SUPPLEMENTAL INFORMATION

Supplemental Figures and Legends

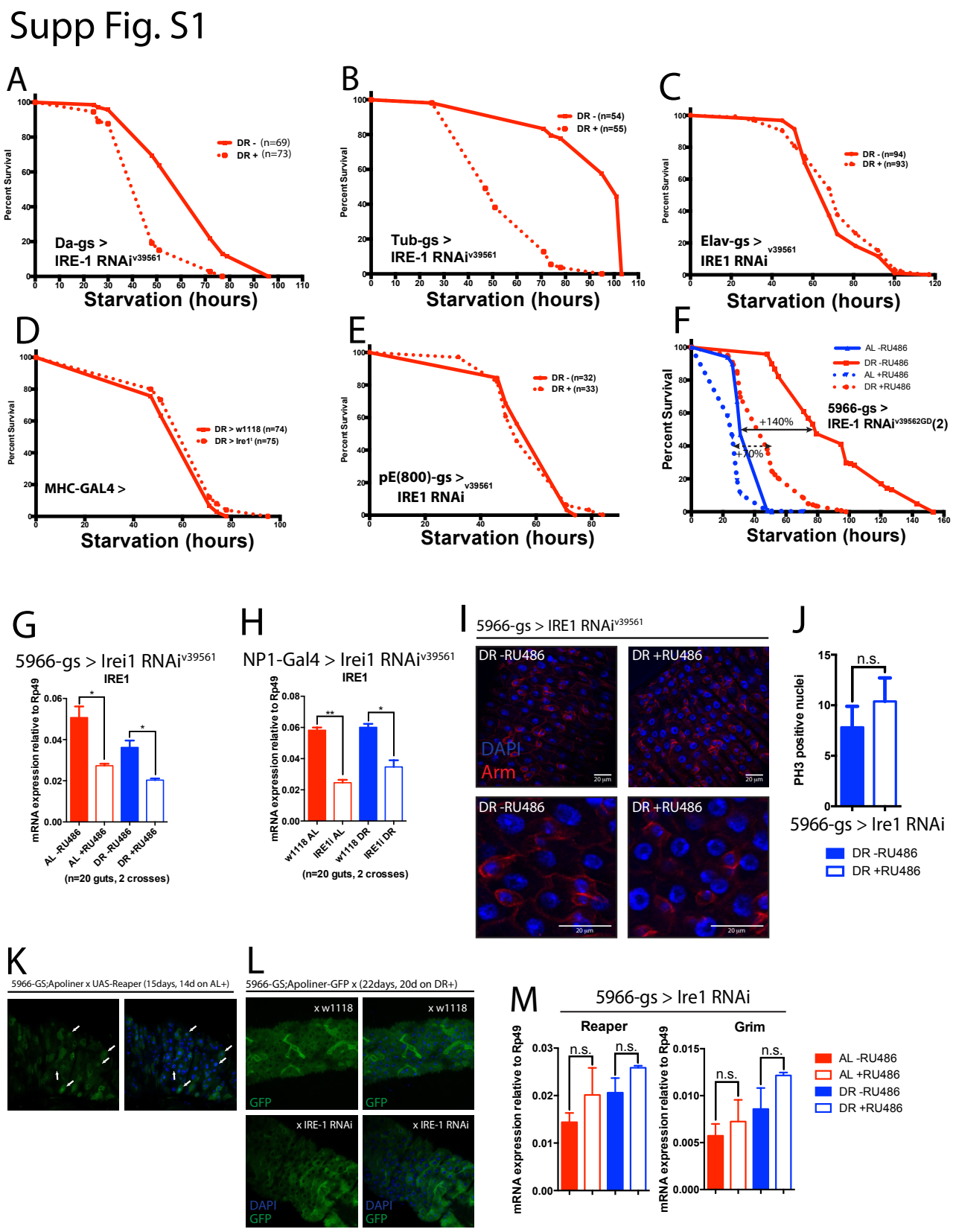

Figure S1 (related to Figure 1). A-E. Starvation resistance upon tissue-specific targeted IRE1 depletion using the indicated GAL4 drivers. For all experiences, unless otherwise indicated, IRE1 was depleted via the v39561 line. 2-3 days mated female flies were fed on DR food for 10-12 day after which they were placed on agar-only containing vials and starved. The living population at each time point scored is shown. Flies were transferred to fresh agar vials every 24 h. In the case that a gene-switch driver was used, (+) denotes the presence of the inducer RU486 in the food and (-) indicates just ethanol added. Non-gene-switch drivers were crossed to the *w1118* control, used to backcross the RNAi line used. Number of flies used per condition, from at least 3 independent crosses reared separately, is indicated in the plots. (**A.** Ubiquitous knockdown via the gene-switch driver Daughterless-gs. **B.** Ubiquitous knockdown via the gene-switch driver Tubulin-gs. **C.** Pan-neuronal knockdown via the gene-switch driver Elav-gs. **D.** Thorax muscle knockdown via the MHC-GAL4 driver. **E.** Oenocyte-targeted knockdown via the promE(800)-gs gene-switch driver) **F.** IRE1 was knocked down using a second independent RNAi line 39562GD, indicated in the plot, via the EC-specific gene switch driver 5966GS-GAL4, and starvation resistance of 10-12 days old flies fed on AL or DR diets, supplemented with ethanol only (-RU486) or with RU486 (+RU486) to induce GAL4 expression, was assayed. Results are comparable to the ones described in Fig 1A, where starvation resistance is reduced drastically upon IRE1 depletion on either diet. **G, H.** mRNA levels of IRE1 from dissected guts were measured by RT-qPCR, upon tissue-specific IRE1 knockdown via the midgut-specific drivers **(G)** 5966-gs or **(H)** NP1-GAL4. **I.** Armadillo (beta-catenin) staining of midgut enterocytes upon 10-12 days of IRE1 depletion. **J.** PH3 staining of 10-12 days old midguts of flies IRE1 knockdown flies fed on DR +/-RU486, shows no significant induction of stem cell, an indication of healthy guts. (n=11-16 midguts). **K.** Positive control for (L), Apoliner flies were used to overexpress Reaper and induce apoptosis, via the *5966GS-GAL4* driver. White arrows point to increased GFP nuclear signal, indicative of apoptotic cells. **L.** Flies carrying apoptosis reporter UAS-Apoliner and the 5966-gs driver were crossed with $IRE1^{RNAi}$ or *w1118* and fed on DR supplemented with RU486 for 20 days to assess activation of the apoptotic cascade – which triggers the translocation of a membrane GFP, from the Apoliner construct, into the nucleus. No changes were observed. **M.** Expression levels of the apoptosis transducers Reaper and Grim in the midguts of 10day old 5966-gs>IRE1RNAi flies, measured by RT-qPCR, show no significant alteration. (n=20 guts, from 2 independent crosses).

