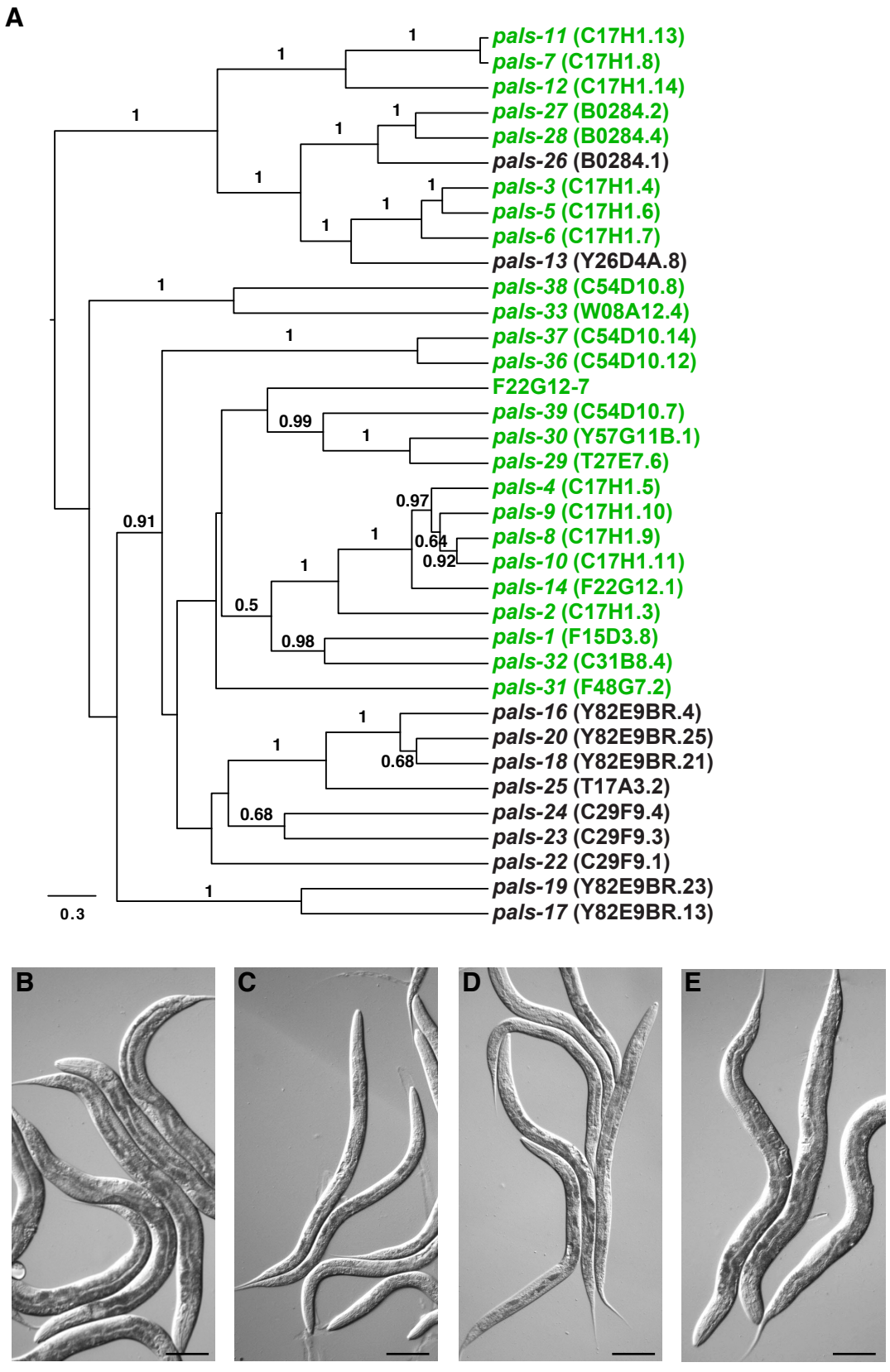
A
pals-11 (C17H1.13)
pals-7 (C17H1.8)
pals-12 (C17H1.14)
pals-27 (B0284.2)
pals-28 (B0284.4)
pals-26 (B0284.1)
pals-3 (C17H1.4)
pals-5 (C17H1.6)
pals-6 (C17H1.7)
pals-13 (Y26D4A.8)
pals-38 (C54D10.8)
pals-33 (W08A12.4)
pals-37 (C54D10.14)
pals-36 (C54D10.12)
F22G12-7
pals-39 (C54D10.7)
pals-30 (Y57G11B.1)
pals-29 (T27E7.6)
pals-4 (C17H1.5)
pals-9 (C17H1.10)
pals-8 (C17H1.9)
pals-10 (C17H1.11)
pals-14 (F22G12.1)
pals-2 (C17H1.3)
pals-1 (F15D3.8)
pals-32 (C31B8.4)
pals-31 (F48G7.2)
pals-16 (Y82E9BR.4)
pals-20 (Y82E9BR.25)
pals-18 (Y82E9BR.21)
pals-25 (T17A3.2)
pals-24 (C29F9.4)
pals-23 (C29F9.3)
pals-22 (C29F9.1)
pals-19 (Y82E9BR.23)
pals-17 (Y82E9BR.13)
0.3
B
C
D
E

