

Table S2 Reproductive status of *let-418* alleles

Genotype	temp.	brood size	n=	% fertile
wt control	25°C ^a	205 ± 22	9	n.d.
<i>let-418(n3536)</i>		152 ± 18	10	n.d.
<i>swEX661</i>		150 ± 15	10	n.d.
<i>swEX662</i>		163 ± 18	10	n.d.
<i>let-418(n3536);swEX661</i>		53.9 ± 13	10	n.d.
<i>let-418(n3536);swEX662</i>		60 ± 22	10	n.d.
wt control	25°C ^b	n.d.	369	100
<i>let-418(n3536)</i>		n.d.	344	0.003
<i>swEX661</i>		n.d.	321	98.8
<i>swEX662</i>		n.d.	344	98.4
<i>let-418(n3536);swEX661</i>		n.d.	244	1
<i>let-418(n3536);swEX662</i>		n.d.	206	5
<i>unc-46(e177) control</i>	25°C ^a	145 ± 25	14	n.d.
<i>let-418(s1617) (m+z-)</i>		5 ± 4	13	n.d.
<i>let-418(ar113) (m+z-)</i>		10 ± 7	9	n.d.
<i>let-418(ar114) (m+z-)</i>		0.7 ± 0.9	15	n.d.
<i>unc-46(e177) control</i>	20°C ^a	193 ± 21	10	n.d.
<i>let-418(s1617) (m+z-)</i>		10 ± 8	14	n.d.
<i>let-418(ar113) (m+z-)</i>		12 ± 12	13	n.d.
<i>let-418(ar114) (m+z-)</i>		4.3 ± 4.8	15	n.d.

^aanimals are maintained at 15°C and then shifted to the indicated temperature at the L4 stage

^banimals were shifted at 25 °C at the L1 stage

Table S1 Mutations in *let-418* increase lifespan

Genotype	Mean survival \pm SEM (Days)	Total number of animals Died/Total	P value vs control
<i>wt control</i>	13.4 \pm 0.4	85/100	
<i>let-418(n3536ts)</i>	15.1 \pm 0.6	67/82	0.0003
<i>wt control</i>	13.4 \pm 0.4	80/82	
<i>let-418(n3536ts)</i>	14.8 \pm 0.5	65/80	0.0183
<i>wt control</i>	10.6 \pm 0.5	64/75	
<i>let-418(n3536ts)</i>	14.2 \pm 0.3	68/75	<0.0001
<i>let-418(n3536ts);swEx661</i>	9.5 \pm 0.4	46/75	0.1818
<i>let-418(n3536ts);swEx662</i>	11.4 \pm 0.7	35/75	0.2111
<i>wt control</i>	9.5 \pm 0.3	66/80	
<i>let-418(n3536ts)</i>	12 \pm 0.3	76/80	<0.0001
<i>let-418(n3536ts);swEx661</i>	9.5 \pm 0.3	64/80	0.8918
<i>let-418(n3536ts);swEx662</i>	9.3 \pm 0.3	68/80	0.6398
<i>swEx661</i>	9 \pm 0.4	68/80	0.5133
<i>swEx662</i>	9.7 \pm 0.4	53/80	0.8526
<i>unc-46(e177) control</i>	8.7 \pm 0.4	52/80	
<i>unc-46(-); let-418(s1617)</i>	11.1 \pm 0.3	67/80	<0.0001
<i>unc-46(e177) control</i>	7.9 \pm 0.3	46/80	
<i>unc-46(-); let-418(s1617)</i>	11.2 \pm 0.4	69/80	<0.0001
<i>unc-46(e177) control</i>	8.8 \pm 0.5	22/80	
<i>unc-46(-); let-418(s1617)</i>	10.3 \pm 0.4	64/80	0.0297
<i>unc-46(-); let-418(ar113)</i>	10.6 \pm 0.4	55/80	0.0032
<i>unc-46(-); let-418(ar114)</i>	12.3 \pm 0.3	72/80	<0.0001
<i>unc-46(e177) control 20°C</i>	10.8 \pm 0.4	48/80	
<i>unc-46(-); let-418(s1617)</i>	12.67 \pm 0.4	42/80	0.0074
<i>unc-46(-); let-418(ar113)</i>	12.2 \pm 0.4	42/80	0.0424
<i>unc-46(-); let-418(ar114)</i>	14.6 \pm 0.4	57/80	<0.0001
<i>wt control</i>	9.0 \pm 0.4	58/75	
<i>chd-3(eh4)</i>	9.0 \pm 0.3	75/84	0.4069
<i>wt control</i>	10.7 \pm 0.7	55/75	
<i>chd-3(ok1651)</i>	9.7 \pm 0.6	72/75	0.1028
<i>wt control</i>	9.6 \pm 0.5	58/75	
<i>mep-1(q660)</i>	10.4 \pm 0.3	73/75	0.4272
<i>lin-53(n3368)</i>	6.5 \pm 0.1	75/75	<0.0001
<i>wt control</i>	13.5 \pm 0.3	64/75	
<i>hda-1(RNAi)</i>	13.13 \pm 0.2	75/75	0.1071
<i>wt control</i>	13.5 \pm 0.4	74/75	
<i>egr-1(RNAi)</i>	13.2 \pm 0.4	72/75	0.4258

