

SUPPLEMENTARY INFORMATION

Supplementary Table 1. Lifespan and lifetime egg production of mated female Canton-S flies on 0.1X or 1.0X diets containing 0, 1, 10, or 100 mM Met.

Fig.	GB	Sex	Diets		Lifespan			Reproduction		
			AA	Met	n	Mean \pm s.e.m.	% increase*	n	Egg production \pm s.d.**	% increase***
1	S	F	0.1X	0 mM	146	51.10 \pm 0.73	-32.85	40	14.62 \pm 4.62	-67.55
	S	F		1 mM	144	76.10 \pm 1.02	Control	40	45.04 \pm 3.85	Control
	S	F		10 mM	150	69.30 \pm 1.32	-8.94	40	35.96 \pm 2.22	-20.17
	S	F	1.0X	0 mM	191	41.31 \pm 0.77	-19.69	40	49.54 \pm 4.90	-73.04
	S	F		1.5 mM	205	52.33 \pm 1.10	1.74	40	84.71 \pm 9.11	-53.90
	S	F		10 mM	205	51.44 \pm 1.14	Control	40	183.77 \pm 9.63	Control
	S	F		100 mM	205	40.30 \pm 1.17	-21.65	40	137.82 \pm 20.10	-25.00

GB: Genetic Background, S: Canton-S, F: Female, AA: Amino acids

*: % increase of mean lifespan over flies on the control diets (1 mM Met-0.1X and 10 mM Met-1.0X)

**: Average of lifetime egg production counted on for 24 hours every three day from 4 independent experiments

***: % increase of egg production over flies on the control diets (1 mM Met-0.1X and 10 mM Met-1.0X)

Supplementary Table 2. Test of homogeneity of survivorship and lifetime egg production shown in Supplementary Table 1.

Fig.	GB	Sex	AA	Diets for comparison		Lifespan		Reproduction
				Met		Log-Rank		Student's <i>t</i> -test
						χ^2	$p > \chi^2$	
1	S	F	0.1X	1 mM	0 mM	253.5835	<.0001	p<.01
	S	F		1 mM	10 mM	9.103	0.0026	p=0.048
	S	F	1X	10 mM	1.5 mM	0.0016	0.9678	p<.01
	S	F		10 mM	100 mM	36.3905	<.0001	p=0.039
	S	F		1.5 mM	0 mM	106.701	<.0001	p<.01

Supplementary Table 3. Lifespan and test of homogeneity of survivorship.

Fig.	GB	Sex	Diets		Lifespan		Log-Rank		
			AA	Met	n	Mean \pm s.e.m.	% increase*	χ^2	$\rho > \chi^2$
2&3	S	F	0.1X	0.15 mM	195	47.49 \pm 0.81	-0.29	3.4203	0.0644
	S	F		1 mM	196	47.63 \pm 0.60		Control	
	S	F		10 mM	184	42.64 \pm 0.69	-10.48	37.468	<.0001
	S	M		0.15 mM	191	45.31 \pm 0.69	7.93	12.1657	0.0005
	S	M		1 mM	187	41.98 \pm 0.67		Control	
	S	M		10 mM	196	43.73 \pm 0.65	4.17	2.3669	0.1239
	R	F		0.15 mM	203	37.92 \pm 0.57	-13.64	62.7935	<.0001
	R	F		1 mM	203	43.91 \pm 0.57		Control	
	R	F		10 mM	201	39.09 \pm 0.51	-10.98	43.5385	<.0001
	R	M		0.15 mM	202	35.03 \pm 0.55	-9.48	20.3038	<.0001
	R	M		1 mM	198	38.70 \pm 0.50		Control	
	R	M		10 mM	206	38.23 \pm 0.46	-1.21	0.3137	0.5754
	W	F		0.15 mM	91	53.08 \pm 0.89	-7.75	10.7038	0.0011
	W	F		1 mM	94	57.54 \pm 0.85		Control	
	W	F		10 mM	81	43.96 \pm 1.21	-23.6	43.3324	<.0001
W	M	0.15 mM	99	57.55 \pm 0.75	-2.74	7.7404	0.0054		
W	M	1 mM	94	59.17 \pm 0.97		Control			
W	M	10 mM	85	57.64 \pm 1.20	-2.59	0.0301	0.8623		

GB: Genetic Background, S: Canton-S, R: Oregon-R, W: *w¹¹¹⁸*, F: Female, M: Male, AA: Amino acids

*: % increase of mean lifespan over flies on the control diets (1 mM Met)

Supplementary Table 4. Lifespan and lifetime egg production of mated female Canton-S flies on 0.1X, 0.4X, or 1.0X diets containing 0, 0.15, or 1 mM Met.