Supp Fig. S2

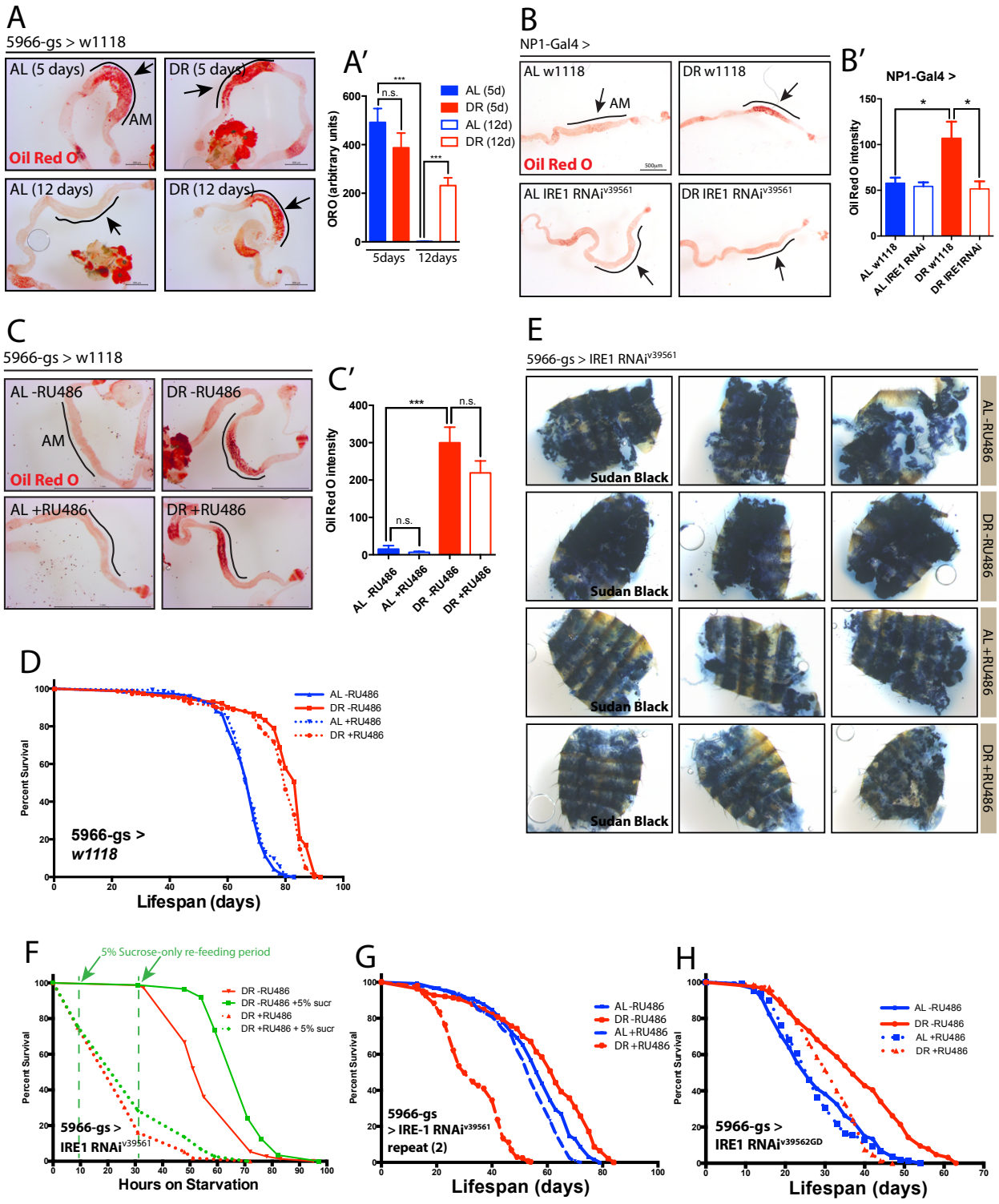

Figure S2 (related to Figure 1). A. Oil Red O (ORO) was used to stain total neutral lipids on dissected midguts of 5 day and 12 day fed control flies (5966-gs> *w1118*) on either AL or DR diets; the black line denotes the anterior midgut (AM) area measured, where lipids accumulate; scale bar = 200 mm. **A'.** Quantification of the ORO signal (details in Methods section) in the anterior midgut area (n=10-11/condition). **B.** Female flies carrying the enterocyte-specific driver NP1-GAL4 were crossed with either *w1118* or IRE1^{RNAi} males and reared for 10-12days

on AL or DR food. Midguts were dissected and stained with Oil Red O to assess lipid content. Black lines and arrows point to the anterior midgut area, where lipids accumulate under DR. **B'.** Quantification of the intensity of ORO stain from (B), details in the methods section; n=8-12 flies/condition/replicate, representative of 3 independent biological replicates/crosses. **C.** In order to test for RU486 interfering with lipid accumulation via Oil Red O staining, at the concentration used in our diets, we crossed 5966-GS females with w1118 males and fed them for 10-12 days on each of the 4 diets (AL/DR with or without RU486) prior to dissecting their guts for ORO stain. **C'.** Quantification of the intensity of ORO signal from (P), details in the methods section; n=10-14 flies/condition/replicate. **D.** To test if RU486 affects lifespan of flies carrying the intestinal geneswitch driver used, we established 6 independent crosses of 5966-gs female virgins with *w1118* mutants males and sorted from their progeny 600 female flies into 4 groups of 150 flies distributed by 6 vials in each test condition (AL or DR, -/+RU486). We find that at the concentration of RU486 diluted in our food, there is no effect over lifespan on either diet. **E.