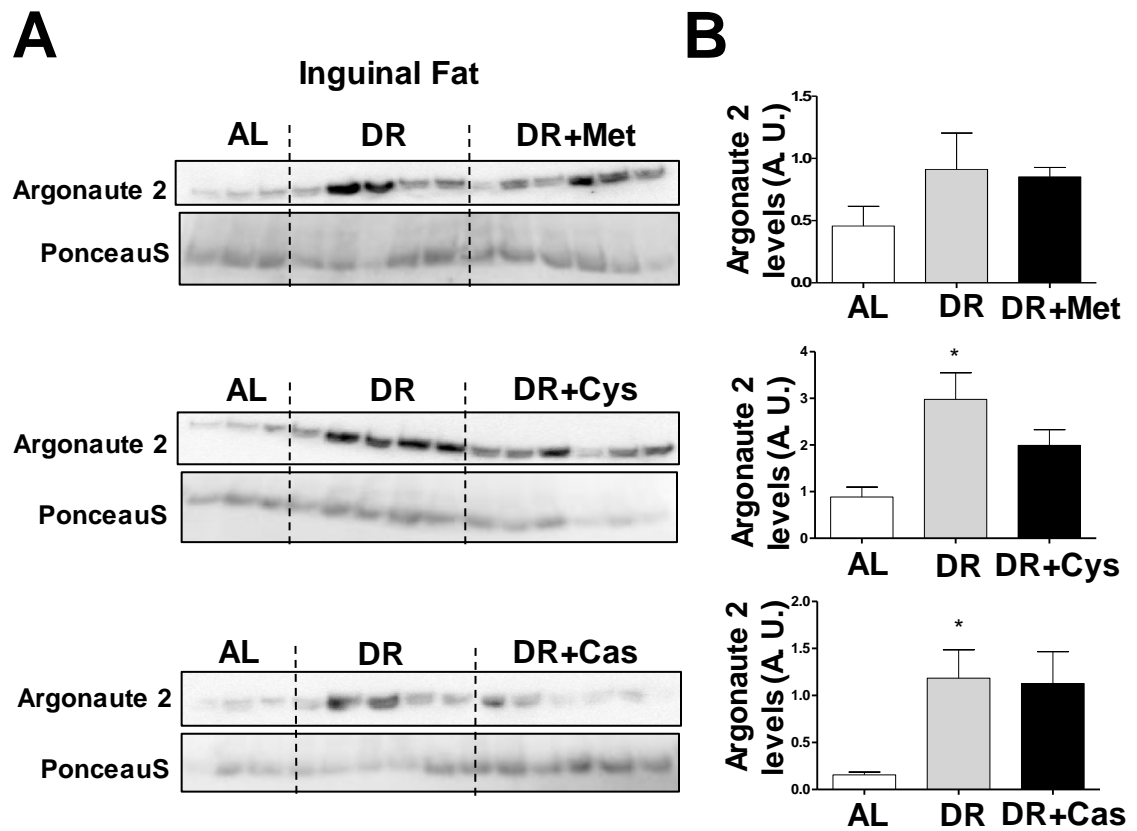
