygous Eri hermaphrodite are compared for Eri phenotypes. Assuming a single-locus recessive trait, the expectation is that the F<sub>1</sub> should be 50% Eri in both reciprocal crosses. (A) The cross progeny of *eri-1*, *eri-6/7*, and *eri-8* show expected levels ( $p > 0.48$ ) of Eri phenotype when the mother is homozygous Eri. (B) The cross progeny of *eri-1*, *eri-6/7*, and *eri-8* show significantly lower than expected levels ( $p < 10^{-13}$ ) of Eri phenotype when the mother is heterozygous Eri. See Tables S30 and S31 for data used in determining  $p$  values.

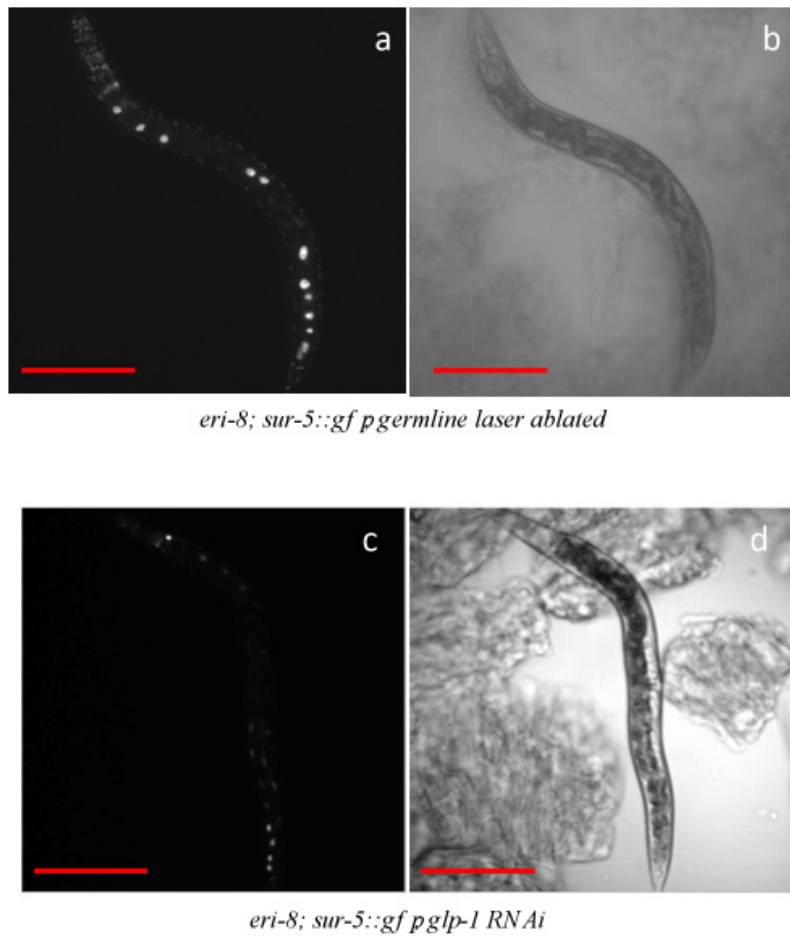


FIGURE S7.—Transgene silencing seen in Eri mutants is not from a germline source. *eri-8 (gg100); sur-5::gfp* animals exhibit spontaneous transgene silencing (A) even with a laser ablated germline (B) (see File S1). *eri-8 (gg100); sur-5::gfp* animals fed RNAi targeting *glp-1* still exhibit spontaneous transgene silencing (C), despite also lacking germlines (D). GFP images were exposed for 100 milliseconds. Red scale bar indicates 0.2 mm.

**TABLE S1****Phenotypes scored for RNAi foods**

Tissue	Food	Phenotype	Reference
Epidermis	<i>bli-1</i>	Large blisters on animals	Myllyharju and Kivirikko 2004
Epidermis	<i>dpy-11</i>	Severely dumpy animals whose length is at most 3X its width	Ko and Chow 2003
Epidermis	<i>dpy-13</i>	Severely dumpy animals whose length is at most 3X its width	Bird 1992
Gonad	<i>flh-6</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Chang <i>et al.</i> 2004
Gonad	<i>gon-1</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Tamai and Nishiwaki 2007
Gonad	<i>gon-4</i>	Severely protruding or absent gonad	Church and Lambie 2003
Intestine	<i>act-5</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	MacQueen <i>et al.</i> 2005
Intestine	<i>gtl-1*</i>	Brood size reduction in developed L3s or older worms Affected animals are significantly smaller in morphology	Xing <i>et al.</i> 2008
Intestine	<i>ifc-2</i>	Bent posterior body morphology that paralyzes locomotion	Hüsken <i>et al.</i> 2007
Muscle	<i>act-3</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Meissner <i>et al.</i> 2009
Muscle	<i>myo-3</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Ahn and Fire 1994
Muscle	<i>unc-22</i>	Severe twitching that paralyzes locomotion	Fire <i>et al.</i> 1991
Neuron	<i>hbl-1**</i>	Paralysis	Thompson-Peer, K.L. 2009 ( <i>unpublished</i> )
Neuron	<i>hmr-1*</i>	Brood size reduction in developed L3s or older worms Affected animals are significantly smaller in morphology	Broadbent and Pettitt 2002
Neuron	<i>unc-73</i>	Paralysis	Vanderzalm <i>et al.</i> 2009
Pharynx	<i>div-1*</i>	Brood size reduction in developed L3s or older worms Affected animals are significantly smaller in morphology	McKay <i>et al.</i> 2003
Pharynx	<i>pbs-6*</i>	Brood size reduction in developed L3s or older worms Affected animals are significantly smaller in morphology	Wang <i>et al.</i> 2006
Pharynx	<i>pha-4</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Mango 2007
Ubiquitous	<i>cdk-1</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Seydoux and Fire 1994.
Ubiquitous	<i>knl-3</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Cheeseman <i>et al.</i> 2004
Ubiquitous	<i>vha-15</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Hunt-Newbury <i>et al.</i> 2007
Germline	<i>glp-1</i>	Absent germline in adult hermaphrodites	Vought <i>et al.</i> 2005
Germline	<i>par-1</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Bowerman <i>et al.</i> 1997



Germline	<i>pos-1</i>	Brood size reduction in developed L3s or older worms Affected animals are lethally absent	Tabara <i>et al.</i> 1999
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The tissue-specific phenotype for each of the genes targeted by RNAi foods in Figure 1 are listed and referenced. Single asterisk (\*) indicates foods whose gene targets are grouped to a tissue due to high expression in that particular tissue. Double asterisks (\*\*) indicate food whose gene target is grouped to a tissue due to phenotype scored resulting from defects within that particular tissue. The remaining foods are grouped to a tissue due to both expression and phenotype arising from a particular tissue's effects.

TABLE S2

Dilution series results for *ifc-2* feeding

Strain	OD <sub>600</sub>	Penetrance readings						Avg	SD	Eri?
<i>Wild type</i> (N2)	<b>0.5</b>	0/22	0/27	0/20	0/23	1/60		<b>0</b>	<b>0.01</b>	
	<b>1</b>	1/24	3/22	1/26	0/23	0/24		<b>0.04</b>	<b>0.06</b>	
	<b>2</b>	0/20	3/59	3/31	2/24	2/32		<b>0.06</b>	<b>0.04</b>	
	<b>3</b>	2/27	2/30	1/35	4/36	0/23		<b>0.06</b>	<b>0.04</b>	
	<b>4</b>	5/36	2/26	4/30	4/33	8/39	2/31	2/31	<b>0.11</b>	<b>0.05</b>
<i>eri-1</i> ( <i>mg366</i> )	<b>0.5</b>	3/20	1/22	2/32	2/16	10/48		<b>0.12</b>	<b>0.07</b>	<b>Yes</b>
	<b>1</b>	6/21	8/34	5/29	4/33	5/24		<b>0.20</b>	<b>0.06</b>	<b>Yes</b>
	<b>2</b>	7/28	11/18	13/24	21/30	11/29		<b>0.50</b>	<b>0.18</b>	<b>Yes</b>
	<b>3</b>	17/24	20/31	19/32	22/29	23/29		<b>0.70</b>	<b>0.08</b>	<b>Yes</b>
	<b>4</b>	33/33	39/42	54/57	41/43	23/23	21/22	25/28	<b>0.95</b>	<b>0.04</b>
<i>rf-3</i> ( <i>pk1426</i> ) <u>*Best*</u>	<b>0.5</b>	5/25	0/38	4/28	0/10	12/39		<b>0.13</b>	<b>0.13</b>	
	<b>1</b>	20/28	25/28	35/46	20/23	33/33		<b>0.85</b>	<b>0.11</b>	<b>Yes</b>
	<b>2**</b>	32/39	24/25	22/25	13/18	22/28		<b>0.83</b>	<b>0.09</b>	<b>Yes</b>
	<b>3**</b>	15/19	22/23	16/21	45/47	33/39		<b>0.86</b>	<b>0.09</b>	<b>Yes</b>
	<b>4**</b>	29/30	28/30	10/10	29/30	20/20	40/40	29/30	<b>0.98</b>	<b>0.03</b>
<i>eri-3</i> ( <i>tm1361</i> )	<b>0.5</b>	6/80	2/90	5/60	1/20	2/40		<b>0.06</b>	<b>0.02</b>	<b>Yes</b>
	<b>1</b>	6/17	4/23	7/18	6/25	7/19		<b>0.30</b>	<b>0.09</b>	<b>Yes</b>
	<b>2</b>	12/16	5/14	12/30	7/16	6/16		<b>0.46</b>	<b>0.16</b>	<b>Yes</b>
	<b>3</b>	16/19	12/13	12/16	17/23	11/14		<b>0.81</b>	<b>0.08</b>	<b>Yes</b>
	<b>4</b>	15/20	17/19	11/17	12/15	8/17	17/26	16/20	<b>0.72</b>	<b>0.14</b>
<i>eri-5</i> ( <i>tm1705</i> )	<b>0.5</b>	4/80	2/60	0/20	0/20	0/20		<b>0.02</b>	<b>0.02</b>	
	<b>1</b>	0/44	3/60	0/20	3/40	2/50		<b>0.03</b>	<b>0.03</b>	
	<b>2</b>	0/20	2/80	3/80	0/20	2/40		<b>0.02</b>	<b>0.02</b>	
	<b>3</b>	0/28	1/40	1/40	2/60	4/80		<b>0.03</b>	<b>0.02</b>	
	<b>4</b>	1/31	4/30	3/48	3/22	5/33	7/54		<b>0.11</b>	<b>0.05</b>
<i>eri-6/7</i> ( <i>tm1917</i> )	<b>0.5</b>	2/27	3/21	2/34	3/37	2/33		<b>0.08</b>	<b>0.03</b>	<b>Yes</b>
	<b>1</b>	13/26	8/26	6/25	5/19	9/27		<b>0.33</b>	<b>0.10</b>	<b>Yes</b>
	<b>2</b>	8/26	10/33	11/34	8/23	12/39		<b>0.32</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	9/22	13/22	16/30	10/20	13/25		<b>0.51</b>	<b>0.07</b>	<b>Yes</b>
	<b>4</b>	14/36	15/35	10/27	28/37	12/19	8/19	23/30	<b>0.54</b>	<b>0.18</b>
<i>eri-8</i>	<b>0.5</b>	3/23	2/28	4/42	2/39	2/39		<b>0.08</b>	<b>0.03</b>	<b>Yes</b>

<i>(gg100)</i>	<b>1</b>	4/22	2/25	7/25	9/32	6/18			<b>0.23</b>	<b>0.10</b>	<b>Yes</b>
	<b>2</b>	9/23	12/26	13/27	10/23	11/23			<b>0.45</b>	<b>0.04</b>	<b>Yes</b>
	<b>3</b>	11/23	20/24	10/23	12/20	36/47			<b>0.62</b>	<b>0.17</b>	<b>Yes</b>
	<b>4</b>	17/24	24/27	24/28	20/30	31/36	31/34	45/48	<b>0.83</b>	<b>0.10</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.5</b>	2/26	6/26	2/32	5/39	1/35			<b>0.04</b>	<b>0.08</b>	
<i>(gg106)</i>	<b>1</b>	7/32	10/41	8/40	4/37	6/31			<b>0.09</b>	<b>0.05</b>	<b>Yes</b>
	<b>2</b>	3/20	3/27	3/32	4/27	5/41			<b>0.12</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	13/26	21/27	8/25	12/24	11/28			<b>0.50</b>	<b>0.17</b>	<b>Yes</b>
	<b>4</b>	9/21	10/21	14/30	16/28	17/24	13/21	10/10	<b>0.61</b>	<b>0.20</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.5</b>	0/32	1/30	2/30	2/45	3/31			<b>0.05</b>	<b>0.04</b>	
<i>(gg99)</i>	<b>1</b>	6/25	6/29	3/24	10/37	5/27			<b>0.21</b>	<b>0.06</b>	<b>Yes</b>
	<b>2</b>	13/31	13/26	13/28	11/23	10/24			<b>0.46</b>	<b>0.04</b>	<b>Yes</b>
	<b>3</b>	12/20	23/29	14/23	23/37	21/30			<b>0.66</b>	<b>0.08</b>	<b>Yes</b>
	<b>4</b>	18/26	24/25	30/35	19/27	21/30	22/28	18/28	<b>0.76</b>	<b>0.11</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *ifc-2*; 4 days later, the percent of progeny showing the expected bent posterior and accompanying paralysis at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.1, 0.25, and 0.75), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

**TABLE S3****Coefficient of variation for Eri responses by RNAi feeding against *ifc-2****Corresponds with Figure S1*

<b>OD<sub>600</sub></b>	<i>Wild type</i> ( <i>N2</i> )	<i>eri-1</i> ( <i>mg366</i> )	<i>rrf-3</i> ( <i>pk1426</i> )	<i>eri-3</i> ( <i>tm1361</i> )	<i>eri-5</i> ( <i>tm1705</i> )	<i>eri-6/7</i> ( <i>tm1917</i> )	<i>eri-8</i> ( <i>gg100</i> )	<i>eri-9</i> ( <i>gg106</i> )	<i>eri-11</i> ( <i>gg99</i> )
0.5	2.24	0.56	1.02	0.43	1.41	0.41	0.42	0.75	0.75
1	1.29	0.30	0.13	0.31	0.99	0.31	0.44	0.27	0.27
2	0.64	0.36	0.11	0.35	0.99	0.06	0.08	0.19	0.08
3	0.77	0.12	0.11	0.09	0.68	0.13	0.28	0.35	0.12
4	0.44	0.04	0.03	0.19	0.45	0.33	0.12	0.32	0.15

**TABLE S4**  
**Dilution series results for *bli-1* feeding**

<i>Strain</i>	<i>OD</i> <sub>600</sub>	<i>Penetrance readings</i>											<i>Avg</i>	<i>SD</i>	<i>Eri?</i>	
<i>Wildtype</i>	<b>0.1</b>	1/86	0/32	1/64	2/80	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0.01</b>	
( <i>N2</i> )	<b>0.5</b>	23/83	30/123	23/102	23/97	0/20	0/20	0/20	0/20	1/45				<b>0.11</b>	<b>0.13</b>	
	<b>1</b>	24/124	2/18	6/38	5/47	9/47	4/26							<b>0.15</b>	<b>0.04</b>	
	<b>2</b>	81/163	98/178	78/164	46/134	39/113	45/109	45/107	19/40	27/41	9/26			<b>0.45</b>	<b>0.10</b>	
	<b>3</b>	16/27	131/196	132/212	45/53	38/52	46/57	60/70	43/53					<b>0.74</b>	<b>0.10</b>	
<i>eri-1</i>	<b>0.1</b>	9/80	13/73	12/61	11/79	24/76	0/64	0/40	0/20	0/20	0/20	1/60	0/20	<b>0.08</b>	<b>0.11</b>	
( <i>mg366</i> )	<b>0.5</b>	37/82	12/29	37/90	59/116	51/93	48/90	23/58	10/34	10/38	12/51	21/34	6/23	<b>0.41</b>	<b>0.13</b>	<b>Yes</b>
<b>*Best*</b>	<b>1</b>	63/87	34/36	45/56	27/31	40/45	44/48	33/39						<b>0.86</b>	<b>0.07</b>	<b>Yes</b>
	<b>2</b>	71/84	59/73	43/60	69/82	86/102	44/51	31/37	44/53					<b>0.82</b>	<b>0.05</b>	<b>Yes</b>
	<b>3**</b>	57/59	95/110	66/80	68/74	20/20	84/92	68/85						<b>0.90</b>	<b>0.07</b>	<b>Yes</b>
<i>rrf-3</i>	<b>0.1</b>	6/48	0/20	0/20	0/20	0/20	0/20	0/20						<b>0.02</b>	<b>0.05</b>	
( <i>pk1426</i> )	<b>0.5</b>	83/115	55/108	14/27	28/54	21/46	20/45	21/43						<b>0.52</b>	<b>0.09</b>	<b>Yes</b>
	<b>1</b>	88/121	66/84	37/73	70/123	18/35	60/70	58/84	45/60	78/91				<b>0.70</b>	<b>0.14</b>	<b>Yes</b>
	<b>2</b>	102/104	74/87	34/42	33/42	45/56	28/38	44/51	7/9					<b>0.83</b>	<b>0.07</b>	<b>Yes</b>
	<b>3</b>	110/112	73/79	5/7	31/43	39/46	37/42	42/50	60/65					<b>0.85</b>	<b>0.10</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.1</b>	16/81	23/69	22/92	5/87	16/119	17/58	7/57	1/40	0/20	0/20	0/20	0/20	<b>0.12</b>	<b>0.12</b>	
( <i>tm1361</i> )	<b>0.5</b>	88/128	63/64	97/139	32/93	66/126	26/76	24/65	1/30	7/20	10/31	30/47	17/30	<b>0.49</b>	<b>0.25</b>	<b>Yes</b>
	<b>1</b>	62/96	88/105	57/100	7/25	28/106	25/72	9/40	12/58	21/41	12/44	18/42	19/51	<b>0.41</b>	<b>0.19</b>	<b>Yes</b>
	<b>2</b>	76/102	54/68	84/108	41/54	51/55	27/30	35/43	40/45					<b>0.83</b>	<b>0.07</b>	<b>Yes</b>
	<b>3</b>	84/99	54/67	95/103	54/78	43/48	21/26	7/9	42/52	37/44				<b>0.82</b>	<b>0.07</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.1</b>	3/80	2/80	0/23	1/50	0/20	0/20	0/20	0/20	0/20				<b>0.01</b>	<b>0.01</b>	
( <i>tm1705</i> )	<b>0.5</b>	3/63	5/25	0/20	1/60	6/50	5/50	0/20						<b>0.07</b>	<b>0.07</b>	

	<b>1</b>	80/168	60/159	70/184	13/46	41/96	9/24	8/26	2/33	3/49	8/40	4/52	23/109	<b>0.27</b>	<b>0.15</b>	
	<b>2</b>	59/146	60/166	63/162	25/62	10/26	21/63	18/45	15/41					<b>0.38</b>	<b>0.02</b>	
	<b>3</b>	42/54	59/66	47/66	29/44	29/38								<b>0.76</b>	<b>0.09</b>	
<i>eri-6/7</i>	<b>0.1</b>	20/138	14/115	7/59	0/20	0/20	0/20	0/20						<b>0.06</b>	<b>0.07</b>	
<i>(tm1917)</i>	<b>0.5</b>	46/146	74/191	14/59	22/53	11/54	14/49	1/7						<b>0.28</b>	<b>0.10</b>	<b>Yes</b>
	<b>1</b>	40/156	45/145	24/122	1/5	11/64	21/69	14/44	15/33	10/27	13/41	14/45		<b>0.29</b>	<b>0.08</b>	<b>Yes</b>
	<b>2</b>	79/121	29/40	16/35	17/34	16/36								<b>0.56</b>	<b>0.13</b>	<b>Yes</b>
	<b>3</b>	30/48	49/61	19/28	22/29	32/42								<b>0.73</b>	<b>0.07</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.1</b>	6/90	12/120	24/123	11/120	33/128	17/120	10/80	0/20	0/20	0/20	0/20	0/20	<b>0.08</b>	<b>0.09</b>	
<i>(gg100)</i>	<b>0.5</b>	51/134	54/130	54/120	43/105	59/133	41/95	36/117	10/90	0/90	2/90	12/32		<b>0.30</b>	<b>0.17</b>	<b>Yes</b>
	<b>1</b>	76/164	84/188	94/193	48/142	100/181	34/88	5/11	38/79	14/52	3/18	4/19	9/19	<b>0.39</b>	<b>0.12</b>	<b>Yes</b>
	<b>2</b>	66/135	59/126	6/12	33/55	33/54	23/32	24/39	22/32					<b>0.59</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	34/44	29/34	29/39	24/32	39/48								<b>0.79</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.1</b>	7/90	5/69	2/56	0/20	0/20	0/20	0/20	0/20					<b>0.02</b>	<b>0.03</b>	
<i>(gg106)</i>	<b>0.5</b>	90/202	51/154	32/143	49/130	57/124	32/80	42/105	11/34	19/45	6/22			<b>0.37</b>	<b>0.08</b>	<b>Yes</b>
	<b>1</b>	17/29	33/52	31/48	19/28	33/45								<b>0.66</b>	<b>0.05</b>	<b>Yes</b>
	<b>2</b>	65/128	103/181	86/172	46/52	53/60	48/57	32/42	24/39					<b>0.70</b>	<b>0.17</b>	<b>Yes</b>
	<b>3</b>	40/44	54/58	7/8	6/7	23/29								<b>0.87</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.1</b>	6/95	2/107	16/132	13/97	16/75	3/90	11/105	0/20	0/20	0/20	0/20	0/20	<b>0.06</b>	<b>0.07</b>	
<i>(gg99)</i>	<b>0.5</b>	68/170	72/188	52/153	25/91	37/96	37/118	19/112	5/20	7/20	3/22	0/20	13/50	<b>0.27</b>	<b>0.12</b>	<b>Yes</b>
	<b>1</b>	74/189	68/139	25/38	16/27	12/24	15/31	21/36						<b>0.53</b>	<b>0.09</b>	<b>Yes</b>
	<b>2</b>	3/5	6/8	26/32	15/19	32/38								<b>0.76</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	17/22	7/9	20/24	13/24	32/43								<b>0.73</b>	<b>0.11</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *bli-1*; 4 days later, the percent of progeny showing the expected large blisters on the animals at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.025, 0.25, and 4), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

