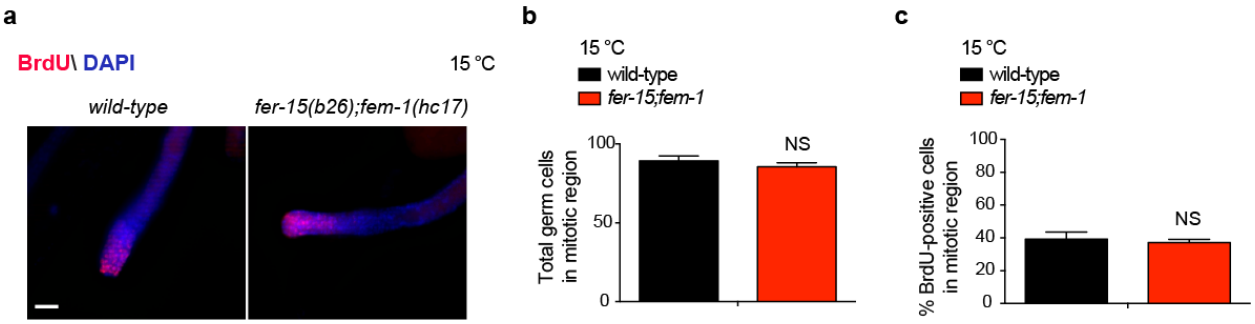
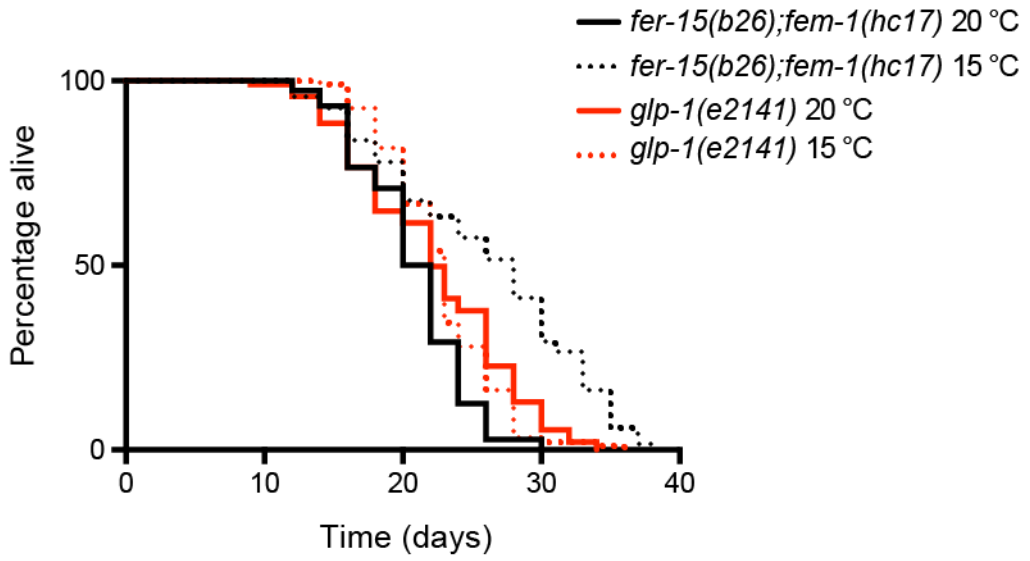
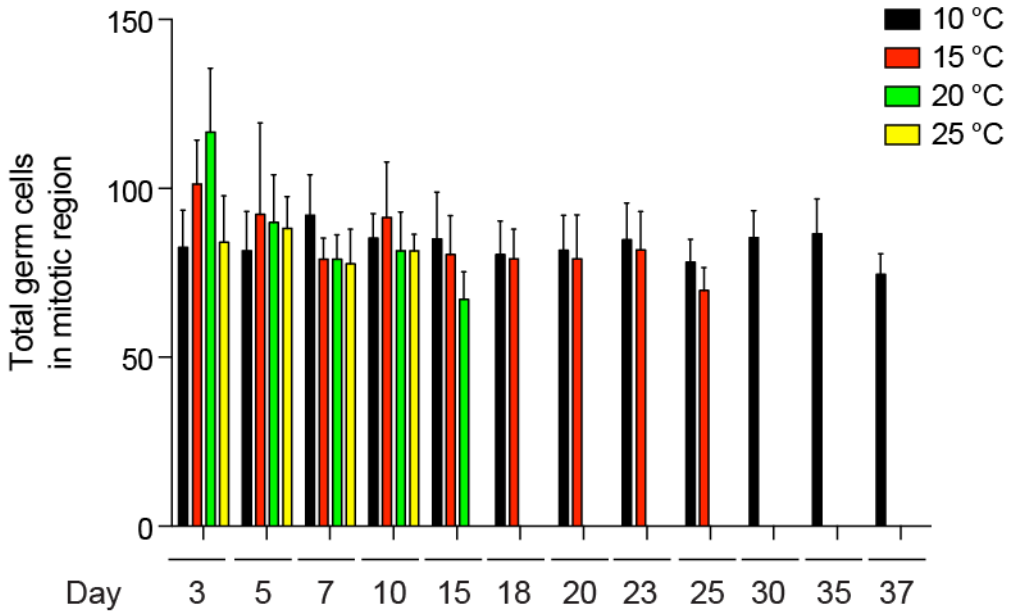


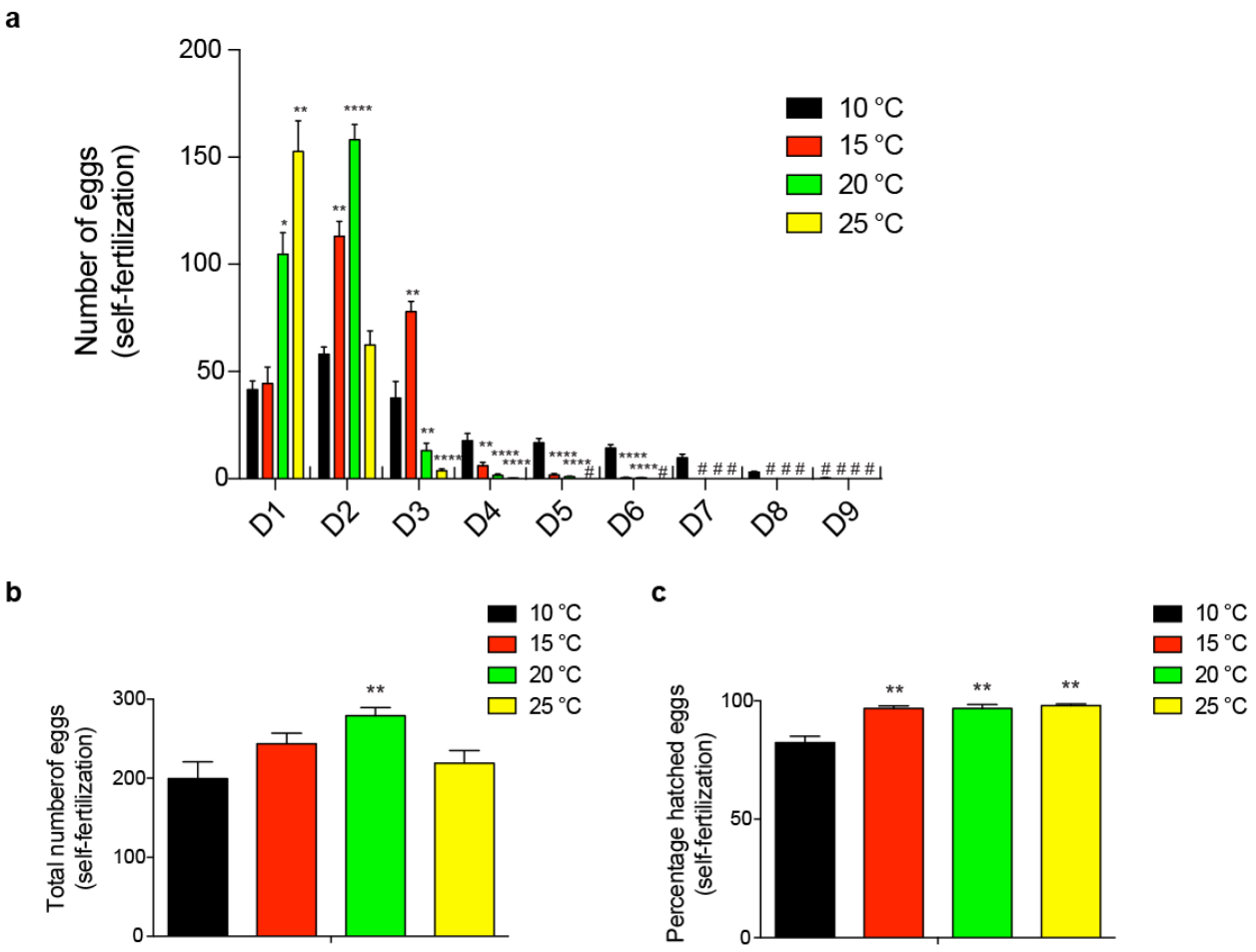
Supplementary Figure 1. The total number of germ cells and percentage of proliferating cells within the mitotic region are not affected in *fer-15;fem-1* sterile mutants. a, Bromodeoxyuridine (BrdU) staining of proliferating germ cells. Wild-type and *fer-15(b26);fem-1(hc17)* worms were raised at 25°C during development and adult worms were shifted to 15°C. The germ lines were extruded after 2 h BrdU treatment at day 6 of adulthood. Cell nuclei were stained with DAPI. Scale bar represents 20 µm. The images are representative of 2 independent experiments. **b,** Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., 16 germ lines scored per condition from 2 independent experiments). NS= not significant (P=0.3564). **c,** Graph represents the percentage of BrdU-positive cells/total nuclei within the mitotic region (mean ± s.e.m., 16 germ lines scored per condition from 2 independent experiments). NS= not significant (P=0.6539). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples.



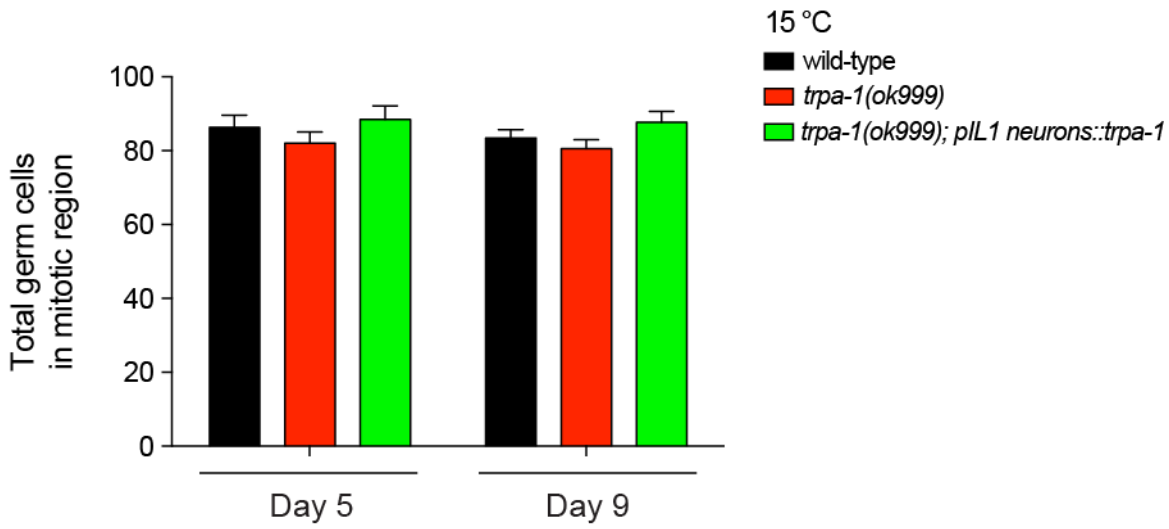
Supplementary Figure 2. Low temperature during adulthood increases lifespan of control sterile *fer-15;fem-1* mutants whereas it does not extend lifespan of germline-lacking worms. Temperature reduction (15°C) extends lifespan of control sterile *fer-15;fem-1* mutants with proliferating germ line (*fer-15;fem-1* 20°C mean ± s.e.m: 20.44 ± 0.44, *fer-15;fem-1* 15°C: 26.90 ± 0.89, P<0.0001), but not *glp-1* germline-lacking worms (*glp-1* 20°C: 22.23 ± 0.60, *glp-1* 15°C: 22.73 ± 0.42, P= 0.6075). Sterile control worms are long lived compared with *glp-1* mutant worms at cold temperature (*fer-15;fem-1* 15°C versus *glp-1* 15°C, P<0.0001). P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



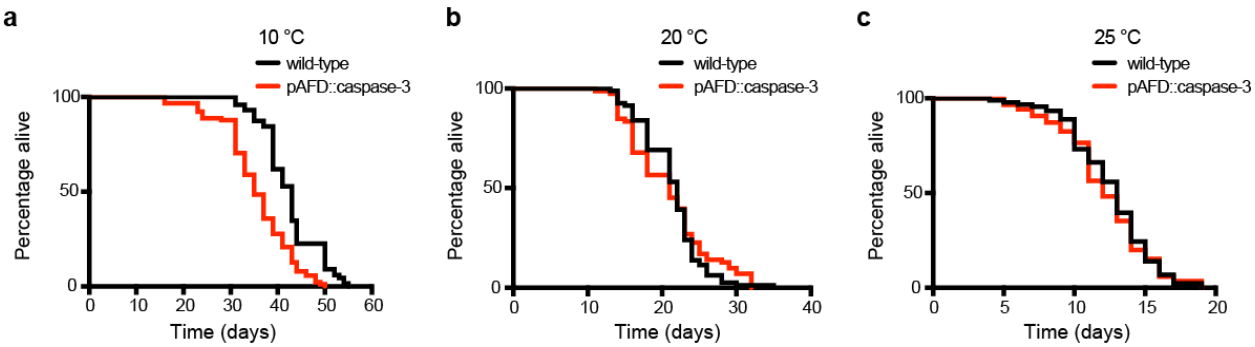
Supplementary Figure 3. The total number of germ cells within the mitotic region did not change with age or temperature. Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., 10°C D3-37, 15°C D3-23 (n=20 germ lines), 15°C D23, 20°C D3-15, 25°C D3-10 (n= 15), germ lines were scored per each condition from 3 independent experiments). We did not examine the germ line after day 15 at 25°C, day 18 at 20°C, day 25 at 15°C and day 37 at 10°C as the percentage of BrdU-positive cells was below 10% at the indicated ages/temperatures (please see **Figure 2d**). Wild-type larvae were raised at 20°C until adulthood and then shifted to the indicated temperatures. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. No significant differences were found (P>0.05 was considered not significant).