Fig.	GB	Sex	Diets		Lifespan			Reproduction		
			AA	Met	n	Mean \pm s.e.m.	% increase*	n	Egg production \pm s.d.**	% increase***
4	S	F		0 mM	147	49.69 \pm 0.66	-34.95	40	45.66 \pm 4.93	-14.09
	S	F	0.4X	0.15 mM	123	76.39 \pm 1.44	Control	40	53.15 \pm 5.92	Control
	S	F		1 mM	150	66.82 \pm 0.96	-12.53	40	108.32 \pm 10.38	103.80
	S	F		0 mM	151	47.40 \pm 0.52	-21.39	40	44.54 \pm 4.63	-20.02
	S	F	0.7X	0.15 mM	150	60.30 \pm 1.11	Control	40	55.69 \pm 2.84	Control
	S	F		1 mM	150	60.42 \pm 1.05	0.20	40	131.13 \pm 18.65	135.45
	S	F		0 mM	134	40.70 \pm 0.63	-12.57	40	49.54 \pm 5.99	-21.61
	S	F	1.0X	0.15 mM	143	46.55 \pm 1.06	Control	40	63.20 \pm 3.06	Control
	S	F		1 mM	144	55.60 \pm 1.27	19.44	40	148.76 \pm 12.53	135.38

GB: Genetic Background, S: Canton-S, F: Female, AA: Amino acids

*: % increase of mean lifespan over flies on the control diets (0.15 mM Met in each amino acid diet)

** : Average of lifetime egg production counted on for 24 hours every three day from 4 independent experiments

***: % increase of egg production over flies on the control diets (0.15 mM Met in each amino acid diet)

Supplementary Table 5. Test of homogeneity of survivorship and lifetime egg production shown in Supplementary Table 4.

Fig.	GB	Sex	AA	Diets for comparison		Lifespan		Reproduction
				Met		Log-Rank		Student's <i>t</i> -test
						χ^2	$p > \chi^2$	
4	S	F	0.4X	0.15 mM	0 mM	195.4226	<.0001	p=0.308
	S	F		0.15 mM	1 mM	53.1079	<.0001	p<.01
	S	F	0.7X	0.15 mM	0 mM	115.4874	<.0001	p=0.03
	S	F		0.15 mM	1 mM	0.0004	0.9842	p=0.02
	S	F	1.0X	0.15 mM	0 mM	33.3613	<.0001	p=0.01
	S	F		0.15 mM	1 mM	31.7566	<.0001	p<.01

GB: Genetic Background, S: Canton-S, F: Female, AA: Amino acids

Supplementary Table 6. Test of homogeneity of survivorship and lifetime egg production shown in Supplementary Table 4.

Fig.	GB	Sex	Met	Diets for comparison		% increase*	Lifespan		Reproduction
				AA			Log-Rank		Student's <i>t</i> -test
							χ^2	$p > \chi^2$	
4	S	F	0 mM	0.4X	1.0X	-22.09	88.3917	<.0001	p=0.828
	S	F	0.15 mM	0.4X	1.0X	-64.10	183.4938	<.0001	p=0.185
	S	F	1 mM	0.4X	1.0X	-20.17	26.3467	<.0001	p=0.09

GB: Genetic Background, S: Canton-S, F: Female, AA: Amino acids

*: % increase of mean lifespan over flies on the 0.4X diets (0.4X Vs 1.0X)

Supplementary Table 7. Correlation between mean lifespan and lifetime egg production shown in Supplementary Table 4.