** Whole abdomens (cuticle was opened to allow dye penetration) were stained with Sudan Black to observe total lipid stores, from 10-12 day old flies, reared on AL or DR food, depleted of IRE1 in the midgut via 5966-gs. The difference is striking and easily observable at the microscope. Representative images are shown. **F.** 5966-gs>IRE1^{RNAi} flies were reared on DR -/+RU486 food for 10 days prior to being placed on agar-only containing vials to test starvation resistance. Vertical green lines indicate periods of temporary 5% sucrose re-feeding (8 hrs, not plotted) of the populations depicted in green, in order to test the capacity to regenerate lipid stores. This allows for extended survival when placed again under starvation conditions (a "reset" to the initial conditions) - green solid curve. Note the lack of a post-sucrose effect when IRE1 is depleted, when compared to its "non-re fed" control (green dotted curve vs. red dotted curve). **G.** Lifespan curve of flies where IRE1 has been specifically knocked down via the gene switch driver 5966-gs; shown as a replicate repeat to lifespan presented on Figure 1A. 6 independent populations of mated female flies were divided into 6 groups of 25 flies/condition (total of 600 flies) and survival scored. Flies were transferred into fresh vials every 2-3 days. **H.** Lifespan curve of flies where IRE1 has been specifically knocked down as in Fig 1F and Fig S1S using a second independent RNAi line 39562GD. The experiment was set up and flies aged in the same conditions as described above and in the methods section.