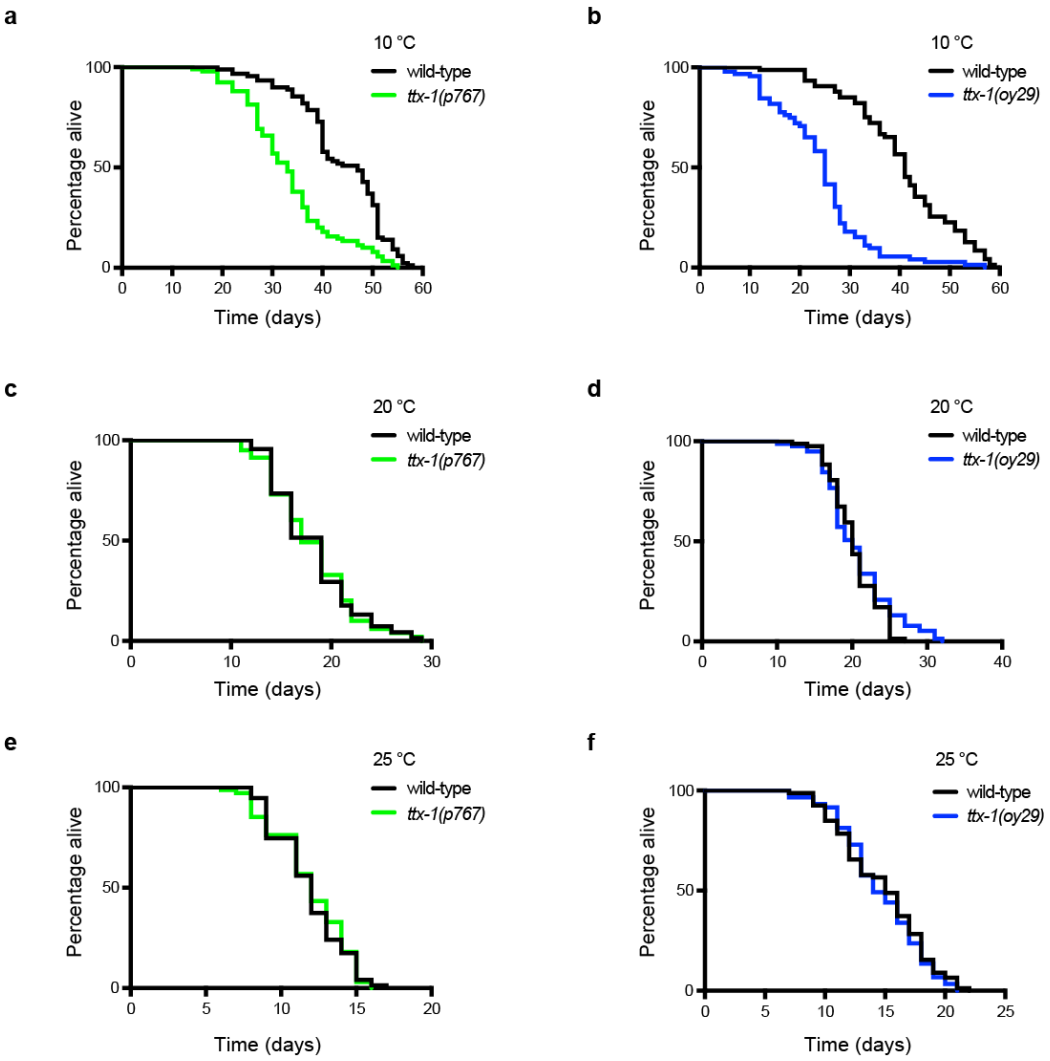
Supplementary Figure 4. Exposure to different temperatures during adulthood does not have strong effects on self-fertility. a, Number of eggs laid per wild-type hermaphrodite every 24 h during the self-reproductive period at different temperatures (mean ± s.e.m., n= 63 worms scored per condition from 3 independent experiments). Worms were exposed to the indicated temperatures during adulthood. (#) no eggs were laid. **b,** Total number of eggs laid at different temperatures during the self-fertilization period (mean ± s.e.m., n= 63 worms scored per condition from 3 independent experiments). **c,** Percentage of hatched eggs at different temperatures (mean ± s.e.m., n= 4 independent experiments). Almost all the eggs produced by hermaphrodites at 15°C, 20°C and 25°C were viable (96-98%). Despite a slight but significant decrease at 10°C, most of the eggs were also viable (82%) at this temperature. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: *(P<0.05), **(P<0.01), ****(P<0.0001).



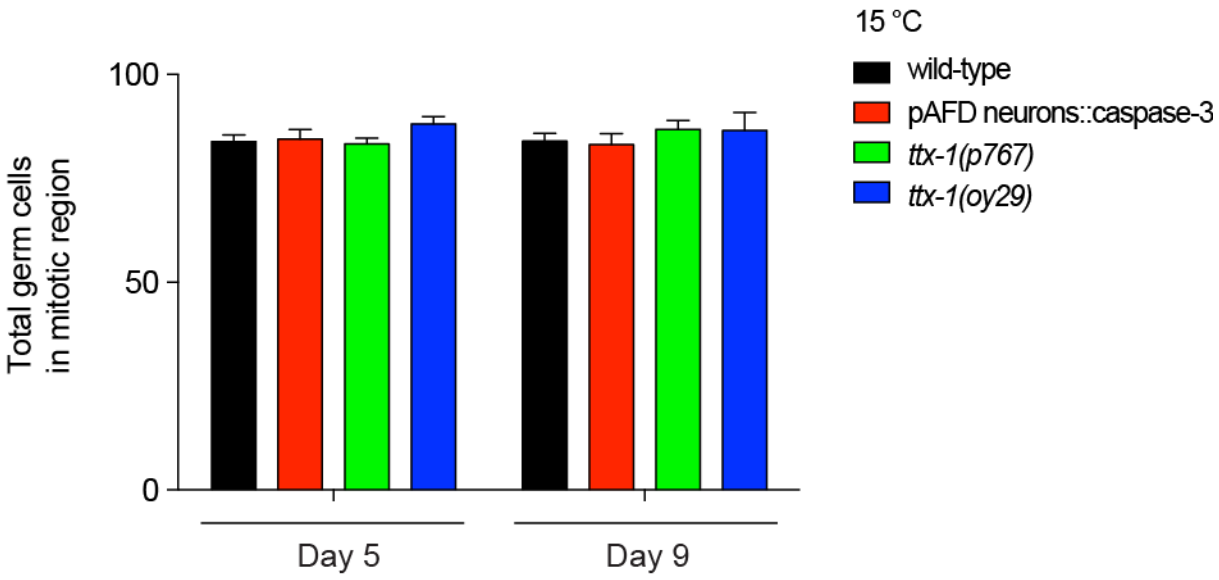
Supplementary Figure 5. Loss of *trpa-1* channel does not affect the total number of germ cells within the mitotic region. Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining in the indicated strains at day 5 and 9 of adulthood (mean ± s.e.m., 15 germ lines scored per condition from 2 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. No significant differences were found. Day 5: wild-type versus *trpa-1* (P=0.3515); wild-type versus *trpa-1;pIL1::trpa-1* (P=0.6666). Day 9: wild-type versus *trpa-1* (P=0.3780); wild-type versus *trpa-1;pIL1::trpa-1* (P=0.2478).



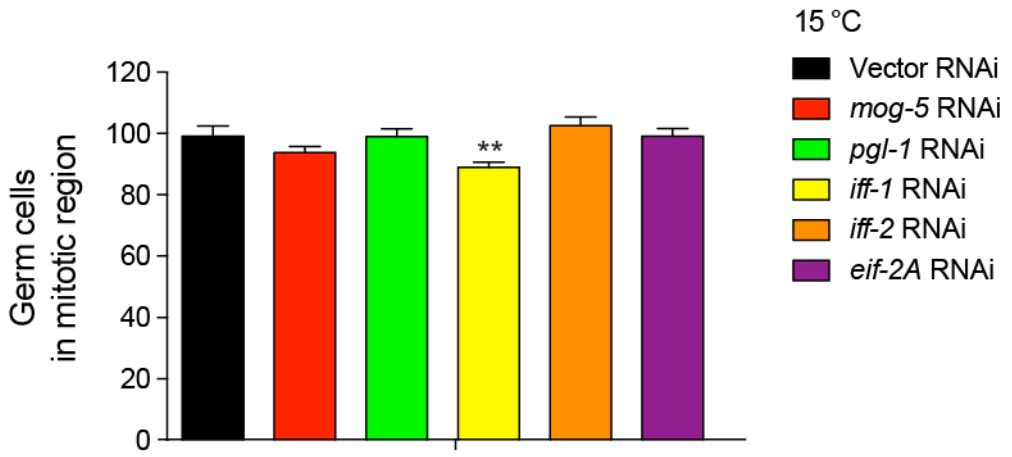
Supplementary Figure 6. Ablation of AFD neurons diminishes cold-induced longevity. a, AFD-ablated transgenic worms live shorter when compared to wild-type strain at 10°C (N2 wild-type mean ± s.e.m: 42.51 ± 0.70, pAFD::caspase-3: 35.55 ± 0.77, P< 0.0001). **b,** AFD-ablated transgenic worms do not live shorter when compared to wild-type strain at 20°C (N2: 21.24 ± 0.45, pAFD::caspase-3: 20.85 ± 0.64, P= 0.6869). **c,** Lifespan of AFD-ablated transgenic worms compared with wild-type strain at 25°C (N2: 12.57 ± 0.30, pAFD::caspase-3: 12.16 ± 0.34, P= 0.6240). P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



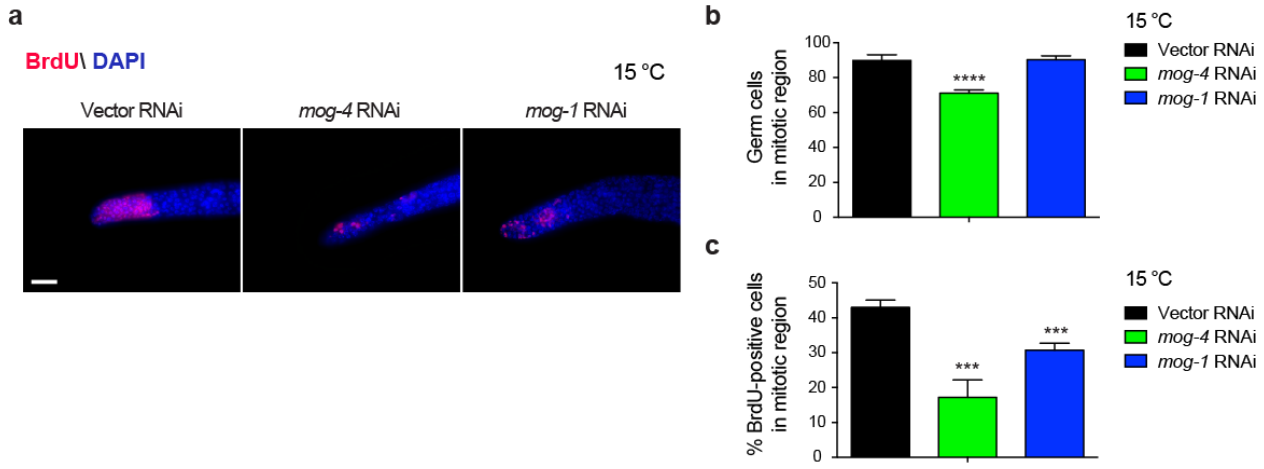
Supplementary Figure 7. *ttx-1* mutant worms are short-lived at cold-temperature. a, *ttx-1(p767)* mutant worms live shorter when compared to wild-type strain at 10°C (N2 wild-type mean ± s.e.m: 43.88 ± 0.95, *ttx-1(p767)*: 33.34 ± 0.97, P< 0.0001). **b,** *ttx-1(oy29)* mutant worms live shorter when compared to wild-type strain at 10°C (N2 wild-type mean ± s.e.m: 40.71 ± 1.23, *ttx-1(oy29)*: 24.35 ± 1.10, P< 0.0001). **c,** Lifespan of *ttx-1(p767)* worms compared with wild-type strain at 20°C (N2 mean ± s.e.m: 18.21 ± 0.49, *ttx-1(p767)*: 18.11 ± 0.56, P= 0.9486). **d,** Lifespan of *ttx-1(oy29)* worms compared with wild-type strain at 20°C (N2 mean ± s.e.m: 20.24 ± 0.36, *ttx-1(oy29)*: 20.60 ± 0.51, P= 0.2874). **e,** Lifespan of *ttx-1(p767)* worms compared with wild-type strain at 25°C (N2 mean ± s.e.m: 11.84 ± 0.26, *ttx-1(p767)*: 12.00 ± 0.32, P= 0.8799). **f,** Lifespan of *ttx-1(oy29)* worms compared with wild-type strain at 25°C (N2 mean ± s.e.m: 14.80 ± 0.41, *ttx-1(oy29)*: 14.65 ± 0.44, P= 0.3118). P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



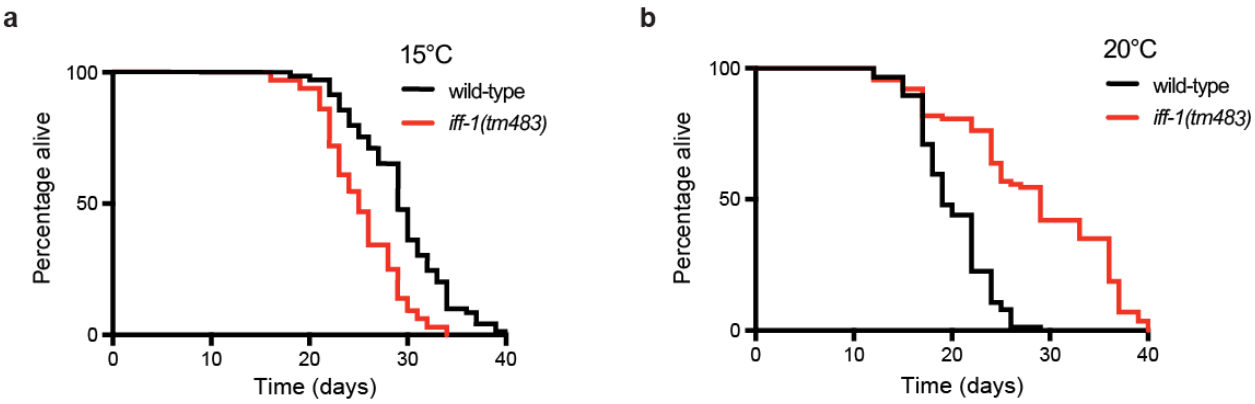
Supplementary Figure 8. Dysfunction of AFD neurons does not affect the total number of germ cells within the mitotic region. Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining in the indicated strains at day 5 and 9 of adulthood (mean ± s.e.m., day 5 (n=30 germ lines), day 9 (n=15), germ lines were scored per each condition from 3 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. No significant differences were found (P>0.05 was considered not significant).