Changes in Met	AA	Correlation between mean lifespan and lifetime egg production*	
		Pearson Coefficient	p-value
Decrease from 1.0 mM Met to 0.15mM Met	0.4X	-0.963 ~ -0.864	0.0021 ~ 0.0265
	0.7X	-0.184 ~ 0.278	0.5941 ~ 0.9923
	1.0X	0.662 ~ 0.963	0.0020 ~ 0.1522

* Three independent measurements of mean lifespan and three independent measurements of lifetime egg production were taken at each diet. Pearson correlation coefficients and p-values were computed for all potential combinations of the measurements, and the ranges were indicated above. Under methionine restriction, there was a strong negative correlation between mean lifespan and lifetime egg production on the low amino acid status, but no correlation or weak correlation on the high amino acid status.

Supplementary Table 8. Lifespan of virgin female Canton-S flies on 0.1X, 0.4X, or 1.0X diets containing 0, 0.15, or 1 mM Met.

Fig.	GB	Sex	Diets		Lifespan		
			AA	Met	n	Mean \pm s.e.m.	% increase*
7	S	F(V)		0 mM	103	46.37 \pm 0.82	-33.79
	S	F(V)	0.4X	0.15 mM	92	70.04 \pm 2.18	Control
	S	F(V)		1 mM	93	57.06 \pm 1.40	-18.53
	S	F(V)		0 mM	111	43.00 \pm 0.59	-31.98
	S	F(V)	0.7X	0.15 mM	97	63.22 \pm 1.47	Control
	S	F(V)		1 mM	93	56.74 \pm 1.24	-10.25
	S	F(V)		0 mM	100	39.63 \pm 0.67	-20.60
	S	F(V)	1.0X	0.15 mM	105	49.91 \pm 1.30	Control
	S	F(V)		1 mM	101	54.06 \pm 1.44	8.31

GB: Genetic Background, S: Canton-S, F(V): Virgin female, AA: Amino acids

*: % increase of mean lifespan over flies on the control diets (0.15 mM Met in each amino acid diet)

Supplementary Table 9. Test of homogeneity of survivorship shown in Supplementary Table 8.

Fig.	GB	Sex	AA	Diets for comparison		Lifespan	
				Met		Log-Rank	
						χ^2	$p > \chi^2$
7	S	F(V)	0.4X	0.15 mM	0 mM	112.9819	<.0001
	S	F(V)		0.15 mM	1 mM	35.7991	<.0001
	S	F(V)	0.7X	0.15 mM	0 mM	138.8413	<.0001
	S	F(V)		0.15 mM	1 mM	14.632	0.0001
	S	F(V)	1.0X	0.15 mM	0 mM	70.4184	<.0001
	S	F(V)		0.15 mM	1 mM	6.9342	0.0085

GB: Genetic Background, S: Canton-S, F(V): Virgin female, AA: Amino acids

Supplementary Table 10. Yeast replicative lifespan on various Met diets.

Fig.	GB	Diets		n	Mean lifespan (Replication times)
		AA	Met (mg/ml)		
7	Yeast	1.0X	1	30	16.30
			0.5	30	18.50
			0.1	30	17.63
			0.05	30	22.03**
			0.005	30	23.40**

GB: Genetic Background, AA: Amino acids

*Rank sum test was performed on all tested samples and ** means $p < .05$ when compared with yeast lifespan on 1, 0.5, and 0.1 mg/ml Met diets

Supplementary Table 11. Yeast replicative lifespan on various Met and amino acids diets.

Fig.	GB	Diets		n	Mean lifespan (Replication times)	% increase	Rank sum
		AA	Met (mg/ml)				
7	Yeast	1.0X	0.5	30	16.27	Control	p<.05
			0.05	30	19.73	21.31	
		0.2X	0.5	30	14.97	Control	p<.0001
			0.05	30	21.03	40.53	

GB: Genetic Background, AA: Amino acids

*: % increase of mean lifespan over yeast on control diets (0.5 mg/ml Met in each amino acid diet)

Supplementary Table 12. Lifespan and test of homogeneity of survivorship of mated female flies on 0.4X or 1.0X diets containing 0.2 or 1 mM Met.