Figure S1. Phylogeny of *pals* genes, and *pals-22* mutant developmental phenotypes. Related to Figure 1.

(A) Phylogenetic relationships of *pals* genes were inferred from the amino acid alignment using Bayesian MCMC. Internal branch labels indicate the posterior probability, labels with less than 0.5 support are not shown. Genes that are upregulated upon infection are highlighted in green. [S1-S3] (B-E) Smaller size of *pals-22* mutants shown with images of (B) wild type, (C) *pals-22(jy1)*, (D) *pals-22(jy3)*, and (E*) pals-22(jy3); jyEx193[pals-22(+)]* animals at 48 hours after the L1 larval stage. Scale bar, 100 μm.

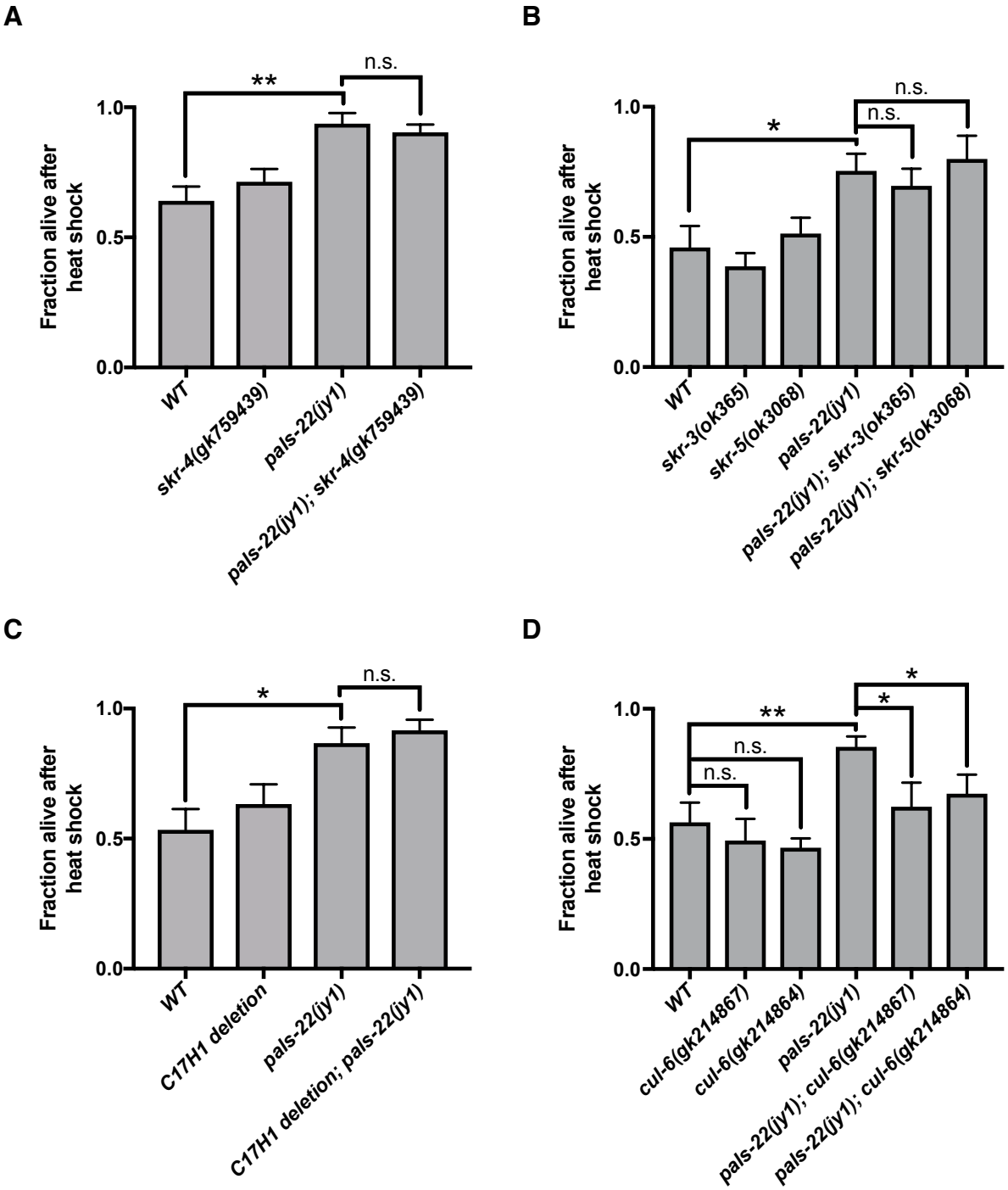
A
Fraction alive after heat shock
1.0
0.5
0.0
**
n.s.
WT
skr-4(gk759439)
pals-22(jy1)
pals-22(jy1); skr-4(gk759439)
B
Fraction alive after heat shock
1.0
0.5
0.0
*
n.s.
n.s.
WT
skr-3(ok365)
skr-5(ok3068)
pals-22(jy1)
pals-22(jy1); skr-3(ok365)
pals-22(jy1); skr-5(ok3068)
C
Fraction alive after heat shock
1.0
0.5
0.0
*
n.s.
WT
C17H1 deletion
pals-22(jy1)
C17H1 deletion; pals-22(jy1)
D
Fraction alive after heat shock
1.0
0.5
0.0
**
n.s.
n.s.
*
*
WT
cul-6(gk214867)
cul-6(gk214864)
pals-22(jy1)
pals-22(jy1); cul-6(gk214867)
pals-22(jy1); cul-6(gk214864)