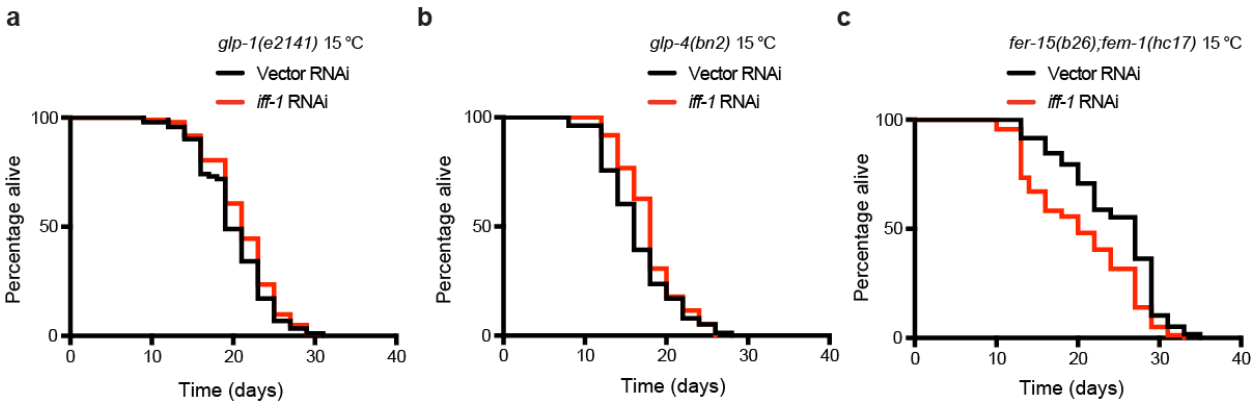
Supplementary Figure 9. Total number of germ cells within the mitotic region upon knockdown during adulthood of distinct regulators of GSC proliferation. Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., Vector, *mog-5*, *iff-1* RNAi (n= 33 germ lines), *pgl-1*, *iff-2, eif-2A* RNAi (n= 36), germ lines were scored per each condition from 3 independent experiments). Wild-type worms were examined at day 5 of adulthood. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: **(P<0.01).



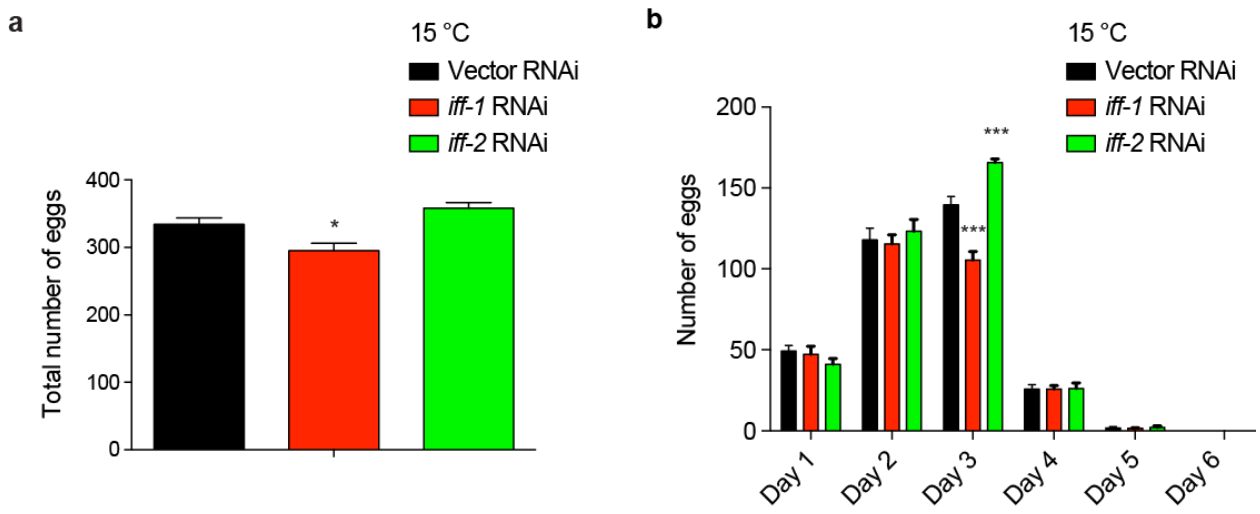
Supplementary Figure 10. Knockdown of either *mog-4* or *mog-1* during adulthood reduces germ-cell proliferation within the mitotic region. a, BrdU staining of germ lines from wild-type *C. elegans* fed with the indicated RNAi from day 1 of adulthood at 15°C. Worms were examined at day 5 of adulthood. Cell nuclei were stained with DAPI. Scale bar represents 20 µm. The images are representative of 2 independent experiments. **b,** Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., 11 germ lines scored per condition from 2 independent experiments). **c,** Graph represents the percentage of BrdU-positive cells/total nuclei (mean ± s.e.m., 11 germ lines scored per condition from 2 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: ***(P<0.001), **** (P<0.0001).



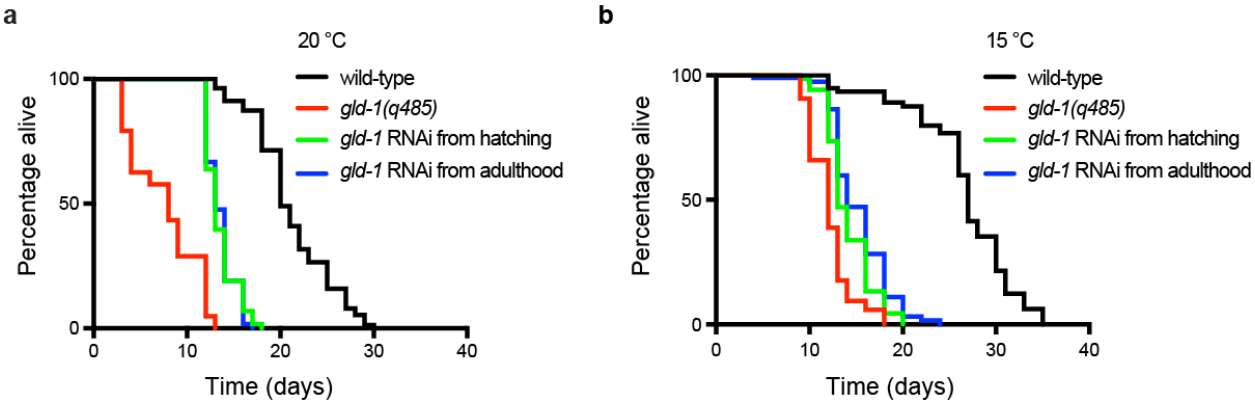
Supplementary Figure 11. *iff-1* germline-less worms are short-lived at 15°C, whereas they are long-lived at 20°C. a, *iff-1(tm483)* germline-lacking mutant *C. elegans* are short lived compared with N2 wild-type worms at cold temperature (two-sided log rank, P<0.0001). *N2* 15°C mean ± s.e.m: 29.24 ± 0.57, *iff-1* 15°C: 25.29 ± 0.49 (n= 96 worms/condition). **b,** *iff-1* germline-lacking mutant worms are long lived at 20°C (two-sided log rank, P<0.0001). *N2* 20°C mean ± s.e.m: 19.88 ± 0.42, *iff-1* 20°C: 28.14 ± 0.88 (n= 96 worms/condition). See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



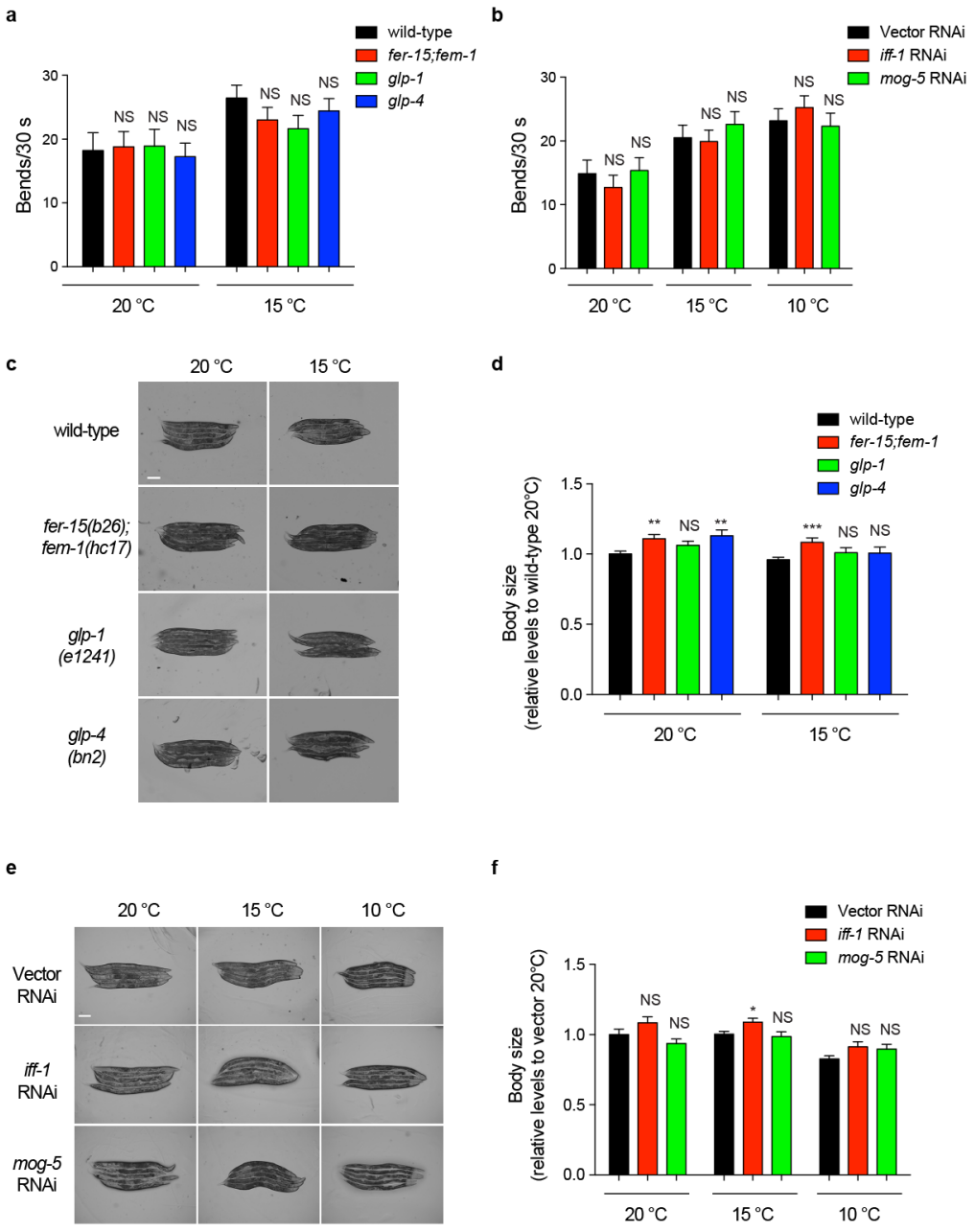
Supplementary Figure 12. Knockdown of *iff-1* does not further shorten the lifespan of germline-lacking worms at 15°C, but reduces cold-induced longevity in sterile worms with a proliferating germ line. a, Knockdown of *iff-1* during adulthood does not reduce lifespan of *glp-1(e2141)* germline-lacking worms at 15°C (two-sided log rank, P= 0.1538). Empty vector RNAi: mean ± s.e.m: 20.09 ± 0.45, *iff-1* RNAi: 21.08 ± 0.46 (n= 96 worms/condition). **b,** Loss of *iff-1* does not reduce lifespan of *glp-4(bn2)* germline-lacking worms at 15°C (two-sided log rank, P= 0.0827). Empty vector RNAi: mean ± s.e.m: 16.45 ± 0.49, *iff-1* RNAi: 17.92 ± 0.40 (n= 96 worms/condition). **c,** Loss of *iff-1* during adulthood decreases longevity induced by cold temperature (15°C) in sterile worms with a proliferating germ line (*fer-15(b26);fem-1(hc17)*). Empty vector RNAi: mean ± s.e.m: 24.35 ± 0.74, *iff-1* RNAi: 20.35 ± 0.72 (n= 96 worms/condition; two-sided log rank, P= 0.0005). See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



Supplementary Figure 13. Knockdown of *iff-1* does not strongly affect the number of eggs laid by self-fertilizing hermaphrodites. a, Total number of eggs laid at 15°C during the self-reproductive period (mean ± s.e.m., n= 30 worms scored per condition from 3 independent experiments). RNAi was initiated during adulthood of wild-type worms. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: *(P<0.05). **b,** Number of eggs laid every 24 h during the self-reproductive period at 15°C (mean ± s.e.m., n= 30 worms scored per condition from 3 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: ***(P<0.001).

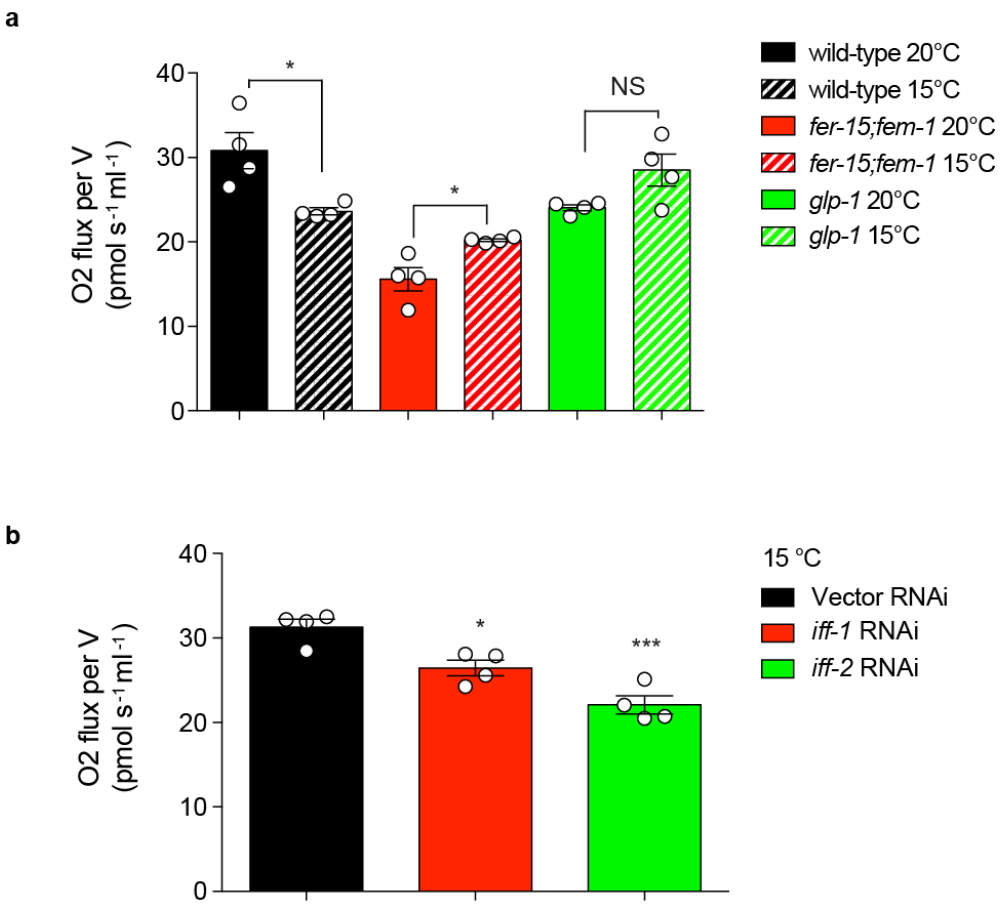


Supplementary Figure 14. Over-proliferation of the germline caused by either tumorous *gld-1* mutations or *gld-1* knockdown kills *C. elegans* early in life. a, *gld-1(q485)* allele and *gld-1* RNAi shortens lifespan at 20°C. Wild type + empty vector RNAi: 21.17 ± 0.47; *gld-1(q485)* + empty vector RNAi: 7.54 ± 0.43, P<0.0001; wild-type + *gld-1* RNAi from hatching: 13.50 ± 0.21, P<0.0001; wild-type + *gld-1* RNAi from adulthood: 13.54 ± 0.18, P<0.0001. **b,** *gld-1(q485)* allele and *gld-1* RNAi shortens lifespan at 15°C. Wild type + empty vector RNAi mean ± s.e.m: 26.58 ± 0.65; *gld-1(q485)* + empty vector RNAi: 12.09 ± 0.24, P<0.0001; wild-type + *gld-1* RNAi from hatching: 14.10 ± 0.30, P<0.0001; wild-type + *gld-1* RNAi from adulthood: 15.17 ± 0.38, P<0.0001. Statistical tests were made by two-sided log rank, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.