p-values (Log-Rank test) calculated for each individual experiment are shown.

Table S3 *let-418* genetic interactions with other mutations influencing ageing

Genotype	Mean survival ± SEM (Days)	Total number of animals Died/Total	P value vs control	vs strain	P value
<i>wt control</i>	10.9 ± 0.6	57/75			
<i>let-418(n3536)</i>	13.0 ± 0.6	67/75	0.0096		
<i>daf-16(mu86)</i>	10.1 ± 0.5	65/75	0.1972		
<i>daf-16(-); let-418(-)</i>	11.3 ± 0.3	71/75	0.8111	<i>daf-16(-)</i> <i>let-418(n3536)</i>	0.4335 0.001
<i>unc-46(e177) control</i>	7.4 ± 0.4	23/80			
<i>unc-46(-); let-418(s1617)</i>	8.7 ± 0.3	55/80	0.0059		
<i>daf-16(mu86); unc-46(-)</i>	6.5 ± 0.3	31/80	0.0319		
<i>daf-16(-); unc-46(-) let-418(-)</i>	7.3 ± 0.2	63/80	0.5745	<i>unc-46(-); daf-16(-)</i> <i>unc-46(-); let-418(s1617)</i>	0.0097 <0.0001
<i>unc-46(e177) control</i>	6.9 ± 0.5	22/80			
<i>unc-46(-); let-418(s1617)</i>	8.6 ± 0.2	59/80	<0.0001		
<i>daf-16(mu86); unc-46(-)</i>	6.1 ± 0.2	37/80	0.0461		
<i>daf-16(-); unc-46(-) let-418(-)</i>	7.2 ± 0.2	75/80	0.8126	<i>unc-46(-); daf-16(-)</i> <i>unc-46(-); let-418(s1617)</i>	0.0003 <0.0001
<i>unc-46(e177) control</i>	12.8 ± 0.3	5/80			
<i>unc-46(-); let-418(s1617)</i>	14.9 ± 0.4	1/80	0.0007		
<i>unc-46(-); hsf-1(RNAi)</i>	6.8 ± 0.1	7/80	<0.0001		
<i>unc-46(-); let-418(-); hsf-1(RNAi)</i>	6.9 ± 0.1	7/80	<0.0001	<i>unc-46(-); hsf-1(RNAi)</i> <i>unc-46(-); let-418(s1617)</i>	0.3441 <0.0001
<i>unc-46(-); skn-1(RNAi)</i>	12.5 ± 0.3	4/80	0.2053		
<i>unc-46(-); let-418(-); skn-1(RNAi)</i>	12.0 ± 0.4	8/80	0.0745	<i>unc-46(-); skn-1(RNAi)</i> <i>unc-46(-); let-418(s1617)</i>	0.74 <0.0001
<i>unc-46(e177) control</i>	8.4 ± 0.4	52/80			
