

Table S1

IIS RNAi (Figure 7C,D,E)	EV(RNAi)	5 mM caffeine	15°C	28.0	30.2	213	EV(RNAi)	0 mM caffeine	15°C	25.0	25.9	253	8.62E-09	16.6%	increased
	EV(RNAi)	10 mM caffeine	15°C	31.0	35.7	195	EV(RNAi)	0 mM caffeine	15°C	25.0	25.9	253	5.64E-28	37.6%	increased
	daf-2(RNAi)	0 mM caffeine	15°C	47.0	45.6	218	EV(RNAi)	0 mM caffeine	15°C	25.0	25.9	253	4.30E-46	75.7%	increased
	daf-2(RNAi)	5 mM caffeine	15°C	46.0	46.4	266	EV(RNAi)	5 mM caffeine	15°C	28.0	30.2	213	1.80E-40	53.5%	increased
	daf-2(RNAi)	10 mM caffeine	15°C	47.5	49.1	206	EV(RNAi)	10 mM caffeine	15°C	31.0	35.7	195	1.40E-26	37.6%	increased
	daf-2(RNAi)	5 mM caffeine	15°C	46.0	46.4	266	daf-2(RNAi)	0 mM caffeine	15°C	47.0	45.6	218	0.6015	1.9%	no effect
	daf-2(RNAi)	10 mM caffeine	15°C	47.5	49.1	206	daf-2(RNAi)	0 mM caffeine	15°C	47.0	45.6	218	0.0148	7.7%	increased
	daf-16(RNAi)	0 mM caffeine	15°C	20.0	21.5	215	EV(RNAi)	0 mM caffeine	15°C	25.0	25.9	253	1.79E-20	-16.9%	decreased
	daf-16(RNAi)	5 mM caffeine	15°C	24.0	22.3	272	EV(RNAi)	5 mM caffeine	15°C	28.0	30.2	213	6.61E-35	-26.2%	decreased
	daf-16(RNAi)	10 mM caffeine	15°C	24.0	25.8	180	EV(RNAi)	10 mM caffeine	15°C	31.0	35.7	195	9.79E-28	-27.7%	decreased
	daf-16(RNAi)	5 mM caffeine	15°C	24.0	22.3	272	daf-16(RNAi)	0 mM caffeine	15°C	20.0	21.5	215	0.0884	3.6%	no effect
	daf-16(RNAi)	10 mM caffeine	15°C	24.0	25.8	180	daf-16(RNAi)	0 mM caffeine	15°C	20.0	21.5	215	4.51E-12	19.7%	increased
Longevity Pathway Epistasis (Figure 6;7A,B)		5 mM caffeine	15°C	31.0	34.6	419		0 mM caffeine	15°C	25.0	26.6	416	1.25E-38	29.8%	increased
		10 mM caffeine	15°C	36.0	36.5	426		0 mM caffeine	15°C	25.0	26.6	416	3.10E-54	37.1%	increased
	daf-16	0 mM caffeine	15°C	24.0	26.8	243		0 mM caffeine	15°C	25.0	26.6	416	0.8121	0.7%	no effect
	daf-16	5 mM caffeine	15°C	25.5	27.8	216		5 mM caffeine	15°C	31.0	34.6	419	4.04E-16	-19.7%	decreased
	daf-16	10 mM caffeine	15°C	25.5	26.9	242		10 mM caffeine	15°C	36.0	36.5	426	1.06E-36	-26.3%	decreased
	daf-16	5 mM caffeine	15°C	25.5	27.8	216	daf-16	0 mM caffeine	15°C	24.0	26.8	243	0.0613	3.5%	no effect
	daf-16	10 mM caffeine	15°C	25.5	26.9	242	daf-16	0 mM caffeine	15°C	24.0	26.8	243	0.0196	0.4%	increased
	cep-1	0 mM caffeine	15°C	32.0	33.5	186		0 mM caffeine	15°C	25.0	26.6	416	3.77E-10	25.8%	increased
	cep-1	5 mM caffeine	15°C	43.0	39.8	177		5 mM caffeine	15°C	31.0	34.6	419	0.0003	15.3%	increased
	cep-1	10 mM caffeine	15°C	39.0	37.2	160		10 mM caffeine	15°C	36.0	36.5	426	0.5192	1.8%	no effect
	cep-1	5 mM caffeine	15°C	43.0	39.8	177	cep-1	0 mM caffeine	15°C	32.0	33.5	186	2.81E-06	18.9%	increased
