# Figure S1. Related to Figure 1

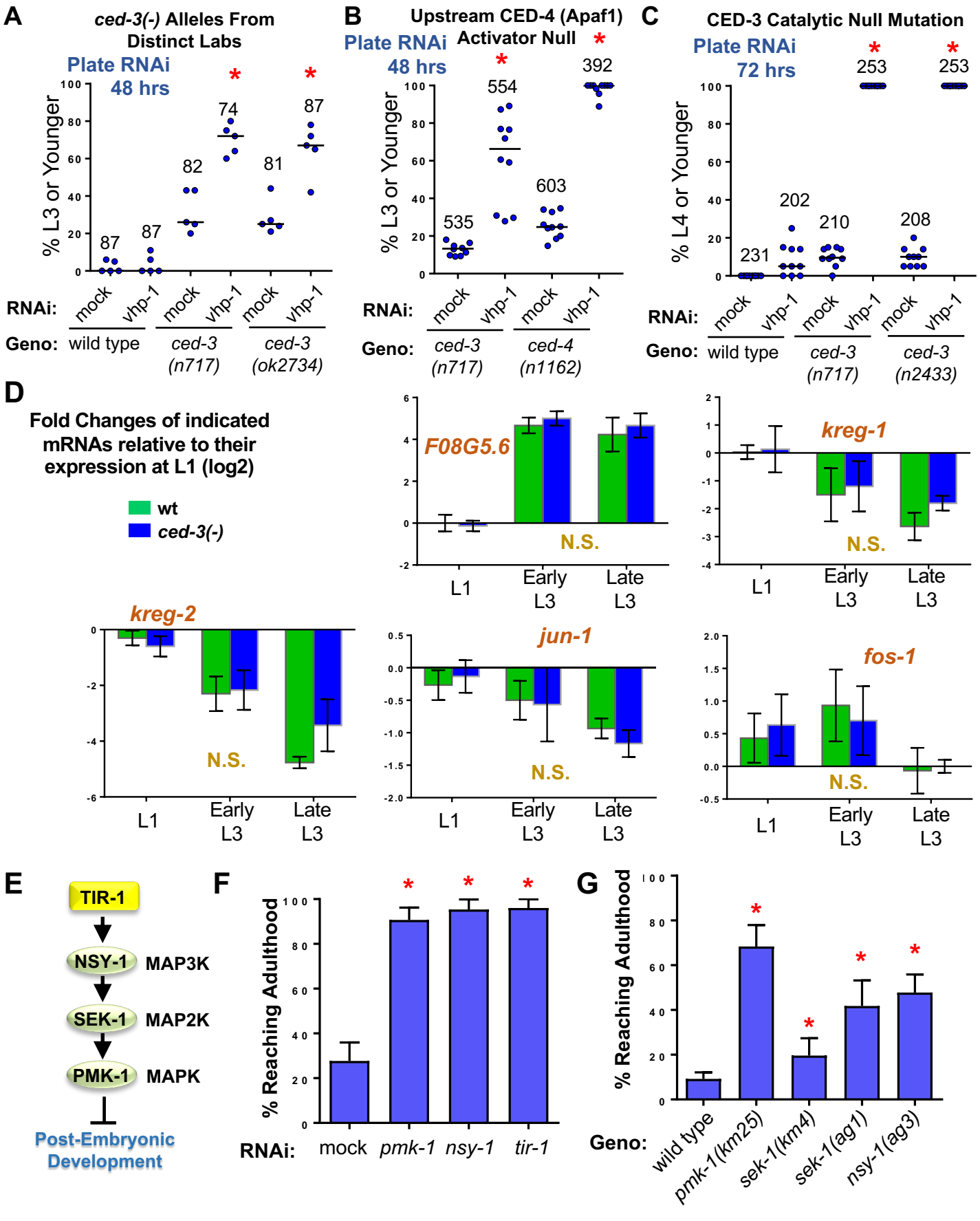


**Figure S1. Related to Figure 1. Confirmation of Caspase and Epidermal p38 MAPK Pathway**

**(A-C)** Confirmation of a *ced-3(-)* null mutation originating from distinct labs, a null mutation in the upstream *ced-4/Apaf1* gene, and a *ced-3* catalytic activity null mutation for synthetic larval delay phenotypes with *vhp-1(RNAi).* *Significant, wt on *vhp-1(RNAi)* vs *ced-3* or *ced-4* alleles on *vhp-1(RNAi), p* < 0.05 (A), *p* < 0.001 (B-C), Mann-Whitney, median values (bars).