Supp Fig S3

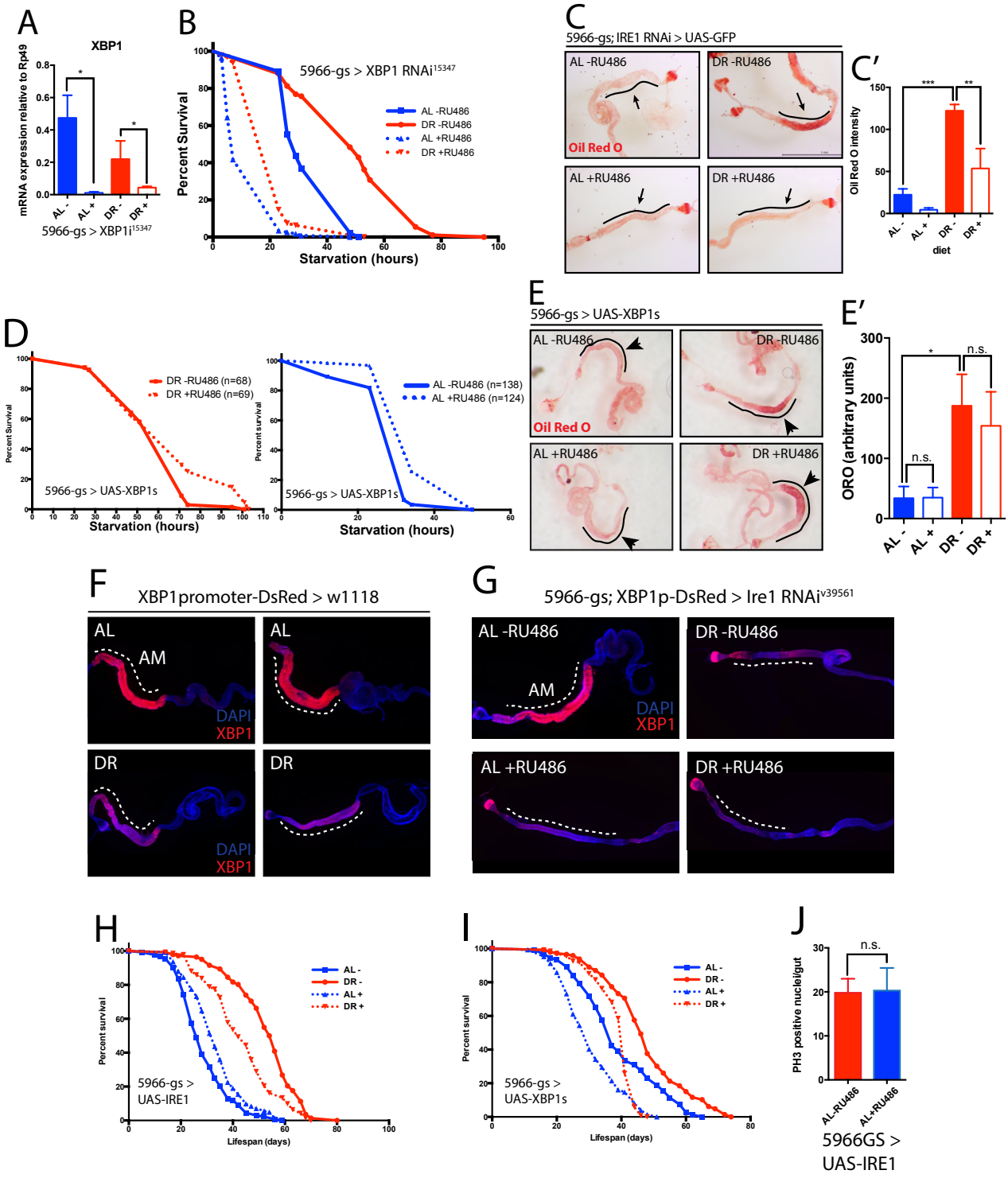

Figure S3 (related to Figure 2) Overexpression of a spliced form of XBP1 does not further increase starvation resistance under DR. A. RT-qPCRs for full XBP1 mRNA levels in 10 day old flies, where XBP1 is knocked down via the RNAi v15347 construct under *5966GS-GAL4* control. **B.** Starvation resistance of flies

depleted of XPB1, using a second independent RNAi line v15347, in the midgut enterocytes was assayed. 5966-gs>XBP1^{15347} targeted XBP1 depletion to the midgut enterocytes and after 10-12 days of feeding in differentiated food (without or with RU486 to induce the knockdown) flies were transferred to vials containing only agar (to prevent desiccation). n=100 flies/condition, from 4 independent crosses. **C.** Recombinant flies carrying both the *5966GS-GAL4* driver and IRE1 RNAi were crossed with flies carrying a UAS-GFP insert in order to determine if the presence of a second UAS insert affected the IRE1 RNAi efficiency. After 10-11d of feeding on either AL or DR, supplemented with (+) or without (-) RU486 guts were dissected and stained with ORO for direct neutral lipid quantification, showing a very strong reduction in lipid stores upon IRE1 depletion under DR. **D.** Starvation resistance of flies overexpressing spliced XBP1 message driven by the *5966GS-GAL4* gene switch driver. By itself, increasing XBP1 levels does not significantly alter starvation resistance on either diet, although it is sufficient to rescue IRE1 depletion, as shown in Fig 2D. **E.