Figure S2. Analysis of the effects of IPR gene mutations on thermotolerance of *pals-22* mutants. Related to Figure 2.

(A-D) Survival of animals after 2h heat shock treatment at 37°C, followed by 24h at 20°C. Strains were tested in triplicate. Mean fraction alive indicates the average survival among the triplicates, errors bars are SD. ** $p < 0.01$, * $p < 0.05$, n.s., not significant with Student's t-test. Assays were repeated three independent times with similar results, and data from a representative experiment are shown.

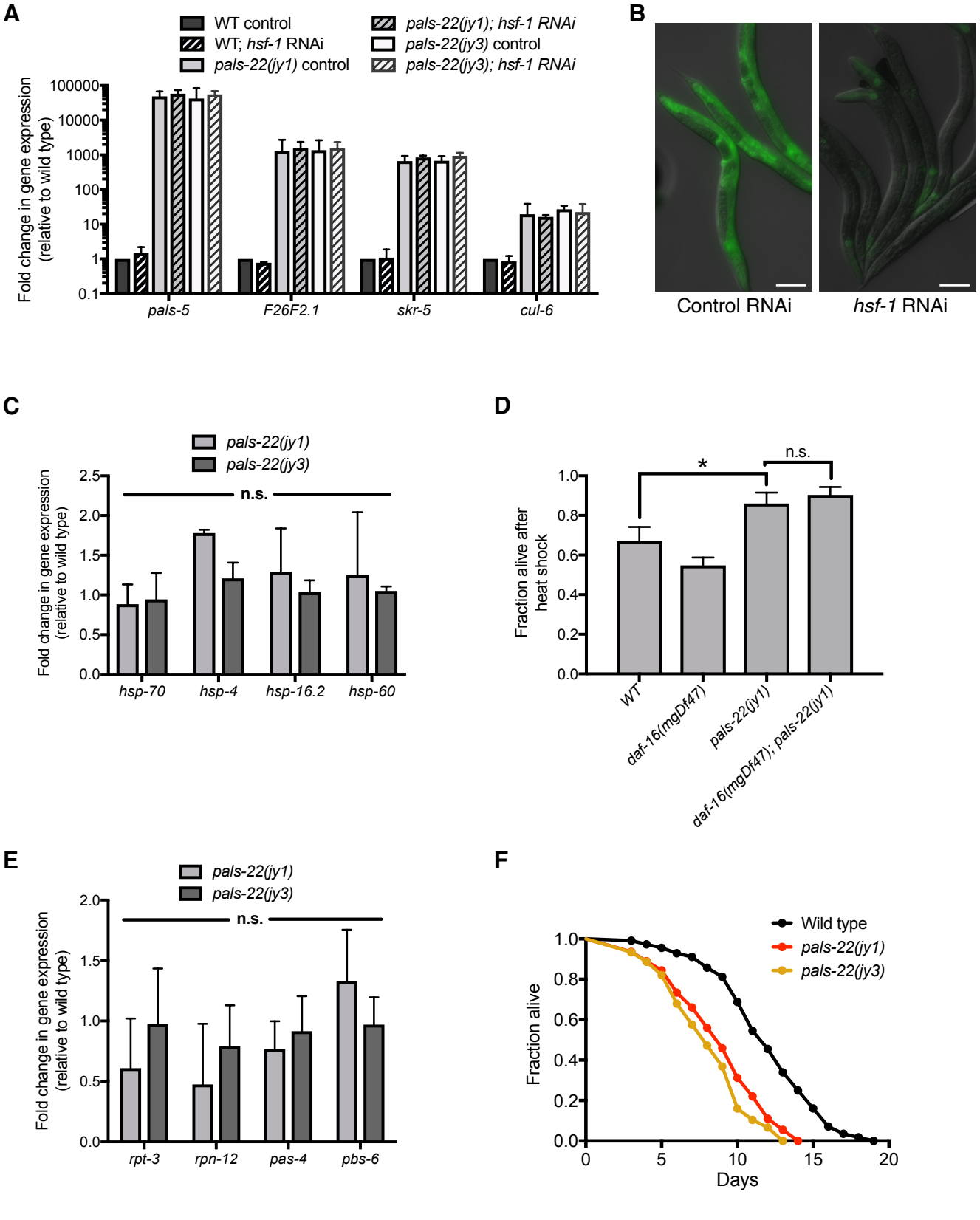
A
WT control
WT; hsf-1 RNAi
pals-22(jy1) control
pals-22(jy1); hsf-1 RNAi
pals-22(jy3) control
pals-22(jy3); hsf-1 RNAi
Fold change in gene expression (relative to wild type)
100000
10000
1000
100
10
1
0.1
pals-5
F26F2.1
skr-5
cul-6
B
Control RNAi
hsf-1 RNAi
C
pals-22(jy1)
pals-22(jy3)
Fold change in gene expression (relative to wild type)
n.s.
2.5
2.0
1.5
1.0
0.5
0.0
hsp-70
hsp-4
hsp-16.2
hsp-60
D
Fraction alive after heat shock
*
n.s.
1.0
0.8
0.6
0.4
0.2
0.0
WT
daf-16(mgDf47)
pals-22(jy1)
daf-16(mgDf47); pals-22(jy1)
E
pals-22(jy1)
pals-22(jy3)
Fold change in gene expression (relative to wild type)
n.s.
2.0
1.5
1.0
0.5
0.0
rpt-3
rpn-12
pas-4
pbs-6
F
Wild type
pals-22(jy1)
pals-22(jy3)
Fraction alive
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
Days

Figure S3. Analysis of the interaction between *pals-22* and previously characterized stress resistance pathways. Related to Figure 2.