	cep-1	10 mM caffeine	15°C	39.0	37.2	160	cep-1	0 mM caffeine	15°C	32.0	33.5	186	0.0033	11.0%	increased
	sir-2.1	0 mM caffeine	15°C	28.0	31.9	159		0 mM caffeine	15°C	25.0	26.6	416	3.05E-09	19.7%	increased
	sir-2.1	5 mM caffeine	15°C	35.0	34.8	181		5 mM caffeine	15°C	31.0	34.6	419	0.9844	0.8%	no effect
	sir-2.1	10 mM caffeine	15°C	36.0	36.4	158		10 mM caffeine	15°C	36.0	36.5	426	0.8455	-0.3%	no effect
	sir-2.1	5 mM caffeine	15°C	35.0	34.8	181	sir-2.1	0 mM caffeine	15°C	28.0	31.9	159	0.0055	9.3%	increased
	sir-2.1	10 mM caffeine	15°C	36.0	36.4	158	sir-2.1	0 mM caffeine	15°C	28.0	31.9	159	3.17E-06	14.2%	increased
	hlf-1	0 mM caffeine	15°C	27.0	27.2	404		0 mM caffeine	15°C	25.0	26.6	416	1.09E-07	2.0%	increased
	hlf-1	5 mM caffeine	15°C	31.0	31.6	340		5 mM caffeine	15°C	31.0	34.6	419	0.0023	-8.6%	decreased
	hlf-1	10 mM caffeine	15°C	31.0	33.0	294		10 mM caffeine	15°C	36.0	36.5	426	2.06E-05	-9.7%	decreased
	hlf-1	5 mM caffeine	15°C	31.0	31.6	340	hlf-1	0 mM caffeine	15°C	27.0	27.2	404	2.92E-14	16.2%	increased
	hlf-1	10 mM caffeine	15°C	31.0	33.0	294	hlf-1	0 mM caffeine	15°C	27.0	27.2	404	7.95E-20	21.3%	increased
Intervention						Control						Change			
Experiment	Name	Temp.	Median Life Span	Mean Life Span	N	Name	Temp.	Median Life Span	Mean Life Span	N	Rank Sum P-Value	in Mean Life	Effect on Life Span		
Dose response (Figures 1;2)	5 mM caffeine	15°C	35.0	36.7	977	0 mM caffeine	15°C	27.0	28.6	1037	1.84E-83	28.5%	increased		
	7.5 mM caffeine	15°C	34.0	34.2	186	0 mM caffeine	15°C	27.0	28.6	1037	8.92E-20	19.6%	increased		
	10 mM caffeine	15°C	39.0	39.1	644	0 mM caffeine	15°C	27.0	28.6	1037	2.97E-98	36.7%	increased		
	20 mM caffeine	15°C	34.0	34.7	227	0 mM caffeine	15°C	27.0	28.6	1037	3.10E-22	21.6%	increased		
	50 mM caffeine	15°C	17.0	16.9	188	0 mM caffeine	15°C	27.0	28.6	1037	3.70E-55	-40.9%	decreased		
	75 mM caffeine	15°C	3.0	4.9	57	0 mM caffeine	15°C	27.0	28.6	1037	7.07E-37	-82.8%	decreased		
	100 mM caffeine	15°C	3.0	3.0	83	0 mM caffeine	15°C	27.0	28.6	1037	5.02E-52	-89.5%	decreased		
	0.5 mM caffeine	20°C	26.0	26.5	186	0 mM caffeine	20°C	23.0	24.6	575	0.0001	7.7%	increased		
	2.5 mM caffeine	20°C	28.0	28.8	167	0 mM caffeine	20°C	23.0	24.6	575	1.12E-15	17.2%	increased		
	5 mM caffeine	20°C	26.0	27.3	523	0 mM caffeine	20°C	23.0	24.6	575	8.27E-13	10.8%	increased		
Bacteria Deprivation (Figure 5A,B)	7.5 mM caffeine	20°C	28.0	26.7	243	0 mM caffeine	20°C	23.0	24.6	575	8.54E-08	8.7%	increased		