** Females virgins carrying the intestinal geneswitch *5966GS-GAL4* driver were crossed to males carrying a UAS-XBP1s in order to overexpress a spliced XBP1 in the enterocytes. Progeny was sorted at 1-2 days posteclosion and female flies were reared on either AL or DR diets, in the presence or absence of RU486 to induce XBP1s expression. Flies were collected after 10 days feeding on the diets, the guts were dissected and stained with Oil Red O for local lipid quantification in the anterior midgut. **E'.** Quantification of the intensity of ORO signal from (E), details in the methods section; n=10-12 flies/condition. **F.** XBP1-DsRed reporter flies, carrying the XBP1 promoter fused to DsRed crossed to *w* controls were fed for 10-11d on either of our AL or DR diets. Guts were dissected and immediately fixed in PFA and directly imaged with a fluorescence microspe. **G.** XBP1-DsRed reporter flies, carrying the XBP1 promoter fused to DsRed and expressing the midgut-specific gene-switch driver 5966-gs were crossed with IRE1 RNAi males and fed for 10-11d on either AL/DR, with (+) or without (-) RU486, after which midguts were dissected. Higher levels of XBP1 expression are observed under an AL diet, and are diminished in both AL and DR upon IRE1 depletion. **H.** Lifespan curves of flies overexpressing IRE1 (+RU486) under control of the intestinal specific 5966GS-GAL4 driver on either AL or DR. **I.** Lifespan curves of flies overexpressing spliced XBP1 (UAS-XBP1s; +RU486 denotes induction of GAL4) under control of the intestinal specific *5966GS-GAL4* driver on either AL or DR. **J.** phospho-histone H3 positive (PH3+) nuclei/gut in 30day old female flies, shows no beneficial effect from IRE1 overexpression on age-related ISC activation, fed an AL diet.