**(D)** Analyses of mRNA levels by qRT-PCR for additional MAPK targets. None of these other targets were significantly upregulated by *ced-3(-)* mutation. No significance found by t-test.

**(E-G)** Confirmation of PMK-1 pathway factors for roles in negatively regulating post-embryonic developmental rate in the absence of stress. (F) RNAi treatment of wild-type P0 animals started at the L4 stage. The resulting F1 day 1 adults were put on fresh RNAi plates and allowed to lay eggs for 3 hours before being removed. The F2 offspring were phenotyped for stages 54 hours later on RNAi. (G) Gravid P0 adults (5 per plate) were put on OP50 plates and allowed to lay eggs for 3 hrs. The adults were removed from plates and F1 animals were staged 52 hrs later at 20°C. SEK-1 mutations had varying degrees of impact on developmental rate. *Significant, mock vs *pmk-1(RNAi), nsy-1(RNAi),* and *tir-1(RNAi), p* < 0.05, t-test from 3 experiments, standard deviation (bars) (F) and wild-type vs *pmk-1, sek-1,* and *nsy-1* alleles, *p* < 0.05, t-test from 5 experiments, standard deviation (bars) (G).

# Figure S2. Related to Figure 2

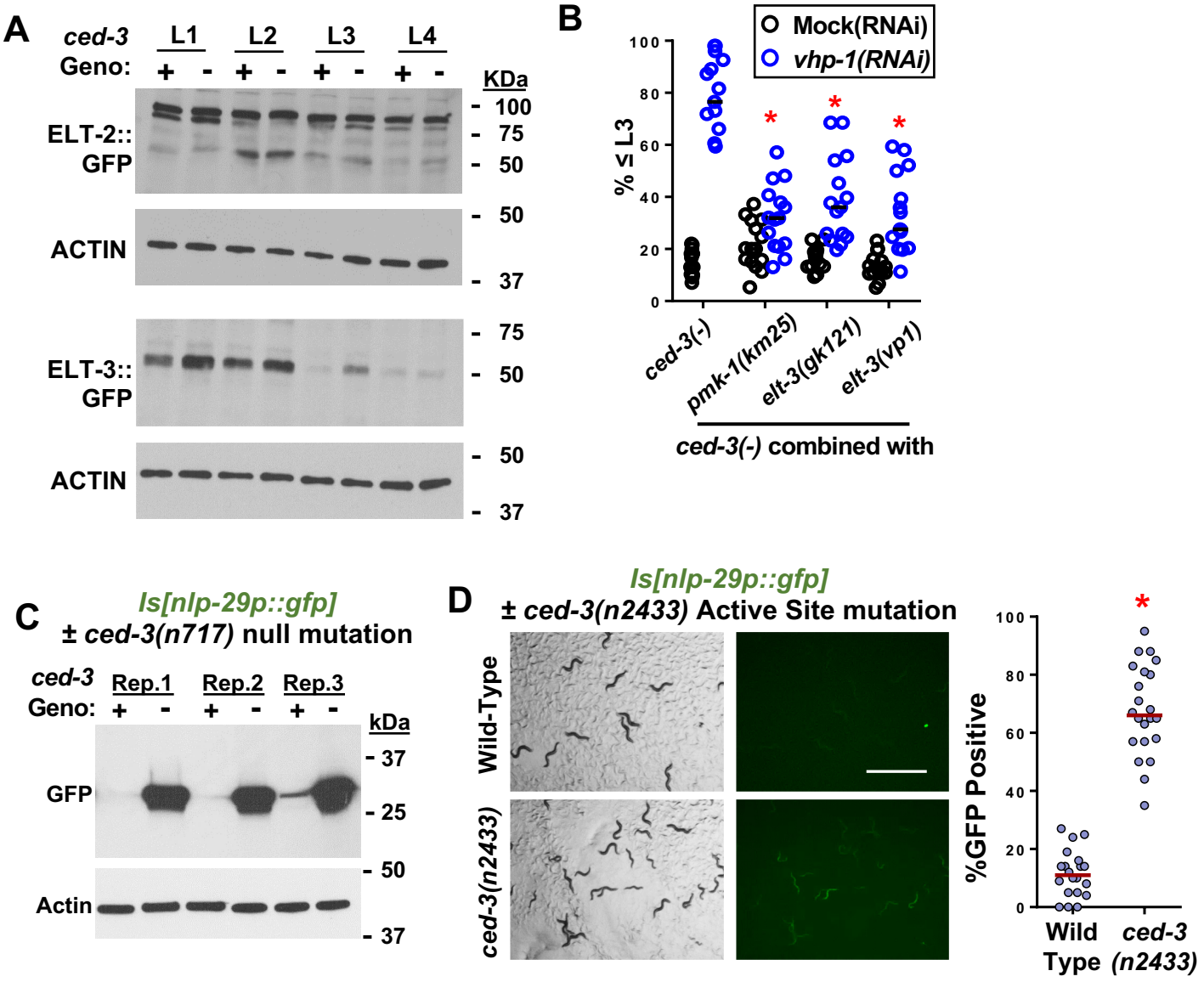


**Figure S2. Related to Figure 2. CED-3 Limits Epidermal but Not Intestinal p38 MAPK Response**

**(A)** Western blot analyses of ELT-2::GFP and ELT-3::GFP using anti-GFP antibody (Clontech, JL8) and anti-actin antibody (Sigma A2066) through larval stages. For ELT-3::GFP blot, lane of no transgene strain (wt) demonstrating high Mw non-specific band removed on left side.

**(B)** Suppression test for *ced-3(-)* larval growth delay effect with *vhp-1(RNAi).* The *elt-3* mutants restored *ced-3(-)* development as well as *pmk-1(-)* consistent with PMK-1 acting through ELT-3 in the epidermis.

**(C)** Confirmation of GFP expression by *ced-3* null mutation confirmed by Western blot. Remainder of blot (left side) shown in **Figure 2F** showing comparable induction at same exposure time.

**(D)** Confirmation of GFP expression by *ced-3* caspase catalytic null mutation G360S. Scored in the blind three times. $p<0.0001$, Mann-Whitney. Pseudo-colored images, same magnification. Scale bar, 1 mm.