<i>unc-46(-); let-418(s1617)</i>	11.1 ± 0.3	67/80	<0.0001		
<i>daf-2(e1370); unc-46(-)</i>	38.3 ± 1.8	54/80	<0.0001		
<i>daf-2(-); unc-46(-) let-418(-)</i>	31.9 ± 1.3	80/80	<0.0001	<i>daf-2(e1370); unc-46(-)</i> <i>unc-46(-); let-418(-)</i>	0.0007 <0.0001
<i>unc-46(e177) control</i>	7.9 ± 0.3	46/80			
<i>unc-46(-); let-418(s1617)</i>	11.2 ± 0.4	69/80	<0.0001		
<i>daf-2(e1370); unc-46(-)</i>	39.4 ± 1.5	45/80	<0.0001		
<i>daf-2(-); unc-46(-) let-418(-)</i>	32.6 ± 1.2	79/80	<0.0001	<i>daf-2(e1370); unc-46(-)</i> <i>unc-46(-); let-418(-)</i>	0.0016 <0.0001
<i>wt control</i>	7.9 ± 0.3	46/80			
<i>let-418(n3536)</i>	11.2 ± 0.4	69/80	0.0044		
<i>daf-2(e1370)</i>	39.4 ± 1.5	45/80	<0.0001		
<i>daf-2(-); let-418(n3536)</i>	32.6 ± 1.2	79/80	<0.0001	<i>daf-2(e1370)</i> <i>let-418(n3536)</i>	0.0023 <0.0001
<i>unc-46(e177) control</i>	9.1 ± 0.2	63/80			
<i>unc-46(-); let-418(s1617)</i>	10.8 ± 0.2	14/80	0.0001		
<i>unc-46(-); age-1(RNAi)</i>	13.8 ± 0.5	50/80	<0.0001		
<i>unc-46(-); let-418(-); age-1(RNAi)</i>	11.9 ± 0.3	75/80	<0.0001	<i>unc-46(-); let-418(-)</i> <i>unc-46(-); age-1(RNAi)</i>	0.0042 <0.0001
<i>unc-46(-); akt-2(ok393); akt-1(RNAi)</i>	17.5 ± 0.6	48/80	<0.0001		
<i>unc-46(-) let-418(-); akt-2(ok393) akt-1(RNAi)</i>	15.6 ± 0.4	78/80	<0.0001	<i>unc-46(-); akt-2(ok393); akt-1(RNAi)</i> <i>unc-46(-); let-418(-)</i>	0.0012 <0.0001
<i>unc-46(e177) 20° control</i>	9.7 ± 0.7	18/80			
<i>unc-46(-) let-418(s1617)</i>	12.8 ± 0.5	69/80	0.0006		
<i>glp-1(q224); unc-46(-)</i>	16.5 ± 1.5	71/80	0.0486	<i>unc-46(-); let-418(-)</i>	0.231
<i>glp-1(-); unc-46(-) let-418(-)</i>	12.5 ± 0.5	44/80	0.0013	<i>unc-46(-); let-418(-)</i>	0.4755