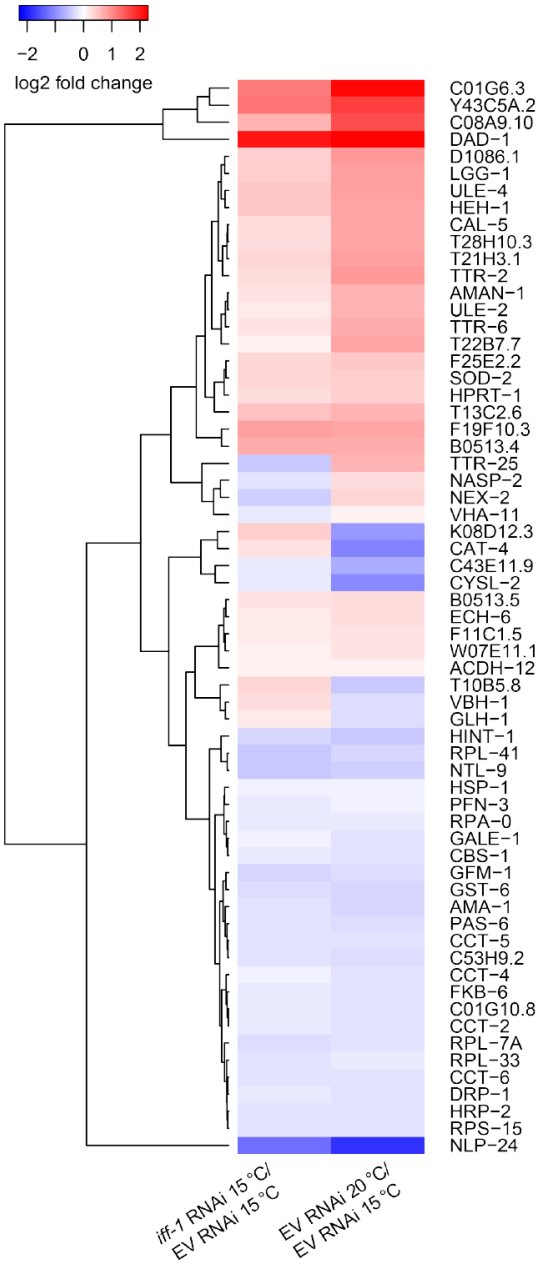


Supplementary Figure 15. Ablation of germ line and inhibition of adult germline proliferation do not affect motility or body size at cold temperature. a, Bar graphs represent the mean ± s.e.m. (n=25 worms) of thrashing movements over a 30 s period. We examined wild-type, sterile *fer-15(b26);fem-1(hc17)* and *glp-1(e2141)/glp-4(bn2)* germline-lacking worms on day 6 of adulthood. No significant (NS) differences were found when sterile and germline-lacking worms were compared with wild-type worms at the same temperature (P>0.05 was considered not significant). **b,** Graph represents the mean ± s.e.m. (n=25 per condition from 2 independent experiments) of thrashing movements/30 s at day 6 of adulthood. RNAi treatment was initiated at day 1 of adulthood. No significant differences were found when *iff-1* or *mog-5*

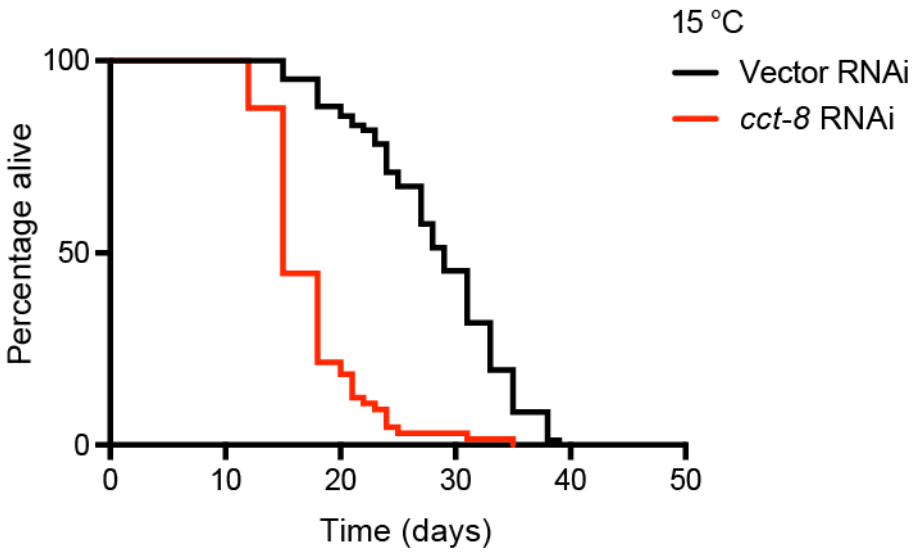
RNAi-treated worms were compared with empty-vector control worms at the same temperature (P>0.05 was considered not significant). **c,** Differential interference contrast images of wild-type, sterile *fer-15(b26);fem-1(hc17)* and *glp-1(e2141)/glp-4(bn2)* germline-lacking worms on day 6 of adulthood. Scale bar, 200 μm. Images are representative of two independent experiments. **d,** Quantification of body size at the indicated temperatures. Graph represents the mean ± s.e.m. relative to wild-type 20°C (20°C: wild-type (n=20 worms), *fer-15;fem-1* (n=15), *glp-1* (n=15), *glp-4* (n=15). 15°C: wild-type (n=25 worms), *fer-15;fem-1* (n=15), *glp-1* (n=15), *glp-4* (n=15). Worms were analyzed per each condition from 2 independent experiments). No significant differences were found in body size when germline-lacking worms were compared with wild-type worms at 15°C (P>0.05 was considered not significant). **e,** Differential interference contrast images of wild-type worms at day 6 of adulthood. Worms were shifted to the indicated temperature and RNAi at day 1 of adulthood. Scale bar, 200 μm. Images are representative of two independent experiments. **f,** Quantification of body size upon the indicated RNAi treatment and temperatures. Graph represents the mean ± s.e.m. relative to Vector RNAi 20°C (11 worms per condition from 2 independent experiments). *iff-1* or *mog-5* RNAi-treatment did not have a notable effect on body size when compared with empty vector control at the same temperature (NS= not significant, P>0.05). All the statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: *(P<0.05), ** (P<0.01), ***(P<0.001).



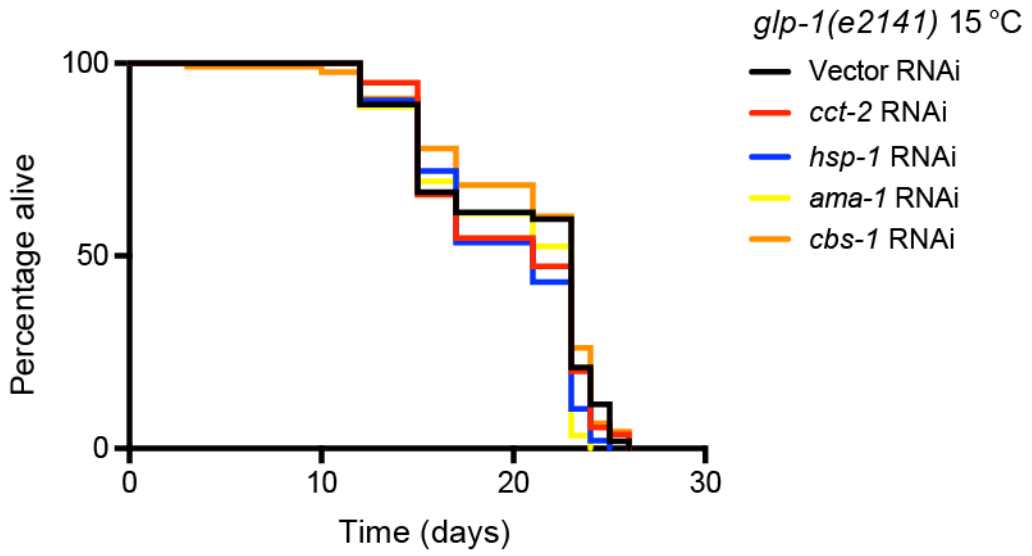
Supplementary Figure 16. Inhibition of adult germline proliferation does not increase metabolic rates. a, Graph represents oxygen consumption (pmol s^{-1} ml^{-1}) of wild-type, sterile *fer-15(b26);fem-1(hc17)* and *glp-1(e2141)* germline-lacking worms cultured at the indicated temperatures during adulthood (mean ± s.e.m., n= 4). Oxygen consumption was measured at day 5 of adulthood. NS= not significant (P=0.0608). **b,** Graph represents oxygen consumption (pmol s^{-1} ml^{-1}) of wild-type worms treated with *iff-1* and *iff-2* RNAi from adulthood at 15°C (mean ± s.e.m., n= 4). Oxygen consumption was measured at day 6 of adulthood. All the statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: *(P<0.05), ***(P<0.001).



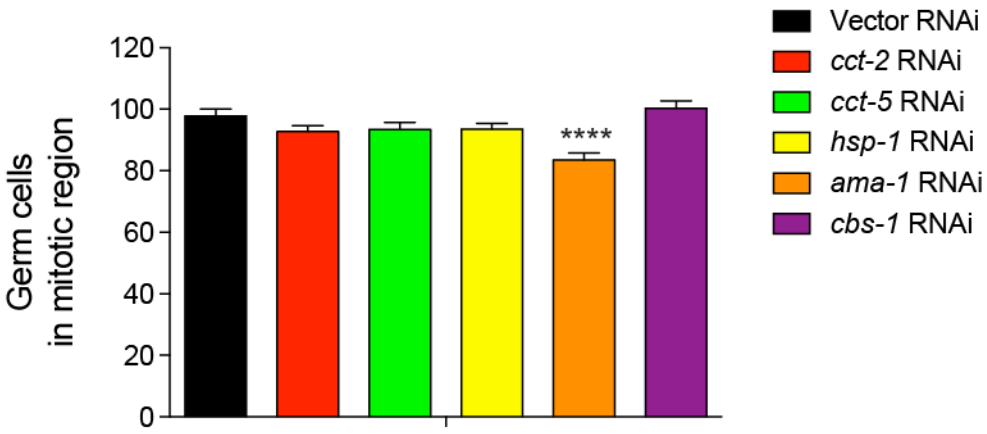
Supplementary Figure 17. Heatmap with the full list of significantly changed proteins in both *iff-1* RNAi treated worms and 20°C conditions. Log_2-fold change of differentially expressed proteins in both *iff-1* RNAi-treated worms at 15°C and EV RNAi-treated worms at 20°C when compared with EV RNAi-treated worms at 15°C. *fer-15(b26);fem-1(hc17)* control strain was raised at the restrictive temperature (25°C) during development to obtain sterile worms with a proliferating germline, which were then shifted to the indicated temperatures and RNAi treatment until day 6 of adulthood. Statistical comparisons were made by two-tailed Student's t-test (n= 3, P-value <0.05 was considered significant).



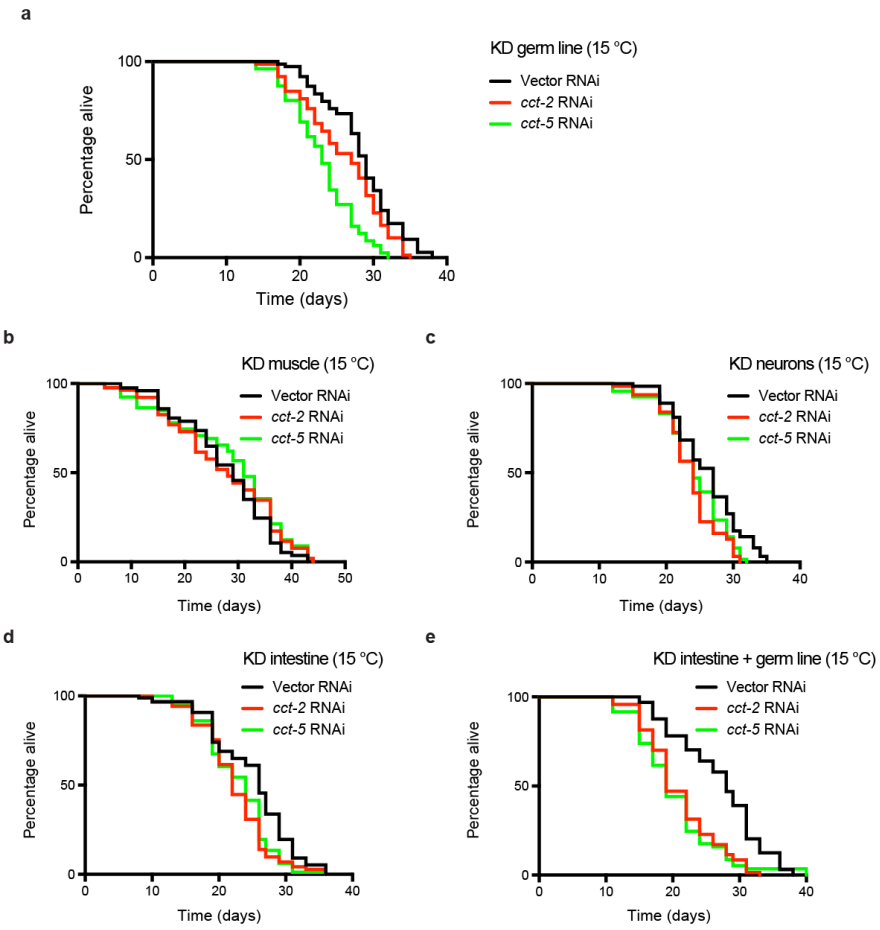
Supplementary Figure 18. Similar to other *cct* subunits, knockdown of *cct-8* during adulthood also decreases lifespan at 15°C. Wild-type worms fed with *cct-8* RNAi from adulthood live shorter when compared with control worms at 15°C. Empty vector RNAi mean ± s.e.m: 28.26 ± 0.69; *cct-8* RNAi: 17.20 ± 0.53, P<0.0001. P-values: two-sided log-rank test, n= 96 worms/condition, RNAi starting at day 1 of adulthood. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