	10 mM caffeine	20°C	28.0	28.8	227	0 mM caffeine	20°C	23.0	24.6	575	1.87E-14	16.9%	increased		
	30 mM caffeine	20°C	19.0	18.6	92	0 mM caffeine	20°C	23.0	24.6	575	1.55E-18	-24.4%	decreased		
	5 mM caffeine	25°C	14.0	15.4	178	0 mM caffeine	25°C	17.0	17.8	170	1.97E-07	-13.6%	decreased		
	7.5 mM caffeine	25°C	15.0	15.8	165	0 mM caffeine	25°C	17.0	17.8	170	2.54E-05	-11.6%	decreased		
	0 mM caffeine BD	15°C	48.0	44.0	136	0 mM caffeine	15°C	31.0	33.6	248	1.57E-16	31.2%	increased		
	5 mM caffeine BD	15°C	45.0	45.1	131	5 mM caffeine	15°C	48.0	44.5	228	0.8533	1.5%	no effect		
	10 mM caffeine BD	15°C	43.0	42.4	146	10 mM caffeine	15°C	47.0	44.0	218	0.0764	-3.7%	no effect		
	20 mM caffeine BD	15°C	38.0	37.9	58	20 mM caffeine	15°C	38.0	37.1	159	0.5511	2.4%	no effect		
	50 mM caffeine BD	15°C	14.0	14.7	95	50 mM caffeine	15°C	19.0	19.1	141	4.47E-08	-23.1%	decreased		
	5 mM caffeine	15°C	48.0	44.5	228	0 mM caffeine	15°C	31.0	33.6	248	3.09E-29	32.5%	increased		
	10 mM caffeine	15°C	47.0	44.0	218	0 mM caffeine	15°C	31.0	33.6	248	1.90E-24	31.1%	increased		
	20 mM caffeine	15°C	38.0	37.1	159	0 mM caffeine	15°C	31.0	33.6	248	0.0004	10.4%	increased		
	50 mM caffeine	15°C	19.0	19.1	141	0 mM caffeine	15°C	31.0	33.6	248	2.82E-42	-43.0%	decreased		
	5 mM caffeine BD	15°C	45.0	45.1	131	0 mM caffeine BD	15°C	48.0	44.0	136	0.9406	2.5%	no effect		
	10 mM caffeine BD	15°C	43.0	42.4	146	0 mM caffeine BD	15°C	48.0	44.0	136	0.0649	-3.8%	no effect		
	20 mM caffeine BD	15°C	38.0	37.9	58	0 mM caffeine BD	15°C	48.0	44.0	136	0.0001	-13.9%	decreased		
	50 mM caffeine BD	15°C	14.0	14.7	95	0 mM caffeine BD	15°C	48.0	44.0	136	3.79E-35	-66.6%	decreased		
	0 mM caffeine BD	20°C	23.0	24.4	61	0 mM caffeine	20°C	21.0	21.3	70	0.0001	14.4%	increased		
	5 mM caffeine BD	20°C	26.0	25.6	73	5 mM caffeine	20°C	26.0	25.3	92	0.5703	1.4%	no effect		
10 mM caffeine BD	20°C	23.0	24.2	66	10 mM caffeine	20°C	23.0	23.5	72	0.1699	3.1%	no effect			
30 mM caffeine BD	20°C	4.0	16.0	16	30 mM caffeine	20°C	4.0	19.0	18.6	1.17E-05	-15.8%	decreased			
	5 mM caffeine	20°C	26.0	25.3	92	0 mM caffeine	20°C	21.0	21.3	70	2.66E-07	18.8%	increased		
	10 mM caffeine	20°C	23.0	23.5	72	0 mM caffeine	20°C	21.0	21.3	70	0.0061	10.4%	increased		
	30 mM caffeine	20°C	4.0	19.0	19	0 mM caffeine	20°C	21.0	21.3	70	0.0012	-10.7%	decreased		

Table S2

Strain	Genotype
N2	wild type
CF1038	<i>daf-16(mu86) I</i>
VC199	<i>sir-2.1(ok434) IV</i>
TJ1	<i>cep-1(gk138) I</i>
ZG31	<i>hif-1(ia4) V</i>
TJ356	<i>zls356[pdaf-16::daf-16-gfp; rol-6]</i>
MQ35	<i>Q35::YFP</i>