Table S3 *let-418* genetic interactions with other mutations influencing ageing

				<i>glp-1(-); unc-46(-)</i>	0.5953
<i>unc-46(e177) 20° control</i>	10.6 ± 0.4	27/80			
<i>unc-46(-) let-418(s1617)</i>	13.8 ± 0.4	66/80	<0.0001		
<i>glp-1(e2141); unc-46(-)</i>	14.7 ± 1	51/80	0.001	<i>unc-46(-); let-418(-)</i>	0.675
<i>glp-1(-); unc-46(-) let-418(-)</i>	12.8 ± 0.4	59/80	0.0001	<i>unc-46(-); let-418(-)</i>	0.0885
				<i>glp-1(-); unc-46(-)</i>	0.2168
<i>dpy-18(e363); unc-46(e177) control (FuDr)</i>	8.2 ± 0.3	63/75			
<i>dpy-18(-); unc-46(-); kri-1(RNAi)</i>	9.4 ± 0.4	66/77	0.0225		
<i>dpy-18(-); unc-46(-) l418(s1617)</i>	10.3 ± 0.3	75/75	<0.0001		
<i>dpy-18(-); unc-46(-) l418(-); kri-1(RNAi)</i>	11.2 ± 0.3	75/75	<0.0001	<i>dpy-18(-); unc-46(-) l418(-)</i>	0.2143
<i>dpy-18(e363); unc-46(e177) control</i>	11.5 ± 0.5	35/75			
<i>dpy-18(-); unc-46(-); kri-1(RNAi)</i>	11.3 ± 0.7	18/75	0.995		
<i>dpy-18(-); unc-46(-) l418(s1617)</i>	14.8 ± 0.5	75/75	<0.0001		
<i>dpy-18(-); unc-46(-) l418(-); kri-1(RNAi)</i>	14.7 ± 0.4	75/75	<0.0001	<i>dpy-18(-); unc-46(-) l418(-)</i>	0.6164
<i>unc-46(e177) 20 °C control</i>	10.8 ± 0.4	48/80			
<i>unc-46(-); let-418(s1617)</i>	12.6 ± 0.4	42/80	0.0074		
<i>tcer-1(tm1452); unc-46(-)</i>	12.1 ± 0.5	40/80	0.0517		
<i>tcer-1(-); unc-46(-) let-418(s1617)</i>	13.0 ± 0.4	58/80	0.0004	<i>unc-46(-); let-418(-)</i>	0.3359
<i>unc-46(e177) 25 °C control</i>	8.7 ± 0.5	58/80			
<i>unc-46(-); let-418(s1617)</i>	10.2 ± 0.4	64/80	0.0297		
<i>tcer-1(tm1452); unc-46(-)</i>	8.7 ± 0.3	67/80	0.9555		
<i>tcer-1(-); unc-46(-) let-418(s1617)</i>	9.2 ± 0.3	61/80	0.5281	<i>unc-46(-); let-418(-)</i>	0.0767
<i>dpy-18(e363); unc-46(e177) control</i>	10 ± 0.4	50/80			
<i>dpy-18(-); unc-46(-) clk-1(RNAi)</i>	11.2 ± 0.4	48/80	<0.0001		
<i>dpy-18(-); unc-46(-) l418(s1617)</i>	13.6 ± 0.5	55/80	<0.0001		
<i>dpy-18(-); unc-46(-) l418(s1617) clk-1(RNAi)</i>	15.7 ± 0.6	55/80	<0.0001	<i>dpy-18(-); unc-46(-) l418(-) clk-1(RNAi)</i>	0.0024
					<0.0001
<i>dpy-18(e363); unc-46(e177) control</i>	8.9 ± 0.4	31/80			
<i>dpy-18(-); unc-46(-) clk-1(RNAi)</i>	9.1 ± 0.3	41/80	0.9008		
<i>dpy-18(-); unc-46(-) l418(s1617)</i>	14.7 ± 0.6	65/80	<0.0001		
<i>dpy-18(-); unc-46(-) l418(s1617) clk-1(RNAi)</i>	16.4 ± 0.6	63/80	<0.0001	<i>dpy-18(-); unc-46(-) l418(-) clk-1(RNAi)</i>	0.0066
					<0.0001
<i>unc-46(e177) control</i>	8.5 ± 0.6	26/80			
<i>unc-46(-); let-418(s1617)</i>	10.5 ± 0.5	74/80	0.0032		
<i>eat-2(ad1116); unc-46(-)</i>	12.4 ± 0.5	59/80	<0.0001		
<i>eat-2(-); unc-46(-) let-418(-)</i>	18.7 ± 0.8	57/80	<0.0001	<i>unc-46(-); let-418(-) eat-2(-)</i>	<0.0001
					<0.0001
<i>unc-46(e177) control</i>	8.2 ± 0.5	12/80			
<i>unc-46(-); let-418(s1617)</i>	13.5 ± 0.7	20/80	<0.0001		
<i>eat-2(ad1116); unc-46(-)</i>	13 ± 0.5	63/80	<0.0001		
<i>eat-2(-); unc-46(-) let-418(-)</i>	17.1 ± 0.6	46/80	<0.0001	<i>unc-46(-); let-418(-) eat-2(-)</i>	0.0002
					<0.0001

p-values(Log-Rank test) calculated for each individual experiment are shown.