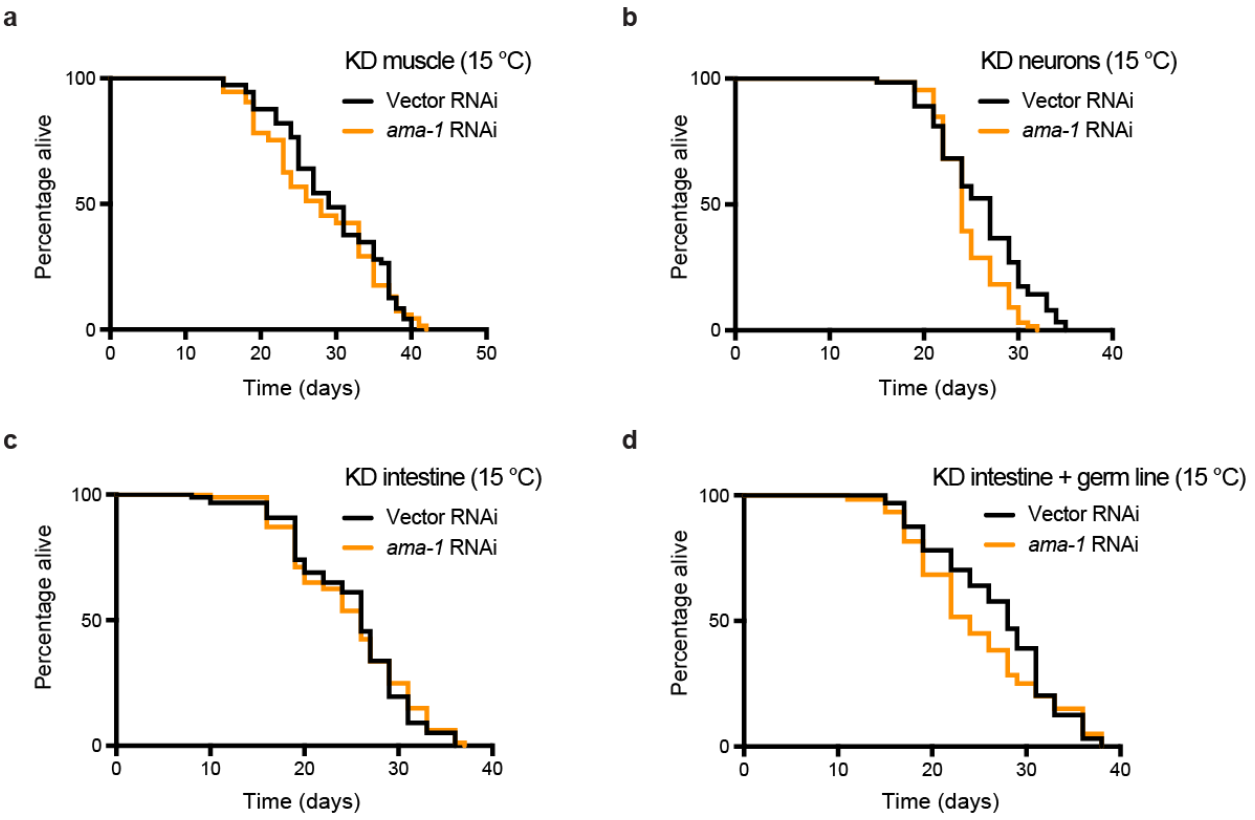
Supplementary Figure 19. Knockdown of *cct-2*, *hsp-1*, *ama-1* or *cbs-1* does not further decrease the short lifespan of germline-lacking worms at 15°C. *cct-2*, *hsp-1*, *ama-1*, or *cbs-1* RNAi does not significantly shorten lifespan of *glp-1* germline-lacking worms at 15°C. Empty vector RNAi mean ± s.e.m: 20.00 ± 0.58; *cct-2* RNAi: 19.59 ± 0.52, P=0.5878; *hsp-1* RNAi: 19.28 ± 0.51, P=0.1008; *ama-1* RNAi: 19.57 ± 0.52, P=0.0570; *cbs-1* RNAi: 20.49 ± 0.59, P=0.7775. P-values: two-sided log-rank test, n= 96 worms/condition, RNAi starting at day 1 of adulthood. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



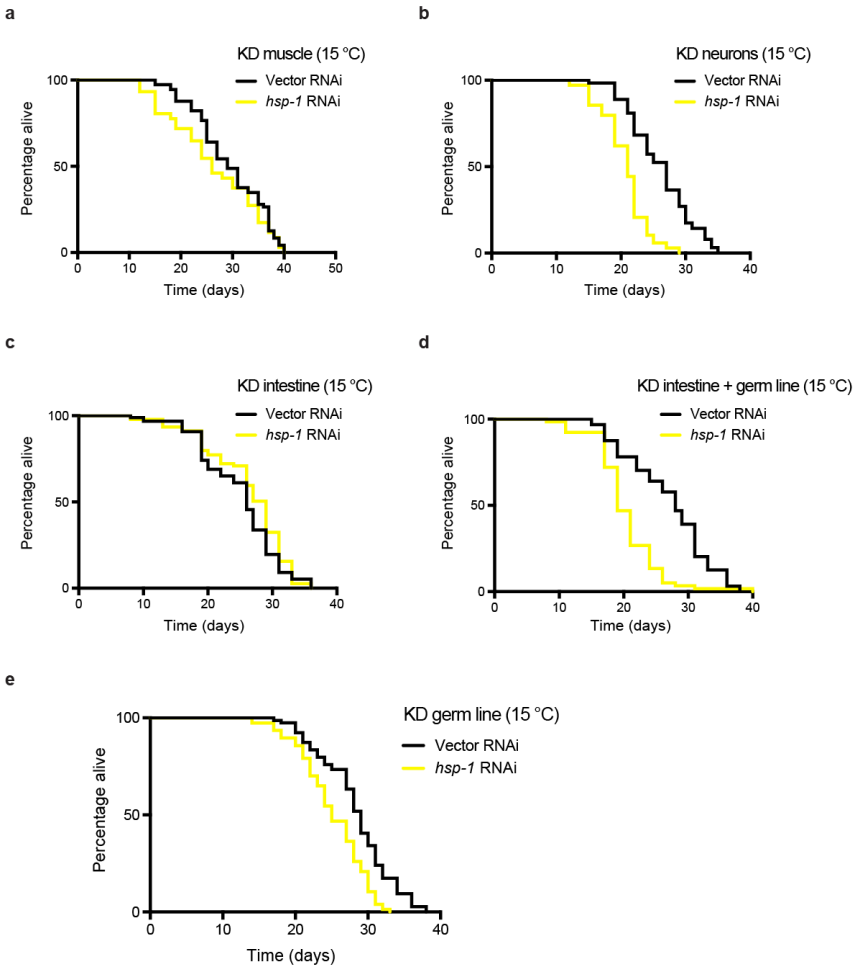
Supplementary Figure 20. Total number of germ cells within the mitotic region upon knockdown of distinct regulators of cold-induced longevity. Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., Vector, *cbs-1* RNAi (n= 46 germ lines), *cct-2*, *cct-5, hsp-1, ama-1* RNAi (n= 40), germ lines scored per each condition from 3 independent experiments). Wild-type worms treated with the indicated RNAis were examined at day 5 of adulthood. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: ****(P<0.0001).



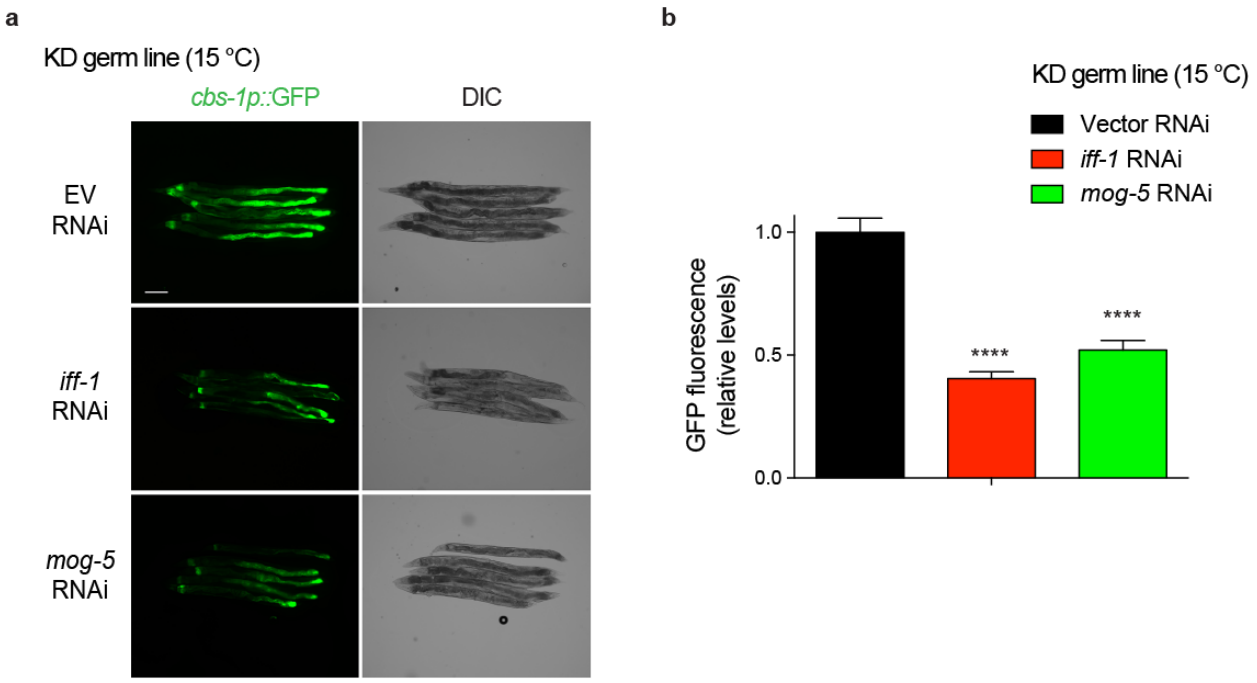
Supplementary Figure 21. Both somatic and germline knockdown of CCT subunits diminish cold-induced longevity. a, Knockdown (KD) of *cct* subunits in the germ line alone decreases cold-induced longevity at 15°C. RNAi rescued in the germ line of RNAi-deficient worms (*rde-1(mkc36); sun-1p::rde-1::sun-1 3'UTR* strain). Empty vector RNAi mean ± s.e.m: 28.32 ± 0.55; *cct-2* RNAi: 25.94 ± 0.61, P=0.0119; *cct-5* RNAi 23.07 ± 0.49, P<0.0001. **b,** Muscle-specific knockdown of *cct* subunits does not affect longevity at 15°C. RNAi rescued in the muscle of RNAi-deficient worms (*rde-1(ne300)*; *myo-3p*::*rde-1* strain). Empty vector RNAi: 27.64 ± 1.08; *cct-2* RNAi: 27.36 ± 1.31, P= 0.5002; *cct-5* RNAi: 28.46 ± 1.31, P=0.2381. **c,** Neuronal-specific knockdown of *cct* subunits decreases longevity at 15°C. RNAi rescued in the neurons of RNAi-deficient worms (*sid-1(pk3321)*; *unc-119p*::*sid-1* strain). Empty vector RNAi: 26.09 ± 0.60; *cct-2* RNAi: 23.56 ± 0.52, P= 0.0010; *cct-5* RNAi: 24.05 ± 0.59, P=0.0088. **d,** Intestinal-specific knockdown of *cct* subunits decreases longevity at 15°C. RNAi rescued in the intestine of RNAi-deficient worms (*rde-1(ne219)*; *nhx-2p*::*rde-1* strain). Empty vector RNAi: 25.02 ± 0.65; *cct-2* RNAi: 22.37 ± 0.59, P= 0.0010; *cct-5* RNAi: 22.90 ± 0.53, P=0.0012. **e,** Intestinal and germline-knockdown of *cct* subunits induces a strong decrease in longevity at 15°C. RNAi rescued in both the intestine and germ line of RNAi-deficient worms (*rde-1(ne219)*; *mex-5p*::*rde-1* strain). Empty vector RNAi: 26.97 ± 0.79; *cct-2* RNAi: 21.01 ± 0.64, P<0.0001; *cct-5* RNAi 20.36 ± 0.82, P<0.0001. P-values: two-sided log-rank test, n= 96 worms/condition. In all the experiments, RNAi was started at day 1 of adulthood. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