# Figure S3. Related to Figure 3

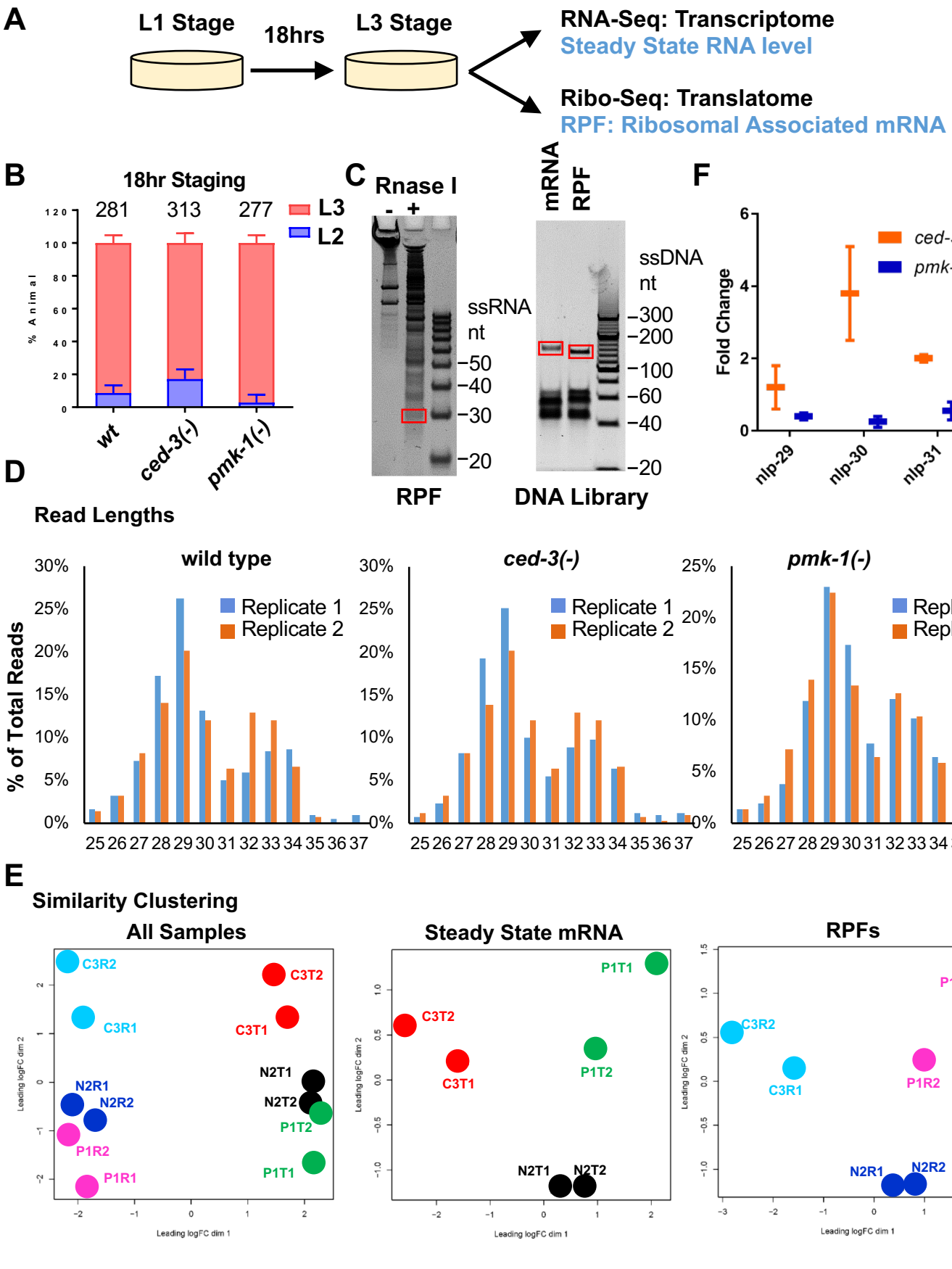


**Figure S3. Related to Figure 3. Ribosome Profiling Workflow and Controls**

**(A)** Synchronous L1 animals were fed normal food for 18 hours to get L3 stage animals and processed for ribosome profiling (see **STAR methods**). The L3 stage was chosen because this stage lacks programmed cell death events in hermaphrodites and represents mid-larval development.