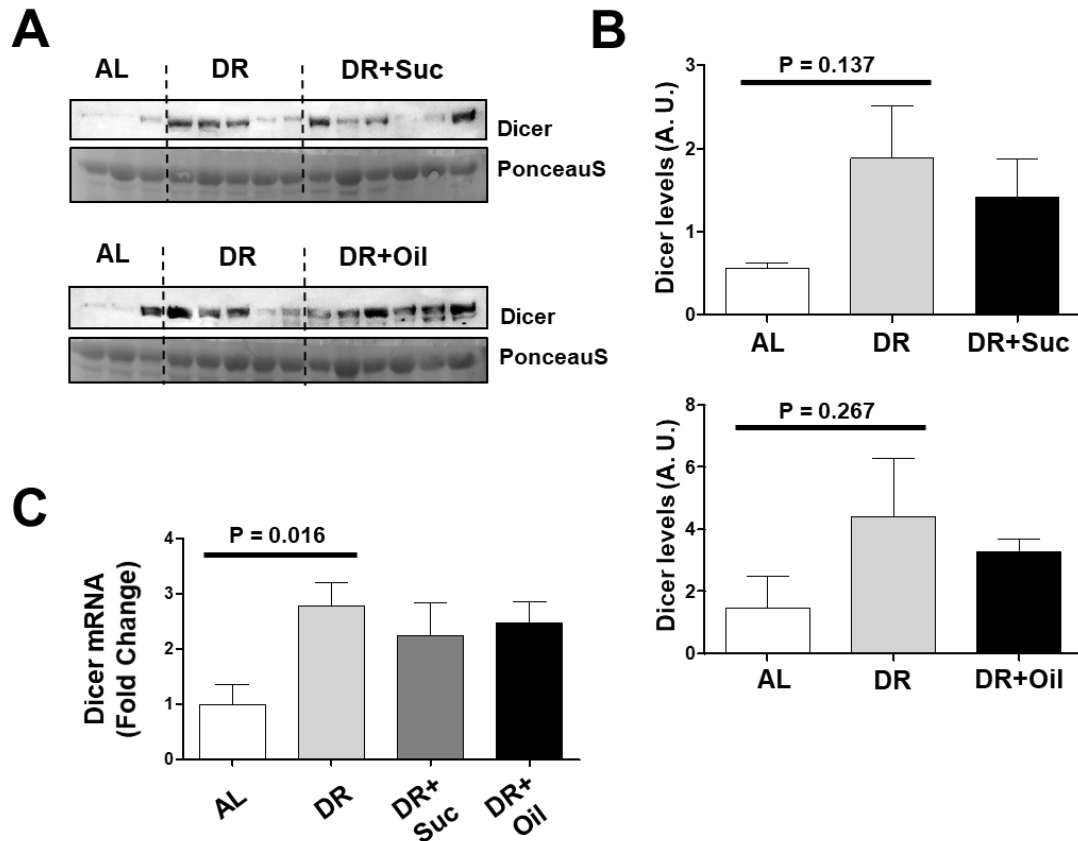