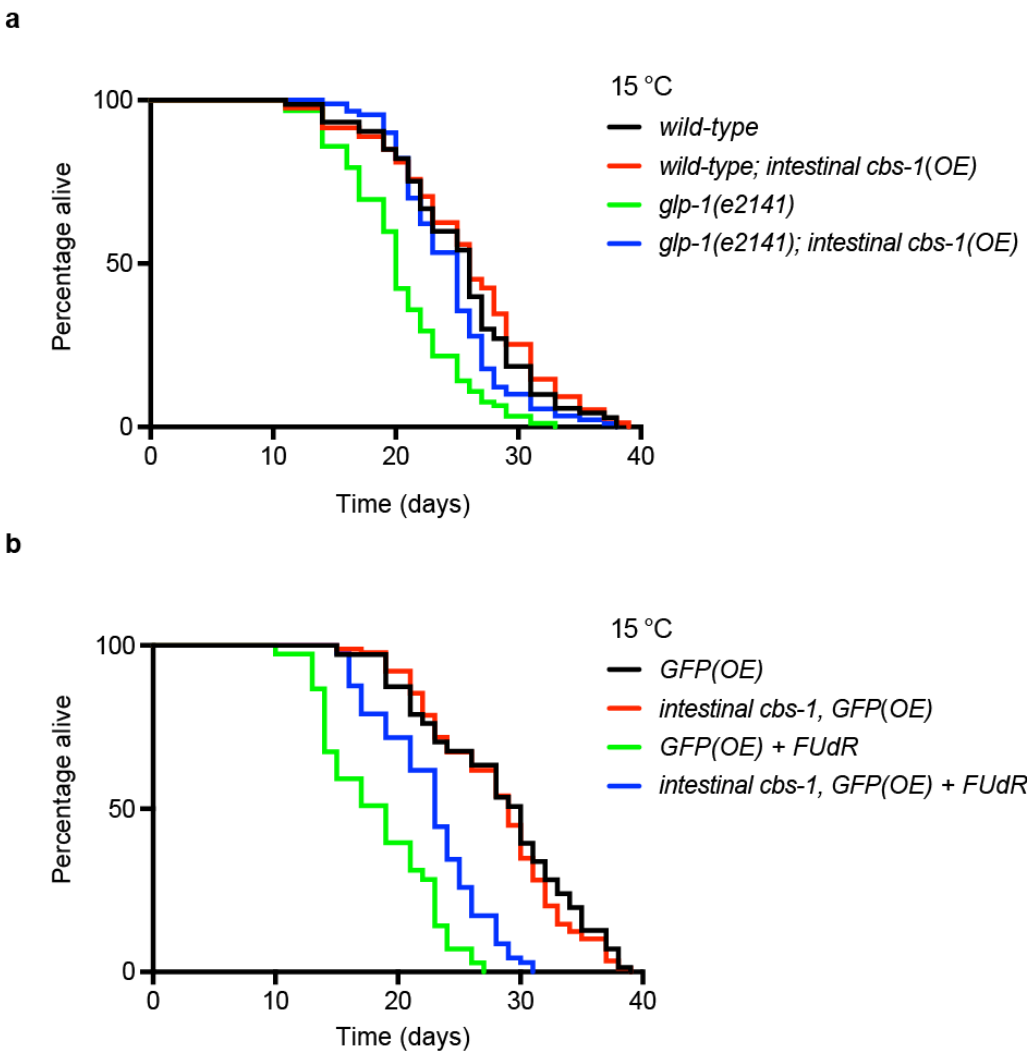
Supplementary Figure 22. Knockdown of *ama-1* in the intestine alone does not affect lifespan, whereas it reduces cold-induced longevity when the RNAi is also efficient in the germ line. a, Muscle-specific knockdown (KD) of *ama-1* does not decrease lifespan extension induced by cold temperature (15°C). RNAi rescued in the muscle of RNAi-deficient worms (*rde-1(ne300)*; *myo-3p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 29.49 ± 0.81; *ama-1* RNAi: 28.04 ± 0.91, P=0.5692. **b,** Neuronal-specific KD of *ama-1* slightly decreases longevity at 15°C. RNAi rescued in the neurons of RNAi-deficient worms (*sid-1(pk3321)*; *unc-119p*::*sid-1* strain). Empty vector RNAi mean ± s.e.m: 26.09 ± 0.60; *ama-1* RNAi: 24.53 ± 0.40, P=0.0035. **c,** Intestinal-specific KD of *ama-1* does not affect cold-induced longevity at 15°C. RNAi rescued in the intestine of RNAi-deficient worms (*rde-1(ne219)*; *nhx-2p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 25.02 ± 0.66; *ama-1* RNAi: 24.98 ± 0.68, P=0.7588. **d,** *ama-1* RNAi shortens cold-induced longevity when the knockdown is also efficient in the germ line. RNAi rescued in both the intestine and germ line of RNAi-deficient worms (*rde-1(ne219)*; *mex-5p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 26.97 ± 0.79; *ama-1* RNAi: 24.92 ± 0.91, P=0.0302. P-values: two-sided log-rank test, n= 96 worms/condition. In all the experiments, RNAi was started at day 1 of adulthood. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



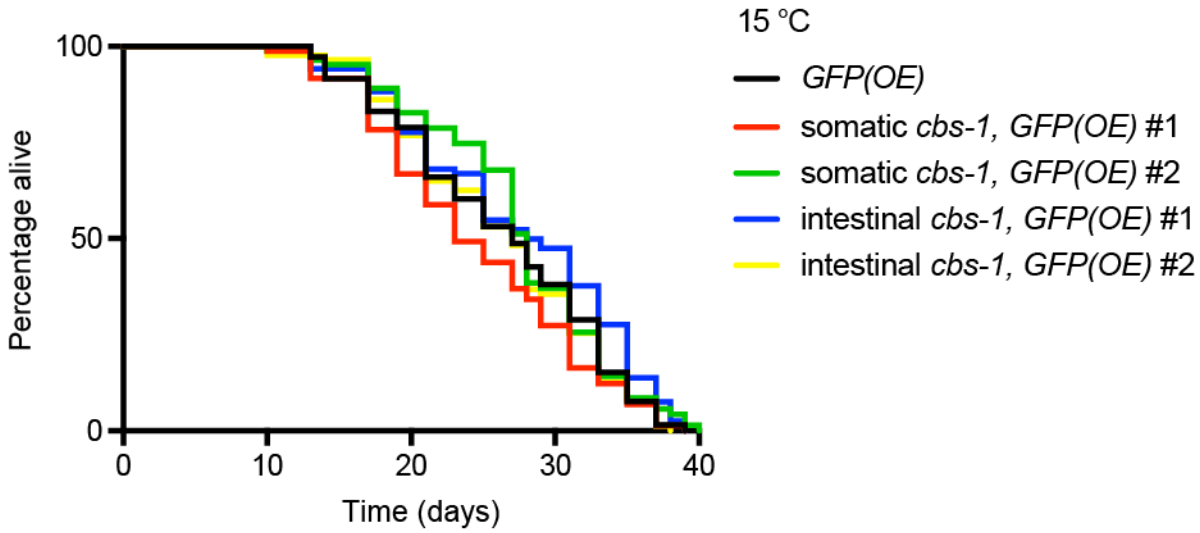
Supplementary Figure 23. Knockdown of *hsp-1* in either neurons or germ line reduces cold-induce longevity. a, Muscle-specific knockdown (KD) of *hsp-1* does not decrease lifespan extension induced by cold temperature (15°C). RNAi rescued in the muscle of RNAi-deficient worms (*rde-1(ne300)*; *myo-3p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 29.49 ± 0.81; *hsp-1* RNAi: 26.56 ± 1.03, P=0.1574. **b,** Neuronal-specific KD of *hsp-1* decreases longevity at 15°C. RNAi rescued in the neurons of RNAi-deficient worms (*sid-1(pk3321)*; *unc-119p*::*sid-1* strain). Empty vector RNAi mean ± s.e.m: 26.09 ± 0.60; *hsp-1* RNAi: 20.60 ± 0.43, P<0.0001. **c,** Intestinal-specific KD of *hsp-1* does not affect cold-induced longevity at 15°C. RNAi rescued in the intestine of RNAi-deficient worms (*rde-1(ne219)*; *nhx-2p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 25.02 ± 0.66; *hsp-1* RNAi: 26.29 ± 0.68, P=0.1258. **d,** *hsp-1* RNAi shortens cold-induced longevity when the knockdown is also efficient in the germ line. RNAi rescued in both the intestine and germ line of RNAi-deficient worms (*rde-1(ne219)*; *mex-5p*::*rde-1* strain). Empty vector RNAi mean ± s.e.m: 26.97 ± 0.79; *hsp-1* RNAi: 20.33 ± 0.64, P<0.0001. **e,** Knockdown of *hsp-1* in the germ line alone decreases cold-induced longevity at 15°C. RNAi rescued in the germ line of RNAi-deficient worms (*rde-1(mkc36); sun-1p::rde-1::sun-1 3'UTR* strain). Empty vector RNAi mean ± s.e.m: 28.32 ± 0.55; *hsp-1* RNAi: 25.12 ± 0.51, P<0.0001. P-values: two-sided log-rank test, n= 96 worms/condition. In all the experiments, RNAi was started at day 1 of adulthood. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



Supplementary Figure 24. Tissue-specific knockdown of either *iff-1* or *mog-5* in the germ line alone decreases somatic expression of *cbs-1*. a, Representative images of GFP expressed under control of the *cbs-1* promoter in germline-specific RNAi strain at day 9 of adulthood. RNAi rescued in the germ line of RNAi-deficient worms (*rde-1(mkc36); sun-1p::rde-1::sun-1 3'UTR* strain). Knockdown of either *iff-1* or *mog-5* during adulthood in the germ line alone decreases *cbs-1* expression in somatic tissues such as the intestine when compared to empty vector (EV) RNAi control. Scale bar, 50 µm. Images are representative of two independent experiments. **b,** Quantification of *cbs-1p::*GFP expression in germline-specific RNAi strain fed with either *iff-1* or *mog-5* RNAi at 15°C. Graph represents the mean ± s.e.m. relative to EV RNAi (Vector and *iff-1* RNAi (n=18 worms), *mog-5* RNAi (n=20), worms were analyzed per each condition from 2 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: ****(P<0.0001).

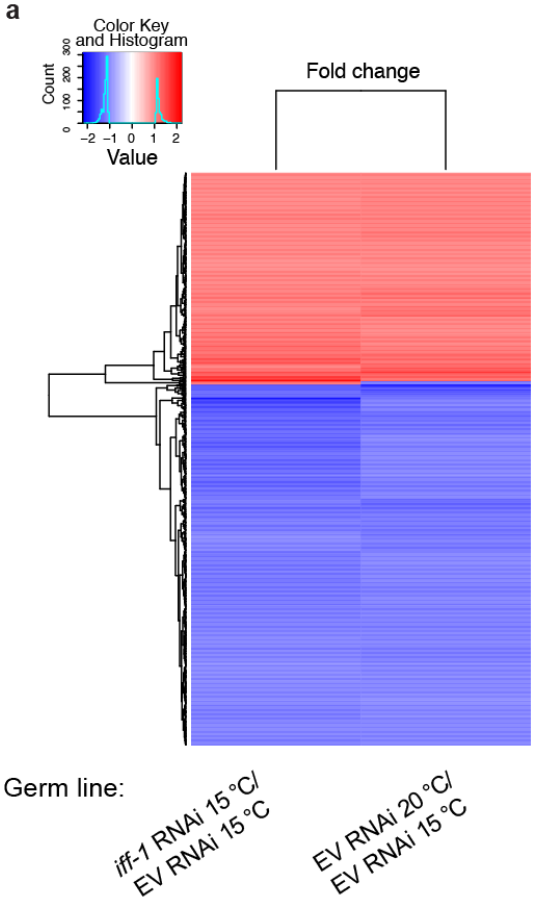


Supplementary Figure 25. Intestinal overexpression of *cbs-1* extends the short lifespan of germline-defective animals at cold temperature. a, Tissue-specific overexpression (OE) of *cbs-1* in the intestine does not further increase cold-induced longevity of wild-type worms (wild-type versus wild type + intestinal *cbs-1(OE)*, P=0.3734), but it extends the short lifespan of *glp-1(e2141)* germline-lacking mutants (*glp-1* versus *glp-1* + intestinal *cbs-1(OE)*, P<0.0001). Wild-type mean ± s.e.m: 25.17 ± 0.67; wild type + intestinal *cbs-1(OE)*: 25.74 ± 0.71; *glp-1*: 20.39 ± 0.49, *glp-1* + intestinal *cbs-1(OE)*: 24.33 ± 0.46. **b,** Intestinal overexpression of *cbs-1* does not further increase cold-induced longevity of worms with an intact adult proliferating germ line (*GFP(OE)* versus intestinal *cbs-1, GFP(OE)*, P=0.3964). However, it partially rescues the short lifespan of worms treated with 100 µg ml^{-1} FUdR during adulthood at cold temperature (*GFP(OE)* + FUdR versus intestinal *cbs-1, GFP(OE)* + FUdR, P<0.0001). *GFP(OE)* mean ± s.e.m: 28.34 ± 0.35; intestinal *cbs-1,GFP(OE)*: 28.06 ± 0.59; *GFP(OE)* + FUdR: 18.36 ± 0.53; intestinal *cbs-1,GFP(OE)* + FUdR: 22.66 ± 0.51. P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



Supplementary Figure 26. Neither ubiquitous somatic overexpression nor intestinal overexpression of *cbs-1* further extends cold-induced longevity. Ubiquitous overexpression (OE) of *cbs-1* under *sur-5* promoter does not extend cold-induced longevity. Likewise, *cbs-1* overexpression in the intestine alone under *gly-19* promoter does not increase longevity at cold temperature. *GFP(OE)* mean ± s.e.m: 26.29 ± 0.85; *cbs-1, GFP(OE)* #1: 24.57 ± 0.81, P=0.1982; *cbs-1, GFP(OE)* #2: 27.37 ± 0.75, P=0.5257; intestinal *cbs-1(OE),GFP(OE)* #1: 27.54 ± 0.83, P= 0.1330; intestinal *cbs-1(OE),GFP(OE)* #2: 26.17 ± 0.74, P=0.7372. P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.

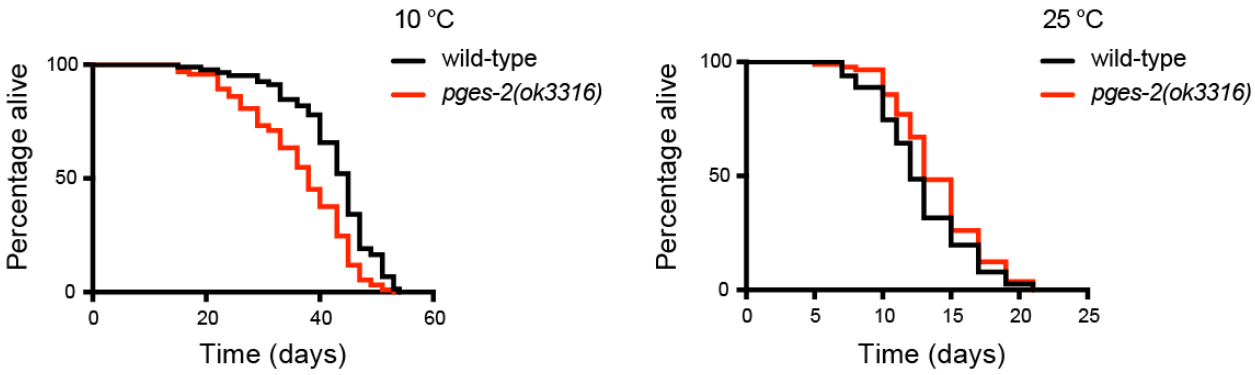
a



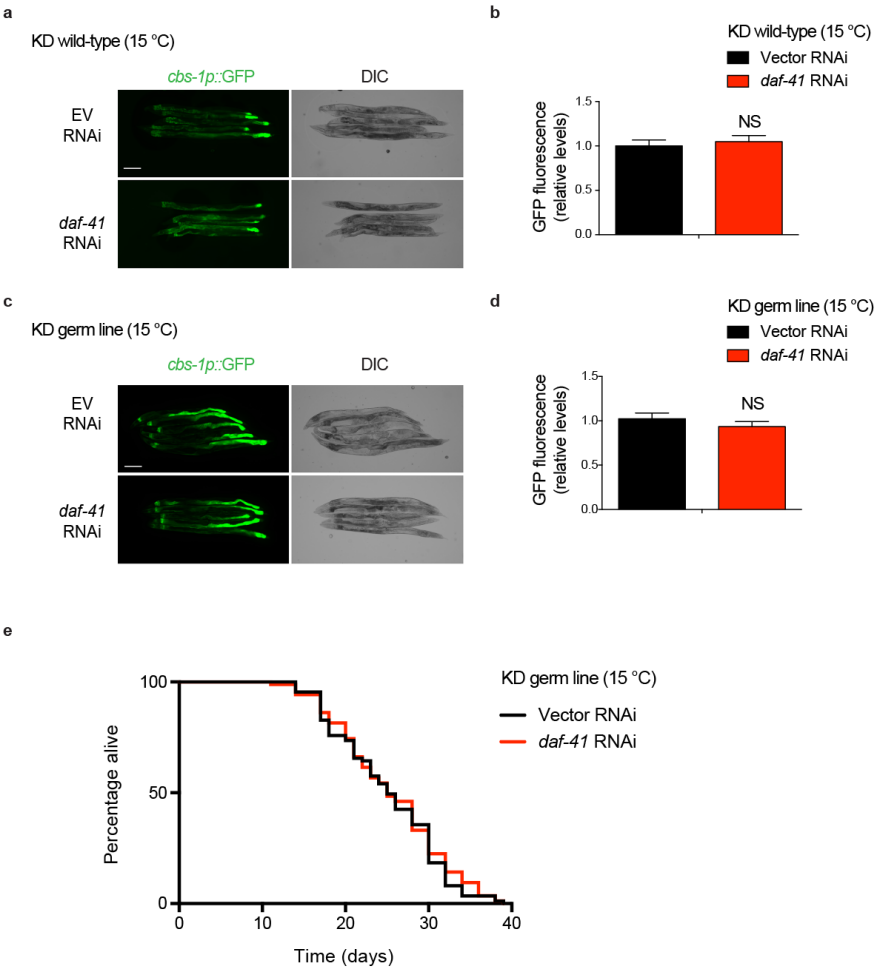
b

	EV-RNAi 20°C/EV-RNAi 15°C		*iff-1*-RNAi 15°C/EV-RNAi 15°C	
	Fold change	P-value	Fold change	P-value
pges-2	-1.23	<0.0001	-1.17	<0.0001