**(B)** Confirmation of stages at 18 hours. The predominate mass of tissue for each strain was L3. Standard deviation (error bars) is shown.

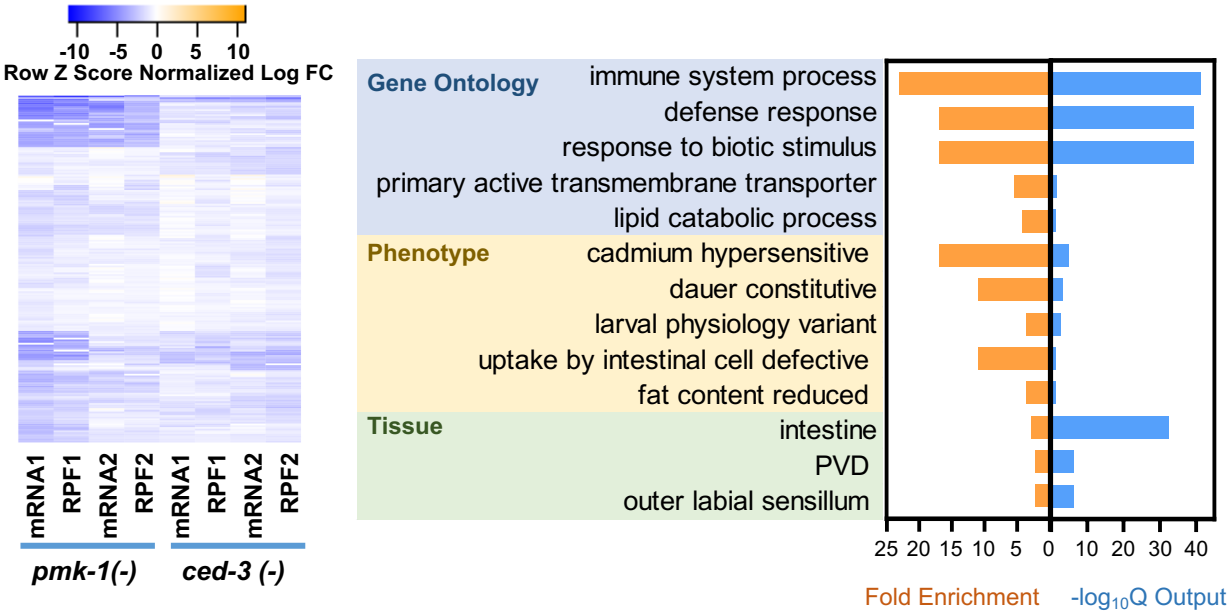
**(C-D)** RNAse I was titrated to obtain ribosome protected fragments (RPFs) around 28-30 nt in length. mRNA and RPF libraries were gel purified prior to sequencing. Red boxes indicate region of gel cut for purification. Replicates were collected and processed by ribosome profiling independently on different days. Distribution of read lengths shows peak length at 28-30 nt for all samples.