**TABLE S5**  
**Dilution series results for *dpy-11* feeding**

<i>Strain</i>	<i>OD</i> <sub>600</sub>	<i>Penetrance readings</i>						<i>Avg</i>	<i>SD</i>	<i>Eri?</i>	
<i>Wildtype</i>	<b>0.05</b>	0/20	0/20	0/40	1/70	0/20	0/20	0/20	<b>0</b>	<b>0.01</b>	
<i>(N2)</i>	<b>0.1</b>	0/20	0/60	0/20	0/20	0/20	0/20	1/45	<b>0</b>	<b>0.01</b>	
	<b>0.5</b>	4/78	16/78	8/49	6/38	3/20	11/27	4/30	<b>0.18</b>	<b>0.11</b>	
	<b>1</b>	27/43	13/20	18/28	13/27	13/25	29/59	14/29	<b>0.56</b>	<b>0.08</b>	
	<b>3</b>	41/42	36/38	14/19	20/20	20/20	18/20	29/31	<b>0.93</b>	<b>0.09</b>	
<i>eri-1</i>	<b>0.05</b>	9/38	14/32	11/47	9/30	4/31	7/47	12/37	<b>0.26</b>	<b>0.11</b>	<b>Yes</b>
<i>(mg366)</i>	<b>0.1</b>	6/62	15/75	19/29	20/44	22/49	5/16	9/29	<b>0.35</b>	<b>0.18</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.5**</b>	39/49	51/54	49/50	20/20	63/75	20/20	20/20	<b>0.94</b>	<b>0.08</b>	<b>Yes</b>
	<b>1**</b>	20/20	20/20	20/20	20/20	40/40	20/20	20/20	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	59/60	20/20	20/20	<b>1.00</b>	<b>0.01</b>	
<i>rff-3</i>	<b>0.05</b>	2/30	2/41	4/57	4/47	3/53	5/52	7/46	<b>0.08</b>	<b>0.03</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.1</b>	31/82	35/96	9/35	14/46	11/32	14/39	10/28	<b>0.34</b>	<b>0.04</b>	<b>Yes</b>
	<b>0.5</b>	38/53	26/27	20/20	20/20	20/20	20/20		<b>0.95</b>	<b>0.11</b>	<b>Yes</b>
	<b>1</b>	20/20	20/20	30/30	20/20	20/21	20/20		<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	20/20	20/20		<b>1.00</b>	<b>0</b>	
<i>eri-3</i>	<b>0.05</b>	3/29	2/32	9/52	6/41	3/30	5/52	9/66	<b>0.12</b>	<b>0.04</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.1</b>	5/25	6/74	14/60	11/35	23/71	9/39	7/39	<b>0.22</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.5</b>	36/52	32/43	15/22	27/34	15/24	18/23	24/29	<b>0.74</b>	<b>0.07</b>	<b>Yes</b>
	<b>1</b>	20/20	20/20	20/20	20/20	29/30	20/20	20/20	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	59/60	20/20	20/20	<b>1.00</b>	<b>0.01</b>	
<i>eri-5</i>	<b>0.05</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>	
<i>(tm1705)</i>	<b>0.1</b>	0/60	0/60	0/28	0/20	0/20	0/30	0/20	<b>0</b>	<b>0</b>	
	<b>0.5</b>	18/69	10/74	11/34	7/25	10/28	14/37	13/40	<b>0.29</b>	<b>0.08</b>	
	<b>1</b>	15/29	25/40	11/38	11/19	12/26	14/40	15/31	<b>0.47</b>	<b>0.12</b>	
	<b>3</b>	79/80	80/80	20/20	20/20	20/20	39/40	54/60	<b>0.98</b>	<b>0.04</b>	
<i>eri-6/7</i>	<b>0.05</b>	2/40	0/20	0/20	9/70	3/30	0/20	7/40	<b>0.06</b>	<b>0.07</b>	
<i>(tm1917)</i>	<b>0.1</b>	0/8	16/35	8/35	7/27	9/27	6/24	9/29	<b>0.26</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.5</b>	27/43	27/35	20/20	20/20	30/35	20/20	40/45	<b>0.88</b>	<b>0.14</b>	<b>Yes</b>
	<b>1</b>	20/20	20/20	60/60	30/30	39/40	77/80	20/20	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	42/42	18/19	20/20	20/20	20/20	20/20	20/20	<b>0.99</b>	<b>0.02</b>	
<i>eri-8</i>	<b>0.05</b>	3/21	3/17	10/39	8/27	3/19	6/28	7/34	<b>0.21</b>	<b>0.05</b>	<b>Yes</b>



<i>(gg100)</i>	<b>0.1</b>	4/79	29/107	3/14	15/18	8/18	13/31	6/24	<b>0.35</b>	<b>0.25</b>	<b>Yes</b>
	<b>0.5</b>	65/82	44/58	20/20	20/20	20/20	20/20	36/40	<b>0.92</b>	<b>0.11</b>	<b>Yes</b>
	<b>1</b>	20/20	20/20	20/20	39/40	20/20	20/20	69/70	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	20/20	20/20	20/20	<b>1.00</b>	<b>0</b>	
<i>eri-9</i>	<b>0.05</b>	9/24	8/21	6/29	4/15	2/35	11/34	17/37	<b>0.30</b>	<b>0.13</b>	<b>Yes</b>
<i>(gg106)</i>	<b>0.1</b>	19/84	4/73	12/21	23/33	20/34	13/26	24/38	<b>0.47</b>	<b>0.24</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.5**</b>	50/59	38/38	20/20	19/20	20/20	20/20	40/40	<b>0.97</b>	<b>0.06</b>	<b>Yes</b>
	<b>1**</b>	20/20	20/20	20/20	74/80	20/20	20/20	20/20	<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	20/20	20/20	20/20	<b>1.00</b>	<b>0</b>	
<i>eri-11</i>	<b>0.05</b>	5/19	5/25	4/25	3/20	2/18	3/25	7/34	<b>0.17</b>	<b>0.05</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.1</b>	14/98	4/22	4/21	6/18	8/19	5/18	3/21	<b>0.24</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.5</b>	27/37	20/26	20/20	20/20	20/20	20/20	48/53	<b>0.91</b>	<b>0.12</b>	<b>Yes</b>
	<b>1</b>	16/20	20/20	20/20	20/20	20/20	20/20	20/20	<b>0.97</b>	<b>0.08</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	20/20	20/20	20/20	20/20	<b>1.00</b>	<b>0</b>	

Single L3-stage larvae were placed on RNAi food targeting *dpy-11*; 4 days later, the percent of progeny showing the expected severe dumpiness, in which an animal's length is at most three times its width, at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, one bacterial culture concentration (OD<sub>600nm</sub> of 4), which produced similar Eri penetrances as adjacent concentrations, is not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the "best *eri*" criterion described in text is marked as "best", with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

**TABLE S6**  
**Dilution series results for *dpy-13* feeding**

<i>Strain</i>	<i>OD</i> <sub>600</sub>	<i>Penetrance readings</i>										<i>Avg</i>	<i>SD</i>	<i>Eri?</i>
<i>Wildtype</i>	<b>0.04</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20			<b>0</b>	<b>0</b>	
<i>(N2)</i>	<b>0.1</b>	0/20	0/20	0/20	0/20	0/20	0/20	1/37	0/20			<b>0</b>	<b>0.01</b>	
	<b>0.25</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20			<b>0</b>	<b>0</b>	
	<b>0.75</b>	0/20	0/20	0/20	0/20	0/20	1/105	0/20	0/20			<b>0</b>	<b>0.01</b>	
	<b>3</b>	5/98	22/122	4/84	14/165	4/131	4/103	1/112	3/119	6/116		<b>0.06</b>	<b>0.05</b>	
<i>eri-1</i>	<b>0.04</b>	0/12	0/8	0/36	0/73	0/20	0/20	0/20				<b>0</b>	<b>0</b>	
<i>(mg366)</i>	<b>0.1</b>	4/46	12/30	8/68	36/68	35/60	13/82	22/54	31/50			<b>0.36</b>	<b>0.22</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.25</b>	17/28	44/44	9/19	67/78	60/73	4/5	20/20	20/20	20/20		<b>0.84</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.75**</b>	34/35	20/20	58/60	51/51	20/20	20/20	20/20				<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3**</b>	9/9	6/6	12/12	58/58	20/20	20/22	20/20				<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
<i>rf-3</i>	<b>0.04</b>	0/20	0/20	0/20	0/20	0/20	0/20					<b>0</b>	<b>0</b>	
<i>(pk1426)</i>	<b>0.1</b>	0/20	0/20	0/20	7/62	10/96	2/44	4/54	2/50	2/61		<b>0.05</b>	<b>0.04</b>	<b>Yes</b>
	<b>0.25</b>	3/58	6/57	80/115	71/78	37/48	25/56	38/65	23/61			<b>0.49</b>	<b>0.31</b>	<b>Yes</b>
	<b>0.75</b>	51/80	36/56	43/100	44/45	20/20	20/20	66/70	56/57	58/59		<b>0.84</b>	<b>0.21</b>	<b>Yes</b>
	<b>3</b>	67/67	20/20	42/44	20/20	20/20	20/20	20/20				<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.04</b>	0/20	0/20	0/20	0/20	0/20	0/20					<b>0</b>	<b>0</b>	
<i>(tm1361)</i>	<b>0.1</b>	3/62	0/55	3/77	13/88	5/80	3/44	1/14	7/55			<b>0.07</b>	<b>0.05</b>	<b>Yes</b>
	<b>0.25</b>	6/52	3/54	6/52	22/54	38/51	32/87	41/74	17/64	24/58		<b>0.34</b>	<b>0.23</b>	<b>Yes</b>
	<b>0.75</b>	37/75	64/80	48/81	76/89	87/94	94/101	62/84	86/90	43/52		<b>0.79</b>	<b>0.16</b>	<b>Yes</b>
	<b>3</b>	62/67	80/85	48/49	20/20	20/20	20/20					<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.04</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20			<b>0</b>	<b>0</b>	
<i>(tm1705)</i>	<b>0.1</b>	0/20	0/20	0/20	0/20	0/27	0/20					<b>0</b>	<b>0</b>	

	<b>0.25</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>		
	<b>0.75</b>	0/52	0/67	0/42	0/20	0/20	0/20	2/50		<b>0.01</b>	<b>0.02</b>		
	<b>3</b>	3/80	2/67	8/90	17/95	11/80	6/61	24/88	10/103	<b>0.12</b>	<b>0.08</b>		
<i>eri-6/7</i>	<b>0.04</b>	0/25	0/22	0/20	0/20	0/20				<b>0</b>	<b>0</b>		
( <i>tm1917</i> )	<b>0.1</b>	2/63	1/60	1/84	3/74	0/58	1/82	0/20		<b>0.02</b>	<b>0.02</b>		
	<b>0.25</b>	1/60	4/56	2/51	23/101	29/129	33/144	22/111	8/81	17/95	<b>0.14</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.75</b>	102/103	30/87	75/102	71/80	136/154	94/105	125/155	80/126	70/137	<b>0.74</b>	<b>0.21</b>	<b>Yes</b>
	<b>3</b>	94/96	88/91	61/70	20/20	96/100					<b>0.96</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.04</b>	0/29	0/33	1/120	0/20	0/20	2/100				<b>0</b>	<b>0.01</b>	
( <i>gg100</i> )	<b>0.1</b>	2/68	1/86	0/70	8/101	20/113	16/82	9/99	1/85		<b>0.07</b>	<b>0.08</b>	
	<b>0.25</b>	6/106	4/83	11/72	82/100	49/94	52/94	110/131	91/128	36/37	<b>0.52</b>	<b>0.35</b>	<b>Yes</b>
	<b>0.75</b>	55/60	57/80	52/57	118/120	117/120	20/20	20/20	114/161	20/20	<b>0.91</b>	<b>0.12</b>	<b>Yes</b>
	<b>3</b>	102/105	77/81	99/106	20/20	99/100					<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.04</b>	0/64	0/55	0/57	0/20	0/20					<b>0</b>	<b>0</b>	
( <i>gg106</i> )	<b>0.1</b>	0/67	0/58	0/49	5/76	8/86	3/109	8/103	2/63	5/74	<b>0.04</b>	<b>0.04</b>	
	<b>0.25</b>	7/79	10/106	4/79	24/126	39/109	35/108	22/131	14/98	68/122	<b>0.22</b>	<b>0.16</b>	<b>Yes</b>
	<b>0.75</b>	76/114	81/108	82/130	20/20	20/20	103/108	116/120	80/95	95/103	<b>0.86</b>	<b>0.14</b>	<b>Yes</b>
	<b>3</b>	95/100	74/78	89/94	20/20	99/100					<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.04</b>	0/20	0/20	0/20	4/77	2/70	0/20	0/20			<b>0.01</b>	<b>0.02</b>	
( <i>gg99</i> )	<b>0.1</b>	4/85	9/77	6/65	55/64	53/83	39/75	3/80	1/80		<b>0.29</b>	<b>0.33</b>	
<u>*Best*</u>	<b>0.25</b>	53/72	40/60	37/58	67/97	77/95	45/67	57/91	54/73	35/60	<b>0.68</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.75**</b>	20/20	20/20	125/130	20/20	20/20	99/100	56/60	73/76		<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>3**</b>	20/20	94/100	20/20	20/20	20/20	20/20	20/20	98/100	20/20	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *dpy-13*; 4 days later, the percent of progeny showing the expected severe dumpiness, in which an animal's length is at most three times its width, at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, four bacterial culture

concentrations ( $OD_{600nm}$  of 0.01, 0.02, 1.5, and 4), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S7

Dilution series results for *fkh-6* feeding

Strain	OD <sub>600</sub>	Brood Size						Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.002</b>	207	230	208	233	220		<b>220</b>	<b>12</b>	<b>0.03</b>	<b>0.10</b>	
(N2)	<b>0.01</b>	200	184	232	184	248	240	<b>215</b>	<b>29</b>	<b>0.05</b>	<b>0.15</b>	
	<b>0.02</b>	120	224	160	232	272	176	<b>197</b>	<b>55</b>	<b>0.13</b>	<b>0.26</b>	
	<b>0.04</b>	167	128	103	55	106	80	<b>107</b>	<b>39</b>	<b>0.53</b>	<b>0.18</b>	
	<b>0.1</b>	2	4	7	4	59	0	<b>13</b>	<b>23</b>	<b>0.94</b>	<b>0.10</b>	
<i>eri-1</i>	<b>0.002</b>	46	67	25	42	56		<b>47</b>	<b>16</b>	<b>0.70</b>	<b>0.10</b>	<b>Yes</b>
( <i>mg366</i> )	<b>0.01</b>	57	37	43	31	24	22	<b>36</b>	<b>13</b>	<b>0.77</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.02</b>	38	21	1	27	23	22	<b>22</b>	<b>12</b>	<b>0.86</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.04</b>	0	38	55	35	6	33	<b>28</b>	<b>21</b>	<b>0.82</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.1</b>	3	0	6	28	8	4	<b>8</b>	<b>10</b>	<b>0.95</b>	<b>0.06</b>	
<i>rif-3</i>	<b>0.002</b>	36	33	21	19	41	23	<b>29</b>	<b>9</b>	<b>0.78</b>	<b>0.07</b>	<b>Yes</b>
( <i>pk1426</i> )	<b>0.01**</b>	14	18	29	16	10	43	<b>22</b>	<b>12</b>	<b>0.84</b>	<b>0.09</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.02**</b>	27	13	0	28	30	17	<b>19</b>	<b>12</b>	<b>0.86</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.04**</b>	20	16	5	22	18	0	<b>14</b>	<b>9</b>	<b>0.90</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.1**</b>	0	0	13	0	0	0	<b>2</b>	<b>5</b>	<b>0.98</b>	<b>0.04</b>	
<i>eri-3</i>	<b>0.002</b>	112	171	140	128	108	148	<b>135</b>	<b>24</b>	<b>0.14</b>	<b>0.17</b>	
( <i>tm1361</i> )	<b>0.01</b>	120	125	88	104	42	68	<b>91</b>	<b>32</b>	<b>0.41</b>	<b>0.21</b>	<b>Yes</b>
	<b>0.02</b>	15	96	15	41	46	15	<b>38</b>	<b>32</b>	<b>0.76</b>	<b>0.20</b>	<b>Yes</b>
	<b>0.04</b>	68	43	45	37	31	1	<b>38</b>	<b>22</b>	<b>0.76</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.1</b>	26	2	16	0	0	9	<b>9</b>	<b>10</b>	<b>0.94</b>	<b>0.07</b>	
<i>eri-5</i>	<b>0.002</b>	152	154	192	184	203		<b>177</b>	<b>23</b>	<b>0</b>	<b>0.17</b>	
( <i>tm1705</i> )	<b>0.01</b>	188	199	184	205	152	167	<b>183</b>	<b>20</b>	<b>0</b>	<b>0.16</b>	
	<b>0.02</b>	148	120	112	114	125	137	<b>126</b>	<b>14</b>	<b>0.26</b>	<b>0.11</b>	
	<b>0.04</b>	70	97	71	79	112	84	<b>86</b>	<b>16</b>	<b>0.50</b>	<b>0.11</b>	
	<b>0.1</b>	1	17	5	3	33	4	<b>11</b>	<b>12</b>	<b>0.94</b>	<b>0.07</b>	
<i>eri-6/7</i>	<b>0.002</b>	184	156	184	160	148		<b>166</b>	<b>17</b>	<b>0</b>	<b>0.14</b>	
( <i>tm1917</i> )	<b>0.01</b>	75	90	144	160	88	168	<b>121</b>	<b>41</b>	<b>0.22</b>	<b>0.27</b>	
	<b>0.02</b>	192	160	64	45	92		<b>111</b>	<b>63</b>	<b>0.29</b>	<b>0.41</b>	
	<b>0.04</b>	80	58	27	81	105	20	<b>62</b>	<b>33</b>	<b>0.60</b>	<b>0.22</b>	
	<b>0.1</b>	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-8</i>	<b>0.002</b>	215	162	162	182	160	152	<b>172</b>	<b>23</b>	<b>0.23</b>	<b>0.11</b>	<b>Yes</b>

<i>(gg100)</i>	<b>0.01</b>	148	160	203	154	159	158	<b>164</b>	<b>20</b>	<b>0.26</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.02</b>	162	92	112	152	192	136	<b>141</b>	<b>36</b>	<b>0.37</b>	<b>0.16</b>	
	<b>0.04</b>	136	128	144	120	120	125	<b>129</b>	<b>10</b>	<b>0.42</b>	<b>0.05</b>	
	<b>0.1</b>	1	7	20	1	0	0	<b>5</b>	<b>8</b>	<b>0.98</b>	<b>0.04</b>	
<i>eri-9</i>	<b>0.002</b>	208	217	188	272	211	216	<b>219</b>	<b>28</b>	<b>0.09</b>	<b>0.13</b>	
<i>(gg106)</i>	<b>0.01</b>	175	216	180	184	171	153	<b>180</b>	<b>21</b>	<b>0.25</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.02</b>	184	248	224	205	153	168	<b>197</b>	<b>36</b>	<b>0.18</b>	<b>0.16</b>	
	<b>0.04</b>	32	136	200	168	154	198	<b>148</b>	<b>62</b>	<b>0.38</b>	<b>0.26</b>	
	<b>0.1</b>	0	39	0	7	46	3	<b>16</b>	<b>21</b>	<b>0.93</b>	<b>0.09</b>	
<i>eri-11</i>	<b>0.002</b>	216	224	270	233	312		<b>251</b>	<b>40</b>	<b>0.08</b>	<b>0.16</b>	
<i>(gg99)</i>	<b>0.01</b>	109	82	115	120	192	152	<b>128</b>	<b>38</b>	<b>0.53</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.02</b>	86	85	156	160	64	96	<b>108</b>	<b>40</b>	<b>0.61</b>	<b>0.15</b>	<b>Yes</b>
	<b>0.04</b>	140	76	108	9	35	30	<b>66</b>	<b>51</b>	<b>0.76</b>	<b>0.19</b>	
	<b>0.1</b>	1	0	0	1	39	4	<b>8</b>	<b>16</b>	<b>0.97</b>	<b>0.06</b>	<b>Yes</b>

Single L1-stage larvae were placed on RNAi food targeting *fkh-6*; 5 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.25 and 0.5), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S8

Dilution series results for *gon-1* feeding

<i>Strain</i>	<i>OD<sub>600</sub></i>	<i>Brood Size</i>							<i>Avg</i>	<i>SD</i>	<i>N.Avg</i>	<i>SEM</i>	<i>Eri?</i>
<i>Wildtype</i>	<b>0.25</b>	238	259	208	160	216	240	168	<b>213</b>	<b>37</b>	<b>0.06</b>	<b>0.19</b>	
<i>(N2)</i>	<b>0.5</b>	208	192	162	120	246	208	171	<b>187</b>	<b>40</b>	<b>0.18</b>	<b>0.19</b>	
	<b>1</b>	66	59	101	166	160	150	152	<b>122</b>	<b>46</b>	<b>0.46</b>	<b>0.21</b>	
	<b>2</b>	35	75	120	132	138	118		<b>103</b>	<b>40</b>	<b>0.55</b>	<b>0.18</b>	
	<b>3</b>	4	19	28	21	39	60	0	<b>24</b>	<b>21</b>	<b>0.89</b>	<b>0.09</b>	
<i>eri-1</i>	<b>0.25</b>	102	72	20	32	43	11		<b>47</b>	<b>34</b>	<b>0.71</b>	<b>0.22</b>	<b>Yes</b>
<i>(mg366)</i>	<b>0.5</b>	2	4	11	42	25	2		<b>14</b>	<b>16</b>	<b>0.91</b>	<b>0.10</b>	<b>Yes</b>
<b>*Best*</b>	<b>1**</b>	0	5	14	1	1	3	9	<b>5</b>	<b>5</b>	<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
	<b>2**</b>	1	2	1	10	3	11	1	<b>4</b>	<b>4</b>	<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
	<b>3**</b>	4	3	1	0	20	20	2	<b>7</b>	<b>9</b>	<b>0.95</b>	<b>0.06</b>	
<i>rff-3</i>	<b>0.25</b>	54	40	43	0	11	13		<b>27</b>	<b>22</b>	<b>0.80</b>	<b>0.16</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.5</b>	53	31	40	15	8	2	11	<b>23</b>	<b>19</b>	<b>0.83</b>	<b>0.14</b>	<b>Yes</b>
<b>*Best*</b>	<b>1**</b>	1	0	0	1	1	11	2	<b>2</b>	<b>4</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>2**</b>	1	5	1	0	1	18	2	<b>4</b>	<b>6</b>	<b>0.97</b>	<b>0.05</b>	<b>Yes</b>
	<b>3**</b>	0	0	0	0	0	2	0	<b>0</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.25</b>	44	61	4	72	40	64		<b>48</b>	<b>25</b>	<b>0.70</b>	<b>0.16</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.5</b>	95	72	5	49	37	18		<b>46</b>	<b>34</b>	<b>0.70</b>	<b>0.22</b>	<b>Yes</b>
	<b>1</b>	74	42	8	39	80	30		<b>46</b>	<b>27</b>	<b>0.71</b>	<b>0.18</b>	<b>Yes</b>
	<b>2</b>	54	64	8	36	33	13		<b>35</b>	<b>22</b>	<b>0.78</b>	<b>0.14</b>	<b>Yes</b>
	<b>3</b>	5	4	2	1	1	0	0	<b>2</b>	<b>2</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.25</b>	152	144	166	168	125	136		<b>149</b>	<b>17</b>	<b>0.13</b>	<b>0.13</b>	
<i>(tm1705)</i>	<b>0.5</b>	144	126	137	90	128			<b>125</b>	<b>21</b>	<b>0.27</b>	<b>0.14</b>	
	<b>1</b>	11	78	1	78	87			<b>51</b>	<b>41</b>	<b>0.70</b>	<b>0.24</b>	
	<b>2</b>	100	10	2	28	82	76	66	<b>52</b>	<b>38</b>	<b>0.69</b>	<b>0.23</b>	
	<b>3</b>	1	1	1	40	0			<b>9</b>	<b>18</b>	<b>0.95</b>	<b>0.10</b>	
<i>eri-6/7</i>	<b>0.25</b>	97	139	188	70	104	99		<b>116</b>	<b>42</b>	<b>0.25</b>	<b>0.27</b>	
<i>(tm1917)</i>	<b>0.5</b>	141	190	86	92	88	80	99	<b>111</b>	<b>40</b>	<b>0.29</b>	<b>0.27</b>	
	<b>1</b>	1	26	30	40	64	98	64	<b>46</b>	<b>32</b>	<b>0.70</b>	<b>0.21</b>	
	<b>2</b>	1	0	0	0	9	1	1	<b>2</b>	<b>3</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	0	2	2	2	1	2	2	<b>2</b>	<b>1</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.25</b>	192	162	184	96	144			<b>156</b>	<b>38</b>	<b>0.30</b>	<b>0.17</b>	<b>Yes</b>

<i>(gg100)</i>	<b>0.5</b>	64	108	30	81	54	47	97	<b>69</b>	<b>28</b>	<b>0.69</b>	<b>0.13</b>	<b>Yes</b>
	<b>1</b>	2	0	4	80	56	43	52	<b>34</b>	<b>32</b>	<b>0.85</b>	<b>0.14</b>	<b>Yes</b>
	<b>2</b>	1	0	2	1	1	49	12	<b>9</b>	<b>18</b>	<b>0.96</b>	<b>0.08</b>	<b>Yes</b>
	<b>3</b>	30	0	1	0	2	3	0	<b>5</b>	<b>11</b>	<b>0.98</b>	<b>0.05</b>	
<i>eri-9</i>	<b>0.25</b>	144	160	148	88	97			<b>127</b>	<b>33</b>	<b>0.47</b>	<b>0.14</b>	<b>Yes</b>
<i>(gg106)</i>	<b>0.5</b>	114	120	80	71	94			<b>96</b>	<b>21</b>	<b>0.60</b>	<b>0.09</b>	<b>Yes</b>
	<b>1</b>	4	0	1	63	104	42		<b>36</b>	<b>42</b>	<b>0.85</b>	<b>0.18</b>	<b>Yes</b>
	<b>2</b>	1	0	1	42	58	0		<b>17</b>	<b>26</b>	<b>0.93</b>	<b>0.11</b>	<b>Yes</b>
	<b>3</b>	0	1	0	8	23	2	57	<b>13</b>	<b>21</b>	<b>0.95</b>	<b>0.09</b>	
<i>eri-11</i>	<b>0.25</b>	102	112	112	57	120	144		<b>108</b>	<b>29</b>	<b>0.61</b>	<b>0.11</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.5</b>	94	128	3	47	0	2		<b>46</b>	<b>55</b>	<b>0.83</b>	<b>0.20</b>	<b>Yes</b>
	<b>1</b>	1	60	62	46	47	85	87	<b>55</b>	<b>29</b>	<b>0.80</b>	<b>0.11</b>	<b>Yes</b>
	<b>2</b>	0	1	0	1	58	34	34	<b>18</b>	<b>24</b>	<b>0.93</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	1	0	34	0	0	0	0	<b>5</b>	<b>13</b>	<b>0.98</b>	<b>0.05</b>	<b>Yes</b>

Single L1-stage larvae were placed on RNAi food targeting *gon-1*; 5 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, one bacterial culture concentration (OD<sub>600nm</sub> of 0.1), which produced similar Eri penetrances as adjacent concentrations, is not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.