## Supplementary Data

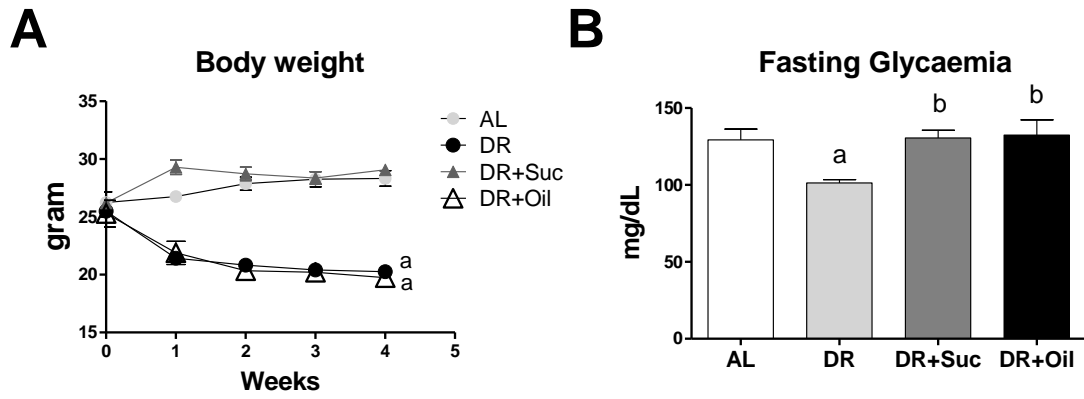
### Supplementary Figures



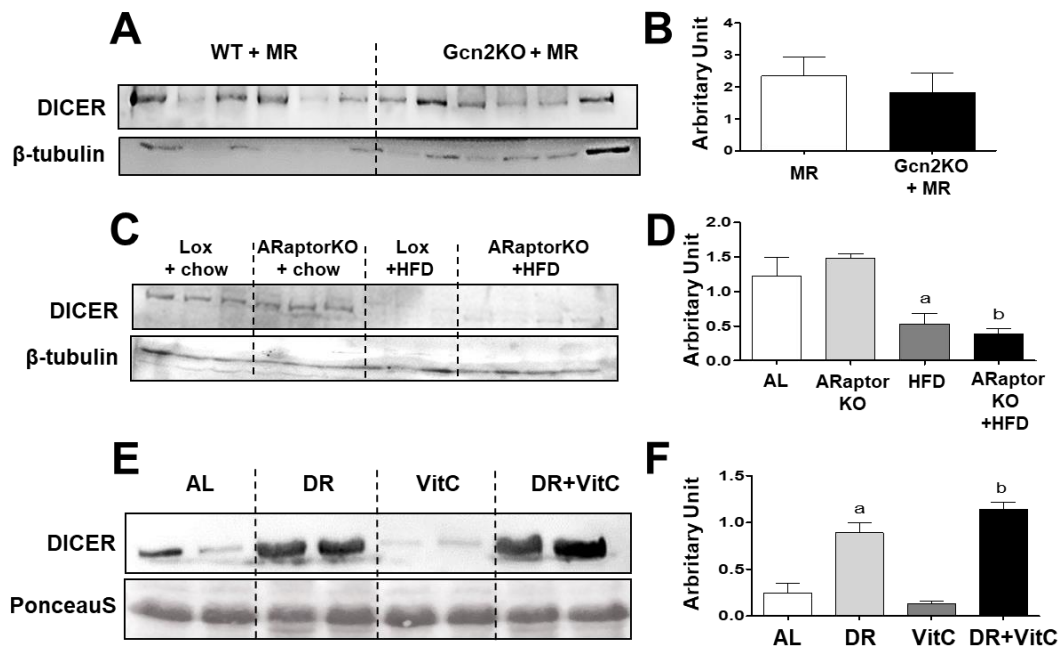
**Fig. S1. Effects of sulfur amino acid availability on the abundance of components of the miRNA processing pathway in adipose tissue.** (A and B) Mice were subjected to 4 weeks of *ad libitum* diet (AL, N = 3), dietary restriction (DR, N = 5) or DR plus 40% of methionine (DR+Met, N = 6), cysteine (DR+Cys, N = 6) or casein (DR+Cas, N = 6). A = Argonaute-2 (AGO2) protein abundance in inguinal fat. Ponceau S staining was used as loading control. B = band densitometry. \* $p < 0.001$  vs. AL. One-way ANOVA test with Tukey's as post-test. A.U. = arbitrary units.



**Fig. S2. Effects of dietary oil or sucrose availability on DICER abundance in adipose tissue.** Mice were subjected to 4 weeks of *ad libitum* diet (AL, N = 4), dietary restriction (DR, N = 5), DR plus sucrose (DR+Suc, N = 6) or oil (DR+Oil, N = 6). A = DICER protein abundance in inguinal fat. Ponceau S staining was used as loading control. B = band densitometry. C = *Dicer* mRNA expression. P values were obtained using one-way ANOVA test with Tukey's as post-test.