**(E)** Multidimensional scaling plots show that strains and sample types (total vs. RPFs) clustered more closely to their cognate replicate than any other sample. Additionally, *pmk-1(-)* samples showed the most variability.

**(F)** Biological replicates of RPFs for the *nlp-29-31* family showing opposing regulation by CED-3 and PMK-1. Five out of six biological replicates showed upregulation of the *nlp-29-31* family in *ced-3(-)* mutants and all replicates showed down-regulation by *pmk-1(-)* mutants.

## Figure S4. Related to Figure 3

## Genes down-regulated in both *ced-3(-)* and *pmk-1(-)*




## Genes up-regulated in both *ced-3(-)* and *pmk-1(-)*

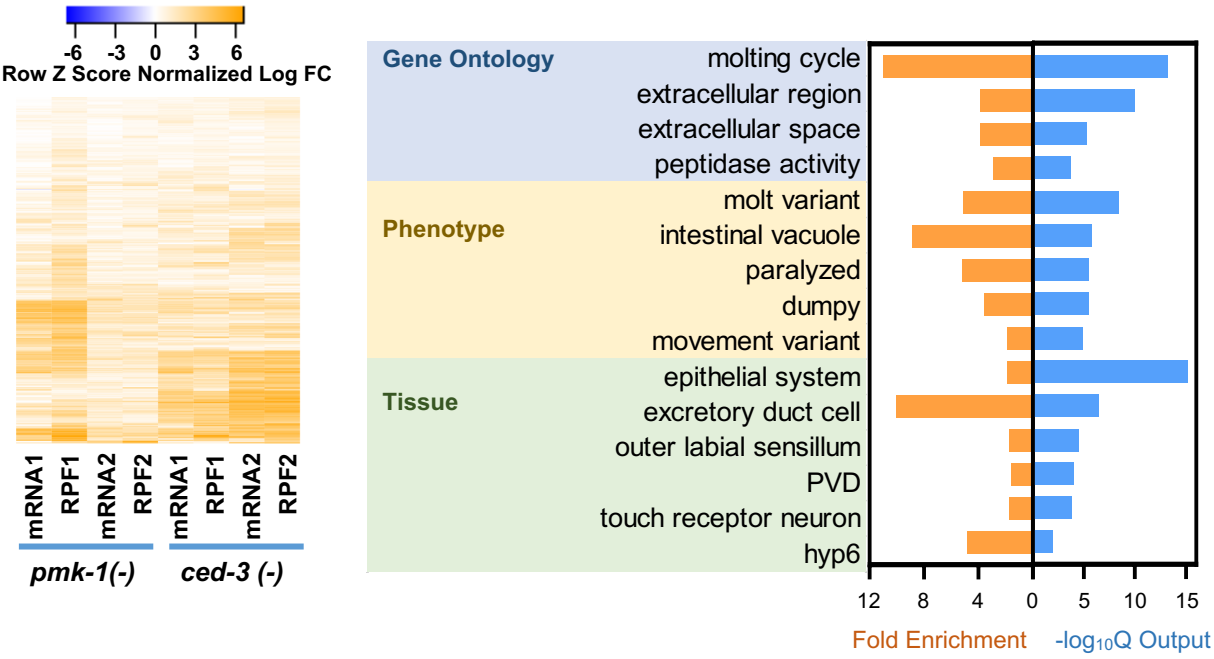



**Figure S4. Related to Figure 3. Analyses of genes found up- and down-regulated in both *ced-3(-)* and *pmk-1(-)* mutants.**