Supp Fig S4

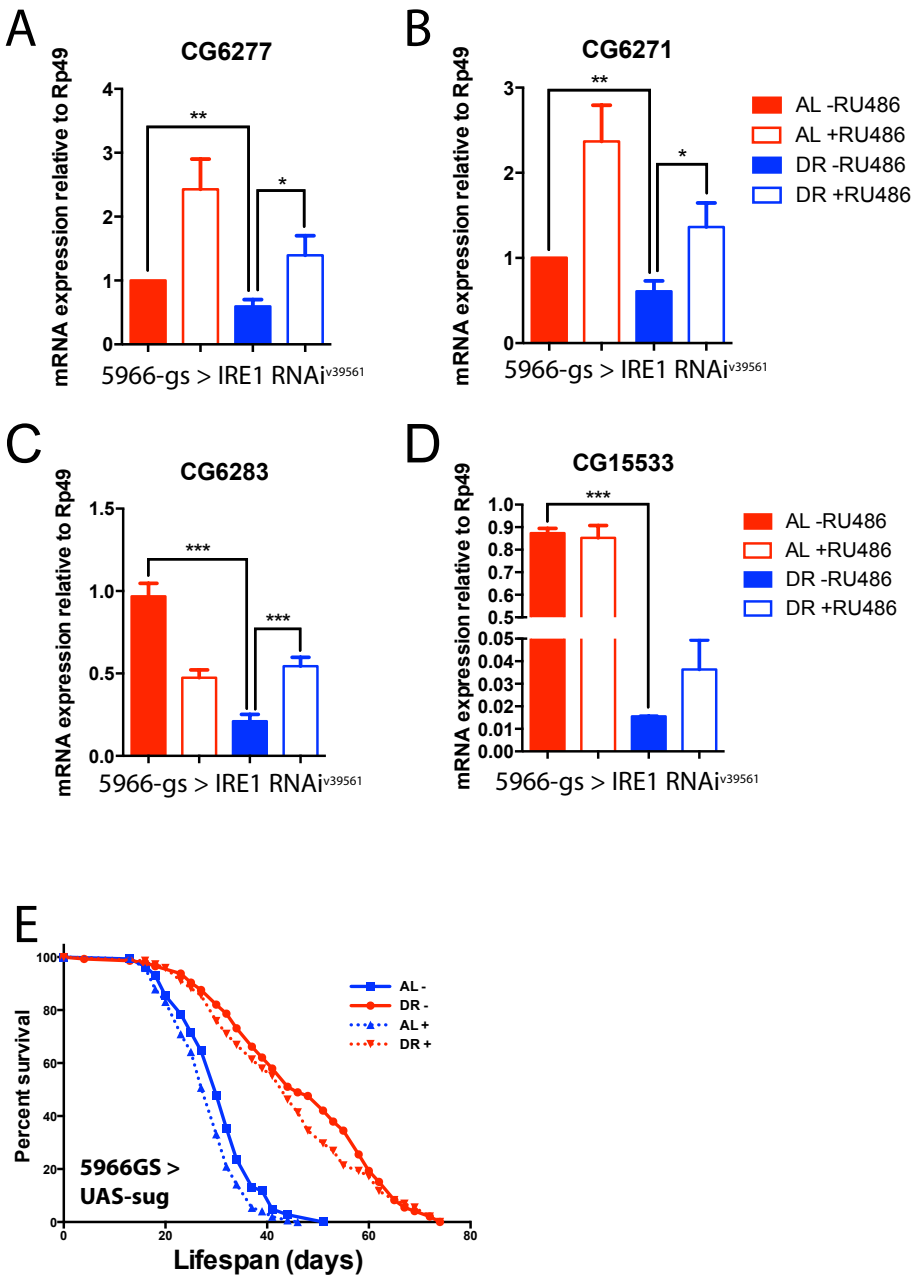

Figure S4 (related to Figure 3 and Figure 4) IRE1 is required for DR-mediated repression of dietary lipases. **A-D.** transcription levels (from dissected guts) of several DR-regulated genes measured by RT-qPCR, validating some regulated genes from the RNA-Seq. 5966-gs>IRE1^{RNAi} flies were fed under AL or DR for 10 days; RU486 was mixed with the (+) food to induce IRE1 depletion under 5966-gs control, showing that these lipid metabolism genes are also regulated by IRE1. Error bars are SEMs and p-values were calculated by pairwise student's t-test. **E.** Lifespan curves of flies overexpressing Sugarbabe (+RU486) under control of the intestinal driver 5966GS-GAL4 raised either on AL or DR, showing no significant alteration from controls (-RU486).