(A) qRT-PCR measurement of IPR gene expression in wild type, *pals-22(jy1)*, and *pals-22(jy3)* animals treated with either control RNAi (L4440) or *hsf-1* RNAi, shown as the fold change relative to wild-type control. Results shown are the average of two independent biological replicates, error bars are SD. (B) Control for *hsf-1* RNAi efficacy. Robust induction of *hsp-16.2p::GFP* after heat shock (left, L4440 RNAi control) is strongly reduced by *hsf-1* RNAi treatment (right). Images are overlays of green and Nomarski channels and were taken with the same camera exposure. Scale bar, 100 μm. (C) qRT-PCR measurement of *hsp* gene expression in wild type, *pals-22(jy1)*, and *pals- 22(jy3).* Results shown are the average of two independent biological replicates, error bars are SD. n.s., not significant with Student's t-test. (D) Survival of animals after 2h heat shock treatment at 37°C followed by 24h at 20°C. Strains were tested in triplicate. Mean fraction alive indicates the average survival among the triplicates, errors bars are SD. * $p < 0.05$, n.s., not significant with Student's t-test. Heat shock assay was repeated three independent times with similar results, and data from a representative experiment are shown. (E) qRT-PCR measurement of proteasome subunit gene expression in *pals-22(jy1)* and *pals-22(jy3)* animals, shown