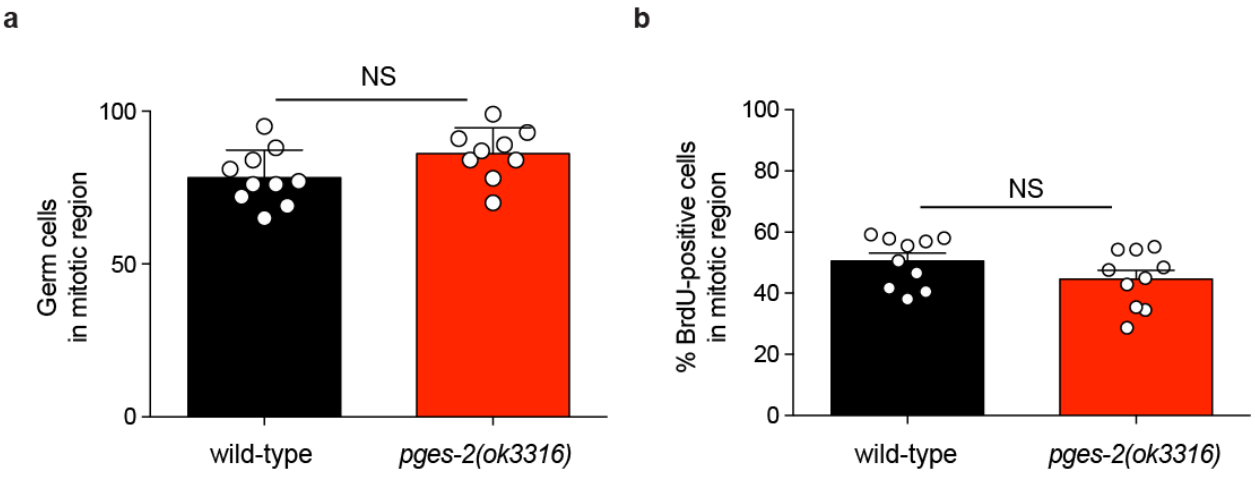
Supplementary Figure 27. The transcript levels of *pges-2* decrease in the germ line upon *iff-1* knockdown at 15°C or temperature increase. a, The heat map presents the 681 transcripts changed in the same direction in the germ line of both *iff-1* RNAi-treated worms at 15°C and empty vector (EV) RNAi-treated worms at 20°C when compared to the germ line of EV RNAi-treated worms at 15°C. Among them, 248 transcripts were up-regulated whereas 433 were down-regulated. n= 3 (each replicate contains 150 extruded germ lines from N2 wild-type worms), two-tailed t-test, P-value<0.01 was considered significant. Germ lines were extruded at day 6 of adulthood. **b,** Fold-change of *pges-2* expression from the RNA-sequencing data presented in **Supplementary Data 2 and Supplementary Fig. 27a**. *pges-2* transcript levels decrease in the germ line upon either *iff-1* knockdown or temperature increase when compared to the germ line of control worms at 15°C. Statistical comparisons were made by two-tailed Student's t-test for unpaired samples (n= 3, each replicate contains 150 extruded germ lines from N2 wild-type worms, P-values<0.0001).



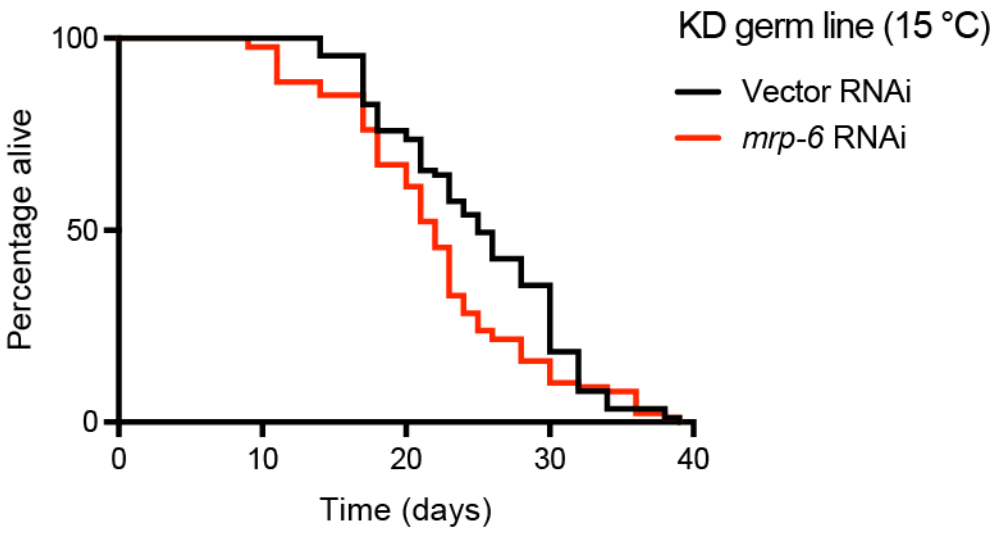
Supplementary Figure 28. *pges-2(ok3316)* are short lived at cold temperature (10°C), but not at 25°C. *pges-2(ok3316)* are short lived at cold temperature (10°C) compared with N2 wild-type animals (*pges-2* 10°C mean ± s.e.m: 42.55 ± 0.87 versus *N2* 10°C mean ± s.e.m: 36.50 ± 0.94, P<0.0001). In contrast, *pges-2* mutant worms do not live shorter at warm temperatures (25°C) (*pges-2* 25°C: 12.83 ± 0.38 versus *N2* 25°C: 13.99 ± 0.36, P=0.0491). P-values: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



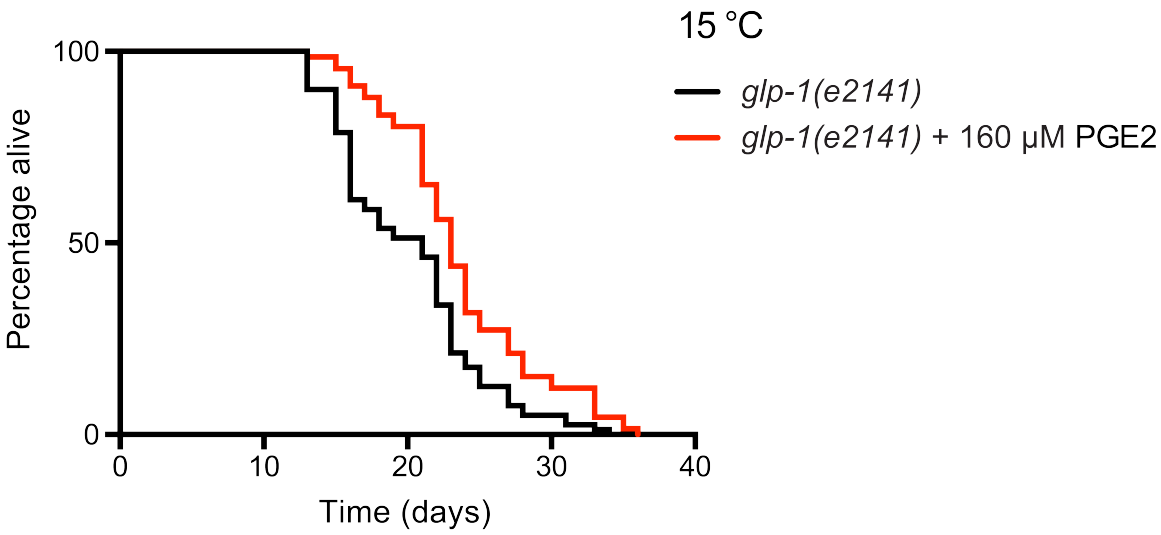
Supplementary Figure 29. Tissue-specific knockdown of *daf-41/p23* in the germ line alone does not impair cold-induced *cbs-1* somatic expression and longevity. a, Representative images of GFP expressed under control of the *cbs-1* promoter in wild-type worms at day 9 of adulthood. Knockdown (KD) of *daf-41* during adulthood does not decrease *cbs-1* expression in somatic tissues compared to empty vector (EV) RNAi control. Scale bar, 50 µm. Images are representative of two independent experiments. **b,** Quantification of *cbs-1p::*GFP expression in N2 worms treated with *daf-41* RNAi at 15°C. Graph represents the mean ± s.e.m. relative to EV RNAi (15 worms per condition from 2 independent experiments). NS= no significant differences (P=0.6723, two-tailed Student's t-test for unpaired samples). **c,** Representative images of *cbs-1p::*GFP in germline-specific RNAi strain at day 6 of adulthood. RNAi rescued in the germ line of RNAi-deficient worms (*rde-1(mkc36); sun-1p::rde-1::sun-1 3'UTR* strain). Scale bar, 50 µm. Images are representative of two independent experiments. **d,** Quantification of *cbs-1p::*GFP expression in germline-specific RNAi strain fed with *daf-41* RNAi at 15°C. Graph represents the mean ± s.e.m. relative to EV RNAi (15 worms per condition from 2 independent experiments). NS= no significant differences (P=0.3179, two-tailed Student's t-test for unpaired samples). **e,** Germline-specific knockdown of *daf-41* does not affect lifespan at 15°C (Empty vector RNAi: 25.10 ± 0.67; *daf-41* RNAi: 25.49 ± 0.72, P=0.5938). P-value: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



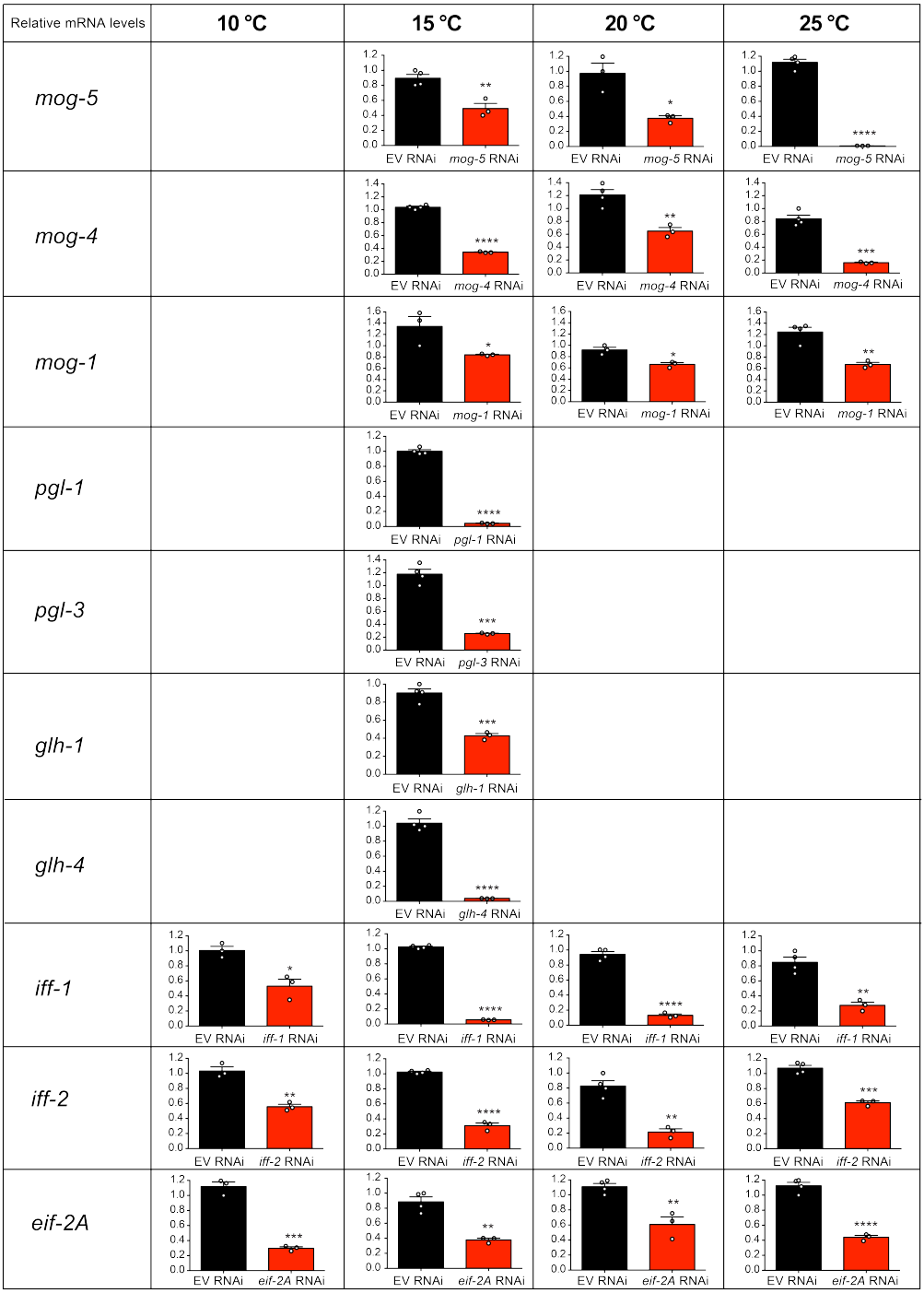
Supplementary Figure 30. *pges-2* mutants have normal number of proliferating germ cells within the mitotic region. a, Graph represents the total number of germ cells in the mitotic region quantified by DAPI staining (mean ± s.e.m., 10 germ lines scored per condition from 2 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples, P= 0.0582. **b,** Graph represents the percentage of BrdU-positive cells/total nuclei (mean ± s.e.m., 10 germ lines scored per condition from 2 independent experiments). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples, P= 0.1483. Worms were examined at day 6 of adulthood. NS= no significant differences.