Gene enrichment analysis showed that genes down-regulated by both *ced-3(-)* and *pmk-1(-)* were enriched for intestinal immune genes, whereas genes upregulated by both *ced-3(-)* and *pmk-1(-)* were enriched for epithelial, secretory, and molting genes.

# Figure S5. Related to Figure 3

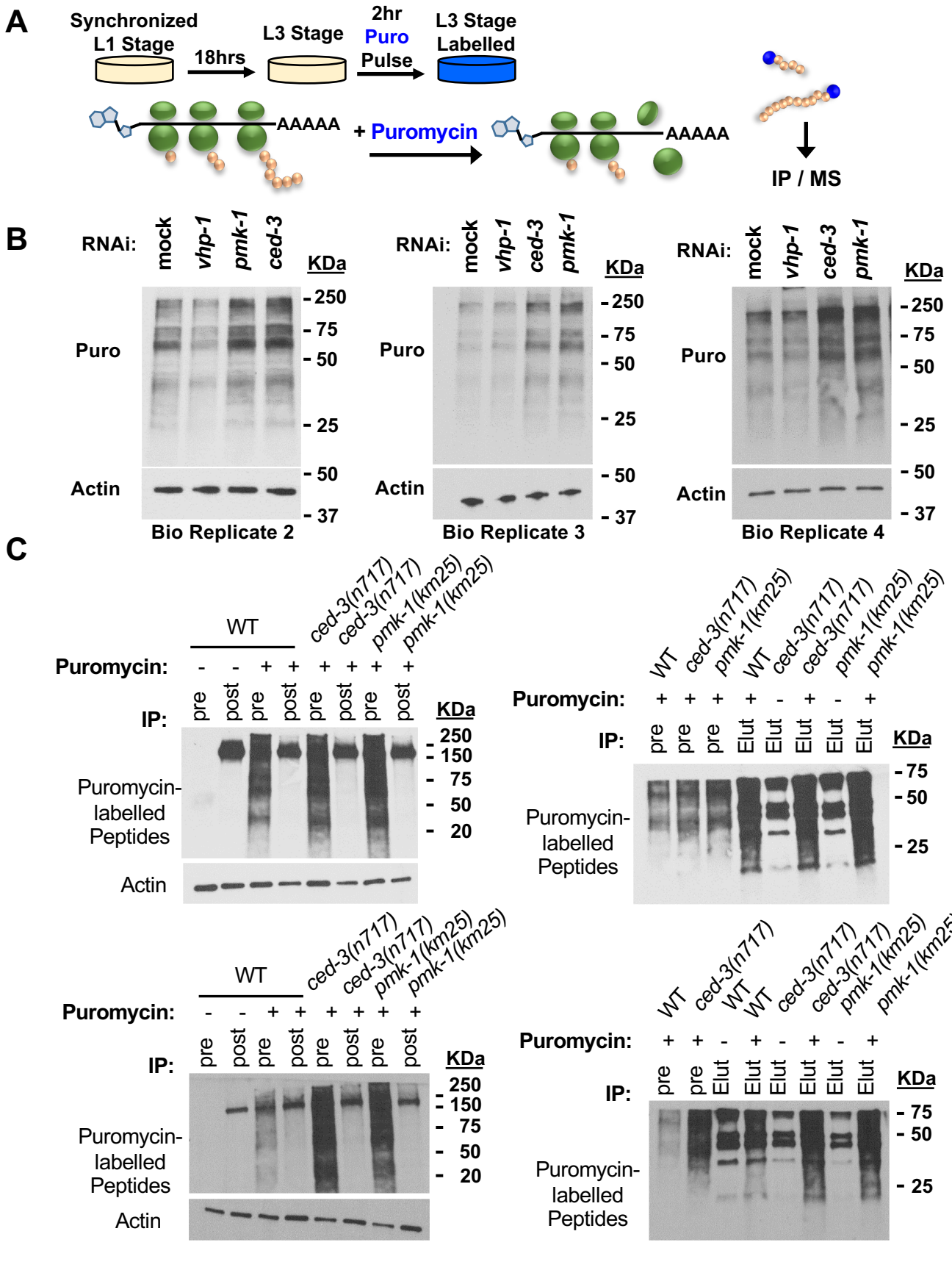


**Figure S5. Related Figure 3. Replicates for Puromycin Labeling of Translating Peptides**

**(A)** Cartoon summary of Puromycin pulse labeling for mass-spectrometry.

**(B)** Raw images of independent replicates used for quantification shown in **Figure 3E**. Lanes on right sides of each replicate removed as these were unrelated experiments.

**(C)** Raw images of two biological replicates for puromycin pull downs prior to mass-spectrometry. Images show quantitative depletion of puromycin-labeled proteins from supernatants. Bands seen in the puromycin (-) lanes correspond to the anti-puromycin antibody. The puromycin (-) samples were also assayed by mass-spectrometry to confirm there was very little background binding of proteins in the absence of puromycin (control versus puro columns in **Table S2**).

## Figure S6. Related to Figure 4

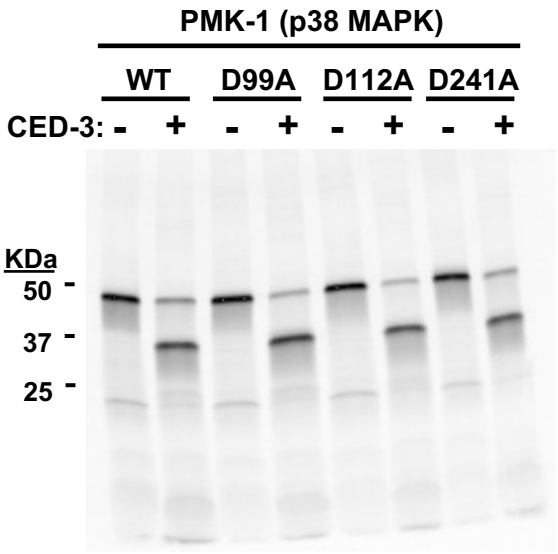