**TABLE S9**  
**Dilution series results for *gon-4* feeding**

<i>Strain</i>	<i>OD</i> <sub>600</sub>	<i>Penetrance readings</i>							<i>Avg</i>	<i>SD</i>	<i>Eri?</i>
<i>Wildtype</i>	<b>0.5</b>	1/29	1/39	0/40	0/20	0/20	1/40		<b>0.01</b>	<b>0.02</b>	
( <i>N2</i> )	<b>1</b>	0/22	0/18	2/43	0/20	2/40	0/20	1/30	<b>0.02</b>	<b>0.02</b>	
	<b>2</b>	2/24	2/30	2/21	0/20	2/60			<b>0.06</b>	<b>0.04</b>	
	<b>3</b>	6/19	5/24	1/18	5/56	0/47	2/28	5/64	<b>0.12</b>	<b>0.11</b>	
	<b>4</b>	1/6	11/76	2/30	1/5	1/20			<b>0.13</b>	<b>0.06</b>	
<i>eri-1</i>	<b>0.5</b>	2/22	3/32	1/23	0/20	0/20	1/30		<b>0.04</b>	<b>0.04</b>	
( <i>mg366</i> )	<b>1</b>	9/18	6/30	3/28	0/20	0/20	2/12		<b>0.16</b>	<b>0.19</b>	
	<b>2</b>	22/26	24/24	15/18	4/25	0/20	6/18		<b>0.53</b>	<b>0.42</b>	<b>Yes</b>
	<b>3</b>	34/47	17/17	28/32	5/12	7/17	7/21		<b>0.63</b>	<b>0.28</b>	<b>Yes</b>
	<b>4</b>	19/20	10/21	20/22	7/16	11/13			<b>0.72</b>	<b>0.25</b>	<b>Yes</b>
<i>rif-3</i>	<b>0.5</b>	2/20	1/20	0/20	1/30	1/13	0/20		<b>0.04</b>	<b>0.04</b>	
( <i>pk1426</i> )	<b>1</b>	0/20	0/20	0/20	1/20	0/20	0/20		<b>0.01</b>	<b>0.02</b>	
<u>*Best*</u>	<b>2</b>	21/40	21/25	18/32	11/19	0/20	17/40		<b>0.49</b>	<b>0.28</b>	<b>Yes</b>
	<b>3</b>	28/35	29/34	29/41	17/20	15/21	22/23		<b>0.81</b>	<b>0.09</b>	<b>Yes</b>
	<b>4**</b>	20/20	20/20	19/23	7/9	20/20	17/19		<b>0.92</b>	<b>0.10</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.5</b>	0/20	1/20	1/16	0/20	1/24	0/20		<b>0.03</b>	<b>0.03</b>	
( <i>tm1361</i> )	<b>1</b>	4/30	3/20	1/30	1/20	0/20	1/30		<b>0.07</b>	<b>0.06</b>	
	<b>2</b>	9/20	17/31	19/31	10/20	18/55			<b>0.49</b>	<b>0.11</b>	<b>Yes</b>
	<b>3</b>	27/30	27/28	17/20	5/15	9/20	18/20		<b>0.73</b>	<b>0.27</b>	<b>Yes</b>
	<b>4</b>	33/35	21/25	32/35	26/30	12/14	39/50	26/35	<b>0.85</b>	<b>0.07</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.5</b>	2/20	2/20	3/20	0/20	0/8	0/62	0/20	<b>0.05</b>	<b>0.06</b>	
( <i>tm1705</i> )	<b>1</b>	3/40	6/50	0/20	0/20	0/20	1/40		<b>0.04</b>	<b>0.05</b>	
	<b>2</b>	3/22	10/25	6/21	0/20	0/20	1/20	0/20	<b>0.12</b>	<b>0.16</b>	
	<b>3</b>	3/15	8/24	8/34	4/39	0/20	0/20	11/56	<b>0.15</b>	<b>0.12</b>	
	<b>4</b>	0/20	5/34	4/42	0/20	0/20	4/20	3/42	<b>0.07</b>	<b>0.08</b>	
<i>eri-6/7</i>	<b>0.5</b>	2/33	2/26	2/43	0/20	0/20	1/40	1/50	<b>0.03</b>	<b>0.03</b>	
( <i>tm1917</i> )	<b>1</b>	2/40	1/80	3/27	0/20	4/60	13/34	11/80	<b>0.11</b>	<b>0.13</b>	
	<b>2</b>	3/31	2/22	6/30	2/40	14/90	11/80		<b>0.12</b>	<b>0.05</b>	
	<b>3</b>	5/14	8/20	10/19	2/8	13/18	8/22		<b>0.44</b>	<b>0.17</b>	<b>Yes</b>
	<b>4</b>	11/20	7/9	16/19	21/29	3/8			<b>0.65</b>	<b>0.19</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.5</b>	0/20	0/20	1/40	0/20	2/40	0/20	0/20	<b>0.01</b>	<b>0.02</b>	

<i>(gg100)</i>	<b>1</b>	3/40	0/20	0/20	0/20	1/60	0/20	0/20	<b>0.01</b>	<b>0.03</b>	
	<b>2</b>	15/45	24/46	13/33	0/20	1/11	0/20	0/20	<b>0.19</b>	<b>0.22</b>	
	<b>3</b>	7/20	10/23	28/35	4/10	14/64	9/39		<b>0.41</b>	<b>0.21</b>	<b>Yes</b>
	<b>4</b>	8/12	9/19	19/24	12/15	5/8			<b>0.67</b>	<b>0.13</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.5</b>	1/60	1/20	0/20	0/20	1/20	0/20	0/20	<b>0.02</b>	<b>0.02</b>	
<i>(gg106)</i>	<b>1</b>	1/20	4/30	0/15	2/8	12/90	2/30		<b>0.11</b>	<b>0.09</b>	
	<b>2</b>	14/17	11/15	15/19	11/19	20/35	30/65		<b>0.66</b>	<b>0.14</b>	<b>Yes</b>
	<b>3</b>	10/13	10/14	20/27	11/16	20/38			<b>0.69</b>	<b>0.10</b>	<b>Yes</b>
	<b>4</b>	24/35	24/36	20/25	10/14	11/15			<b>0.72</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.5</b>	0/20	1/40	1/40	0/20	0/20	1/30	0/20	<b>0.01</b>	<b>0.02</b>	
<i>(gg99)</i>	<b>1</b>	0/20	1/40	0/20	0/20	1/10	0/20		<b>0.02</b>	<b>0.04</b>	
	<b>2</b>	7/55	14/56	6/32	11/30	8/28			<b>0.24</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	6/29	7/27	12/36	6/12	15/40			<b>0.33</b>	<b>0.11</b>	<b>Yes</b>
	<b>4</b>	7/14	19/20	20/22	6/20	7/31			<b>0.58</b>	<b>0.34</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *gon-4*; 5 days later, the percent of progeny showing the expected severely protruding or absent gonads at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S10

Dilution series results for *act-5* feeding

<i>Strain</i>	<i>OD<sub>600</sub></i>	<i>Brood Size</i>						<i>Avg</i>	<i>SD</i>	<i>N.Avg</i>	<i>SEM</i>	<i>Eri?</i>	
<i>Wildtype</i>	<b>0.001</b>	288	264	248	216	224	198	<b>240</b>	<b>32</b>	<b>0</b>	<b>0.18</b>		
<i>(N2)</i>	<b>0.002</b>	175	160	157	166	94	134	172	<b>151</b>	<b>29</b>	<b>0.33</b>	<b>0.14</b>	
	<b>0.005</b>	112	118	71	61	69	118	66	<b>88</b>	<b>27</b>	<b>0.61</b>	<b>0.12</b>	
	<b>0.01</b>	79	97	76	82	118			<b>90</b>	<b>17</b>	<b>0.60</b>	<b>0.09</b>	
	<b>0.02</b>	76	80	0	0	3	41		<b>33</b>	<b>38</b>	<b>0.85</b>	<b>0.17</b>	
<i>eri-1</i>	<b>0.001</b>	99	108	81	85	107	102		<b>97</b>	<b>11</b>	<b>0.39</b>	<b>0.08</b>	<b>Yes</b>
<i>(mg366)</i>	<b>0.002</b>	57	91	97	50	44	65	59	<b>66</b>	<b>20</b>	<b>0.58</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.005</b>	65	77	23	41	24	86	65	<b>54</b>	<b>25</b>	<b>0.66</b>	<b>0.16</b>	
	<b>0.01</b>	18	29	26	23	25			<b>24</b>	<b>4</b>	<b>0.85</b>	<b>0.03</b>	<b>Yes</b>
	<b>0.02</b>	1	0	4	21	0	8		<b>6</b>	<b>8</b>	<b>0.96</b>	<b>0.05</b>	
<i>rf-3</i>	<b>0.001</b>	66	85	89	76	115	88		<b>87</b>	<b>16</b>	<b>0.35</b>	<b>0.13</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.002</b>	1	8	39	0	15	12	18	<b>13</b>	<b>13</b>	<b>0.90</b>	<b>0.10</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.005**</b>	0	0	1	26	0	1	5	<b>5</b>	<b>10</b>	<b>0.96</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.01**</b>	30	5	0	0	1	1	6	<b>6</b>	<b>11</b>	<b>0.95</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.02**</b>	0	1	0	2	0	1	0	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.001</b>	47	84	51	80	69			<b>66</b>	<b>17</b>	<b>0.57</b>	<b>0.11</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.002</b>	52	74	30	42	31	41	62	<b>47</b>	<b>16</b>	<b>0.70</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.005</b>	40	18	26	6	40	54	27	<b>30</b>	<b>16</b>	<b>0.81</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.01</b>	12	8	25	22	18	25		<b>18</b>	<b>7</b>	<b>0.88</b>	<b>0.05</b>	<b>Yes</b>
	<b>0.02</b>	0	2	1	1	22	14	15	<b>8</b>	<b>9</b>	<b>0.95</b>	<b>0.06</b>	
<i>eri-5</i>	<b>0.001</b>	192	168	180	164	204			<b>182</b>	<b>17</b>	<b>0</b>	<b>0.15</b>	
<i>(tm1705)</i>	<b>0.002</b>	168	87	142	164	134	144		<b>140</b>	<b>29</b>	<b>0.18</b>	<b>0.19</b>	
	<b>0.005</b>	73	92	108	93	78			<b>89</b>	<b>14</b>	<b>0.48</b>	<b>0.10</b>	
	<b>0.01</b>	114	17	17	69	92	89		<b>66</b>	<b>41</b>	<b>0.61</b>	<b>0.24</b>	
	<b>0.02</b>	55	39	0	0	0	18	3	<b>16</b>	<b>22</b>	<b>0.90</b>	<b>0.13</b>	
<i>eri-6/7</i>	<b>0.001</b>	158	151	189	157	144			<b>160</b>	<b>17</b>	<b>0</b>	<b>0.14</b>	
<i>(tm1917)</i>	<b>0.002</b>	85	90	61	109	119			<b>93</b>	<b>23</b>	<b>0.40</b>	<b>0.15</b>	
	<b>0.005</b>	40	99	111	55	46			<b>70</b>	<b>32</b>	<b>0.55</b>	<b>0.21</b>	
	<b>0.01</b>	17	3	20	11	26			<b>15</b>	<b>9</b>	<b>0.90</b>	<b>0.06</b>	<b>Yes</b>
	<b>0.02</b>	1	7	8	32	0	42	5	<b>14</b>	<b>17</b>	<b>0.91</b>	<b>0.11</b>	
<i>eri-8</i>	<b>0.001</b>	144	120	104	148	168	256	153	<b>156</b>	<b>49</b>	<b>0.30</b>	<b>0.22</b>	<b>Yes</b>

<i>(gg100)</i>	<b>0.002</b>	57	78	154	97	97	125		<b>101</b>	<b>34</b>	<b>0.54</b>	<b>0.15</b>	<b>Yes</b>
	<b>0.005</b>	34	82	103	38	95	29	74	<b>65</b>	<b>31</b>	<b>0.71</b>	<b>0.14</b>	
	<b>0.01</b>	28	1	38	16	17			<b>20</b>	<b>14</b>	<b>0.91</b>	<b>0.06</b>	<b>Yes</b>
	<b>0.02</b>	1	67	37	0	9	27	0	<b>20</b>	<b>25</b>	<b>0.91</b>	<b>0.11</b>	
<i>eri-9</i>	<b>0.001</b>	128	128	138	103	125			<b>124</b>	<b>13</b>	<b>0.48</b>	<b>0.06</b>	<b>Yes</b>
<i>(gg106)</i>	<b>0.002</b>	125	118	99	69	109	110	95	<b>104</b>	<b>18</b>	<b>0.57</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.005</b>	42	140	84	97	47	100		<b>85</b>	<b>37</b>	<b>0.65</b>	<b>0.15</b>	
	<b>0.01</b>	18	0	0	1	1	1		<b>4</b>	<b>7</b>	<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
	<b>0.02</b>	81	0	1	1	0	25	21	<b>18</b>	<b>30</b>	<b>0.92</b>	<b>0.12</b>	
<i>eri-11</i>	<b>0.001</b>	128	216	152	232	140	168	212	<b>178</b>	<b>41</b>	<b>0.35</b>	<b>0.16</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.002</b>	75	111	99	88	98	176		<b>108</b>	<b>36</b>	<b>0.61</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.005</b>	68	62	71	18	52	122	97	<b>70</b>	<b>33</b>	<b>0.74</b>	<b>0.12</b>	
	<b>0.01</b>	11	0	88	85	55	22		<b>44</b>	<b>38</b>	<b>0.84</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.02</b>	0	16	1	4	1	31	29	<b>12</b>	<b>14</b>	<b>0.96</b>	<b>0.05</b>	

Single L3-stage larvae were placed on RNAi food targeting *act-5*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri<sup>?</sup>), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S11

Dilution series results for *gtl-1* feeding

Strain	<i>OD</i> <sub>600</sub>	Brood Size							<i>Avg</i>	<i>SD</i>	<i>N.Avg</i>	<i>SEM</i>	<i>Eri?</i>
<i>Wildtype</i>	<b>0.04</b>	216	216	207	162	189	200	192	<b>197</b>	<b>19</b>	<b>0.13</b>	<b>0.12</b>	
<i>(N2)</i>	<b>0.1</b>	190	220	240	224	64	112	128	<b>168</b>	<b>67</b>	<b>0.26</b>	<b>0.30</b>	
	<b>0.5</b>	224	210	232	207	189	180	187	<b>204</b>	<b>20</b>	<b>0.10</b>	<b>0.12</b>	
	<b>1</b>	204	168	160	128	144	84	88	<b>139</b>	<b>43</b>	<b>0.38</b>	<b>0.20</b>	
	<b>2</b>	189	168	160	22	28	40	52	<b>94</b>	<b>74</b>	<b>0.58</b>	<b>0.33</b>	
<i>eri-1</i>	<b>0.04</b>	192	144	76	80	136	112	176	<b>131</b>	<b>45</b>	<b>0.17</b>	<b>0.29</b>	
<i>(mg366)</i>	<b>0.1</b>	144	96	104	81	88	80	72	<b>95</b>	<b>24</b>	<b>0.40</b>	<b>0.16</b>	
	<b>0.5</b>	128	104	128	56	72	64	79	<b>90</b>	<b>30</b>	<b>0.43</b>	<b>0.19</b>	Yes
	<b>1</b>	36	7	60	37	13	35	35	<b>32</b>	<b>17</b>	<b>0.80</b>	<b>0.11</b>	Yes
	<b>2</b>	40	48	45	48	54	39	40	<b>45</b>	<b>6</b>	<b>0.72</b>	<b>0.04</b>	
<i>rff-3</i>	<b>0.04</b>	36	77	62	65	108	65	71	<b>69</b>	<b>21</b>	<b>0.48</b>	<b>0.16</b>	Yes
<i>(pk1426)</i>	<b>0.1</b>	49	42	63	38	63	73	62	<b>56</b>	<b>13</b>	<b>0.58</b>	<b>0.10</b>	Yes
<u>*Best*</u>	<b>0.5</b>	39	45	54	40	24	34	45	<b>40</b>	<b>9</b>	<b>0.70</b>	<b>0.07</b>	Yes
	<b>1**</b>	19	8	16	30	30	0	28	<b>19</b>	<b>12</b>	<b>0.86</b>	<b>0.09</b>	Yes
	<b>2**</b>	7	16	8	22	15	18	38	<b>18</b>	<b>10</b>	<b>0.87</b>	<b>0.08</b>	Yes
<i>eri-3</i>	<b>0.04</b>	152	128	135	88	112	102	68	<b>112</b>	<b>29</b>	<b>0.28</b>	<b>0.20</b>	
<i>(tm1361)</i>	<b>0.1</b>	21	136	96	76	44	72	72	<b>74</b>	<b>37</b>	<b>0.53</b>	<b>0.24</b>	
	<b>0.5</b>	25	95	15	68	6	72	40	<b>46</b>	<b>33</b>	<b>0.71</b>	<b>0.21</b>	Yes
	<b>1</b>	80	27	56	20	15	35	20	<b>36</b>	<b>24</b>	<b>0.77</b>	<b>0.15</b>	Yes
	<b>2</b>	20	45	17	40	32	40	10	<b>29</b>	<b>13</b>	<b>0.81</b>	<b>0.09</b>	
<i>eri-5</i>	<b>0.04</b>	184	240	231	168	216	153	160	<b>193</b>	<b>36</b>	<b>0</b>	<b>0.24</b>	
<i>(tm1705)</i>	<b>0.1</b>	174	176	200	128	112	128	144	<b>152</b>	<b>32</b>	<b>0.11</b>	<b>0.21</b>	
	<b>0.5</b>	204	210	176	88	184	160	125	<b>164</b>	<b>44</b>	<b>0.04</b>	<b>0.28</b>	
	<b>1</b>	148	94	141	84	81	72	96	<b>102</b>	<b>30</b>	<b>0.40</b>	<b>0.19</b>	
	<b>2</b>	152	144	182	52	48	44	42	<b>95</b>	<b>61</b>	<b>0.44</b>	<b>0.37</b>	
<i>eri-6/7</i>	<b>0.04</b>	60	76	75	176	136	184	202	<b>130</b>	<b>59</b>	<b>0.16</b>	<b>0.39</b>	
<i>(tm1917)</i>	<b>0.1</b>	47	43	74	61	62	104	90	<b>69</b>	<b>22</b>	<b>0.56</b>	<b>0.15</b>	Yes
	<b>0.5</b>	44	36	84	82	79	100	67	<b>70</b>	<b>23</b>	<b>0.55</b>	<b>0.15</b>	Yes
	<b>1</b>	16	20	22	65	34	42	17	<b>31</b>	<b>18</b>	<b>0.80</b>	<b>0.12</b>	Yes
	<b>2</b>	4	9	22	29	21	9	15	<b>16</b>	<b>9</b>	<b>0.90</b>	<b>0.06</b>	Yes
<i>eri-8</i>	<b>0.04</b>	120	136	85	137	88	104	120	<b>113</b>	<b>21</b>	<b>0.49</b>	<b>0.10</b>	Yes

<i>(gg100)</i>	<b>0.1</b>	104	112	114	52	51	82		<b>86</b>	<b>29</b>	<b>0.61</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.5</b>	44	44	68	68	79	72	80	<b>65</b>	<b>15</b>	<b>0.71</b>	<b>0.07</b>	<b>Yes</b>
	<b>1</b>	39	28	23	42	43	64	27	<b>38</b>	<b>14</b>	<b>0.83</b>	<b>0.06</b>	<b>Yes</b>
	<b>2</b>	12	20	20	12	17	14	24	<b>17</b>	<b>5</b>	<b>0.92</b>	<b>0.02</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.04</b>	232	296	248	128	160	120	152	<b>191</b>	<b>68</b>	<b>0.20</b>	<b>0.29</b>	
<i>(gg106)</i>	<b>0.1</b>	48	246	120	50	64	100	81	<b>101</b>	<b>69</b>	<b>0.58</b>	<b>0.29</b>	
	<b>0.5</b>	144	175	128	64	80	104		<b>116</b>	<b>41</b>	<b>0.52</b>	<b>0.17</b>	<b>Yes</b>
	<b>1</b>	32	39	49	84	72	68	98	<b>63</b>	<b>24</b>	<b>0.74</b>	<b>0.10</b>	<b>Yes</b>
	<b>2</b>	16	19	32	14	20	25	14	<b>20</b>	<b>7</b>	<b>0.92</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.04</b>	192	160	196	120	104	104	192	<b>153</b>	<b>42</b>	<b>0.44</b>	<b>0.16</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.1</b>	98	168	128	96	72	90	88	<b>106</b>	<b>32</b>	<b>0.61</b>	<b>0.12</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.5</b>	80	96	104	48	56	104	60	<b>78</b>	<b>24</b>	<b>0.71</b>	<b>0.09</b>	<b>Yes</b>
	<b>1**</b>	70	72	68	20	45	9	41	<b>46</b>	<b>25</b>	<b>0.83</b>	<b>0.09</b>	<b>Yes</b>
	<b>2**</b>	35	43	85	21	28	14	16	<b>35</b>	<b>25</b>	<b>0.87</b>	<b>0.09</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *gtl-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.01 and 0.02), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S12