as the fold change relative to wild-type control. Results shown are the average of two independent biological replicates, error bars are SD. n.s., not significant with Student's t-test. (F) Lifespan of wild type, *pals-22(jy1)*, and *pals-22(jy3)* animals. Assays were performed with at least 30 animals per plate, and three plates per strain per experiment. Experiment was repeated two independent times with similar results, with data from a representative experiment shown. *p*-value for *pals-22(jy1)* and *pals-22(jy3)* compared to wild type is <0.0001 using the Log-rank test.

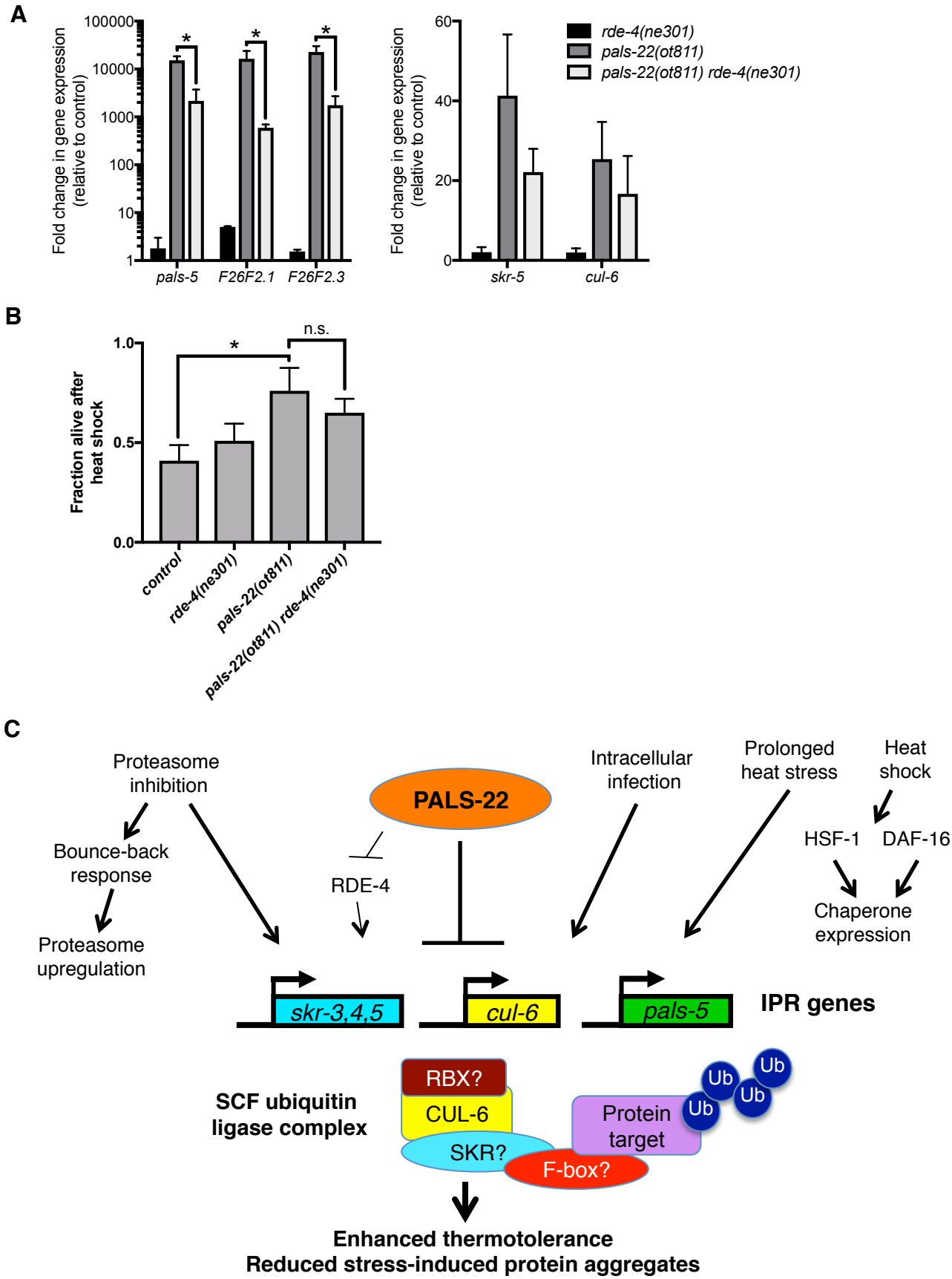
A
Fold change in gene expression (relative to control)
100000
10000
1000
100
10
1
*
*
*
pals-5
F26F2.1
F26F2.3
Fold change in gene expression (relative to control)
60
40
20
0
rde-4(ne301)
pals-22(ot811)
pals-22(ot811) rde-4(ne301)
skr-5
cul-6
B
Fraction alive after heat shock
1.0
0.5
0.0
*
n.s.
control
rde-4(ne301)
pals-22(ot811)
pals-22(ot811) rde-4(ne301)
C
Proteasome inhibition
Bounce-back response
Proteasome upregulation
PALS-22
RDE-4
Intracellular infection
Prolonged heat stress
Heat shock
HSF-1
DAF-16
Chaperone expression
skr-3,4,5
cul-6
pals-5
IPR genes
SCF ubiquitin ligase complex
RBX?
CUL-6
SKR?
F-box?
Protein target
Ub
Ub
Ub
Enhanced thermotolerance
Reduced stress-induced protein aggregates