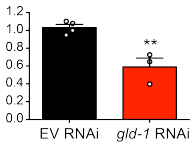
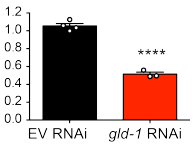
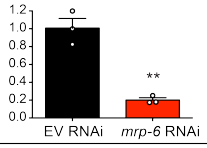
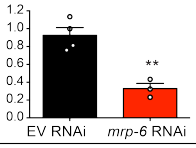
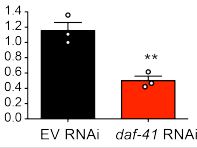
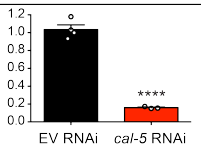
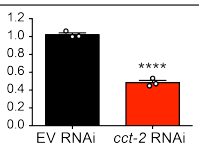
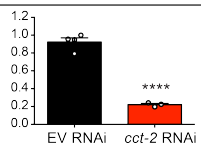
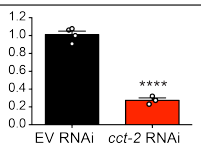
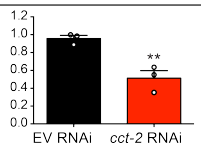
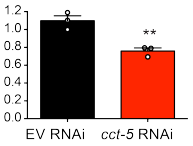
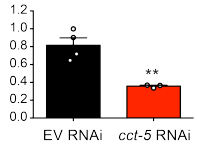
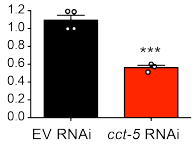
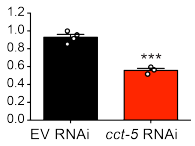
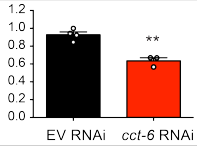
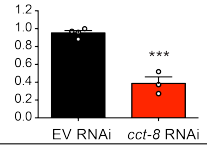
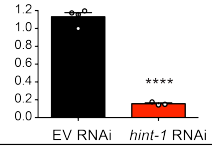
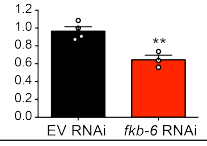
Supplementary Figure 31. Tissue-specific knockdown of *mrp-6* in the germ line alone decreases cold-induced longevity. Germline-specific knockdown (KD) of *mrp-6* shortens lifespan at 15°C (Empty vector RNAi: 25.10 ± 0.67; *mrp-6* RNAi: 22.07 ± 0.74, P=0.0184). P-value: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



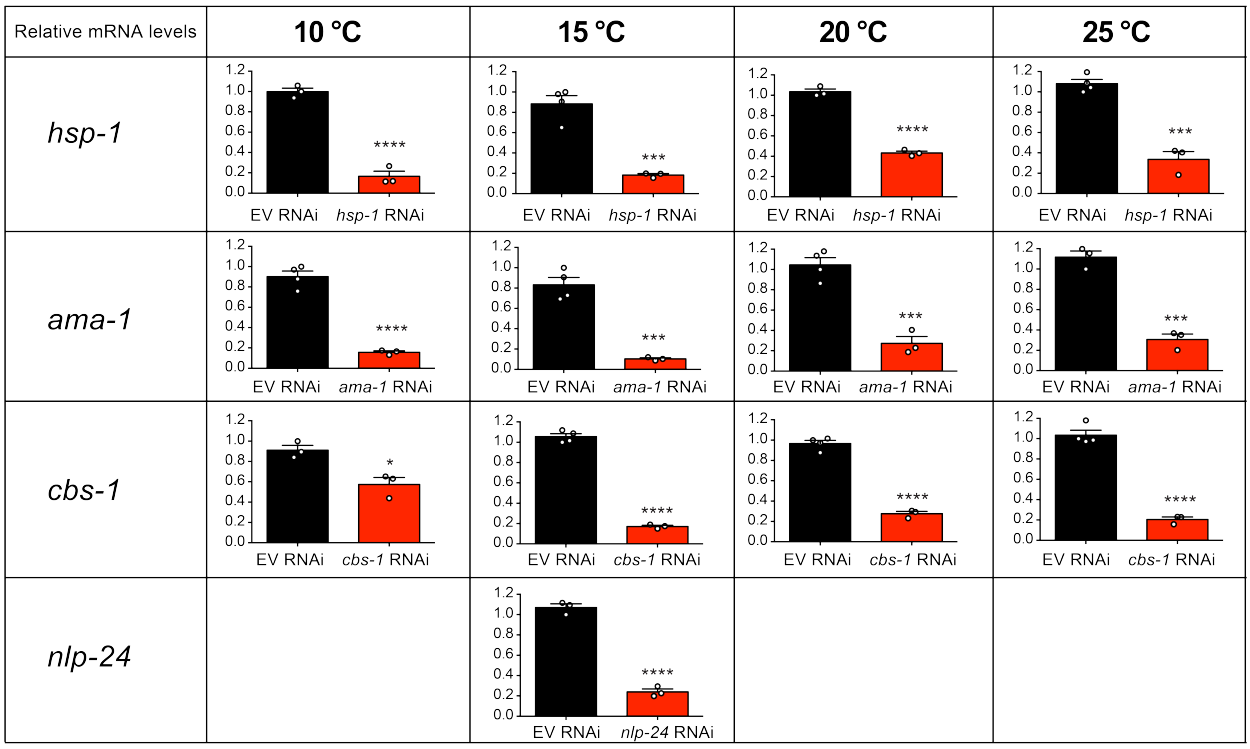
Supplementary Figure 32. Application of exogenous PGE2 extends lifespan of *glp-1* germline-lacking worms at cold temperature. Lifespan analysis of *glp-1(e2141)* germline-lacking mutants treated with PGE2 hormone at 15°C (*glp-1* mean ± s.e.m: 20.08 ± 0.57; *glp-1* + PGE2: 23.66 ± 0.64, P=0.0004). P-value: two-sided log-rank test, n= 96 worms/condition. See **Supplementary Data 3** for statistical analysis and replicate data of lifespan experiments.



Supplementary Figure 33. Knockdown levels at the indicated temperatures. We performed qPCR analysis of day 5-adult wild-type worms to assess knockdown efficiency of the distinct RNAi used in this study. For each RNAi, we tested the temperatures at which the RNAi was used in the manuscript. Graphs represent the relative expression to Empty Vector (EV) RNAi control (mean ± s.e.m., EV RNAi n=4, all the other RNAi n=3). Statistical comparisons were made by two-tailed Student's t-test for unpaired samples. P-value: *(P<0.05), **(P<0.01), ***(P<0.001), ***(P<0.0001).

Relative mRNA levels	10 °C	15 °C	20 °C	25 °C
gld-1				
mrp-6				
daf-41				
cal-5				
cct-2				
cct-5				
cct-6				
cct-8				
hint-1				
fkb-6				

Supplementary Figure 33 (continuation). Knockdown levels at the indicated temperatures.



Supplementary Figure 33 (continuation). Knockdown levels at the indicated temperatures.

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**28.26 ± 0.69**			82/96
cct-2	**18.58 ± 0.71**	-34.25	<0.0001	70/96
cct-6	**16.15 ± 0.66**	-42.85	<0.0001	59/96
cct-5	**17.83 ± 0.68**	-36.91	<0.0001	77/96
F11C1.5	**27.95 ± 0.74**	-1.10	0.6190	65/96
cal-5	**28.09 ± 0.78**	-0.60	0.8688	63/96
T21H3.1	**26.25 ± 0.72**	-7.11	0.0556	63/96
cbs-1	**24.54 ± 0.69**	-13.16	0.0005	63/96
nlp-24	**27.16 ± 0.78**	-3.89	0.0664	54/96

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**26.07 ± 0.76**			80/96
gale-1	**25.64 ± 0.90**	-1.65	0.3961	79/96
C43E11.9	**26.23 ± 0.73**	0.61	0.5300	87/96
drp-1	**25.39 ± 0.91**	-2.61	0.2705	71/96
C53H9.2	**25.39 ± 0.93**	-2.61	0.2245	90/96
gfm-1	**26.41 ± 0.97**	1.30	0.0788	66/96
acdh-12	**25.58 ± 0.85**	-1.88	0.9321	60/96
sod-2	**25.70 ± 0.78**	-1.42	0.8186	82/96
D1086.1	**26.47 ± 0.77**	1.53	0.3438	76/96
heh-1	**26.06 ± 0.88**	-0.04	0.3030	74/96
B0513.4	**26.63 ± 0.78**	2.15	0.2511	80/96
ule-4	**23.92 ± 0.94**	-8.25	0.4438	71/96
pfn-3	**26.67 ± 0.92**	2.30	0.0273	76/96

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**27.23 ± 0.72**			81/96
ule-2	**25.62 ± 0.92**	-5.91	0.9451	84/96
Y43C5A.2	**27.58 ± 0.82**	1.29	0.2169	71/96
C01G6.3	**29.37 ± 0.64**	7.87	0.0164	66/96
B0513.5	**25.20 ± 0.91**	-7.56	0.6471	80/96
C08A9.10	**25.91 ± 0.89**	-4.85	0.7154	76/96
gst-6	**27.60 ± 0.77**	1.36	0.3350	70/96
ntl-9	**27.39 ± 0.84**	0.59	0.2851	73/96
F19F10.3	**28.50 ± 0.69**	4.66	0.0633	84/96
dad-1	**26.86 ± 0.93**	-1.36	0.3543	73/95

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**25.49 ± 0.62**			73/96
hsp-1	**19.84 ± 0.49**	-22.17	<0.0001	71/96
fkb-6	**24.10 ± 0.73**	-5.45	0.2535	62/96
hint-1	**25.05 ± 0.79**	-1.73	0.8929	60/95
hprt-1	**24.03 ± 0.80**	-5.73	0.6952	74/96
pas-6[#]	**14.30 ± 0.30**	-44.96	<0.0001	74/96

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**28.54 ± 0.68**			66/96
hrp-2[*]	**25.40 ± 0.49**	-11.00	<0.0001	83/96
ttr-6	**27.95 ± 0.65**	-2.07	0.4734	79/96
ttr-25	**27.50 ± 0.66**	-3.64	0.3134	76/96
ama-1	**23.67 ± 0.42**	-17.06	<0.0001	84/96

RNAi	Mean lifespan ± s.e.m. (days)	% change in mean lifespan	Log Rank P Value	Total animals died/total
Empty vector	**31.42 ± 0.40**			72/96
lgg-1	**30.40 ± 0.73**	-3.25	0.2303	79/96
T28H10.3	**30.26 ± 0.43**	-3.69	0.0710	76/96

Supplementary Table 1. RNAi screen to identify potential modulators of cold-induced longevity. RNAi screen against genes encoding differentially expressed proteins in both *iff-1* RNAi-treated worms at 15°C and empty vector (EV) RNAi-treated worms at 20°C when compared with EV RNAi-treated worms at 15°C. Lifespan analysis was performed in wild-type worms fed with the indicated RNAi from day 1 of adulthood at 15°C. All statistical

comparisons were made by two-sided log-rank test, n= 96 worms/condition. In red, RNAis that significantly decreased lifespan and were further validated by additional replicates and tested at different temperatures (please see **Figure 5**). [*]It has been recently reported that knockdown of the RNA-binding protein *hrp-2* also decreases lifespan at 20°C (Heintz et al, Nature (2017))[1]. Thus, these data indicate that the effects of *hrp-2* on lifespan are not specific for cold temperature and we did not further assess this factor in the context of cold-induced longevity. [#]*pas-6* is a central component of the proteasome and its knockdown also strongly decreases lifespan at 20°C, representing an essential gene for viability (Ghazi et al, PNAS (2007))[2]. Therefore, we did not further assess this proteasome subunit in the context of cold-induced longevity.

Gene	Forward (5' → 3')	Reverse (5' → 3')
cdc-42	CTGCTGGACAGGAAGATTACG	CTCGGACATTCTCGAATGAAG
pmp-3	GTTCCCGTGTTCATCACTCAT	ACACCGTCGAGAAGCTGTAGA
mog-5	ATTGCTACGAATATTGCCGAAAC	CTGCGGCTTGTGAGATTGG
mog-4	TGCTGATGAAGTTGGATGCAA	TGTGCAATCCTCGAAACGAA
mog-1	CTCAAGCTTCCATTGATCTCAAAC	GAAATACGCAGAGCAAATGCAT
pgl-1	ACTTTTTTGGTTTCATCCATTTCAC	CCCACCGAAATCCACAATTT
pgl-3	GCCGGATTCTTTGGTGGAT	AAAAAGAGAACCTAAAACTTGTGAATACG
glh-1	GATGGTTGGAGTGATAGCGAAAG	CCGAAACCGCCTCCACTAC
glh-4	ACTGTGCTGTTTAGTGCATCCTTCT	TAACCCTCTTTGACGAACTTTGG
iff-1	TGGCTTCGGAGGGTGGAT	TGATCTTCGGACATACTCTCTATGGT
iff-2	ACGCCCATGCAAGATCGT	AGCGTGACCGTGCTTTCC
eif-2A	AGGAAAGCATTCCAACTCAAAAAG	CGCCACTCGTTGCTTGAGA
gld-1	TGTTCAATCCAAAGAGCAGAAGTATC	CAGGCTCTTGTCCATCGATGA
mrp-6	GAGTGGATTCTTCTCGTGGATCA	CGGAAACCATCCCGTTCTC
daf-41	AAACAAGCTTCACTTCCAAGGAA	ACGGATGCAGGATCGATTTC
cal-5	GGATGATTTGAAGGGAATTTTTAGAG	CGCAGTTCTTCCCTTTGAATG
cct-2	CCAAAGGGAATGGACAAAATTC	TTGATTCCTCCTGCGCTTTC
cct-5	ATGAAGGAGCAGAAGGTTATCGA	AACCACCTGAGTGGCCAATG
cct-6	CTTCACGAAATGGCGATTCA	CGTCGAAGCCTTGGCAAT
cct-8	CGGACCAAATGGAATGAACAA	GTCGTTGGTGACGAAGAGCTT
hint-1	GATTCGGATGCTGCGCTTA	AGCTGCTTTGCAACCTTTGAA
fkb-6	CCGAGATGCCATGAAGTTGTT	GAGCGGCGGCCTTATTCT
hsp-1	CGGAGATGCTGCCAAGAATC	TTGGCATCGAAAACAGTGTTATG
ama-1	CGGAGGAGATTAAACGCATGTC	GCTTTCCGTTCTCGTAGACTTCTG
cbs-1	AGCTTTCCAGTTTGCTGAAGAGA	CCGGCGGTCACAAAAACTT
nlp-24	AAATGCTCATCAGTTGCCAGAA	GGTTGGTGAGTGGAATTTGTACTTATT

S**upplementary Table 2.** List of primers used for qPCR assays with *C. elegans* extracts.

Supplementary References

1. Heintz, C.*, et al.* Splicing factor 1 modulates dietary restriction and TORC1 pathway longevity in C. elegans. *Nature* **541**, 102-106 (2017).
2. Ghazi, A., Henis-Korenblit, S. & Kenyon, C. Regulation of Caenorhabditis elegans lifespan by a proteasomal E3 ligase complex. *Proc Natl Acad Sci U S A* **104**, 5947-5952 (2007).