Fig.	GB	Sex	Diets for comparison			Lifespan		Log-Rank	
			AA	Met	n	Mean \pm s.e.m.	% increase*	χ^2	$\rho > \chi^2$
8	<i>Da-GAL4>dInRDN</i>	F	1.0X	0.2 mM	104	48.87 \pm 1.00	-16.55	41.00	<.0001
	<i>Da-GAL4>dInRDN</i>	F		1 mM	106	58.56 \pm 1.29	Control		
	<i>Da-GAL4>dInRDN</i>	F	0.4X	0.2 mM	106	64.50 \pm 0.93	-2.88	2.70	0.10
	<i>Da-GAL4>dInRDN</i>	F		1 mM	103	66.41 \pm 1.03	Control		
	<i>+>dInRDN</i>	F	1.0X	0.2 mM	94	52.69 \pm 0.90	-12.82	30.01	<.0001
	<i>+>dInRDN</i>	F		1 mM	81	60.44 \pm 1.16	Control		
	<i>+>dInRDN</i>	F	0.4X	0.2 mM	101	66.83 \pm 1.01	15.86	31.22	<.0001
	<i>+>dInRDN</i>	F		1 mM	88	57.68 \pm 1.22	Control		
	<i>Da-GAL4>dTSC2</i>	F	1.0X	0.2 mM	149	49.77 \pm 0.87	-18.44	59.56	<.0001
	<i>Da-GAL4>dTSC2</i>	F		1 mM	147	61.02 \pm 1.20	Control		
	<i>Da-GAL4>dTSC2</i>	F	0.4X	0.2 mM	142	66.44 \pm 0.68	-21.88	239.31	<.0001
	<i>Da-GAL4>dTSC2</i>	F		1 mM	152	85.05 \pm 0.72	Control		
	<i>+>dTSC2</i>	F	1.0X	0.2 mM	106	53.89 \pm 0.93	-17.85	54.65	<.0001
	<i>+>dTSC2</i>	F		1 mM	104	65.60 \pm 1.21	Control		
	<i>+>dTSC2</i>	F	0.4X	0.2 mM	111	74.57 \pm 1.17	4.03	6.21	0.01
	<i>+>dTSC2</i>	F		1 mM	111	71.68 \pm 1.07	Control		

GB: Genetic Background, F: Female, AA: Amino acids, +: *w¹¹¹⁸*

*: % increase of mean lifespan over flies on the control diets (1 mM Met in each amino acid diet)

Supplementary Table 13. Lifespan and test of homogeneity of survivorship of mated female flies on 0.4X or 1.0X diets containing 0.2 or 1 mM Met.

Fig.	GB	Sex	Diets		Lifespan			Log-Rank	
			AA	Met	n	Mean \pm s.e.m.	% increase	χ^2	$\rho > \chi^2$
8	<i>Da-GAL4>dInRDN</i>	F	1.0X	0.2 mM	104	48.87 \pm 1.00	-7.25	3.29	0.07
	<i>+>dInRDN</i>	F			94	52.69 \pm 0.90	Control		
	<i>Da-GAL4>dInRDN</i>	F		1 mM	106	58.56 \pm 1.29	-3.11		
	<i>+>dInRDN</i>	F			81	60.44 \pm 1.16	Control		
	<i>Da-GAL4>dInRDN</i>	F	0.4X	0.2 mM	106	64.50 \pm 0.93	-3.49	3.37	0.07
	<i>+>dInRDN</i>	F			101	66.83 \pm 1.01	Control		
	<i>Da-GAL4>dInRDN</i>	F		1 mM	103	66.41 \pm 1.03	15.14		
	<i>+>dInRDN</i>	F			88	57.68 \pm 1.22	Control		
	<i>Da-GAL4>dTSC2</i>	F	1.0X	0.2 mM	149	49.77 \pm 0.87	-7.65	5.54	0.02
	<i>+>dTSC2</i>	F			106	53.89 \pm 0.93	Control		
	<i>Da-GAL4>dTSC2</i>	F		1 mM	147	61.02 \pm 1.20	-6.98		
	<i>+>dTSC2</i>	F			104	65.60 \pm 1.21	Control		
	<i>Da-GAL4>dTSC2</i>	F	0.4X	0.2 mM	142	66.44 \pm 0.68	-10.90	50.28	<.0001
	<i>+>dTSC2</i>	F			111	74.57 \pm 1.17	Control		
	<i>Da-GAL4>dTSC2</i>	F		1 mM	152	85.05 \pm 0.72	18.65		
	<i>+>dTSC2</i>	F			111	71.68 \pm 1.07	Control		

GB: Genetic Background, F: Female, AA: Amino acids, +: w^{1118}

*: % increase of mean lifespan over control flies