Dilution series results for *act-3* feeding

<i>Strain</i>	<i>OD<sub>600</sub></i>	<i>Brood Size</i>						<i>Avg</i>	<i>SD</i>	<i>N.Avg</i>	<i>SEM</i>	<i>Eri?</i>	
<i>Wildtype</i>	<b>0.002</b>	200	208	232	200	192	216	<b>208</b>	<b>14</b>	<b>0.08</b>	<b>0.10</b>		
<i>(N2)</i>	<b>0.005</b>	206	234	198	184	210	208	<b>207</b>	<b>16</b>	<b>0.09</b>	<b>0.11</b>		
	<b>0.01</b>	176	216	207	203	180	210	216	<b>201</b>	<b>17</b>	<b>0.11</b>	<b>0.11</b>	
	<b>0.02</b>	230	234	54	165	80	204	154	<b>160</b>	<b>71</b>	<b>0.29</b>	<b>0.32</b>	
	<b>0.05</b>	9	19	28	6	9	58	18	<b>21</b>	<b>18</b>	<b>0.91</b>	<b>0.08</b>	
<i>eri-1</i>	<b>0.002</b>	132	144	148	120	136	104	136	<b>131</b>	<b>15</b>	<b>0.17</b>	<b>0.11</b>	
<i>(mg366)</i>	<b>0.005</b>	24	53	132	102	84	90	82	<b>81</b>	<b>35</b>	<b>0.49</b>	<b>0.22</b>	<b>Yes</b>
	<b>0.01</b>	36	63	57	34	69	37	88	<b>55</b>	<b>20</b>	<b>0.65</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.02</b>	2	5	32	5	37	77	0	<b>23</b>	<b>28</b>	<b>0.86</b>	<b>0.18</b>	<b>Yes</b>
	<b>0.05</b>	0	4	0	1	0	12	0	<b>2</b>	<b>4</b>	<b>0.98</b>	<b>0.03</b>	
<i>rf-3</i>	<b>0.002</b>	200	56	116	78	117	129	112	<b>115</b>	<b>45</b>	<b>0.13</b>	<b>0.34</b>	
<i>(pk1426)</i>	<b>0.005</b>	65	28	49	93	67	104	88	<b>71</b>	<b>27</b>	<b>0.47</b>	<b>0.20</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.01</b>	17	31	39	66	21	18	23	<b>31</b>	<b>17</b>	<b>0.77</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.02*</b>								<b>3</b>	<b>7</b>	<b>0.98</b>	<b>0.05</b>	<b>Yes</b>
	<b>*</b>	2	19	2	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>0.05*</b>								<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>*</b>	0	0	0	0	1	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.002</b>	73	32	128	133	104	94	89	<b>93</b>	<b>34</b>	<b>0.40</b>	<b>0.23</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.005</b>	40	31	33	101	58	66	100	<b>61</b>	<b>30</b>	<b>0.61</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.01</b>	59	43	37	89	83	39	66	<b>59</b>	<b>21</b>	<b>0.62</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.02</b>	46	9	8	0	59	16	1	<b>20</b>	<b>23</b>	<b>0.87</b>	<b>0.15</b>	<b>Yes</b>
	<b>0.05</b>	0	0	0	0	62	39	0	<b>14</b>	<b>26</b>	<b>0.91</b>	<b>0.16</b>	
<i>eri-5</i>	<b>0.002</b>	222	203	116	176	144	150	168	<b>168</b>	<b>36</b>	<b>0.01</b>	<b>0.23</b>	
<i>(tm1705)</i>	<b>0.005</b>	180	188	210	200	126	140	130	<b>168</b>	<b>35</b>	<b>0.02</b>	<b>0.23</b>	
	<b>0.01</b>	123	116	136	144	152	112		<b>131</b>	<b>16</b>	<b>0.23</b>	<b>0.12</b>	
	<b>0.02</b>	148	72	36	41	133	28		<b>76</b>	<b>52</b>	<b>0.55</b>	<b>0.31</b>	
	<b>0.05</b>	0	3	21	26	12	4		<b>11</b>	<b>11</b>	<b>0.94</b>	<b>0.06</b>	
<i>eri-6/7</i>	<b>0.002</b>	184	168	31	115	128	62	71	<b>108</b>	<b>57</b>	<b>0.30</b>	<b>0.37</b>	
<i>(tm1917)</i>	<b>0.005</b>	189	147	55	114	61	115	114	<b>114</b>	<b>47</b>	<b>0.27</b>	<b>0.31</b>	
	<b>0.01</b>	135	34	64	88	16	27	104	<b>67</b>	<b>44</b>	<b>0.57</b>	<b>0.29</b>	<b>Yes</b>
	<b>0.02</b>	81	3	4	2	3	1	2	<b>14</b>	<b>30</b>	<b>0.91</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.05</b>	1	0	0	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>

<i>eri-8</i>	<b>0.002</b>	272	264	112	160	128	96	136	<b>167</b>	<b>72</b>	<b>0.25</b>	<b>0.32</b>	
( <i>gg100</i> )	<b>0.005</b>	63	42	112	160	160	162	174	<b>125</b>	<b>53</b>	<b>0.44</b>	<b>0.24</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.01</b>	121	69	144	56	72	51	128	<b>92</b>	<b>38</b>	<b>0.59</b>	<b>0.17</b>	<b>Yes</b>
	<b>0.02*</b>								<b>14</b>	<b>15</b>	<b>0.94</b>	<b>0.07</b>	<b>Yes</b>
	*	34	2	1	1	11	15	35					
	<b>0.05*</b>								<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	*	0	1	1	0	1	1	3					
<i>eri-9</i>	<b>0.002</b>	205	192	180	170	190	192	66	<b>171</b>	<b>47</b>	<b>0.29</b>	<b>0.20</b>	<b>Yes</b>
( <i>gg106</i> )	<b>0.005</b>	176	186	176	174	161	152	168	<b>170</b>	<b>11</b>	<b>0.29</b>	<b>0.06</b>	<b>Yes</b>
	<b>0.01</b>	164	56	141	156	174	210	155	<b>151</b>	<b>47</b>	<b>0.37</b>	<b>0.20</b>	<b>Yes</b>
	<b>0.02</b>	88	60	152	0	70	23	95	<b>70</b>	<b>50</b>	<b>0.71</b>	<b>0.21</b>	<b>Yes</b>
	<b>0.05</b>	1	28	1	12	4	5	0	<b>7</b>	<b>10</b>	<b>0.97</b>	<b>0.04</b>	
<i>eri-11</i>	<b>0.002</b>	195	224	188	232	276	152	216	<b>212</b>	<b>39</b>	<b>0.23</b>	<b>0.15</b>	
( <i>gg99</i> )	<b>0.005</b>	155	160	288	176	248	203	176	<b>201</b>	<b>50</b>	<b>0.27</b>	<b>0.19</b>	
	<b>0.01</b>	138	152	152	160	208	162	41	<b>145</b>	<b>51</b>	<b>0.47</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.02</b>	172	23	72	6	59	100	76	<b>73</b>	<b>54</b>	<b>0.73</b>	<b>0.20</b>	<b>Yes</b>
	<b>0.05</b>	5	0	8	17	16	12	46	<b>15</b>	<b>15</b>	<b>0.95</b>	<b>0.05</b>	

Single L3-stage larvae were placed on RNAi food targeting *act-3*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.1, 0.25, and 0.5), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.



TABLE S13

Dilution series results for *myo-3* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.5</b>	241	205	164	170	228	181	226	<b>202</b>	<b>31</b>	<b>0.11</b>	<b>0.16</b>	
<i>(N2)</i>	<b>0.75</b>	248	256	196	193	259	168	202	<b>217</b>	<b>36</b>	<b>0.04</b>	<b>0.18</b>	
	<b>1</b>	220	230	201	183	147	129	127	<b>177</b>	<b>43</b>	<b>0.22</b>	<b>0.20</b>	
	<b>2</b>	176	165	146	139	196	128	90	<b>149</b>	<b>35</b>	<b>0.34</b>	<b>0.16</b>	
	<b>3</b>	102	91	69	94	65	78	106	<b>86</b>	<b>16</b>	<b>0.62</b>	<b>0.08</b>	
<i>eri-1</i>	<b>0.5</b>	92	98	68	74	85	55	58	<b>76</b>	<b>17</b>	<b>0.52</b>	<b>0.11</b>	<b>Yes</b>
<i>(mg366)</i>	<b>0.75</b>	82	54	49	55	42	42	78	<b>57</b>	<b>16</b>	<b>0.64</b>	<b>0.10</b>	<b>Yes</b>
	<b>1</b>	13	58	9	25	18	19	40	<b>26</b>	<b>17</b>	<b>0.84</b>	<b>0.11</b>	<b>Yes</b>
	<b>2</b>	0	2	2	5	12	0		<b>4</b>	<b>5</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>3</b>	0	0	0	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>rif-3</i>	<b>0.5</b>	74	58	68	18	42	55	19	<b>48</b>	<b>22</b>	<b>0.64</b>	<b>0.17</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.75</b>	31	0	0	2	45	0	5	<b>12</b>	<b>18</b>	<b>0.91</b>	<b>0.14</b>	<b>Yes</b>
<b>*Best*</b>	<b>1**</b>	0	0	2	3	0	0	1	<b>1</b>	<b>1</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
	<b>2**</b>	0	0	0	0	2	0	9	<b>2</b>	<b>3</b>	<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
	<b>3**</b>	1	2	0	0	0	4	0	<b>1</b>	<b>2</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.5</b>	105	122	78	105	84	100	99	<b>99</b>	<b>15</b>	<b>0.36</b>	<b>0.11</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.75</b>	76	122	66	75	74	64	47	<b>75</b>	<b>23</b>	<b>0.52</b>	<b>0.15</b>	<b>Yes</b>
	<b>1</b>	12	95	94	69	29	24	90	<b>59</b>	<b>36</b>	<b>0.62</b>	<b>0.24</b>	<b>Yes</b>
	<b>2</b>	3	25	0	2	0	5	0	<b>5</b>	<b>9</b>	<b>0.97</b>	<b>0.06</b>	<b>Yes</b>
	<b>3</b>	0	0	0	0	0	1	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.5</b>	176	192	196	180	188	204		<b>189</b>	<b>10</b>	<b>0</b>	<b>0.10</b>	
<i>(tm1705)</i>	<b>0.75</b>	174	118	176	180	130	120	112	<b>144</b>	<b>31</b>	<b>0.15</b>	<b>0.31</b>	
	<b>1</b>	168	176	84	146	192	188		<b>159</b>	<b>40</b>	<b>0.07</b>	<b>0.40</b>	
	<b>2</b>	166	167	168	76	144	132	132	<b>141</b>	<b>33</b>	<b>0.17</b>	<b>0.33</b>	
	<b>3</b>	96	45	40	32	30	48	58	<b>50</b>	<b>22</b>	<b>0.71</b>	<b>0.22</b>	
<i>eri-6/7</i>	<b>0.5</b>	196	186	206	218	180	206	196	<b>198</b>	<b>13</b>	<b>0</b>	<b>0.13</b>	
<i>(tm1917)</i>	<b>0.75</b>	82	111	96	94	114	110	120	<b>104</b>	<b>13</b>	<b>0.33</b>	<b>0.10</b>	<b>Yes</b>
	<b>1</b>	104	49	106	46	106	80	101	<b>85</b>	<b>27</b>	<b>0.46</b>	<b>0.18</b>	<b>Yes</b>
	<b>2</b>	0	0	2	0	10	0	0	<b>2</b>	<b>4</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	0	0	0	2	0	0	1	<b>0</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.5</b>	238	216	222	216	196	184	206	<b>211</b>	<b>18</b>	<b>0.05</b>	<b>0.09</b>	

<i>(gg100)</i>	<b>0.75</b>	224	240	206	196	180	206		<b>209</b>	<b>21</b>	<b>0.06</b>	<b>0.10</b>	
	<b>1</b>	112	120	96	80	76	86	90	<b>94</b>	<b>16</b>	<b>0.58</b>	<b>0.07</b>	<b>Yes</b>
	<b>2</b>	0	0	0	1	0	2	11	<b>2</b>	<b>4</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	0	0	1	2	0	0		<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.5</b>	264	272	240	232	232	222		<b>244</b>	<b>20</b>	<b>0</b>	<b>0.10</b>	
<i>(gg106)</i>	<b>0.75</b>	224	264	260	196	208	220	201	<b>225</b>	<b>27</b>	<b>0.06</b>	<b>0.13</b>	
	<b>1</b>	11	160	90	5	60	40	55	<b>60</b>	<b>53</b>	<b>0.75</b>	<b>0.22</b>	<b>Yes</b>
	<b>2</b>	0	12	2	11	7	0	5	<b>5</b>	<b>5</b>	<b>0.98</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	1	3	0	0	0	0	1	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.5</b>	272	230	216	224	230	270		<b>240</b>	<b>24</b>	<b>0</b>	<b>0.11</b>	
<i>(gg99)</i>	<b>0.75</b>	232	208	196	238	240	216	208	<b>220</b>	<b>17</b>	<b>0</b>	<b>0.08</b>	
	<b>1</b>	156	181	144	144	106	134	98	<b>138</b>	<b>29</b>	<b>0.50</b>	<b>0.11</b>	<b>Yes</b>
	<b>2</b>	0	2	18	35	30	0	14	<b>14</b>	<b>14</b>	<b>0.95</b>	<b>0.05</b>	<b>Yes</b>
	<b>3</b>	0	0	0	5	0	5	6	<b>2</b>	<b>3</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *myo-3*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.05, 0.1, and 0.25), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

**TABLE S14**  
**Dilution series results for *unc-22* feeding**

<i>Strain</i>	<i>OD</i> <sub>600</sub>	<i>Penetrance readings</i>							<i>Avg</i>	<i>SD</i>	<i>Eri?</i>
<i>Wildtype</i>	<b>0.1</b>	3/28	3/18	1/16	5/31	0/13	3/25	1/17	<b>0.10</b>	<b>0.06</b>	
<i>(N2)</i>	<b>0.25</b>	8/30	9/35	8/29	5/30	5/22	5/20		<b>0.24</b>	<b>0.04</b>	
	<b>0.5</b>	8/31	8/36	10/28	8/27	8/27	8/30	11/26	<b>0.30</b>	<b>0.07</b>	
	<b>1</b>	7/24	7/25	12/21	11/22	6/16	10/19	11/27	<b>0.42</b>	<b>0.11</b>	
	<b>2</b>	26/31	27/36	22/26	25/27	29/36	26/29	28/33	<b>0.84</b>	<b>0.06</b>	
<i>eri-1</i>	<b>0.1</b>	3/26	3/35	1/22	4/32	2/27	0/30	2/19	<b>0.08</b>	<b>0.04</b>	
<i>(mg366)</i>	<b>0.25</b>	8/42	5/23	9/21	8/19	6/25	6/21	10/23	<b>0.32</b>	<b>0.11</b>	
	<b>0.5</b>	18/33	27/33	8/17	19/41	26/37	19/34	19/22	<b>0.63</b>	<b>0.16</b>	<b>Yes</b>
	<b>1</b>	46/55	6/7	20/22	31/32	45/50	19/21	24/30	<b>0.88</b>	<b>0.06</b>	<b>Yes</b>
	<b>2</b>	47/50	37/39	20/20	20/20	19/20	48/50	18/20	<b>0.96</b>	<b>0.04</b>	<b>Yes</b>
<i>rif-3</i>	<b>0.1</b>	15/37	18/27	12/41	2/41	7/33	2/36	6/36	<b>0.26</b>	<b>0.22</b>	
<i>(pk1426)</i>	<b>0.25</b>	20/32	27/37	36/48	24/31	18/24	30/35	34/36	<b>0.78</b>	<b>0.10</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.5**</b>	36/41	51/58	37/41	46/51	32/34	39/46	44/44	<b>0.91</b>	<b>0.05</b>	<b>Yes</b>
	<b>1**</b>	31/33	45/49	20/20	46/50	20/20	20/20	19/21	<b>0.95</b>	<b>0.04</b>	<b>Yes</b>
	<b>2**</b>	54/56	20/20	20/20	40/40	20/20	46/47	20/20	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.1</b>	4/15	9/19	2/30	3/54	6/36	2/31	2/37	<b>0.16</b>	<b>0.16</b>	
<i>(tm1361)</i>	<b>0.25</b>	3/30	5/24	5/24	5/31	9/40	10/35	6/31	<b>0.20</b>	<b>0.06</b>	
	<b>0.5</b>	28/31	20/31	29/46	30/40	14/18	24/34	17/22	<b>0.74</b>	<b>0.09</b>	<b>Yes</b>
	<b>1</b>	42/46	48/52	40/42	20/20	19/20	20/20	31/33	<b>0.95</b>	<b>0.03</b>	<b>Yes</b>
	<b>2</b>	24/26	46/52	20/20	20/20	19/20	20/20	21/23	<b>0.95</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.1</b>	3/28	3/37	2/28	4/30	5/47	4/35	3/26	<b>0.10</b>	<b>0.02</b>	
<i>(tm1705)</i>	<b>0.25</b>	5/49	3/21	1/25	6/25	7/36	7/27	6/34	<b>0.17</b>	<b>0.08</b>	
	<b>0.5</b>	4/33	11/48	19/39	8/29	10/19	4/37		<b>0.29</b>	<b>0.18</b>	
	<b>1</b>	22/47	9/29	19/34	14/28	24/44	19/40	13/30	<b>0.47</b>	<b>0.08</b>	
	<b>2</b>	37/47	26/38	27/30	19/23	20/22	24/27	46/49	<b>0.85</b>	<b>0.09</b>	
<i>eri-6/7</i>	<b>0.1</b>	2/21	13/34	4/39	6/33	13/39	14/30	5/24	<b>0.25</b>	<b>0.14</b>	<b>Yes</b>
<i>(tm1917)</i>	<b>0.25</b>	14/42	15/37	17/36	10/19	6/20	14/29	11/24	<b>0.43</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.5</b>	29/40	22/29	28/32	25/28	30/33	32/37		<b>0.84</b>	<b>0.08</b>	<b>Yes</b>
	<b>1</b>	51/55	20/20	39/40	78/80	30/30	20/20		<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>2</b>	20/20	29/30	20/20	20/20	20/20	20/20	38/41	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.1</b>	4/30	4/25	5/27	1/27	1/35	3/25		<b>0.11</b>	<b>0.06</b>	

<i>(gg100)</i>	<b>0.25</b>	9/22	11/31	6/23	14/34	8/18	5/16	10/27	<b>0.37</b>	<b>0.06</b>	<b>Yes</b>
	<b>0.5</b>	22/30	30/38	26/32	22/30	28/36	12/16	14/17	<b>0.77</b>	<b>0.04</b>	<b>Yes</b>
	<b>1</b>	46/49	44/47	20/20	20/20	37/40	63/69	19/20	<b>0.95</b>	<b>0.03</b>	<b>Yes</b>
	<b>2</b>	17/18	23/25	58/60	20/20	68/70	28/29	20/20	<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.1</b>	5/38	3/34	1/22	0/22	1/14	1/19	1/17	<b>0.06</b>	<b>0.04</b>	
<i>(gg106)</i>	<b>0.25</b>	3/14	3/20	4/21	3/16	14/28	12/30	8/29	<b>0.27</b>	<b>0.13</b>	
	<b>0.5</b>	12/22	18/27	20/26	20/27	14/19	29/37	14/19	<b>0.71</b>	<b>0.08</b>	<b>Yes</b>
	<b>1</b>	10/11	37/41	37/41	20/20	20/20	70/72	31/32	<b>0.95</b>	<b>0.04</b>	<b>Yes</b>
	<b>2</b>	51/56	44/46	20/20	20/20	44/47	40/40	20/20	<b>0.97</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.1</b>	6/37	12/26	2/31	8/33	6/26	6/21	6/31	<b>0.23</b>	<b>0.12</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.25</b>	13/37	9/29	6/18	11/21	11/30	12/19	10/30	<b>0.41</b>	<b>0.12</b>	<b>Yes</b>
	<b>0.5</b>	13/18	10/19	22/30	18/29	31/33	17/22	20/26	<b>0.73</b>	<b>0.13</b>	<b>Yes</b>
	<b>1</b>	10/24	18/23	22/23	41/42	20/20	17/20		<b>0.83</b>	<b>0.22</b>	<b>Yes</b>
	<b>2</b>	29/33	37/41	38/40	37/42	20/20	20/20	69/72	<b>0.94</b>	<b>0.05</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *unc-22*; 4 days later, the percent of progeny showing the expected paralysis due to severe twitching at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 3 and 4), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S15

Dilution series results for *hbl-1* feeding

Strain	OD <sub>600</sub>	Penetrance readings								Avg	SD	Eri?
<i>Wildtype</i>	<b>0.1</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>	
<i>(N2)</i>	<b>0.25</b>	0/20	0/20	2/78	1/98	0/62	0/20			<b>0.01</b>	<b>0.01</b>	
	<b>0.75</b>	0/20	2/100	1/100	12/89	16/104	16/83	1/80	4/90	<b>0.07</b>	<b>0.08</b>	
	<b>1.5</b>	5/95	6/80	4/83	43/110	14/93	17/81	12/124	16/135	<b>0.14</b>	<b>0.11</b>	
	<b>3</b>	16/59	15/76	22/91	24/105	23/109	34/108	46/143	21/140	<b>0.24</b>	<b>0.06</b>	
<i>eri-1</i>	<b>0.1</b>	3/50	2/50	0/50	0/20	0/20	0/20	3/74	1/56	<b>0.02</b>	<b>0.02</b>	
<i>(mg366)</i>	<b>0.25</b>	7/62	10/44	0/20	6/90	2/50	68/71	20/60		<b>0.25</b>	<b>0.33</b>	
	<b>0.75</b>	8/13	13/33	34/53	24/67	20/20	17/21	16/29	17/33	<b>0.61</b>	<b>0.21</b>	<b>Yes</b>
	<b>1.5</b>	11/14	37/45	25/27	74/78	84/88	65/100	37/41	21/32	<b>0.83</b>	<b>0.12</b>	<b>Yes</b>
	<b>3</b>	17/22	8/10	6/8	51/56	69/75	46/50	48/70	14/16	<b>0.83</b>	<b>0.09</b>	<b>Yes</b>
<i>rrf-3</i>	<b>0.1</b>	4/50	6/60	6/60	1/50	0/20	0/20	7/79		<b>0.06</b>	<b>0.05</b>	
<i>(pk1426)</i>	<b>0.25</b>	15/38	16/52	16/75	13/82	10/72	26/64	12/54		<b>0.26</b>	<b>0.11</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.75</b>	37/57	31/72	51/99	20/20	27/30	26/30	34/43	34/55	<b>0.72</b>	<b>0.20</b>	<b>Yes</b>
	<b>1.5**</b>	20/20	20/20	20/20	20/20	28/30	20/20	33/35	27/29	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>3**</b>	20/20	20/20	20/20	20/20	20/20	20/20	20/20		<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.1</b>	9/81	1/15	5/78	0/20	5/80	0/20	3/68	4/60	<b>0.05</b>	<b>0.04</b>	
<i>(tm1361)</i>	<b>0.25</b>	12/56	13/38	11/58	0/53	9/77	14/79	20/73	19/80	<b>0.19</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.75</b>	15/27	13/18	28/54	19/20	29/30	159/174	34/40	24/36	<b>0.77</b>	<b>0.18</b>	<b>Yes</b>
	<b>1.5</b>	20/20	20/20	20/20	20/20	20/20	145/155	20/20	20/20	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	18/19	20/20	90/127	20/20	20/20	<b>0.96</b>	<b>0.10</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.1</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>	
<i>(tm1705)</i>	<b>0.25</b>	0/20	0/20	0/20	0/20	0/20	0/20	2/50	1/50	<b>0.01</b>	<b>0.01</b>	
	<b>0.75</b>	3/100	3/100	5/100	5/93	17/107	28/149	2/31	10/68	<b>0.09</b>	<b>0.06</b>	
	<b>1.5</b>	19/107	20/100	23/81	9/111	1/12	8/79	16/50	15/46	<b>0.20</b>	<b>0.10</b>	
	<b>3</b>	27/87	31/109	25/71	14/111	13/80	24/132	10/57	24/56	<b>0.25</b>	<b>0.11</b>	
<i>eri-6/7</i>	<b>0.1</b>	9/66	0/20	1/50	3/50	1/50	1/15	1/58		<b>0.05</b>	<b>0.06</b>	
<i>(tm1917)</i>	<b>0.25</b>	23/118	16/86	7/89	11/56	10/120	16/84	8/54	24/63	<b>0.18</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.75</b>	23/89	5/69	28/59	20/20	59/82	79/90	36/50	20/20	<b>0.64</b>	<b>0.34</b>	<b>Yes</b>
	<b>1.5</b>	24/88	30/32	20/20	34/43	20/20	50/90	24/48	38/40	<b>0.75</b>	<b>0.28</b>	<b>Yes</b>
	<b>3</b>	20/20	20/20	20/20	73/80	20/20	28/30	20/20		<b>0.98</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.1</b>	3/100	9/100	7/150	4/70	5/150	1/90			<b>0.04</b>	<b>0.03</b>	

