

Strain	Genotype and RNAi treatment	Trial	Mean lifespan ± SEM (days)	% Difference	N (total)	<i>p</i>
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	1	29.2 ± 0.98		73 (98)	-
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	1	28.0 ± 0.72	-3.8 ^b	78 (96)	0.047 ^a
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-5</i> RNAi	1	27.5 ± 1.08	-5.6 ^b	56 (82)	NS ^a
NL2099	<i>rrf-3</i> control RNAi	2	14.8 ± 0.52		86 (99)	
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	2	28.4 ± 1.08		86 (88)	<0.0001 ^b
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	2	23.2 ± 0.79	-18.4 ^b	109 (109)	<0.0001 ^a
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-5</i> RNAi	2	25.9 ± 0.99	-9.0 ^b	108 (108)	0.07 ^a
NL2099	<i>rrf-3</i> control RNAi	3	13.7 ± 0.47		82 (82)	-
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	3	26.5 ± 0.83		106 (118)	<0.0001 ^b
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	3	22.9 ± 0.70	-13.7 ^b	108 (108)	<0.0001 ^a
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-5</i> RNAi	3	26.0 ± 1.10	-2.1 ^b	81 (81)	NS ^a
NL2099	<i>rrf-3</i> control RNAi	4	12.6 ± 0.34		119 (123)	-
NL2099	<i>rrf-3 aakg-4</i> RNAi	4	11.8 ± 0.35	-6.5 ^a	79 (81)	0.08 ^b
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	4	26.6 ± 0.86		127 (127)	<0.0001 ^b
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	4	20.0 ± 0.72	-24.8 ^b	102 (102)	<0.0001 ^{a/b}
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-5</i> RNAi	4	17.8 ± 0.72	-32.9 ^b	114 (114)	<0.0001 ^{a/b}
NL2099	<i>rrf-3</i> control RNAi	5	11.6 ± 0.39		49 (50)	-
NL2099	<i>rrf-3 aakg-4</i> RNAi	5	10.8 ± 0.36	-6.9 ^a	49 (50)	NS ^b
NL2099	<i>rrf-3 aakg-5</i> RNAi	5	10.9 ± 0.39	-5.9 ^a	50 (50)	NS ^b
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	5	27.9 ± 1.01		43 (50)	<0.0001 ^b
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	5	22.9 ± 0.53	-18.0 ^b	47 (50)	<0.0001 ^{a/b}
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-5</i> RNAi	5	29.0 ± 0.72	+4.0 ^b	47 (50)	NS ^a <0.0001 ^b
NL2099	<i>rrf-3</i> control RNAi	6	9.2 ± 0.27		75(75)	-
NL2099	<i>rrf-3 aakg-4</i> RNAi	6	10.3 ± 0.26	+11.8 ^a	73 (75)	0.005 ^a
GA303	<i>rrf-3</i> ; <i>daf-2</i> control RNAi	6	27.1 ± 0.47		56 (60)	<0.0001 ^a
GA303	<i>rrf-3</i> ; <i>daf-2 aakg-4</i> RNAi	6	24.1 ± 0.52	-10.8 ^b	73 (75)	<0.0001 ^a 0.0002 ^b
NL2099	<i>rrf-3</i> control RNAi	7	12.1 ± 0.33		67 (67)	-
NL2099	<i>rrf-3 aakg-4</i> RNAi	7	11.0 ± 0.31	-8.9 ^a	66 (68)	0.02 ^b
NL2099	<i>rrf-3 aakg-5</i> RNAi	7	12.0 ± 0.40	-0.8 ^a	65 (67)	NS ^b
	N2 control RNAi	8	9.7 ± 0.25		96 (99)	
	N2 <i>aakg-4</i> RNAi	8	10.2 ± 0.22	+5.22 ^a	116 (122)	0.1370 ^a
	N2 <i>aakg-5</i> RNAi	8	10.7 ± 0.27	+10.61 ^a	98 (99)	0.0045 ^a
GA1071	<i>aakg-4</i> control RNAi	8	10.8 ± 0.26		96 (99)	0.0027 ^a
GA1071	<i>aakg-4</i> ; <i>aakg-5</i> RNAi	8	12.2 ± 0.21	+12.37 ^c	97 (97)	0.0005 ^c
DR1567	<i>daf-2</i> control RNAi	8	21.5 ± 0.79		80 (85)	<0.0001 ^a
DR1567	<i>daf-2 aakg-4</i> RNAi	8	19.7 ± 0.69	-8.43 ^b	106 (111)	0.0013 ^b

DR1567	<i>daf-2 aakg-5</i> RNAi	8	16.9 ± 0.69	-21.24 ^b	55 (67)	<0.0001 ^b
	N2 control RNAi	9	9.9 ± 0.29		100 (100)	
	N2 <i>aakg-4</i> RNAi	9	9.9 ± 0.34	+0.68 ^a	64 (64)	NS ^a
	N2 <i>aakg-5</i> RNAi	9	10.0 ± 0.31	+1.72 ^a	100 (100)	NS ^a
GA1071	<i>aakg-4</i> control RNAi	9	10.4 ± 0.26		98 (99)	NS ^a
GA1071	<i>aakg-4; aakg-5</i> RNAi	9	10.6 ± 0.29	+2.46 ^c	100 (100)	NS ^c
DR1567	<i>daf-2</i> control RNAi	9	23.8 ± 0.71		85 (87)	<0.0001 ^a
DR1567	<i>daf-2 aakg-4</i> RNAi	9	20.0 ± 0.57	-15.72 ^b	95 (95)	<0.0001 ^b
DR1567	<i>daf-2 aakg-5</i> RNAi	9	20.2 ± 0.74	-14.92 ^b	90 (90)	0.0028 ^b
GA1072	<i>daf-2; aakg-4</i> control RNAi	9	18.2 ± 1.00		38 (38)	<0.0001 ^b
GA1072	<i>daf-2; aakg-4 aakg-5</i> RNAi	9	19.7 ± 0.74	+7.95 ^d	80 (80)	NS ^d
DR1567	<i>daf-2</i> control RNAi	10	24.1 ± 0.73		105 (115)	-
DR1567	<i>daf-2 aakg-5</i> RNAi	10	18.5 ± 0.75	-23.40 ^b	99 (101)	<0.0001 ^b
GA1072	<i>daf-2; aakg-4</i> control RNAi	10	18.9 ± 0.73	-21.65 ^b	71 (71)	<0.0001 ^b
GA1072	<i>daf-2; aakg-4 aakg-5</i> RNAi	10	19.5 ± 0.67	+3.23 ^d	86 (95)	NS ^d

Table S8. *aakg-4* and *aakg-5* RNAi shorten *daf-2* lifespan.