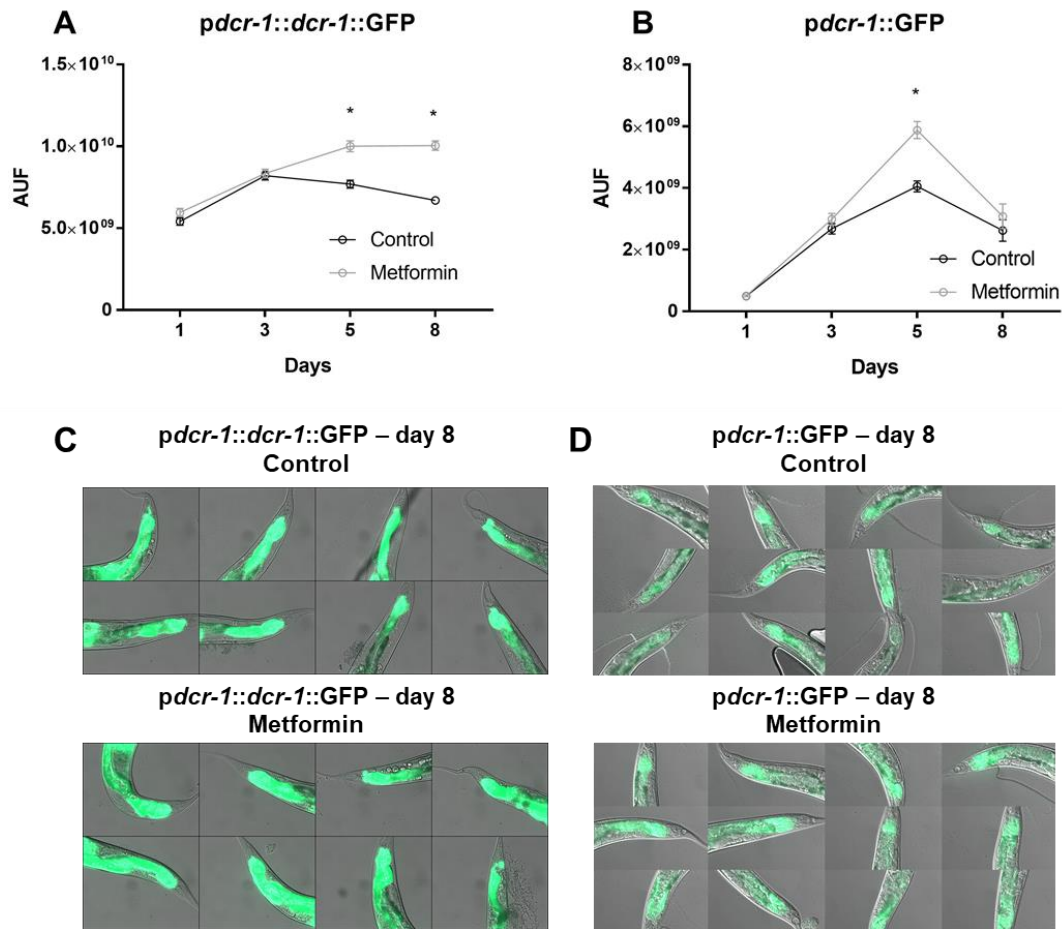


**Fig. S3. Effects of dietary oil or sucrose availability on body weight and blood glucose.** Mice were subjected to 4 weeks of *ad libitum* diet (AL, N = 6), dietary restriction (DR, N = 6), DR plus sucrose (DR+Suc, N = 7) or oil (DR+Oil, N = 5). A = Body weight. B = Glycaemia after 12 hours of fasting.  $p < 0.05$ : a, compared to AL; b, compared to DR. One-way ANOVA test with Tukey's as post-test.



**Fig. S4. Mechanism of DICER regulation by MR.** A = DICER levels in subcutaneous inguinal adipose tissue of *Gcn2* knockout mice (*Gcn2*KO) subjected to MR. B = band densitometry (N = 6 per group). C = DICER levels in subcutaneous inguinal adipose tissue of adipocyte-specific *Raptor* knockout mice (*ARaptor*KO) or *Lox* controls feeding chow diet or high fat diet (HFD). D = band densitometry (*Lox* + Chow, N = 3; *ARaptor*KO + Chow, N = 3; *Lox* + HFD, N = 3; *ARaptor*KO + HFD, N = 4). E = DICER levels in the inguinal adipose tissue of mice subjected to 4 weeks of DR plus or minus vitamin C (VitC). F = band densitometry (N = 4 per group). Results are presented as mean  $\pm$  SEM.  $p < 0.05$ : a, compared to *ad libitum* (AL); b, compared to the *ARaptor*KO or VitC group. In B, unpaired Student t test. In D, two-way ANOVA test with Bonferroni's post-test. In F, one-way ANOVA test with Tukey's as post-test.

**Figure S5**



**Fig. S5. DCR-1 is upregulated in *C. elegans* intestine after metformin exposure.** A = Worms expressing the DCR-1 reporter transgene *mamIs1* (*pdcr-1::dcr-1::gfp*) had their fluorescence levels assessed in the posterior intestine at days 1, 3, 5, and 8 of adulthood. B = *dcr-1* promoter activity in the posterior intestine was measured by GFP fluorescence using the *mamIs3* (*pdcr-1::gfp*) transgene at days 1, 3, 5, and 8 of adulthood. C = Representative images of *pdcr-1::dcr-1::gfp* expressing worms at the 8<sup>th</sup> day of adulthood. D = Representative images of *pdcr-1::gfp* expressing worms at the 8<sup>th</sup> day of adulthood. Approximately 20 worms per group were photographed in each replicate. The experiments were repeated twice. AUF = Arbitrary Units of Fluorescence. \**p*<0.05 when comparing the metformin group with the control group in each time-point using Student t-test.