**Figure S6. Related to Figure 4.** Additional Asp to Ala mutants that do not block cleavage. *In vitro* cleavage analysis with purified CED-3 to test additional Asp sites in PMK-1.

# Table S3. Related to STAR Methods and Key Resources Table

| Oligo | Description | Sequence |
|---|---|---|
| P1 | qPCR primers for reference gene rpl-4 | CGGACGTCTTATCATCTGGACCG |
| P2 | qPCR primers for reference gene rpl-4 | CACTGGGTTCTTCTTTGGAGCTCTG |
| P3 | qRT-PCR primers for pmk-1 epidermal target nlp-29 | CAACCTCTTCAATTCTTGTTCTTGTCGTCC |
| P4 | qRT-PCR primers for pmk-1 epidermal target nlp-29 | CTTTCCCCATCCTCCATACATTCCGCGT |
| P5 | qRT-PCR primers for pmk-1 epidermal target nlp-29 | AGGATATGGAAGAGGATATGGAGGA |
| P6 | qRT-PCR primers for pmk-1 epidermal target nlp-29 | CGCATTGTTACATAACGAAATGAGA |
| P7 | qPCR primers for kgb-1 target mRNA kreg-1 | CAATCCATATGGAGCCTACGGGAATG |
| P8 | qPCR primers for kgb-1 target mRNA kreg-1 | CCAAAATGATGGCCATGATGATGATG |
| P9 | qPCR primers for kgb-1 target mRNA kreg-2 (lys-3) | TGATTAGAAGTGCGAAGAATCTGGGCTT |
| P10 | qPCR primers for kgb-1 target mRNA kreg-2 (lys-3) | GGTCCAAATGGACGGAAATCTTCAAGA |
| P11 | qPCR primer for elt-2 target mRNA F08G5.6 | CGGCAAGTGGCTATATGAATCTGAATCA |
| P12 | qPCR primer for elt-2 target mRNA F08G5.6 | CGAGAAGCACTTTTGATTCACTTGTTGG |