<i>(gg100)</i>	<b>0.25</b>	16/95	9/91	38/143	24/111	26/129	29/105	21/92		<b>0.21</b>	<b>0.06</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.75</b>	20/21	20/21	27/27	138/148	28/30	43/47	48/104	68/98	<b>0.86</b>	<b>0.18</b>	<b>Yes</b>
	<b>1.5**</b>	20/20	20/20	20/20	26/29	20/20	27/29	20/20	140/150	<b>0.97</b>	<b>0.04</b>	<b>Yes</b>
	<b>3**</b>	20/20	20/20	20/20	20/20	20/20	78/89	20/20	20/20	<b>0.98</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.1</b>	5/100	5/100	6/100	0/20	0/20	0/20	0/53	0/20	<b>0.02</b>	<b>0.03</b>	
<i>(gg106)</i>	<b>0.25</b>	20/115	13/85	19/96	7/103	9/160	14/180	34/168	2/6	<b>0.16</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.75</b>	67/78	57/91	39/97	117/147	116/166	96/121	35/124	40/87	<b>0.61</b>	<b>0.21</b>	<b>Yes</b>
	<b>1.5</b>	62/69	49/50	159/178	26/165	27/151	49/69	104/115		<b>0.67</b>	<b>0.36</b>	<b>Yes</b>
	<b>3</b>	22/22	14/14	99/100	81/135	47/50	20/20	96/103		<b>0.92</b>	<b>0.15</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.1</b>	1/100	0/20	0/20	4/150	2/120	0/20	4/150	2/80	<b>0.01</b>	<b>0.01</b>	
<i>(gg99)</i>	<b>0.25</b>	8/86	10/54	7/56	12/105	8/82	9/113	9/61	11/63	<b>0.13</b>	<b>0.04</b>	<b>Yes</b>
	<b>0.75</b>	12/55	8/22	43/85	63/133	55/91	34/66	21/88		<b>0.42</b>	<b>0.15</b>	<b>Yes</b>
	<b>1.5</b>	18/18	20/22	44/77	85/108	76/114	76/129			<b>0.75</b>	<b>0.18</b>	<b>Yes</b>
	<b>3</b>	13/14	14/14	17/19	115/137	20/20	103/143	20/20	20/20	<b>0.92</b>	<b>0.10</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *hbl-1*; 4 days later, the percent of progeny showing the expected paralysis at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.02 and 0.5), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S16

Dilution series results for *hmr-1* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.02</b>	224	208	240	198	232	248		<b>225</b>	<b>19</b>	<b>0.01</b>	<b>0.12</b>	
<i>(N2)</i>	<b>0.05</b>	184	200	240	272	248	256		<b>233</b>	<b>34</b>	<b>0</b>	<b>0.18</b>	
	<b>0.1</b>	252	224	200	240	256	220	238	<b>233</b>	<b>20</b>	<b>0</b>	<b>0.13</b>	
	<b>0.25</b>	288	264	200	210	225	252	224	<b>238</b>	<b>32</b>	<b>0</b>	<b>0.17</b>	
	<b>0.5</b>	225	240	264	259	224	208	228	<b>235</b>	<b>20</b>	<b>0</b>	<b>0.13</b>	
<i>eri-1</i>	<b>0.02</b>	104	128	120	114	144	88	80	<b>111</b>	<b>22</b>	<b>0.30</b>	<b>0.15</b>	<b>Yes</b>
<i>(mg366)</i>	<b>0.05</b>	72	56	78	96	70	84	72	<b>75</b>	<b>12</b>	<b>0.52</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.1</b>	53	25	71	58	83	53	61	<b>58</b>	<b>18</b>	<b>0.64</b>	<b>0.12</b>	<b>Yes</b>
	<b>0.25</b>	54	0	23	14	8	22	0	<b>17</b>	<b>19</b>	<b>0.89</b>	<b>0.12</b>	<b>Yes</b>
	<b>0.5</b>	13	0	0	20	19	0	60	<b>16</b>	<b>21</b>	<b>0.90</b>	<b>0.13</b>	<b>Yes</b>
<i>rnf-3</i>	<b>0.02</b>	78	101	85	48	80	63	71	<b>75</b>	<b>17</b>	<b>0.44</b>	<b>0.13</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.05</b>	89	42	49	53	45	63	100	<b>63</b>	<b>23</b>	<b>0.53</b>	<b>0.17</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.1**</b>	0	0	1	1	0	6	21	<b>4</b>	<b>8</b>	<b>0.97</b>	<b>0.06</b>	<b>Yes</b>
	<b>0.25**</b>	22	0	1	2	24	0	18	<b>10</b>	<b>11</b>	<b>0.93</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.5**</b>	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.02</b>	72	102	72	85	120	128		<b>97</b>	<b>24</b>	<b>0.38</b>	<b>0.17</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.05</b>	120	108	128	144	90			<b>118</b>	<b>20</b>	<b>0.24</b>	<b>0.15</b>	<b>Yes</b>
	<b>0.1</b>	29	23	37	25	13	17	40	<b>26</b>	<b>10</b>	<b>0.83</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.25</b>	0	19	12	3	0	3		<b>6</b>	<b>8</b>	<b>0.96</b>	<b>0.05</b>	<b>Yes</b>
	<b>0.5</b>	0	0	0	0	1	6	3	<b>1</b>	<b>2</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.02</b>	144	184	203	217	152	168	193	<b>180</b>	<b>27</b>	<b>0</b>	<b>0.19</b>	
<i>(tm1705)</i>	<b>0.05</b>	216	168	216	192	152			<b>189</b>	<b>29</b>	<b>0</b>	<b>0.20</b>	
	<b>0.1</b>	152	168	152	176	184	184	128	<b>163</b>	<b>21</b>	<b>0.04</b>	<b>0.15</b>	
	<b>0.25</b>	168	144	116	156	170	125	136	<b>145</b>	<b>21</b>	<b>0.15</b>	<b>0.15</b>	
	<b>0.5</b>	192	184	156	160	176	152	175	<b>171</b>	<b>15</b>	<b>0</b>	<b>0.13</b>	
<i>eri-6/7</i>	<b>0.02</b>	132	105	93	84	108	90	98	<b>101</b>	<b>16</b>	<b>0</b>	<b>0.11</b>	
<i>(tm1917)</i>	<b>0.05</b>	136	160	128	168	104	168	136	<b>143</b>	<b>24</b>	<b>0.08</b>	<b>0.17</b>	
	<b>0.1</b>	33	26	20	46	35	112	68	<b>49</b>	<b>32</b>	<b>0.69</b>	<b>0.21</b>	<b>Yes</b>
	<b>0.25</b>	46	29	0	36	42	45		<b>33</b>	<b>17</b>	<b>0.79</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.5</b>	10	0	0	4	3	0	1	<b>3</b>	<b>4</b>	<b>0.98</b>	<b>0.02</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.02</b>	96	168	136	142	153	160	169	<b>146</b>	<b>25</b>	<b>0</b>	<b>0.12</b>	

<i>(gg100)</i>	<b>0.05</b>	128	72	144	104	128	56	128	<b>109</b>	<b>33</b>	<b>0.51</b>	<b>0.15</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.1**</b>	3	25	17	25	5	16	12	<b>15</b>	<b>9</b>	<b>0.93</b>	<b>0.04</b>	<b>Yes</b>
	<b>0.25**</b>	1	1	0	4	0	8	3	<b>2</b>	<b>3</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
	<b>0.5**</b>	0	1	0	0	0	1	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.02</b>	180	232	168	168	176	196	187	<b>187</b>	<b>22</b>	<b>0.22</b>	<b>0.10</b>	<b>Yes</b>
<i>(gg106)</i>	<b>0.05</b>	160	176	120	200	112	128	204	<b>157</b>	<b>38</b>	<b>0.34</b>	<b>0.16</b>	<b>Yes</b>
	<b>0.1</b>	15	168	160	72	114	104	71	<b>101</b>	<b>54</b>	<b>0.58</b>	<b>0.23</b>	<b>Yes</b>
	<b>0.25</b>	37	87	33	52	27	67	72	<b>54</b>	<b>23</b>	<b>0.78</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.5</b>	8	12	0	9	34	0	15	<b>11</b>	<b>12</b>	<b>0.95</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.02</b>	256	184	208	200	168	184	180	<b>197</b>	<b>29</b>	<b>0.28</b>	<b>0.12</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.05</b>	152	160	180	205	200	198		<b>183</b>	<b>22</b>	<b>0.33</b>	<b>0.09</b>	<b>Yes</b>
	<b>0.1</b>	64	66	95	56	96	162	80	<b>88</b>	<b>36</b>	<b>0.68</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.25</b>	48	0	15	80	30	50	52	<b>39</b>	<b>27</b>	<b>0.86</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.5</b>	6	0	11	0	0	0	7	<b>3</b>	<b>5</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *hmr-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.01, 1, and 2), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Figure S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.



TABLE S17

Dilution series results for *unc-73* feeding

Strain	OD <sub>600</sub>	Penetrance readings							Avg	SD	Eri?
<i>Wildtype</i>	<b>0.1</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>	
<i>(N2)</i>	<b>0.5</b>	0/20	0/20	0/20	0/20	0/20	1/30	0/20	1/40	<b>0.01</b>	<b>0.01</b>
	<b>0.75</b>	0/20	0/20	0/20	0/20	0/20	0/20	0/20	0/20	<b>0</b>	<b>0</b>
	<b>2</b>	0/20	0/20	0/20	2/50	0/30	0/20	2/80	<b>0.01</b>	<b>0.02</b>	
	<b>3</b>	0/20	0/20	0/20	6/90	3/80	0/20	0/20	<b>0.01</b>	<b>0.03</b>	
<i>eri-1</i>	<b>0.1</b>	0/20	0/20	0/20	0/26	0/35	0/20	0/20	<b>0</b>	<b>0</b>	
<i>(mg366)</i>	<b>0.5</b>	5/50	8/67	13/61	17/47	6/27	14/32	12/33	<b>0.26</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.75</b>	12/40	14/50	9/47	13/35	20/57	27/48	26/54	<b>0.36</b>	<b>0.13</b>	<b>Yes</b>
	<b>2</b>	21/23	74/78	22/38	21/31	73/84	30/53		<b>0.76</b>	<b>0.17</b>	<b>Yes</b>
	<b>3</b>	20/20	103/112	20/20	28/30	20/20	42/47		<b>0.96</b>	<b>0.05</b>	<b>Yes</b>
<i>rf-3</i>	<b>0.1</b>	0/20	0/20	0/20	1/29	2/60	0/20	0/20	<b>0.01</b>	<b>0.02</b>	
<i>(pk1426)</i>	<b>0.5</b>	1/60	4/50	3/70	4/15	13/67	6/48		<b>0.12</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.75</b>	3/6	10/42	10/31	13/37	38/61	44/61	21/48	<b>0.46</b>	<b>0.17</b>	<b>Yes</b>
	<b>2</b>	18/39	19/77	22/58	46/54	43/55	81/91	88/97	<b>0.65</b>	<b>0.27</b>	<b>Yes</b>
	<b>3</b>	18/64	18/47	25/54	27/30	88/90	58/68		<b>0.64</b>	<b>0.30</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.1</b>	0/20	0/20	0/12	0/20	1/30	0/20	0/20	<b>0</b>	<b>0.01</b>	
<i>(tm1361)</i>	<b>0.5</b>	2/50	3/60	5/50	1/15	2/23	12/56	15/40	<b>0.13</b>	<b>0.12</b>	<b>Yes</b>
	<b>0.75</b>	18/52	16/48	13/32	13/35	11/22	26/36	13/30	<b>0.44</b>	<b>0.13</b>	<b>Yes</b>
	<b>2</b>	11/44	22/46	16/65	19/46	6/10	32/36	80/82	<b>0.55</b>	<b>0.29</b>	<b>Yes</b>
	<b>3</b>	29/46	25/44	26/48	53/60	18/20	22/24	43/44	<b>0.77</b>	<b>0.19</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.1</b>	0/20	0/20	2/30	0/20	0/20	0/20	1/108	<b>0.01</b>	<b>0.02</b>	
<i>(tm1705)</i>	<b>0.5</b>	0/20	0/20	0/20	0/20	0/20	0/20		<b>0</b>	<b>0</b>	
	<b>0.75</b>	1/40	0/20	0/20	0/20	1/30	12/120	4/120	<b>0.03</b>	<b>0.04</b>	
	<b>2</b>	0/20	0/20	1/20	1/30	0/20	2/89	0/20	<b>0.02</b>	<b>0.02</b>	
	<b>3</b>	1/20	2/30	4/50	2/60	1/30	5/103	0/20	<b>0.04</b>	<b>0.03</b>	
<i>eri-6/7</i>	<b>0.1</b>	0/20	0/20	0/20	0/67	1/53	1/90	0/20	<b>0</b>	<b>0.01</b>	
<i>(tm1917)</i>	<b>0.5</b>	3/40	7/50	2/60	4/57	6/78	1/32	8/69	<b>0.08</b>	<b>0.04</b>	<b>Yes</b>
	<b>0.75</b>	6/22	17/77	17/69	26/39	10/17	11/90	17/83	<b>0.33</b>	<b>0.21</b>	<b>Yes</b>
	<b>2</b>	34/43	47/50	44/50	23/40	38/66	34/40	14/60	<b>0.69</b>	<b>0.25</b>	<b>Yes</b>
	<b>3</b>	46/50	47/50	20/20	20/20	20/20	30/33	50/53	<b>0.96</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.1</b>	0/20	0/20	2/50	2/50	3/60	0/23	0/29	<b>0.02</b>	<b>0.02</b>	

<i>(gg100)</i>	<b>0.5</b>	8/90	8/60	4/70	14/73	28/78	34/82	17/68	<b>0.21</b>	<b>0.14</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.75</b>	56/73	86/101	46/53	41/51	29/45	32/57	30/65	<b>0.71</b>	<b>0.16</b>	<b>Yes</b>
	<b>2**</b>	20/20	20/20	20/20	19/24	20/20	117/122	81/81	<b>0.96</b>	<b>0.08</b>	<b>Yes</b>
	<b>3**</b>	20/20	20/20	20/20	20/20	20/20	124/133	20/20	<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.1</b>	1/50	0/20	0/20	4/71	5/57	1/130	0/20	<b>0.02</b>	<b>0.03</b>	
<i>(gg106)</i>	<b>0.5</b>	3/100	8/100	2/80	9/54	24/83	13/51		<b>0.14</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.75</b>	9/60	8/69	25/78	11/62	6/48	34/64	15/47	<b>0.25</b>	<b>0.15</b>	<b>Yes</b>
	<b>2</b>	40/48	43/65	35/46	29/94	19/71	52/57	31/72	<b>0.60</b>	<b>0.26</b>	<b>Yes</b>
	<b>3</b>	48/50	83/90	89/90	67/88	107/115	41/49		<b>0.90</b>	<b>0.09</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.1</b>	0/20	1/40	0/20	0/20	1/30	0/20	2/80	<b>0.01</b>	<b>0.02</b>	
<i>(gg99)</i>	<b>0.5</b>	11/122	6/72	10/87	7/50	4/72	6/44	21/53	<b>0.15</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.75</b>	24/55	7/64	21/73	36/79	21/66	27/84	29/86	<b>0.32</b>	<b>0.11</b>	<b>Yes</b>
	<b>2</b>	32/79	20/71	22/67	11/59	53/72	12/35	35/66	<b>0.40</b>	<b>0.18</b>	<b>Yes</b>
	<b>3</b>	51/83	112/118	20/20	20/20	56/66	91/107	61/67	<b>0.88</b>	<b>0.13</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *unc-73*; 4 days later, the percent of progeny showing the expected paralysis at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.03, 0.25, and 1), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri<sup>?</sup>), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S18

Dilution series results for *div-1* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.5</b>	95	104	128	105	128	160	146	<b>124</b>	<b>24</b>	<b>0.45</b>	<b>0.12</b>	
(N2)	<b>1</b>	86	57	69	72	33	37	56	<b>59</b>	<b>19</b>	<b>0.74</b>	<b>0.09</b>	
	<b>2</b>	88	53	50	47	79	33	37	<b>55</b>	<b>21</b>	<b>0.76</b>	<b>0.09</b>	
	<b>3</b>	59	62	49	54	84	33	50	<b>56</b>	<b>16</b>	<b>0.75</b>	<b>0.07</b>	
	<b>4</b>	63	50	58	83	50	34	32	<b>53</b>	<b>18</b>	<b>0.77</b>	<b>0.08</b>	
<i>eri-1</i>	<b>0.5</b>	98	100	64	120	66	99	80	<b>90</b>	<b>20</b>	<b>0.43</b>	<b>0.13</b>	
(mg366)	<b>1</b>	60	96	78	68	36	48	46	<b>62</b>	<b>21</b>	<b>0.61</b>	<b>0.13</b>	
	<b>2</b>	29	63	59	10	55	31	40	<b>41</b>	<b>19</b>	<b>0.74</b>	<b>0.12</b>	
	<b>3</b>	50	50	56	44	23	35	59	<b>45</b>	<b>13</b>	<b>0.71</b>	<b>0.08</b>	
	<b>4</b>	51	74	19	64	39	10	47	<b>43</b>	<b>23</b>	<b>0.73</b>	<b>0.15</b>	
<i>rff-3</i>	<b>0.5</b>	64	96	63	84	102	57	54	<b>74</b>	<b>19</b>	<b>0.44</b>	<b>0.15</b>	
(pk1426)	<b>1</b>	36	65	75	35	34	41	26	<b>45</b>	<b>18</b>	<b>0.67</b>	<b>0.14</b>	
	<b>2</b>	36	42	66	27	25	10	11	<b>31</b>	<b>19</b>	<b>0.77</b>	<b>0.15</b>	
	<b>3</b>	26	23	1	25	10	27	15	<b>18</b>	<b>10</b>	<b>0.86</b>	<b>0.07</b>	<b>Yes</b>
	<b>4</b>	20	24	17	17	19	43	15	<b>22</b>	<b>10</b>	<b>0.83</b>	<b>0.07</b>	
<i>eri-3</i>	<b>0.5</b>	47	54	79	55	51	55	37	<b>54</b>	<b>13</b>	<b>0.65</b>	<b>0.09</b>	
(tm1361)	<b>1</b>	94	34	47	25	45	27	50	<b>46</b>	<b>23</b>	<b>0.70</b>	<b>0.15</b>	
<b>*Best*</b>	<b>2**</b>	18	36	13	10	14	19		<b>18</b>	<b>9</b>	<b>0.88</b>	<b>0.06</b>	<b>Yes</b>
	<b>3**</b>	10	24	32	18	15	17	8	<b>18</b>	<b>8</b>	<b>0.89</b>	<b>0.05</b>	<b>Yes</b>
	<b>4**</b>	8	16	9	10	15	32	12	<b>15</b>	<b>8</b>	<b>0.91</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.5</b>	46	72	88	104	112	120	81	<b>89</b>	<b>26</b>	<b>0.48</b>	<b>0.16</b>	
(tm1705)	<b>1</b>	32	28	40	7	48	39	13	<b>30</b>	<b>15</b>	<b>0.83</b>	<b>0.09</b>	
	<b>2</b>	23	25	26	22	18	23	18	<b>22</b>	<b>3</b>	<b>0.87</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	18	20	18	23	9	21	16	<b>18</b>	<b>5</b>	<b>0.90</b>	<b>0.03</b>	<b>Yes</b>
	<b>4</b>	30	25	20	9	22	25	19	<b>21</b>	<b>7</b>	<b>0.87</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-6/7</i>	<b>0.5</b>	106	108	90	88	72	84	105	<b>93</b>	<b>13</b>	<b>0.40</b>	<b>0.10</b>	
(tm1917)	<b>1</b>	38	34	31	36	44	37	61	<b>40</b>	<b>10</b>	<b>0.74</b>	<b>0.07</b>	
	<b>2</b>	52	38	26	29	34	2	30	<b>30</b>	<b>15</b>	<b>0.81</b>	<b>0.10</b>	
	<b>3</b>	44	14	23	51	31	27	48	<b>34</b>	<b>14</b>	<b>0.78</b>	<b>0.09</b>	
	<b>4</b>	19	25	29	28	16	6	33	<b>22</b>	<b>9</b>	<b>0.86</b>	<b>0.06</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.5</b>	104	108	135	162	166	180	168	<b>146</b>	<b>31</b>	<b>0.34</b>	<b>0.14</b>	