Supplementary Table

Experiment	Strain	Allele	Temp. (°C)	Condition	Bacteria	Median Lifespan	N	Median Lifespan Effect (%)	P value vs. control	Censor
I	N2	Wild type	20°	Empty vector	HT115	19	59			2
I	N2	Wild type	20°	<i>dcr-1</i> RNAi	HT115	13	91			0
I	DA1116	eat-2(ad1116) II	20°	Empty vector	HT115	24	94	increased by 24%	< 0.0001	0
I	DA1116	eat-2(ad1116) II	20°	<i>dcr-1</i> RNAi	HT115	12	96	increased by 8%	< 0.0001	0
II	N2	Wild type	20°	Empty vector	HT115	16	80			3
II	N2	Wild type	20°	<i>dcr-1</i> RNAi	HT115	11	112			0
II	DA1116	eat-2(ad1116) II	20°	Empty vector	HT115	27	107	increased by 68%	<0.0001	0
II	DA1116	eat-2(ad1116) II	20°	<i>dcr-1</i> RNAi	HT115	11	89	not changed	0.3456	0
I	N2	Wild type	20°	ad libitum	OP50	19	77			13
I	N2	Wild type	20°	sDR	OP50	21	75	increased by 10%	0.0789	13
I	PD8753	dcr-1(ok247)	20°	ad libitum	OP50	8	42			0
I	PD8753	dcr-1(ok247)	20°	sDR	OP50	8	41	not changed	0.7127	0
II	N2	Wild type	20°	ad libitum	OP50	19	100			17
II	N2	Wild type	20°	sDR	OP50	23	89	increased by 21%	0.0006	27
II	PD8753	dcr-1(ok247)	20°	ad libitum	OP50	10	48			0
II	PD8753	dcr-1(ok247)	20°	sDR	OP50	10	54	not changed	0.375	0
I	N2	Wild type	20°	Vehicle + Empty vector	HT115	19	145			0
I	N2	Wild type	20°	Metformin + Empty vector	HT115	18	69	decreased by 5%	0.4486	0
I	N2	Wild type	20°	Vehicle + <i>dcr-1</i> RNAi	HT115	14	76			2
I	N2	Wild type	20°	Metformin + <i>dcr-1</i> RNAi	HT115	13	81	decreased by 7%	0.0001	1
II	N2	Wild type	20°	Vehicle + Empty vector	HT115	21	97			0
II	N2	Wild type	20°	Metformin + Empty vector	HT115	20	89	decreased by 5%	0.1155	0
II	N2	Wild type	20°	Vehicle + <i>dcr-1</i> RNAi	HT115	11	106			0
II	N2	Wild type	20°	Metformin + <i>dcr-1</i> RNAi	HT115	10	78	decreased by 10%	<0.0001	0
III	N2	Wild type	20°	Vehicle + Empty vector	HT115	21	80			0
III	N2	Wild type	20°	Metformin + Empty vector	HT115	20	85	decreased by 10%	0.1420	0
III	N2	Wild type	20°	Vehicle + <i>dcr-1</i> RNAi	HT115	12	109			0

III	N2	Wild type	20°	Metformin + <i>dcr-1</i> RNAi	HT115	11	117	decreased by 8%	0.6631	0
I	N2	Wild type	20°	Vehicle	OP50	21	135			0
I	N2	Wild type	20°	Metformin	OP50	24	118	increased by 14%	0.0456	15
I	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Vehicle	OP50	11	51			0
I	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Metformin	OP50	11	38	not changed	0.2042	0
II	N2	Wild type	20°	Vehicle	OP50	22	149			0
II	N2	Wild type	20°	Metformin	OP50	27	101	increased by 23%	<0.0001	0
II	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Vehicle	OP50	10	84			0
II	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Metformin	OP50	9	72	decreased by 10%	0.0238	0
III	N2	Wild type	20°	Vehicle	OP50	23	136			0
III	N2	Wild type	20°	Metformin	OP50	28	99	increased by 21%	<0.0001	0
III	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Vehicle	OP50	10	71			0
III	<i>PD875</i> 3	<i>dcr-1</i> (ok247)	20°	Metformin	OP50	9	82	decreased by 10%	0.0278	0

**Table S1. Summary of *C. elegans* lifespan data.**