Figure S4. Interaction of *pals-22* with *rde-4* and model for IPR pathway. Related to Figure 4.

(A) qRT-PCR measurement of IPR gene expression, shown as the fold change relative to control. All strains contain the *otIs381* array. Results shown are the average of two independent biological replicates, error bars are SD. * $p < 0.05$ with Student's t-test. (B) Survival of animals after 2h heat shock treatment at 37°C followed by 24h at 20°C. All strains contain the *otIs381* array. Strains were tested in triplicate. Mean fraction alive indicates the average survival among the triplicates, errors bars are SD. Assay was repeated three independent times with similar results, and data from a representative experiment are shown. In all three replicates, *pals-22(ot811) rde-4(ne301)* animals had decreased average survival after heat shock as compared to *pals-22(ot811)* animals. * $p < 0.05$, n.s., not significant with Student's t-test. (C) Model for IPR pathway providing increased proteostasis capacity, independent of other known stress response pathways.

skr-3 qPCR forward	CCGACAGCCAGAAACAAATCA
skr-3 qPCR reverse	TCTGTGATGGTCTTGGATTGAC
skr-4 qPCR forward	CCGACAGCCAGAAACAAATCA
skr-4 qPCR reverse	GGTCTTGGATTGGCTGATCAC
skr-5 qPCR forward	CGAAGAGCAAGATGTCAAAATTG
skr-5 qPCR reverse	AGAAGCTTGGATTGATTGGCA
cul-6 qPCR forward	CTGGGCTTACTCACAATGCC
cul-6 qPCR reverse	GCAGAGTTGGCTTGCTGTAA
skr-1 qPCR forward	GGCAAAGGAACGCGAAATCA
skr-1 qPCR reverse	TTGAGAGACGGATCACATTGC
pals-5 qPCR forward	CATTGGAAAGCGATATTGGA
pals-5 qPCR reverse	TCTCCAGGCACCTATCTTGTAG
F26F2.1 qPCR forward	TGGAACCAGGTCAGAGACAC
F26F2.1 qPCR reverse	TTGTGAGAATTTCCGCGATA
F26F2.3 qPCR forward	GGAAAGGGAATGCATTATGG
F26F2.3 qPCR reverse	CCGCACGGTTATTTCTCAT
F26F2.4 qPCR forward	CAACAATACACTGCGGATGG
F26F2.4 qPCR reverse	TCGCACTGTTATTCATCTCCA
hsp-70 qPCR forward	CTTGGTTGGGGGATCAACT
hsp-70 qPCR reverse	TGCTTCGTCTGGATTAATGG
hsp-4 qPCR forward	CATCTCGTGGAATCAACCCT
hsp-4 qPCR reverse	ACTTAGTCATGACTCCTCCG
hsp-16.2 qPCR forward	TGCAGAATCTCTCCATCTGAGT
hsp-16.2 qPCR reverse	TGGTTTAAACTGTGAGACGTTGA
hsp-60 qPCR forward	CAAGGCTCCAGGATTCG
hsp-60 qPCR reverse	AAAGATCGTTGCTCCCG