<i>(gg100)</i>	<b>1</b>	192	86	102	60	78	76		<b>99</b>	<b>48</b>	<b>0.56</b>	<b>0.21</b>	
	<b>2</b>	128	108	90	36	32	56	33	<b>69</b>	<b>40</b>	<b>0.69</b>	<b>0.18</b>	
	<b>3</b>	29	70	106	39	44	36	39	<b>52</b>	<b>27</b>	<b>0.77</b>	<b>0.12</b>	
	<b>4</b>	74	78	25	30	27	19		<b>42</b>	<b>26</b>	<b>0.81</b>	<b>0.12</b>	
<i>eri-9</i>	<b>0.5</b>	114	148	120	76	122	88	98	<b>109</b>	<b>24</b>	<b>0.54</b>	<b>0.10</b>	
<i>(gg106)</i>	<b>1</b>	72	130	112	30	24	18	24	<b>59</b>	<b>47</b>	<b>0.76</b>	<b>0.19</b>	
	<b>2</b>	72	42	114	31	26	29	22	<b>48</b>	<b>34</b>	<b>0.80</b>	<b>0.14</b>	
	<b>3</b>	75	88	65	30	35	20	21	<b>48</b>	<b>28</b>	<b>0.80</b>	<b>0.12</b>	
	<b>4</b>	25	43	33	29	23	24	20	<b>28</b>	<b>8</b>	<b>0.88</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.5</b>	112	232	160	136	162	200	176	<b>168</b>	<b>40</b>	<b>0.39</b>	<b>0.15</b>	
<i>(gg99)</i>	<b>1</b>	98	102	118	37	72	96	82	<b>86</b>	<b>26</b>	<b>0.68</b>	<b>0.10</b>	
	<b>2</b>	104	44	90	33	45	28	34	<b>54</b>	<b>30</b>	<b>0.80</b>	<b>0.11</b>	
	<b>3</b>	44	98	96	40	35	34	35	<b>55</b>	<b>29</b>	<b>0.80</b>	<b>0.11</b>	
	<b>4</b>	31	42	34	25	37	37		<b>34</b>	<b>6</b>	<b>0.87</b>	<b>0.02</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *div-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri<sup>?</sup>), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S19

Dilution series results for *pbs-6* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.02</b>	205	227	224	244	207	240	207	<b>222</b>	<b>16</b>	<b>0.02</b>	<b>0.11</b>	
(N2)	<b>0.05</b>	244	256	216	134	264	200	160	<b>211</b>	<b>49</b>	<b>0.07</b>	<b>0.23</b>	
	<b>0.1</b>	172	190	84	53	210	41	93	<b>120</b>	<b>69</b>	<b>0.47</b>	<b>0.31</b>	
	<b>0.25</b>	62	50	39	20	21	60		<b>42</b>	<b>19</b>	<b>0.81</b>	<b>0.08</b>	
	<b>0.5</b>	32	12	15	13	23	20	22	<b>20</b>	<b>7</b>	<b>0.91</b>	<b>0.03</b>	
<i>eri-1</i>	<b>0.02</b>	107	137	120	72	80	80	80	<b>97</b>	<b>25</b>	<b>0.39</b>	<b>0.16</b>	<b>Yes</b>
( <i>mg366</i> )	<b>0.05</b>	134	88	84	64	44	60	75	<b>78</b>	<b>29</b>	<b>0.50</b>	<b>0.18</b>	<b>Yes</b>
	<b>0.1</b>	110	33	56	66	40	33	36	<b>53</b>	<b>28</b>	<b>0.66</b>	<b>0.18</b>	
	<b>0.25</b>	20	48	6	9	4	3	11	<b>14</b>	<b>16</b>	<b>0.91</b>	<b>0.10</b>	
	<b>0.5</b>	4	1	2	11	4	4	0	<b>4</b>	<b>4</b>	<b>0.98</b>	<b>0.02</b>	<b>Yes</b>
<i>rif-3</i>	<b>0.02</b>	122	152	120	128	120	138	112	<b>127</b>	<b>14</b>	<b>0.04</b>	<b>0.12</b>	
( <i>pk1426</i> )	<b>0.05</b>	144	135	96	104	126	84	78	<b>110</b>	<b>26</b>	<b>0.18</b>	<b>0.20</b>	
	<b>0.1</b>	51	85	38	25	96	43	84	<b>60</b>	<b>28</b>	<b>0.55</b>	<b>0.21</b>	
	<b>0.25</b>	0	2	2	7	9	87	23	<b>19</b>	<b>31</b>	<b>0.86</b>	<b>0.23</b>	
	<b>0.5</b>	0	1	1	0	0	0	3	<b>1</b>	<b>1</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.02</b>	152	176	42	144	104	156	75	<b>121</b>	<b>49</b>	<b>0.22</b>	<b>0.32</b>	
( <i>tm1361</i> )	<b>0.05</b>	156	99	32	45	19	84	31	<b>67</b>	<b>49</b>	<b>0.57</b>	<b>0.32</b>	<b>Yes</b>
<u>*Best*</u>	<b>0.1</b>	41	25	72	22	56	80	72	<b>53</b>	<b>24</b>	<b>0.66</b>	<b>0.15</b>	
	<b>0.25**</b>	16	4	2	3	7	8	2	<b>6</b>	<b>5</b>	<b>0.96</b>	<b>0.03</b>	<b>Yes</b>
	<b>0.5**</b>	2	11	0	0	1	0	3	<b>2</b>	<b>4</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.02</b>	170	162	160	152	90	112	95	<b>134</b>	<b>34</b>	<b>0.21</b>	<b>0.22</b>	
( <i>tm1705</i> )	<b>0.05</b>	165	144	66	48	62	49	49	<b>83</b>	<b>50</b>	<b>0.51</b>	<b>0.29</b>	<b>Yes</b>
	<b>0.1</b>	56	133	71	42	30	21	33	<b>55</b>	<b>38</b>	<b>0.68</b>	<b>0.23</b>	
	<b>0.25</b>	16	18	6	20	13	23	13	<b>16</b>	<b>6</b>	<b>0.91</b>	<b>0.03</b>	<b>Yes</b>
	<b>0.5</b>	2	3	4	2	5	2	2	<b>3</b>	<b>1</b>	<b>0.98</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-6/7</i>	<b>0.02</b>	176	192	168	184	232	190	112	<b>179</b>	<b>36</b>	<b>0</b>	<b>0.25</b>	
( <i>tm1917</i> )	<b>0.05</b>	150	162	96	96	100	104	126	<b>119</b>	<b>27</b>	<b>0.23</b>	<b>0.19</b>	
<u>*Best*</u>	<b>0.1</b>	40	35	23	112	66	40		<b>53</b>	<b>32</b>	<b>0.66</b>	<b>0.21</b>	
	<b>0.25**</b>	24	11	3	9	2	3	6	<b>8</b>	<b>8</b>	<b>0.95</b>	<b>0.05</b>	<b>Yes</b>
	<b>0.5**</b>	0	0	2	3	4	3	1	<b>2</b>	<b>2</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.02</b>	234	232	266	248	240	224	232	<b>239</b>	<b>14</b>	<b>0</b>	<b>0.07</b>	

<i>(gg100)</i>	<b>0.05</b>	280	272	144	192	152	193		<b>206</b>	<b>58</b>	<b>0.08</b>	<b>0.26</b>	
	<b>0.1</b>	105	28	77	75	45	120		<b>75</b>	<b>35</b>	<b>0.66</b>	<b>0.16</b>	
	<b>0.25</b>	18	19	11	56	22	19	16	<b>23</b>	<b>15</b>	<b>0.90</b>	<b>0.07</b>	
	<b>0.5</b>	2	3	13	0	3	7	3	<b>4</b>	<b>4</b>	<b>0.98</b>	<b>0.02</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.02</b>	216	192	250	210	192	208	222	<b>213</b>	<b>20</b>	<b>0.11</b>	<b>0.10</b>	
<i>(gg106)</i>	<b>0.05</b>	217	227	190	160	192	184	170	<b>191</b>	<b>24</b>	<b>0.20</b>	<b>0.11</b>	
	<b>0.1</b>	124	66	160	167	126	112	44	<b>114</b>	<b>45</b>	<b>0.52</b>	<b>0.19</b>	
	<b>0.25</b>	26	69	14	16	27	32	16	<b>29</b>	<b>19</b>	<b>0.88</b>	<b>0.08</b>	
	<b>0.5</b>	2	0	2	8	9	13	22	<b>8</b>	<b>8</b>	<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.02</b>	161	227	116	146	136	168	135	<b>156</b>	<b>36</b>	<b>0.43</b>	<b>0.14</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.05</b>	192	224	126	88	112	128		<b>145</b>	<b>52</b>	<b>0.47</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.1</b>	26	158	136	128	128	67	33	<b>97</b>	<b>54</b>	<b>0.65</b>	<b>0.20</b>	
	<b>0.25</b>	51	66	26	24	8	37		<b>35</b>	<b>21</b>	<b>0.87</b>	<b>0.08</b>	
	<b>0.5</b>	0	3	12	7	7	8	8	<b>6</b>	<b>4</b>	<b>0.98</b>	<b>0.01</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *pbs-6*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.005, 0.01, and 1), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table Figure 27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S20

Dilution series results for *pha-4* feeding

Strain	OD <sub>600</sub>	Brood Size						Avg	SD	N.Avg	SEM	Eri?	
<i>Wildtype</i>	<b>0.01</b>	208	199	210	233	240	264	260	<b>231</b>	<b>26</b>	<b>0</b>	<b>0.15</b>	
<i>(N2)</i>	<b>0.02</b>	210	272	280	256	252	244		<b>252</b>	<b>25</b>	<b>0</b>	<b>0.15</b>	
	<b>0.04</b>	176	189	240	255	224	234	200	<b>217</b>	<b>29</b>	<b>0.04</b>	<b>0.16</b>	
	<b>0.1</b>	149	160	176	168	152	140		<b>158</b>	<b>13</b>	<b>0.30</b>	<b>0.09</b>	
	<b>0.25</b>	147	158	164	168	136	174		<b>158</b>	<b>14</b>	<b>0.30</b>	<b>0.09</b>	
<i>eri-1</i>	<b>0.01</b>	98	133	160	128	152	130	176	<b>140</b>	<b>25</b>	<b>0.12</b>	<b>0.17</b>	
<i>(mg366)</i>	<b>0.02</b>	70	85	61	100	73	130	47	<b>81</b>	<b>27</b>	<b>0.49</b>	<b>0.18</b>	<b>Yes</b>
	<b>0.04</b>	11	0	57	46	73	94	108	<b>56</b>	<b>40</b>	<b>0.65</b>	<b>0.25</b>	<b>Yes</b>
	<b>0.1</b>	0	45	28	71	61	62		<b>45</b>	<b>27</b>	<b>0.72</b>	<b>0.17</b>	<b>Yes</b>
	<b>0.25</b>	31	15	47	12	17	13		<b>23</b>	<b>14</b>	<b>0.86</b>	<b>0.09</b>	<b>Yes</b>
<i>rnf-3</i>	<b>0.01</b>	114	101	120	112	104	106		<b>110</b>	<b>7</b>	<b>0.18</b>	<b>0.08</b>	<b>Yes</b>
<i>(pk1426)</i>	<b>0.02</b>	76	81	47	92	64	90		<b>75</b>	<b>17</b>	<b>0.44</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.04</b>	6	54	49	61	43	10		<b>37</b>	<b>23</b>	<b>0.72</b>	<b>0.18</b>	<b>Yes</b>
	<b>0.1</b>	1	0	7	19	34	44	57	<b>23</b>	<b>22</b>	<b>0.83</b>	<b>0.17</b>	<b>Yes</b>
	<b>0.25</b>	6	1	0	0	16	9	0	<b>5</b>	<b>6</b>	<b>0.97</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.01</b>	162	142	115	54	45	42	82	<b>92</b>	<b>49</b>	<b>0.41</b>	<b>0.32</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.02</b>	46	87	72	74	54	75	29	<b>62</b>	<b>20</b>	<b>0.60</b>	<b>0.13</b>	<b>Yes</b>
<b>*Best*</b>	<b>0.04</b>	60	79	15	23	7	4	53	<b>34</b>	<b>29</b>	<b>0.78</b>	<b>0.19</b>	<b>Yes</b>
	<b>0.1**</b>	28	25	23	14	3	16	33	<b>20</b>	<b>10</b>	<b>0.87</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.25**</b>	10	15	3	5	17	3	3	<b>8</b>	<b>6</b>	<b>0.95</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.01</b>	194	192	170	178	190	176	184	<b>183</b>	<b>9</b>	<b>0</b>	<b>0.12</b>	
<i>(tm1705)</i>	<b>0.02</b>	192	182	160	200	170	160	167	<b>176</b>	<b>16</b>	<b>0</b>	<b>0.14</b>	
	<b>0.04</b>	168	144	184	168	152	168		<b>164</b>	<b>14</b>	<b>0.04</b>	<b>0.13</b>	
	<b>0.1</b>	100	86	100	133	132	93	65	<b>101</b>	<b>24</b>	<b>0.41</b>	<b>0.16</b>	
	<b>0.25</b>	55	62	35	57	33	50	20	<b>45</b>	<b>15</b>	<b>0.74</b>	<b>0.09</b>	<b>Yes</b>
<i>eri-6/7</i>	<b>0.01</b>	216	240	169	200	205	163	162	<b>194</b>	<b>30</b>	<b>0</b>	<b>0.22</b>	
<i>(tm1917)</i>	<b>0.02</b>	217	266	156	132	172	182		<b>188</b>	<b>48</b>	<b>0</b>	<b>0.32</b>	
	<b>0.04</b>	179	126	73	62	112	114	88	<b>108</b>	<b>39</b>	<b>0.31</b>	<b>0.26</b>	<b>Yes</b>
	<b>0.1</b>	52	74	41	63	56	63	41	<b>56</b>	<b>12</b>	<b>0.64</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.25</b>	60	0	28	30	64	54	47	<b>40</b>	<b>23</b>	<b>0.74</b>	<b>0.15</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.01</b>	236	248	232	224	216	235		<b>232</b>	<b>11</b>	<b>0</b>	<b>0.06</b>	

<i>(gg100)</i>	<b>0.02</b>	86	164	144	176	176	154	160	<b>151</b>	<b>31</b>	<b>0.32</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.04</b>	61	82	64	84	92	63	100	<b>78</b>	<b>16</b>	<b>0.65</b>	<b>0.07</b>	<b>Yes</b>
	<b>0.1</b>	7	3	28	4	3	47	30	<b>17</b>	<b>18</b>	<b>0.92</b>	<b>0.08</b>	<b>Yes</b>
	<b>0.25</b>	25	10	52	55	63	32	9	<b>35</b>	<b>22</b>	<b>0.84</b>	<b>0.10</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.01</b>	244	246	272	240	256	256		<b>252</b>	<b>12</b>	<b>0</b>	<b>0.08</b>	
<i>(gg106)</i>	<b>0.02</b>	216	176	216	240	280	278		<b>234</b>	<b>40</b>	<b>0.02</b>	<b>0.18</b>	
	<b>0.04</b>	164	171	208	248	224	170	220	<b>201</b>	<b>33</b>	<b>0.16</b>	<b>0.14</b>	
	<b>0.1</b>	36	57	114	92	90	123		<b>85</b>	<b>33</b>	<b>0.64</b>	<b>0.14</b>	<b>Yes</b>
	<b>0.25</b>	89	107	87	106	74	146		<b>102</b>	<b>25</b>	<b>0.58</b>	<b>0.11</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.01</b>	292	260	320	264	274	312		<b>287</b>	<b>25</b>	<b>0</b>	<b>0.11</b>	
<i>(gg99)</i>	<b>0.02</b>	264	254	240	248	341	324	304	<b>282</b>	<b>40</b>	<b>0</b>	<b>0.16</b>	
	<b>0.04</b>	153	116	216	216	200	209	226	<b>191</b>	<b>41</b>	<b>0.30</b>	<b>0.16</b>	<b>Yes</b>
	<b>0.1</b>	85	81	228	200	240	256	176	<b>181</b>	<b>72</b>	<b>0.34</b>	<b>0.27</b>	
	<b>0.25</b>	65	72	80	93	96	112		<b>86</b>	<b>17</b>	<b>0.68</b>	<b>0.07</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *pha-4*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.05 and 0.5), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.



TABLE S21

Dilution series results for *cdk-1* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.1</b>	248	284	222	192	248	248		<b>240</b>	<b>31</b>	<b>0</b>	<b>0.17</b>	
<i>(N2)</i>	<b>0.5</b>	194	244	224	239	157			<b>212</b>	<b>36</b>	<b>0.07</b>	<b>0.18</b>	
	<b>1</b>	124	4	9	17	0			<b>31</b>	<b>52</b>	<b>0.86</b>	<b>0.23</b>	
	<b>2</b>	87	137	4	6	3	51	3	<b>42</b>	<b>53</b>	<b>0.82</b>	<b>0.23</b>	
	<b>3</b>	0	11	0	6	2	2	3	<b>3</b>	<b>4</b>	<b>0.98</b>	<b>0.02</b>	
<i>eri-1</i>	<b>0.1</b>	13	127	192	120	123	84	148	<b>115</b>	<b>56</b>	<b>0.27</b>	<b>0.35</b>	
<i>(mg366)</i>	<b>0.5</b>	77	75	65	36	47			<b>60</b>	<b>18</b>	<b>0.62</b>	<b>0.12</b>	<b>Yes</b>
	<b>1</b>	22	0	2	0	1	0		<b>4</b>	<b>9</b>	<b>0.97</b>	<b>0.06</b>	
	<b>2</b>	2	40	0	0	0	0	0	<b>6</b>	<b>15</b>	<b>0.96</b>	<b>0.09</b>	
	<b>3</b>	1	0	0	1	0	1	0	<b>0</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	
<i>rf-3</i>	<b>0.1</b>	50	76	123	156	160	192	160	<b>131</b>	<b>51</b>	<b>0.02</b>	<b>0.39</b>	
<i>(pk1426)</i>	<b>0.5**</b>	2	0	3	0	0	0	0	<b>1</b>	<b>1</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
<u>*Best*</u>	<b>1**</b>	1	0	0	0	0	0		<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
	<b>2**</b>	0	0	0	0	0	0	1	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
	<b>3**</b>	0	0	0	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-3</i>	<b>0.1</b>	134	6	126	108	104	120	120	<b>103</b>	<b>44</b>	<b>0.34</b>	<b>0.29</b>	
<i>(tm1361)</i>	<b>0.5</b>	67	5	0	0	11	38		<b>20</b>	<b>27</b>	<b>0.87</b>	<b>0.17</b>	<b>Yes</b>
	<b>1</b>	26	65	0	1	0	14	34	<b>20</b>	<b>24</b>	<b>0.87</b>	<b>0.15</b>	
	<b>2</b>	0	0	1	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
	<b>3</b>	9	1	0	0	0	0	0	<b>1</b>	<b>3</b>	<b>0.99</b>	<b>0.02</b>	
<i>eri-5</i>	<b>0.1</b>	189	210	174	186	140	148	195	<b>177</b>	<b>25</b>	<b>0</b>	<b>0.18</b>	
<i>(tm1705)</i>	<b>0.5</b>	106	126	58	8	99			<b>79</b>	<b>47</b>	<b>0.53</b>	<b>0.28</b>	<b>Yes</b>
	<b>1</b>	58	72	0	0	0	0	0	<b>19</b>	<b>32</b>	<b>0.89</b>	<b>0.19</b>	
	<b>2</b>	81	5	0	0	0	0	0	<b>12</b>	<b>30</b>	<b>0.93</b>	<b>0.18</b>	
	<b>3</b>	0	1	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-6/7</i>	<b>0.1</b>	99	220	182	216	176	240	168	<b>186</b>	<b>47</b>	<b>0</b>	<b>0.31</b>	
<i>(tm1917)</i>	<b>0.5</b>	51	9	4	3	11			<b>16</b>	<b>20</b>	<b>0.90</b>	<b>0.13</b>	<b>Yes</b>
	<b>1</b>	33	0	0	0	0	0		<b>6</b>	<b>13</b>	<b>0.96</b>	<b>0.09</b>	
	<b>2</b>	4	1	0	1	0	0	0	<b>1</b>	<b>1</b>	<b>0.99</b>	<b>0.01</b>	
	<b>3</b>	0	2	0	1	0	0	0	<b>0</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	
<i>eri-8</i>	<b>0.1</b>	262	276	194	248	240	240	272	<b>247</b>	<b>28</b>	<b>0</b>	<b>0.13</b>	

<i>(gg100)</i>	<b>0.5</b>	24	93	1	0	6			<b>25</b>	<b>39</b>	<b>0.89</b>	<b>0.18</b>	<b>Yes</b>
	<b>1</b>	8	19	0	0	0	44	17	<b>13</b>	<b>16</b>	<b>0.94</b>	<b>0.07</b>	
	<b>2</b>	0	2	0	0	0	0	0	<b>0</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	
	<b>3</b>	1	0	0	0	0	2	1	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0</b>	
<i>eri-9</i>	<b>0.1</b>	282	270	224	184	214	240	248	<b>237</b>	<b>34</b>	<b>0.01</b>	<b>0.15</b>	<b>Yes</b>
<i>(gg106)</i>	<b>0.5</b>	20	0	4	9	3	0		<b>6</b>	<b>8</b>	<b>0.97</b>	<b>0.03</b>	
<b>1</b>	124	0	0	0	2	2			<b>21</b>	<b>50</b>	<b>0.91</b>	<b>0.21</b>	
<b>2</b>	3	127	0	0	3	1	1		<b>19</b>	<b>48</b>	<b>0.92</b>	<b>0.20</b>	
<b>3</b>	0	0	0	0	0	0	0	1	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-11</i>	<b>0.1</b>	272	298	264	216	272	224	260	<b>258</b>	<b>29</b>	<b>0.06</b>	<b>0.12</b>	<b>Yes</b>
<i>(gg99)</i>	<b>0.5</b>	181	282	64	78	38	104	192	<b>134</b>	<b>87</b>	<b>0.51</b>	<b>0.32</b>	
<b>1</b>	47	0	0	2	5	4	3		<b>9</b>	<b>17</b>	<b>0.97</b>	<b>0.06</b>	
<b>2</b>	32	2	3	0	0	0	0		<b>5</b>	<b>12</b>	<b>0.98</b>	<b>0.04</b>	
<b>3</b>	0	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	

Single L3-stage larvae were placed on RNAi food targeting *cdk-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 0.025, 0.25, and 0.75), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S22