Table S4 Mutations in *let-418* enhance oxidative stress resistance

Genotype	Mean survival \pm SEM (Hours)	Total number of animals Died/Total	P value vs control	vs strain	P value
wt control	43.1 \pm 1.7	34/59			
<i>let-418(n3536ts)</i>	51 \pm 2.1	32/60	0.0049		
wt control	37.1 \pm 2	35/57			
<i>let-418(n3536ts)</i>	50.1 \pm 3	37/52	0.0037		
<i>daf-16(mu86)</i>	35.6 \pm 1.7	51/65	0.6256		
<i>daf-16(-); let-418(-)</i>	37.5 \pm 1.6	50/60	0.8472	<i>daf-16(-)</i>	0.5003
				<i>let-418(-)</i>	0.0003
wt control	48.5 \pm 2.1	39/59			
<i>let-418(n3536ts)</i>	66.8 \pm 3	32/54	<0.0001		
<i>daf-16(mu86)</i>	46.5 \pm 2.7	29/41	0.4653		
<i>daf-16(-); let-418(-)</i>	57.7 \pm 2.6	46/62	0.0143	<i>daf-16(-)</i>	0.0313
				<i>let-418(-)</i>	0.0042
<i>unc-46(e177) control</i>	45.9 \pm 1.6	21/50			
<i>unc-46(-) let-418(s1617)</i>	73.2 \pm 3.2	39/50	<0.0001		
<i>daf-16(mu86); unc-46(-)</i>	44.5 \pm 1.4	31/50	0.6167		
<i>daf-16(-); unc-46(-) let-418(-)</i>	56.8 \pm 2.3	45/50	0.0046	<i>daf-16(-); unc-46(-)</i>	0.0001
				<i>unc-46(-) let-418(-)</i>	<0.0001
<i>dpy-18(e363); unc-46(e177) control</i>	37.0 \pm 2.1	50/64			
<i>dpy-18(-); unc-46(-) let-418(s1617)</i>	73.8 \pm 3.5	57/64	<0.0001		
<i>daf-16(mu86); dpy-18(-); unc-46(-)</i>	24.9 \pm 2.8	37/42	0.0019		
<i>daf-16(-); dpy-18(-); unc-46(-) let-418(-)</i>	45.9 \pm 3.1	45/45	0.0076	<i>daf-16(-); dpy-18(-); unc-46(-)</i>	<0.0001
				<i>dpy-18(-); unc-46(-) let-418(-)</i>	<0.0001
<i>dpy-18(e363); unc-46(e177) control</i>	27.1 \pm 1.2	57/65			
<i>dpy-18(-); unc-46(-) let-418(s1617)</i>	51.3 \pm 2.2	101/106	<0.0001		
<i>daf-16(mu86); dpy-18(-); unc-46(-)</i>	31.9 \pm 1.3	54/59	0.0089		
<i>daf-16(-); dpy-18(-); unc-46(-) let-418(-)</i>	39.2 \pm 1.5	119/121	<0.0001	<i>daf-16(-); dpy-18(-); unc-46(-)</i>	0.002
				<i>dpy-18(-); unc-46(-) let-418(-)</i>	<0.0001

p-values(Log-Rank test) calculated for each individual experiment are shown.

Table S5 Mutations in *let-418* enhance thermic stress resistance

Genotype	Mean survival ± SEM (Hours)	Total number of animals Died/Total	P value vs control	vs strain	P value
wt control	11 ± 0.2	50/50			
<i>let-418(n3536ts)</i>	13.4 ± 0.3	50/50	<0.0001		
<i>unc-46(e177) control</i>	9.8 ± 0.2	50/50			
<i>unc-46(-) let-418(s1617)</i>	12.4 ± 0.2	50/50	<0.0001		
<i>daf-16(mu86); unc-46(-)</i>	9.4 ± 0.1	49/50	0.1608		
<i>daf-16(-); unc-46(-) let-418(-)</i>	10.2 ± 0.2	49/50	0.0939	<i>daf-16(-); unc-46(-)</i>	<0.0001
				<i>unc-46(-) let-418(-)</i>	0.037
<i>dpy-18(e363); unc-46(e177)</i>	13.9 ± 0.3	48/50			
control					
<i>dpy-18(-); unc-46(-) let-418(s1617)</i>	19.7 ± 0.3	50/50	<0.0001		
<i>daf-16(mu86); dpy-18(-); unc-46(-)</i>	12.9 ± 0.3	43/50	0.69		
<i>daf-16(-); dpy-18(-); unc-46(-) let-418(-)</i>	16.7 ± 0.4	49/50	<0.0001	<i>daf-16(-); dpy-18(-); unc-46(-)</i>	<0.0001
				<i>dpy-18(-); unc-46(-) let-418(-)</i>	<0.0001
<i>dpy-18(e363); unc-46(e177)</i>	13.7 ± 0.1	50/50			
control					
<i>dpy-18(-); unc-46(-) let-418(s1617)</i>	19.1 ± 0.4	50/50	<0.0001		
<i>daf-16(mu86); dpy-18(-); unc-46(-)</i>	13.6 ± 0.1	50/50	0.0151		
<i>daf-16(-); dpy-18(-); unc-46(-) let-418(-)</i>	15.7 ± 0.3	50/50	<0.0001	<i>daf-16(-); dpy-18(-); unc-46(-)</i>	<0.0001
				<i>dpy-18(-); unc-46(-) let-418(-)</i>	<0.0001

p-values(Log-Rank test) calculated for each individual experiment are shown.