snb-1 qPCR forward	CCGGATAAGACCATCTTGACG
snb-1 qPCR reverse	GACGACTTCATCAACCTGAGC
rpt-3 qPCR forward	CCCAAGAGGAGTTCTCATGTA
rpt-3 qPCR reverse	ATGAAGGAAGCAGCAGTATT
rpn-12 qPCR forward	CTGCCAACAGATTGTCC
rpn-12 qPCR reverse	GGCGTAGAGATGTAAGCG
pas-4 qPCR forward	CGAGCCATCTGGAGCTTACTA
pas-4 qPCR reverse	TCCTCAAGGTATTCACGCAC
pbs-6 qPCR forward	TGGACAGAGCCATCTCATT
pbs-6 qPCR reverse	CTTCAGCGATGACCAAGTG
pals-22 promoter forward	AGTAGTGCTGAAAAATTTTAAATG
pals-22 promoter reverse	GGATTTCTGTAACATGGG
vha-6 promoter forward	TTCCACCATTGTGGTGAGAC
vha-6 promoter reverse	TAGTCGCCCTGAAATTAAAC
unc-119 promoter forward	TGTGCCAAGCTTCAGTAAAAGAAGTAG
unc-119 promoter reverse	ATATGCTGTTGTAGCTGAAAATTTTG
dpy-7 promoter forward	AATCTCATTCCACGATTTCTCGCAA
dpy-7 promoter reverse	CATTTATCTGGAACAAAATGTAAG

C17H1.3 sgRNA sequence	GAACAGAGTGAAGCAGGAAG
C17H1.7 sgRNA sequence	ACGGGCAGATATACAGAGAC
C17H1 CRISPR ssDNA repair template	ATTTTGCTCTTATCACATTTATAGAAATGACAAAAGTCACCGAGCCCTCGGTTTTTCTTTGCGATAGTTCAGAGCTTCTCAAATCTCTCA
dpy-10(cn64) CRISPR ssDNA repair template	CACTTGAACTTCAATACGGCAAGATGAGAATGACTGGAACCGTACCGCATGCGGTGCCTATGGTAGCGGAGCTTCACATGGCTTCAGACCAACAGCCT
dpy-10(cn64) sgRNA sequence	GCTACCATAGGCACCACGAG
GW503 C17H1 deletion genotyping	GTTAGAAATGCGCTGTGACGT
GW504 C17H1 deletion genotyping	AGCTCGCTCAGCATTGTTG
GW515 C17H1 deletion genotyping	GGAATGGTACTACCAGTGCTG

Table S1. Primers used in this study. Related to STAR methods.

Supplemental References

S1. Bakowski, M.A., Desjardins, C.A., Smelkinson, M.G., Dunbar, T.L., Lopez-Moyado, I.F., Rifkin, S.A., Cuomo, C.A., and Troemel, E.R. (2014). Ubiquitin-mediated response to microsporidia and virus infection in C. elegans. PLoS Pathog *10*, e1004200.

S2. Chen, K., Franz, C.J., Jiang, H., Jiang, Y., and Wang, D. (2017). An evolutionarily conserved transcriptional response to viral infection in Caenorhabditis nematodes. BMC genomics *18*, 303.

S3. Sarkies, P., Ashe, A., Le Pen, J., McKie, M.A., and Miska, E.A. (2013). Competition between virus-derived and endogenous small RNAs regulates gene expression in Caenorhabditis elegans. Genome research *23*, 1258-1270.