Dilution series results for *knl-3* feeding

Strain	<i>OD</i> <sub>600</sub>	Brood Size						<i>Avg</i>	<i>SD</i>	<i>N.Avg</i>	<i>SEM</i>	<i>Eri?</i>	
<i>Wildtype</i>	<b>0.1</b>	256	242	184	210	180	232	200	<b>215</b>	<b>29</b>	<b>0.05</b>	<b>0.16</b>	
<i>(N2)</i>	<b>0.25</b>	264	240	237	216	260	235	224	<b>239</b>	<b>18</b>	<b>0</b>	<b>0.12</b>	
	<b>0.5</b>	240	192	148	168	208	191		<b>191</b>	<b>32</b>	<b>0.16</b>	<b>0.16</b>	
	<b>0.75</b>	212	200	176	162	180	169	203	<b>186</b>	<b>19</b>	<b>0.18</b>	<b>0.11</b>	
	<b>1</b>	99	63	84	47	77			<b>74</b>	<b>20</b>	<b>0.67</b>	<b>0.09</b>	
<i>eri-1</i>	<b>0.1</b>	63	40	168	155	162	151		<b>123</b>	<b>56</b>	<b>0.22</b>	<b>0.36</b>	
<i>(mg366)</i>	<b>0.25</b>	100	152	96	120	120	184	156	<b>133</b>	<b>32</b>	<b>0.16</b>	<b>0.21</b>	
	<b>0.5</b>	50	1	55	111	81	114	77	<b>70</b>	<b>39</b>	<b>0.56</b>	<b>0.25</b>	Yes
	<b>0.75</b>	81	74	50	54	75	56	49	<b>63</b>	<b>13</b>	<b>0.60</b>	<b>0.09</b>	Yes
	<b>1</b>	1	0	0	0	0	66	13	<b>11</b>	<b>25</b>	<b>0.93</b>	<b>0.15</b>	Yes
<i>rf-3</i>	<b>0.1</b>	108	62	97	97	113	91	115	<b>98</b>	<b>18</b>	<b>0.27</b>	<b>0.14</b>	Yes
<i>(pk1426)</i>	<b>0.25</b>	68	130	110	89	78	105	100	<b>97</b>	<b>21</b>	<b>0.27</b>	<b>0.16</b>	Yes
<b>*Best*</b>	<b>0.5</b>	96	62	108	58	96	72	81	<b>82</b>	<b>19</b>	<b>0.39</b>	<b>0.15</b>	Yes
	<b>0.75</b>	69	64	102	93	80	109	89	<b>87</b>	<b>17</b>	<b>0.35</b>	<b>0.13</b>	Yes
	<b>1**</b>	0	0	15	0	10	5	1	<b>4</b>	<b>6</b>	<b>0.97</b>	<b>0.04</b>	Yes
<i>eri-3</i>	<b>0.1</b>	99	91	210	200	195	208	220	<b>175</b>	<b>55</b>	<b>0</b>	<b>0.37</b>	
<i>(tm1361)</i>	<b>0.25</b>	85	184	89	189	78	170		<b>133</b>	<b>54</b>	<b>0.15</b>	<b>0.35</b>	
	<b>0.5</b>	62	83	185	168	76	82		<b>109</b>	<b>53</b>	<b>0.30</b>	<b>0.35</b>	
	<b>0.75</b>	128	123	126	101	96	113	103	<b>113</b>	<b>13</b>	<b>0.28</b>	<b>0.11</b>	
	<b>1</b>	0	22	12	16	59	36	10	<b>22</b>	<b>20</b>	<b>0.86</b>	<b>0.13</b>	Yes
<i>eri-5</i>	<b>0.1</b>	224	184	243	216	236	200	168	<b>210</b>	<b>27</b>	<b>0</b>	<b>0.20</b>	
<i>(tm1705)</i>	<b>0.25</b>	240	244	198	232	200	168	180	<b>209</b>	<b>30</b>	<b>0</b>	<b>0.22</b>	
	<b>0.5</b>	82	109	132	144	157	187	136	<b>135</b>	<b>34</b>	<b>0.21</b>	<b>0.22</b>	
	<b>0.75</b>	114	121	113	132	128	104	117	<b>118</b>	<b>10</b>	<b>0.30</b>	<b>0.09</b>	Yes
	<b>1</b>	0	0	28	22	44	0	23	<b>17</b>	<b>17</b>	<b>0.90</b>	<b>0.10</b>	Yes
<i>eri-6/7</i>	<b>0.1</b>	133	151	170	210	216	214	203	<b>185</b>	<b>34</b>	<b>0</b>	<b>0.24</b>	
<i>(tm1917)</i>	<b>0.25</b>	180	188	216	198	232	232		<b>208</b>	<b>22</b>	<b>0</b>	<b>0.18</b>	
	<b>0.5</b>	105	86	160	155	168	222		<b>149</b>	<b>48</b>	<b>0.04</b>	<b>0.32</b>	
	<b>0.75</b>	133	164	168	144	160	184		<b>159</b>	<b>18</b>	<b>0</b>	<b>0.14</b>	
	<b>1</b>	0	31	1	8	20	0	40	<b>14</b>	<b>16</b>	<b>0.91</b>	<b>0.11</b>	Yes
<i>eri-8</i>	<b>0.1</b>	194	256	292	252	272	216	240	<b>246</b>	<b>33</b>	<b>0</b>	<b>0.15</b>	

<i>(gg100)</i>	<b>0.25</b>	215	220	210	210	214	243	241	<b>222</b>	<b>14</b>	<b>0</b>	<b>0.07</b>	
<b>*Best*</b>	<b>0.5</b>	176	186	200	186	200	202		<b>192</b>	<b>11</b>	<b>0.14</b>	<b>0.06</b>	
	<b>0.75</b>	131	157	142	131	152	140	156	<b>144</b>	<b>11</b>	<b>0.35</b>	<b>0.05</b>	<b>Yes</b>
	<b>1**</b>	0	0	0	13	11	9	7	<b>6</b>	<b>6</b>	<b>0.97</b>	<b>0.03</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.1</b>	234	240	280	272	288	244		<b>260</b>	<b>23</b>	<b>0</b>	<b>0.11</b>	
<i>(gg106)</i>	<b>0.25</b>	192	240	264	240	248	232	225	<b>234</b>	<b>22</b>	<b>0.02</b>	<b>0.11</b>	
	<b>0.5</b>	216	224	137	149	168	174	150	<b>174</b>	<b>34</b>	<b>0.27</b>	<b>0.15</b>	
	<b>0.75</b>	132	126	126	138	131	159	146	<b>137</b>	<b>12</b>	<b>0.43</b>	<b>0.06</b>	<b>Yes</b>
	<b>1</b>	10	5	40	38	19	12	78	<b>29</b>	<b>26</b>	<b>0.88</b>	<b>0.11</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.1</b>	292	280	272	320	258	288	304	<b>288</b>	<b>20</b>	<b>0</b>	<b>0.10</b>	
<i>(gg99)</i>	<b>0.25</b>	248	256	280	264	224	254	320	<b>264</b>	<b>30</b>	<b>0.04</b>	<b>0.13</b>	
<b>*Best*</b>	<b>0.5</b>	236	248	156	288	224	235	256	<b>235</b>	<b>40</b>	<b>0.14</b>	<b>0.16</b>	
	<b>0.75</b>	68	81	116	92	109	97	83	<b>92</b>	<b>17</b>	<b>0.66</b>	<b>0.06</b>	<b>Yes</b>
	<b>1**</b>	1	1	15	0	3	21	6	<b>7</b>	<b>8</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *knl-3*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, three bacterial culture concentrations (OD<sub>600nm</sub> of 2, 3, and 4), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S23

Dilution series results for *vha-15* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.03</b>	231	205	185	216	179	229	208	<b>208</b>	<b>20</b>	<b>0.08</b>	<b>0.12</b>	
<i>(N2)</i>	<b>0.25</b>	170	181	190	288	127	136	183	<b>182</b>	<b>53</b>	<b>0.20</b>	<b>0.24</b>	
	<b>1</b>	73	128	127	97	222	135	122	<b>129</b>	<b>46</b>	<b>0.43</b>	<b>0.21</b>	
	<b>2</b>	117	79	79	164	78	122		<b>107</b>	<b>35</b>	<b>0.53</b>	<b>0.16</b>	
	<b>3</b>	30	66	97	100	65	105		<b>77</b>	<b>29</b>	<b>0.66</b>	<b>0.13</b>	
<i>eri-1</i>	<b>0.03</b>	155	173	77	128	140	151	156	<b>140</b>	<b>31</b>	<b>0.12</b>	<b>0.20</b>	
<i>(mg366)</i>	<b>0.25</b>	45	69	77	41	83	97	68	<b>69</b>	<b>20</b>	<b>0.57</b>	<b>0.13</b>	<b>Yes</b>
	<b>1</b>	3	18	3	42	51	44	30	<b>27</b>	<b>20</b>	<b>0.83</b>	<b>0.12</b>	<b>Yes</b>
	<b>2</b>	0	6	0	40	7	10	12	<b>11</b>	<b>14</b>	<b>0.93</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	1	2	0	0	1	12	0	<b>2</b>	<b>4</b>	<b>0.99</b>	<b>0.03</b>	<b>Yes</b>
<i>rff-3</i>	<b>0.03</b>	144	59	196	148	195	97		<b>140</b>	<b>54</b>	<b>0</b>	<b>0.41</b>	
<i>(pk1426)</i>	<b>0.25</b>	29	3	77	57	34	33	0	<b>33</b>	<b>27</b>	<b>0.75</b>	<b>0.21</b>	<b>Yes</b>
<u>*Best*</u>	<b>1**</b>	0	1	0	24	1			<b>5</b>	<b>11</b>	<b>0.96</b>	<b>0.08</b>	<b>Yes</b>
	<b>2**</b>	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>3**</b>	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-3</i>	<b>0.03</b>	135	155	164	133	162	86	145	<b>140</b>	<b>27</b>	<b>0.10</b>	<b>0.19</b>	
<i>(tm1361)</i>	<b>0.25</b>	63	40	66	52	62	9	19	<b>44</b>	<b>23</b>	<b>0.71</b>	<b>0.15</b>	<b>Yes</b>
	<b>1</b>	0	18	1	0	1	0	46	<b>9</b>	<b>17</b>	<b>0.94</b>	<b>0.11</b>	<b>Yes</b>
	<b>2</b>	0	0	0	0	0	17	0	<b>2</b>	<b>6</b>	<b>0.98</b>	<b>0.04</b>	<b>Yes</b>
	<b>3</b>	0	0	0	0	0	1	1	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
<i>eri-5</i>	<b>0.03</b>	97	126	163	195	208	102	153	<b>149</b>	<b>43</b>	<b>0.12</b>	<b>0.27</b>	
<i>(tm1705)</i>	<b>0.25</b>	127	238	106	165	173	114	85	<b>144</b>	<b>52</b>	<b>0.15</b>	<b>0.32</b>	
	<b>1</b>	34	64	43	11	102	65		<b>53</b>	<b>31</b>	<b>0.69</b>	<b>0.19</b>	<b>Yes</b>
	<b>2</b>	5	7	204	26	34	23	45	<b>49</b>	<b>70</b>	<b>0.71</b>	<b>0.41</b>	
	<b>3</b>	24	19	12	67	113	34		<b>45</b>	<b>39</b>	<b>0.74</b>	<b>0.23</b>	
<i>eri-6/7</i>	<b>0.03</b>	219	143	148	226	127	161		<b>171</b>	<b>42</b>	<b>0</b>	<b>0.28</b>	
<i>(tm1917)</i>	<b>0.25</b>	127	78	51	113	128	78		<b>96</b>	<b>31</b>	<b>0.38</b>	<b>0.21</b>	
	<b>1</b>	0	22	51	9	60	16	5	<b>23</b>	<b>23</b>	<b>0.85</b>	<b>0.15</b>	<b>Yes</b>
	<b>2</b>	2	1	0	15	46	9	26	<b>14</b>	<b>17</b>	<b>0.91</b>	<b>0.11</b>	<b>Yes</b>
	<b>3</b>	1	0	1	1	0	1	15	<b>3</b>	<b>5</b>	<b>0.98</b>	<b>0.04</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.03</b>	180	256	209	242	251	273		<b>235</b>	<b>34</b>	<b>0</b>	<b>0.16</b>	

<i>(gg100)</i>	<b>0.25</b>	48	46	27	125	154	49	25	<b>68</b>	<b>51</b>	<b>0.70</b>	<b>0.23</b>	<b>Yes</b>
<b>*Best*</b>	<b>1**</b>	1	0	20	1	2	0	0	<b>3</b>	<b>7</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>2**</b>	0	0	0	1	1	1	4	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
	<b>3**</b>	0	2	0	3	0	0	0	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-9</i>	<b>0.03</b>	219	238	284	246	233	257	237	<b>245</b>	<b>21</b>	<b>0</b>	<b>0.11</b>	
<i>(gg106)</i>	<b>0.25</b>	192	150	179	55	167	150	114	<b>144</b>	<b>46</b>	<b>0.40</b>	<b>0.20</b>	
	<b>1</b>	102	114	62	6	101	53	49	<b>70</b>	<b>38</b>	<b>0.71</b>	<b>0.16</b>	<b>Yes</b>
	<b>2</b>	3	0	1	34	105	46	28	<b>31</b>	<b>37</b>	<b>0.87</b>	<b>0.16</b>	<b>Yes</b>
	<b>3</b>	1	0	0	1	10	1	0	<b>2</b>	<b>4</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
<i>eri-11</i>	<b>0.03</b>	292	246	239	247	258	285	228	<b>256</b>	<b>24</b>	<b>0.06</b>	<b>0.11</b>	
<i>(gg99)</i>	<b>0.25</b>	123	135	220	224	189	249	185	<b>189</b>	<b>47</b>	<b>0.31</b>	<b>0.18</b>	
	<b>1</b>	24	8	2	50	1	66	43	<b>28</b>	<b>26</b>	<b>0.90</b>	<b>0.09</b>	<b>Yes</b>
	<b>2</b>	5	60	0	125	1	43	15	<b>36</b>	<b>46</b>	<b>0.87</b>	<b>0.17</b>	<b>Yes</b>
	<b>3</b>	0	1	0	1	0	82	0	<b>12</b>	<b>31</b>	<b>0.96</b>	<b>0.11</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *vha-15*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.1 and 0.5), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S24

Dilution series results for *glp-1* feeding

Strain	OD <sub>600</sub>	Penetrance readings							Avg	SD	Eri?
<i>Wildtype</i> (N2)	<b>1</b>	2/56	2/67	1/80	0/20	0/20	0/20	1/60	<b>0.01</b>	<b>0.01</b>	
	<b>2</b>	3/67	1/18	2/40	0/20	2/60			<b>0.04</b>	<b>0.02</b>	
	<b>3</b>	9/31	6/25	8/27	6/25	10/31	12/39	8/24	<b>0.29</b>	<b>0.04</b>	
	<b>4</b>	26/61	24/52	7/14	9/28	9/25	9/26	12/36	<b>0.39</b>	<b>0.07</b>	
	<b>5</b>	11/29	26/53	16/31	13/25	18/28	20/34	19/36	<b>0.52</b>	<b>0.08</b>	
<i>eri-1</i> ( <i>mg366</i> )	<b>1</b>	4/49	5/46	6/42	8/47	3/25	3/20	8/45	<b>0.14</b>	<b>0.03</b>	<b>Yes</b>
	<b>2</b>	12/38	13/33	17/39	9/32	8/23	11/30	18/41	<b>0.37</b>	<b>0.06</b>	<b>Yes</b>
	<b>3</b>	14/28	17/33	14/43	16/32	13/28	24/48	22/39	<b>0.48</b>	<b>0.07</b>	<b>Yes</b>
	<b>4</b>	23/34	29/41	38/52	16/23	24/40			<b>0.68</b>	<b>0.05</b>	<b>Yes</b>
	<b>5</b>	24/28	21/27	28/37	25/35	24/31	32/42	31/38	<b>0.78</b>	<b>0.05</b>	<b>Yes</b>
<i>rff-3</i> ( <i>pk1426</i> )	<b>1</b>	7/47	8/61	12/39	4/39	3/38	5/37		<b>0.15</b>	<b>0.08</b>	<b>Yes</b>
	<b>2</b>	10/41	16/50	26/47	39/54	15/34	14/27	18/38	<b>0.47</b>	<b>0.16</b>	<b>Yes</b>
	<b>3</b>	53/57	41/51	18/36	21/28	41/57	29/39		<b>0.74</b>	<b>0.14</b>	<b>Yes</b>
	<b>4</b>	31/33	42/54	21/27	29/40	36/49	27/40	39/50	<b>0.77</b>	<b>0.08</b>	<b>Yes</b>
	<b>5</b>	31/37	25/30	33/38	28/42	23/25	28/34	28/33	<b>0.83</b>	<b>0.08</b>	<b>Yes</b>
<i>eri-3</i> ( <i>tm1361</i> )	<b>1</b>	3/36	5/45	7/25	2/28	2/29	5/37	4/35	<b>0.12</b>	<b>0.07</b>	<b>Yes</b>
	<b>2</b>	10/36	6/19	19/37	22/63	21/47	12/27	11/35	<b>0.38</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	17/39	22/48	14/30	25/37	15/26	19/36	27/49	<b>0.53</b>	<b>0.08</b>	<b>Yes</b>
	<b>4</b>	14/18	39/48	22/33	40/47	22/30	19/24	44/47	<b>0.80</b>	<b>0.09</b>	<b>Yes</b>
	<b>5</b>	19/24	8/9	27/38	17/22	22/30	23/27	21/25	<b>0.80</b>	<b>0.07</b>	<b>Yes</b>
<i>eri-5</i> ( <i>tm1705</i> ) <b>*Best*</b>	<b>1</b>	3/29	4/28	4/37	3/30	2/60	3/50	0/20	<b>0.08</b>	<b>0.05</b>	<b>Yes</b>
	<b>2</b>	21/34	13/20	10/21	10/30	10/22	12/22		<b>0.51</b>	<b>0.12</b>	<b>Yes</b>
	<b>3</b>	7/11	7/14	11/28	8/21	5/14	25/40	12/28	<b>0.47</b>	<b>0.12</b>	<b>Yes</b>
	<b>4</b>	27/36	25/32	20/29	22/27	14/22	22/29	23/28	<b>0.75</b>	<b>0.07</b>	<b>Yes</b>
	<b>5**</b>	11/13	12/13	34/35	27/29	30/33	19/21	13/13	<b>0.93</b>	<b>0.05</b>	<b>Yes</b>
<i>eri-6/7</i> ( <i>tm1917</i> )	<b>1</b>	2/36	4/61	7/32	5/30	5/34	6/40	6/46	<b>0.13</b>	<b>0.06</b>	<b>Yes</b>
	<b>2</b>	12/28	11/27	9/35	8/33	8/35	6/28	12/26	<b>0.32</b>	<b>0.11</b>	<b>Yes</b>
	<b>3</b>	18/31	24/34	20/29	14/25	11/19	26/37		<b>0.64</b>	<b>0.07</b>	<b>Yes</b>
	<b>4</b>	30/35	24/37	24/31	23/29	13/17	27/36	23/29	<b>0.77</b>	<b>0.06</b>	<b>Yes</b>
	<b>5</b>	19/26	18/21	14/25	23/27	26/30	18/20	24/30	<b>0.80</b>	<b>0.12</b>	<b>Yes</b>
<i>eri-8</i>	<b>1</b>	7/79	8/78	7/29	9/50	6/42	2/23	3/35	<b>0.13</b>	<b>0.06</b>	<b>Yes</b>

<i>(gg100)</i>	<b>2</b>	17/38	7/18	9/54	8/24	10/29	18/47	15/49	<b>0.34</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	17/32	15/29	16/30	29/47	20/43	35/58	27/44	<b>0.55</b>	<b>0.06</b>	<b>Yes</b>
	<b>4</b>	20/23	49/68	26/36	24/40	33/47	12/17	32/54	<b>0.70</b>	<b>0.09</b>	<b>Yes</b>
	<b>5</b>	20/32	33/40	22/25	25/30	24/30	23/26	25/34	<b>0.80</b>	<b>0.09</b>	<b>Yes</b>
<i>eri-9</i>	<b>1</b>	8/75	1/48	8/60	2/28	4/46	6/63	11/93	<b>0.09</b>	<b>0.04</b>	<b>Yes</b>
<i>(gg106)</i>	<b>2</b>	13/39	8/24	11/39	12/39	18/53	5/32	4/16	<b>0.29</b>	<b>0.07</b>	<b>Yes</b>
	<b>3</b>	12/28	20/39	20/36	19/34	21/35	14/25	24/45	<b>0.54</b>	<b>0.05</b>	<b>Yes</b>
	<b>4</b>	28/31	30/40	17/27	20/23	17/28	30/39	15/22	<b>0.74</b>	<b>0.11</b>	<b>Yes</b>
	<b>5</b>	43/65	40/51	16/28	34/38	16/18	24/28	26/32	<b>0.78</b>	<b>0.12</b>	<b>Yes</b>
<i>eri-11</i>	<b>1</b>	4/69	5/53	0/20	0/20	2/40	0/20	0/20	<b>0.03</b>	<b>0.04</b>	
<i>(gg99)</i>	<b>2</b>	17/53	11/37	5/19	3/10	9/28	7/24		<b>0.30</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	24/39	16/25	7/20	23/49	10/19	12/28	27/55	<b>0.50</b>	<b>0.10</b>	<b>Yes</b>
	<b>4</b>	44/57	36/44	27/41	27/39	17/27	41/49	19/25	<b>0.74</b>	<b>0.08</b>	<b>Yes</b>
	<b>5</b>	31/36	52/58	16/20	34/39	13/16	24/26	29/37	<b>0.85</b>	<b>0.05</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *glp-1*; 4 days later, the percent of progeny showing the expected absent germline at each indicated concentration (OD at 600 nm) of initial bacterial culture were determined. The tabulated mean (Avg) and standard deviation (SD) for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.



TABLE S25

Dilution series results for *par-1* feeding

Strain	OD <sub>600</sub>	Brood Size						Avg	SD	N.Avg	SEM	Eri?	
<i>Wildtype</i>	<b>0.1</b>	196	248	256	220	216	232	<b>228</b>	<b>22</b>	<b>0</b>	<b>0.13</b>		
<i>(N2)</i>	<b>0.5</b>	196	184	200	160	212		<b>190</b>	<b>20</b>	<b>0.16</b>	<b>0.12</b>		
	<b>1</b>	133	109	130	108	94		<b>115</b>	<b>16</b>	<b>0.49</b>	<b>0.09</b>		
	<b>2</b>	97	49	65	192	36		<b>88</b>	<b>63</b>	<b>0.61</b>	<b>0.28</b>		
	<b>3</b>	10	14	17	18	17	9	<b>6</b>	<b>13</b>	<b>5</b>	<b>0.94</b>	<b>0.02</b>	
<i>eri-1</i>	<b>0.1</b>	130	208	184	168	192	216	<b>183</b>	<b>31</b>	<b>0</b>	<b>0.21</b>		
<i>(mg366)</i>	<b>0.5</b>	79	95	31	131	104	116	128	<b>98</b>	<b>35</b>	<b>0.38</b>	<b>0.22</b>	
	<b>1</b>	35	57	87	34	6	41		<b>43</b>	<b>27</b>	<b>0.73</b>	<b>0.17</b>	<b>Yes</b>
	<b>2</b>	4	19	6	18	9	18		<b>12</b>	<b>7</b>	<b>0.92</b>	<b>0.04</b>	<b>Yes</b>
	<b>3</b>	7	26	15	12	9	23	5	<b>14</b>	<b>8</b>	<b>0.91</b>	<b>0.05</b>	
<i>rif-3</i>	<b>0.1</b>	18	38	176	112	104	87	118	<b>93</b>	<b>53</b>	<b>0.30</b>	<b>0.40</b>	
<i>(pk1426)</i>	<b>0.5</b>	11	10	10	18	21	14		<b>14</b>	<b>5</b>	<b>0.90</b>	<b>0.04</b>	<b>Yes</b>
	<b>1</b>	7	19	12	12	16	12	2	<b>11</b>	<b>6</b>	<b>0.91</b>	<b>0.04</b>	<b>Yes</b>
	<b>2</b>	7	12	5	13	10	12	9	<b>10</b>	<b>3</b>	<b>0.93</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	8	10	10	6	7	3	4	<b>7</b>	<b>3</b>	<b>0.95</b>	<b>0.02</b>	
<i>eri-3</i>	<b>0.1</b>	27	5	19	90	69	90	144	<b>63</b>	<b>49</b>	<b>0.59</b>	<b>0.32</b>	<b>Yes</b>
<i>(tm1361)</i>	<b>0.5</b>	18	18	11	8	11	4	54	<b>18</b>	<b>17</b>	<b>0.89</b>	<b>0.11</b>	<b>Yes</b>
	<b>1</b>	5	8	3	10	6	40	18	<b>13</b>	<b>13</b>	<b>0.92</b>	<b>0.08</b>	<b>Yes</b>
	<b>2</b>	12	3	1	1	2	1	5	<b>4</b>	<b>4</b>	<b>0.98</b>	<b>0.03</b>	<b>Yes</b>
	<b>3</b>	15	7	21	17	3	2	6	<b>10</b>	<b>7</b>	<b>0.93</b>	<b>0.05</b>	
<i>eri-5</i>	<b>0.1</b>	8	94	77	47	248	136	184	<b>113</b>	<b>82</b>	<b>0.33</b>	<b>0.49</b>	
<i>(tm1705)</i>	<b>0.5**</b>	4	15	10	14	19	11	28	<b>14</b>	<b>8</b>	<b>0.92</b>	<b>0.05</b>	<b>Yes</b>
<b>*Best*</b>	<b>1**</b>	5	10	7	6	10	11	4	<b>8</b>	<b>3</b>	<b>0.96</b>	<b>0.02</b>	<b>Yes</b>
	<b>2**</b>	4	14	9	8	3	4	7	<b>7</b>	<b>4</b>	<b>0.96</b>	<b>0.02</b>	<b>Yes</b>
	<b>3</b>	18	21	10	2	10	9	7	<b>11</b>	<b>6</b>	<b>0.94</b>	<b>0.04</b>	
<i>eri-6/7</i>	<b>0.1</b>	159	168	200	208	232	186		<b>192</b>	<b>27</b>	<b>0</b>	<b>0.20</b>	
<i>(tm1917)</i>	<b>0.5</b>	15	12	35	232	13	31	12	<b>50</b>	<b>81</b>	<b>0.68</b>	<b>0.52</b>	
	<b>1</b>	3	3	5	11	10	8		<b>7</b>	<b>4</b>	<b>0.96</b>	<b>0.02</b>	<b>Yes</b>
	<b>2</b>	45	19	11	12	5	13	11	<b>17</b>	<b>13</b>	<b>0.89</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	6	3	6	5	8	3	8	<b>6</b>	<b>2</b>	<b>0.96</b>	<b>0.01</b>	<b>Yes</b>
<i>eri-8</i>	<b>0.1</b>	228	184	220	243	248	208	270	<b>229</b>	<b>28</b>	<b>0</b>	<b>0.13</b>	

<i>(gg100)</i>	<b>0.5</b>	9	27	268	173	159	100	176	<b>130</b>	<b>91</b>	<b>0.41</b>	<b>0.41</b>	
	<b>1</b>	119	80	188	40	39	64	20	<b>79</b>	<b>58</b>	<b>0.65</b>	<b>0.26</b>	
	<b>2</b>	16	21	8	11	60	12	17	<b>21</b>	<b>18</b>	<b>0.91</b>	<b>0.08</b>	<b>Yes</b>
	<b>3</b>	6	16	9	14	10	26	10	<b>13</b>	<b>7</b>	<b>0.94</b>	<b>0.03</b>	
<i>eri-9</i>	<b>0.1</b>	272	244	232	219	255	244		<b>244</b>	<b>18</b>	<b>0</b>	<b>0.10</b>	
<i>(gg106)</i>	<b>0.5</b>	14	26	148	137	172	200	196	<b>128</b>	<b>77</b>	<b>0.47</b>	<b>0.32</b>	
	<b>1</b>	137	144	86	150	176			<b>139</b>	<b>33</b>	<b>0.42</b>	<b>0.14</b>	
	<b>2</b>	23	17	48	117	13	121	140	<b>68</b>	<b>55</b>	<b>0.71</b>	<b>0.23</b>	
	<b>3</b>	2	8	97	40	12	15	5	<b>26</b>	<b>34</b>	<b>0.89</b>	<b>0.14</b>	
<i>eri-11</i>	<b>0.1</b>	280	292	216	252	270	260	243	<b>259</b>	<b>25</b>	<b>0.05</b>	<b>0.11</b>	
<i>(gg99)</i>	<b>0.5</b>	96	20	113	132	248	164		<b>129</b>	<b>76</b>	<b>0.53</b>	<b>0.28</b>	<b>Yes</b>
	<b>1</b>	86	62	200	196	51	121	99	<b>116</b>	<b>60</b>	<b>0.57</b>	<b>0.22</b>	
	<b>2</b>	60	62	17	10	22	17		<b>31</b>	<b>23</b>	<b>0.89</b>	<b>0.09</b>	<b>Yes</b>
	<b>3</b>	11	6	8	4	16	9	8	<b>9</b>	<b>4</b>	<b>0.97</b>	<b>0.01</b>	<b>Yes</b>

Single L3-stage larvae were placed on RNAi food targeting *par-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.25 and 0.75), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

TABLE S26

Dilution series results for *pos-1* feeding

Strain	OD <sub>600</sub>	Brood Size							Avg	SD	N.Avg	SEM	Eri?
<i>Wildtype</i>	<b>0.1</b>	216	205	272	180	196	232	205	<b>217</b>	<b>30</b>	<b>0.04</b>	<b>0.17</b>	
<i>(N2)</i>	<b>0.25</b>	184	168	10	248	231	240		<b>180</b>	<b>89</b>	<b>0.20</b>	<b>0.40</b>	
	<b>0.5</b>	201	170	169	150	153			<b>169</b>	<b>20</b>	<b>0.26</b>	<b>0.11</b>	
	<b>0.75</b>	147	37	3	2	133	74	118	<b>66</b>	<b>61</b>	<b>0.71</b>	<b>0.28</b>	
	<b>1</b>	30	0	3	2	0	4	71	<b>7</b>	<b>27</b>	<b>0.97</b>	<b>0.05</b>	
<i>eri-1</i>	<b>0.1</b>	123	128	154	164	164	171	192	<b>151</b>	<b>24</b>	<b>0.05</b>	<b>0.14</b>	
<i>(mg366)</i>	<b>0.25</b>	132	107	130	188	220	133	168	<b>152</b>	<b>40</b>	<b>0.04</b>	<b>0.28</b>	
	<b>0.5</b>	39	0	7	6	10			<b>13</b>	<b>15</b>	<b>0.92</b>	<b>0.11</b>	<b>Yes</b>
	<b>0.75</b>	74	0	2	0	0	0	22	<b>13</b>	<b>28</b>	<b>0.92</b>	<b>0.19</b>	
	<b>1</b>	64	55	2	0	1	0	0	<b>20</b>	<b>29</b>	<b>0.87</b>	<b>0.19</b>	
<i>rif-3</i>	<b>0.1</b>	91	176	162	126	168	184	186	<b>151</b>	<b>35</b>	<b>0</b>	<b>0.28</b>	
<i>(pk1426)</i>	<b>0.25</b>	138	61	8	204	8	82		<b>84</b>	<b>77</b>	<b>0.37</b>	<b>0.64</b>	
	<b>0.5</b>	0	50	1	2	0	0	1	<b>8</b>	<b>19</b>	<b>0.93</b>	<b>0.15</b>	<b>Yes</b>
	<b>0.75</b>	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>1</b>	0	0	0	0	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-3</i>	<b>0.1</b>	109	90	124	140	125	192	144	<b>130</b>	<b>32</b>	<b>0.17</b>	<b>0.24</b>	
<i>(tm1361)</i>	<b>0.25</b>	142	136	100	27	10	36	25	<b>75</b>	<b>56</b>	<b>0.52</b>	<b>0.38</b>	
	<b>0.5</b>	11	32	41	2	7	5	7	<b>16</b>	<b>15</b>	<b>0.90</b>	<b>0.10</b>	<b>Yes</b>
	<b>0.75</b>	0	0	0	8	4	0	17	<b>2</b>	<b>6</b>	<b>0.99</b>	<b>0.02</b>	<b>Yes</b>
	<b>1</b>	0	2	2	1	18			<b>5</b>	<b>8</b>	<b>0.97</b>	<b>0.05</b>	
<i>eri-5</i>	<b>0.1</b>	129	174	192	228	85	244	200	<b>175</b>	<b>56</b>	<b>0</b>	<b>0.37</b>	
<i>(tm1705)</i>	<b>0.25</b>	78	85	208	184	35	252	136	<b>140</b>	<b>79</b>	<b>0.18</b>	<b>0.51</b>	
<b>*Best*</b>	<b>0.5**</b>	1	5	3	0	0	2	16	<b>2</b>	<b>6</b>	<b>0.99</b>	<b>0.01</b>	<b>Yes</b>
	<b>0.75**</b>	0	0	0	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	<b>Yes</b>
	<b>1</b>	10	0	0	0	0	0	0	<b>2</b>	<b>4</b>	<b>0.99</b>	<b>0.02</b>	
<i>eri-6/7</i>	<b>0.1</b>	166	156	144	128	164	167		<b>154</b>	<b>15</b>	<b>0.01</b>	<b>0.13</b>	
<i>(tm1917)</i>	<b>0.25</b>	186	200	15	97	128	168	184	<b>132</b>	<b>66</b>	<b>0.15</b>	<b>0.45</b>	
	<b>0.5</b>	68	0	20	0	23	22		<b>22</b>	<b>25</b>	<b>0.86</b>	<b>0.18</b>	<b>Yes</b>
	<b>0.75</b>	1	1	0	0	2	0	0	<b>1</b>	<b>1</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
	<b>1</b>	0	0	1	1	0	0	0	<b>0</b>	<b>0</b>	<b>1.00</b>	<b>0</b>	
<i>eri-8</i>	<b>0.1</b>	232	256	184	252	304	240	204	<b>245</b>	<b>39</b>	<b>0</b>	<b>0.18</b>	

<i>(gg100)</i>	<b>0.25</b>	168	264	99	75	29	129	236	<b>127</b>	<b>85</b>	<b>0.43</b>	<b>0.37</b>	
	<b>0.5</b>	40	0	1	50	84	2		<b>35</b>	<b>34</b>	<b>0.84</b>	<b>0.16</b>	<b>Yes</b>
	<b>0.75</b>	32	11	0	0	0	0	1	<b>7</b>	<b>12</b>	<b>0.97</b>	<b>0.06</b>	<b>Yes</b>
	<b>1</b>	44	30	0	1	1	1	0	<b>13</b>	<b>18</b>	<b>0.94</b>	<b>0.09</b>	
<i>eri-9</i>	<b>0.1</b>	224	248	252	200	168	228	210	<b>220</b>	<b>29</b>	<b>0.08</b>	<b>0.14</b>	
<i>(gg106)</i>	<b>0.25</b>	144	172	164	62	128	192		<b>134</b>	<b>46</b>	<b>0.44</b>	<b>0.19</b>	
	<b>0.5</b>	47	71	4	2	0	1	2	<b>21</b>	<b>29</b>	<b>0.91</b>	<b>0.13</b>	<b>Yes</b>
	<b>0.75</b>	5	0	0	1	0	0	21	<b>1</b>	<b>8</b>	<b>1.00</b>	<b>0.01</b>	<b>Yes</b>
	<b>1</b>	0	0	0	0	0	0	9	<b>0</b>	<b>3</b>	<b>1.00</b>	<b>0</b>	
<i>eri-11</i>	<b>0.1</b>	240	208	250	244	256	224	216	<b>237</b>	<b>18</b>	<b>0.13</b>	<b>0.09</b>	
<i>(gg99)</i>	<b>0.25</b>	252	214	272	258	228	243	192	<b>245</b>	<b>28</b>	<b>0.11</b>	<b>0.10</b>	
	<b>0.5</b>	212	230	296	77	202	128		<b>191</b>	<b>78</b>	<b>0.30</b>	<b>0.29</b>	
	<b>0.75</b>	64	67	0	0	1	3		<b>26</b>	<b>33</b>	<b>0.90</b>	<b>0.13</b>	
	<b>1</b>	0	0	6	0	0	37	8	<b>7</b>	<b>14</b>	<b>0.97</b>	<b>0.05</b>	

Single L3-stage larvae were placed on RNAi food targeting *pos-1*; 4 days later, the number of progeny surviving to L3-stage larvae or older at each indicated concentration (OD at 600 nm) of initial bacterial culture was determined. For clarity, two bacterial culture concentrations (OD<sub>600nm</sub> of 0.03 and 2), which produced similar Eri penetrances as adjacent concentrations, are not included. The tabulated mean (Avg) and standard deviation (SD) were normalized to the brood sizes of each strain fed empty RNAi vector (Table S27), to obtain the normalized mean (N.Avg) and standard error of the mean (SEM). The normalized mean and the standard error of the mean for N2 wild type were used as the basis to indicate an Eri or a Rde phenotype (Eri?), with  $p < 0.05$  as the criterion to denote significant difference from wild type response levels. A strain which fits the “best *eri*” criterion described in text is marked as “best”, with asterisks indicating concentrations of RNAi food at which it fulfilled the criterion.

**TABLE S27****Different Eri strains' brood sizes upon L4440 vector feeding**

Strain	Brood Size										Avg	SD
<i>Wildtype</i> ( <i>N2</i> )	185	218	237	242	208	247	248	222	215	244	<b>227</b>	<b>21</b>
<i>eri-1</i> ( <i>mg366</i> )	168	156	151	162	149	167	167	147			<b>158</b>	<b>9</b>
<i>rf-3</i> ( <i>pk1426</i> )	137	137	142	135	143	138	139	117	127	119	<b>133</b>	<b>9</b>
<i>eri-3</i> ( <i>tm1361</i> )	169	160	146	134	151	176	167	143			<b>156</b>	<b>16</b>
<i>eri-5</i> ( <i>tm1705</i> )	150	188	189	144	173	177	186	172	177	147	<b>170</b>	<b>17</b>
<i>eri-6/7</i> ( <i>tm1917</i> )	145	143	154	176	143	168	168	148	152		<b>155</b>	<b>12</b>
<i>eri-8</i> ( <i>gg100</i> )	226	229	208	230	219	234	219	221	218		<b>223</b>	<b>8</b>
<i>eri-9</i> ( <i>gg106</i> )	221	249	233	231	237	227	262	254	241		<b>239</b>	<b>13</b>
<i>eri-11</i> ( <i>gg99</i> )	285	242	274	284	297	279	268	285	249		<b>274</b>	<b>18</b>
<i>sid-1</i> ( <i>qt9</i> )	178	206	214	238	211	224	218	260	243	231	<b>222</b>	<b>23</b>

The presented means and standard deviations were used for normalized means and standard errors of the means in RNAi feeding assays that caused lethality phenotypes.

**TABLE S28****Transgene silencing penetrance of *eri-1*, *rff-3*, and *eri-8* in the *sur-5::gfp* background**

Strain	Penetrance of spontaneous intestinal TGS at 20°C					Mean	STD
N2 wild type	3/98	1/88	2/109	1/19	0/82	0.02	0.02
<i>eri-1 (mg366)</i>	48/62	28/46	31/54			0.65	0.11
<i>rff-3 (pk1426)</i>	73/83	76/91	38/45	39/57	97/107	0.83	0.09
<i>eri-8 (gg100)</i>	30/38	24/42	25/35	42/53	28/40	0.71	0.09

Single L3-stage larvae were placed on OP50 food; 4 days later, the percent of progeny showing spontaneous transgene silencing in the intestinal nuclei was determined. For consistency, only worms with distinctly absent *gfp* expression in intestinal nuclei, as shown in Figure S3, are scored as having spontaneous transgene silencing.

**TABLE S29****Maternal rescue of Eri phenotype on *dpy-13* feeding via outcrossing**

Strain	F <sub>2</sub> Dpy:Non-Dpy						$\chi^2$ value
<i>eri-1 (mg366)</i>	0:60	0:30	0:40	0:80	0:50		1.5e-23
<i>rf-3 (pk1426)</i>	0:120	0:80	0:80				4.4e-22
<i>eri-3 (tm1361)</i>	0:50	0:40	0:50	0:80	0:80		1.5e-23
<i>eri-6/7 (tm1917)</i>	0:80	0:100	0:100	0:80	0:60		2.7e-32
<i>eri-8 (gg100)</i>	4:29	2:34	4:48	4:25			9.4e-9
<i>eri-9 (gg106)</i>	1:59	0:40	2:78	0:80	1:49	0:60	2.3e-26
<i>eri-11 (gg99)</i>	0:40	3:32	2:31	2:38	0:60		5.8e-13

Strain	F <sub>3</sub> 100% Dpy: 25% Dpy: 100% Non-Dpy						$\chi^2$ value
<i>eri-1 (mg366)</i>	6:0:10	5:0:11	3:0:13				9.1e-15
<i>rf-3 (pk1426)</i>	6:0:10	2:0:12	4:0:12				2.8e-15
<i>eri-3 (tm1361)</i>	2:0:14	4:0:12	3:0:13				2.2e-20
<i>eri-6/7 (tm1917)</i>	5:0:11	5:0:11	5:0:11	3:0:13	5:0:11		2.3e-24
<i>eri-8 (gg100)</i>	5:8:3	4:7:5	2:8:5	3:0:13	6:0:10		4.0e-5
<i>eri-9 (gg106)</i>	4:0:12	3:0:13	2:0:14	5:0:11	3:0:13		1.4e-29
<i>eri-11 (gg99)</i>	5:0:11	5:0:11	3:0:13	4:0:12	6:0:10		2.3e-24

Corresponding to Figure S5A, the observed phenotypic ratios of the outcross progeny in the F<sub>2</sub> and F<sub>3</sub> are as indicated. At the F<sub>2</sub>, the expected phenotypic ratio of 1:3 Dpy:non-Dpy is used as the basis for chi-squared test calculations; at the F<sub>3</sub>, the expected phenotypic ratio of 1:2:1 100% Dpy: 25% Dpy:100% Non-Dpy is used as the basis for chi-squared test calculations. Observed results are summed for chi-squared test calculations.

**TABLE S30**

**Maternal rescue of Eri phenotype on *dpy-13* feeding via a heterozygous Eri male crossed with a homozygous Eri hermaphrodite**

Strain	F <sub>1</sub> Dpy:Non-Dpy					$\chi^2$ value
<i>eri-1 (mg366)</i>	18:20	24:25	10:8	13:16	18:17	0.82
<i>rf-3 (pk1426)</i>	11:10	6:8	13:14			0.80
<i>eri-3 (tm1361)</i>	5:8	4:6	13:10			0.77
<i>eri-6/7 (tm1917)</i>	14:9	6:4	4:6			0.45
<i>eri-8 (gg100)</i>	21:28	12:11	20:18	16:18	8:11	0.48
<i>eri-9 (gg106)</i>	12:18	18:13	10:14	15:15		0.64
<i>eri-11 (gg99)</i>	11:16	10:14	12:10	10:7	13:10	0.93

Corresponding to Figure S6A, the observed phenotypic ratios of the cross progeny are as indicated. The expected phenotypic ratio of 1:1 Dpy:non-Dpy is used as the basis for chi-squared test calculations. Observed results are summed for chi-squared test calculations.



**TABLE S31****Maternal rescue of Eri phenotype on *dpy-13* feeding via a homozygous Eri male crossed with a heterozygous****Eri hermaphrodite**

Strain	F <sub>1</sub> Dpy:Non-Dpy				$\chi^2$ value
<i>eri-1 (mg366)</i>	0:16	0:14	0:33		2.1e-15
<i>rf-3 (pk1426)</i>	0:18	0:13	0:23	0:16	5.9e-17
<i>eri-3 (tm1361)</i>	0:40	0:20	0:20		3.7e-19
<i>eri-6/7 (tm1917)</i>	0:60	0:60	0:80	0:80      0:50	9.6e-74
<i>eri-8 (gg100)</i>	1:14	5:14	4:17	5:28      2:22	1.7e-13
<i>eri-9 (gg106)</i>	0:25	0:29	0:16		5.9e-17
<i>eri-11 (gg99)</i>	0:19	0:20	0:21	0:24	4.9e-20

Corresponding to Figure S6B, the observed phenotypic ratios of the cross progeny are as indicated. The expected phenotypic ratio of 1:1 Dpy:non-Dpy is used as the basis for chi-squared test calculations. Observed results are summed for chi-squared test calculations.

**TABLE S32****Maternal rescue of Eri phenotype on *hmr-1* and *unc-73* feeding via outcrossing**

Strain	Food	F <sub>2</sub> Phenotype:No-Phenotype					$\chi^2$ value
<i>eri-1 (mg366)</i>	<i>unc-73</i>	0:76	0:45	0:35	0:45		2.7e-16
<i>rf-3 (pk1426)</i>	<i>unc-73</i>	0:34	0:36	0:23			2.6e-8
<i>eri-8 (gg100)</i>	<i>unc-73</i>	8:24	3:27	3:28	3:38	2:34	3.1e-5

Strain	Food	F <sub>3</sub> 100% Phenotype: 25%Phenotype:No-Phenotype				$\chi^2$ value
<i>eri-1 (mg366)</i>	<i>unc-73</i>	4:0:12	5:0:11	4:0:12	3:0:13	1.4e-21
<i>rf-3 (pk1426)</i>	<i>unc-73</i>	5:0:11	5:0:11	2:0:14	3:0:13	1.8e-22
<i>eri-3 (tm1361)</i>	<i>hmr-1</i>	6:0:10	2:0:14	3:0:13	4:0:12	1.8e-22
<i>eri-6/7 (tm1917)</i>	<i>hmr-1</i>	3:0:13	3:0:13	2:0:14		2.1e-20
<i>eri-8 (gg100)</i>	<i>hmr-1</i>	2:0:14	1:0:15	3:0:13		7.1e-23

Corresponding to Figure S5A, the observed phenotypic ratios of the outcross progeny in the F<sub>2</sub> and F<sub>3</sub> are as indicated when fed the three respective RNAi foods. At the F<sub>2</sub>, the expected phenotypic ratio of 1:3 with-phenotype:without-phenotype is used as the basis for chi-squared test calculations; at the F<sub>3</sub>, the expected phenotypic ratio of 1:2:1 100% with-phenotype: 25% with-phenotype: 100% without-phenotype is used as the basis for chi-squared test calculations. Observed results are summed for chi-squared test calculations.

**TABLE S33****No maternal rescue of Eri phenotype-related spermatogenesis defects**

Strain	F <sub>2</sub> Sterile:Non-sterile			$\chi^2$ value
<i>eri-1 (mg366)</i>	2:14	3:13	3:12	0.18
<i>rjf-3 (pk1426)</i>	5:11	3:13	5:11	0.74
<i>eri-3 (tm1361)</i>	3:13	4:12	3:13	0.50

Corresponding to Figure S5B, the observed phenotypic ratios of the outcross progeny are as indicated. The expected phenotypic ratio of 1:3 sterile:non-sterile is used as the basis for chi-squared test calculations. Observed results are summed for chi-squared test calculations.

**TABLE S34****Maternal rescue of Eri phenotype on *bli-1* feeding via outcrossing**

Strain	Penetrance of Bli at F <sub>2</sub>				Mean	STD	<i>p</i> value
N2 wild type	39/86	63/144	58/119		0.46	0.03	
<i>eri-1</i> ( <i>mg366</i> )	78/87	66/97	65/70		0.84	0.13	0.008
<i>rf-3</i> ( <i>pk1426</i> )	46/51	34/41	38/41		0.89	0.05	0.0002
<i>eri-8</i> ( <i>gg100</i> )	46/67	45/69	47/80		0.64	0.05	0.006
N2 x <i>eri-1</i>	63/134	51/116	74/139	34/80	0.47	0.05	0.78
N2 x <i>rf-3</i>	36/73	64/123	15/37	32/74	0.46	0.05	1
N2 x <i>eri-8</i>	75/145	48/101	36/72	52/97	0.51	0.03	0.11

Corresponding to Figure S5A, the observed phenotypic penetrances of the outcross progeny in the F<sub>2</sub> are as indicated. The N2 wild type penetrance was used as the basis for a *t* test, to compare an Eri mutant's or an outcrossed-Eri mutant's penetrance, with a two-tailed *p* value as indicated.

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