Tables S1-4 (related to Figure 3) Deep sequencing of polysome-associated mRNA of intestinal enterocytes shows gene regulation changes under a DR intervention. Flies were fed in adulthood (2 days post eclosion) in either DR or AL food. A flag-tagged ribosomal subunit was specifically expressed in the intestinal enterocytes via the GAL4 driver MYO1A-GAL4, allowing for subsequent pulldown of mRNAs directly bound to polysomes in a tissue specific manner. Total RNA was used for massive sequencing to assess early changes induced by DR. The tables include all the transcripts measured (Table S1) and subsets resulting from DR-induced regulation (Tables S2-4):

Table S1 – includes all the data, based on the transcript ID and its associated genomic entity (gene, snRNA, ncRNA, etC). Average FPKM from 5 replicates /condition is shown for DR and AL, as well as their corresponding p-values and false discovery rates (FDR). Provided as individual Excel files.

Table S2 – A list of the genes that are UP regulated after 10 days of DR treatment, by > 2 fold with a p-value < 0.05 is on the first tab and a list of the genes that are DOWN regulated after 10 days of DR treatment, by > 2 fold with a p-value < 0.05 is in a separate tab.

Table S3 – A list of the down regulated genes (using the above criteria) that after Gene Ontology analysis (using freely available Flymine tools), have the GO term "Lipid Metabolic Process". This list was then used for another GO analysis generating the chart presented in Fig 3C.

Table S4 – Here we compared our up- and down-regulated genes under DR (there are two tabs in the file), with the lists of regulated genes upon sugar-feeding larvae, from Zinke et al. 2002 and Matilla et al. 2015, to determine the degree of overlap between our DR intervention and an immediate sugar-response.

Supplemental Experimental Procedures

Fly husbandry and stocks:

The fly lines used in this study are: *5966GS-GAL4* and *NP1-GAL4* (Guo et al., 2014), *promE(800)GS-GAL4* (Chatterjee et al., 2014), *XBP1p::DsRed* (Ryoo HD et al., 2013), *MHC-GAL4* (Demontis and Perrimon 2010), UAS-sug (Michael Pankratz), UAS-XBP1spliced (from Pedro M Domingos, Wang, et al 2014b); *ELAVGS-GAL4*, UAS-IRE1^{RNAi1} (v39561), UAS-IRE1^{RNAi2} (v39562), UAS-XBP1^{RNAi} (v15347), UAS-XBP1^{RNAi} (v109312) are from the Vienna Drosophila RNAi Center. *NP1-GAL4*, *TubGS-GAL4*, *DaGS-GAL4,* UAS-sug^{RNAi} (27026), UAS-ApolinerGFP (32122), UAS-GFP, from the Bloomington Drosophila stock center. UAS-RpL13A-His6FLAG used for the polysome-bound mRNA pulldown was generated in the lab: the RpL13A coding sequence was amplified and inserted into pUASTattB vector; His6 and FLAG tag were directionally cloned in frame to the RpL13A gene. The UAS-RpL13A-His6FLAG plasmid was injected into PhiC31 flies (Bloomington 24749), and transgenic flies were selected according to standard procedure (service provided by Rainbow Transgenic Flies, Inc.).

The description of various fly media recipes that were used in the study is as follows:

Standard media: All fly stocks were maintained on standard lab fly media. The standard lab media is based on the Caltech media recipe, which includes 8.6% (w/v) Cornmeal, 1.6% (w/v) Yeast, 5% (w/v) Sucrose, 0.46% (w/v) Agar, 1% (v/v) Acid mix. To prepare the media, Cornmeal (86 g), Sucrose (50 g), active-dry-yeast (16 g, "Saf-

instant") and Agar (4.6 g) were mixed in a liter of water and brought to boil with constant stirring. The media was allowed to cool down to 60°C, before 10 ml of acid mix was added and mixed in the media. Acid mix was prepared by mixing equal volumes of 10% propionic acid (v/v) and 83.6% orthophosphoric acid. The media was then poured in vials (~10 ml/ vial) or bottles (50 ml/bottle) and allowed to cool down before storing at 4°C for later usage. These vials or bottles were then seeded with some live yeast just before the flies are transferred and used for maintenance of lab stocks or for collecting virgins and setting up the crosses.

Media for survival analyses: All survival and other assays were performed on media with varying yeast extract (YE) concentrations:

AL media: The AL media contained 8.6% (w/v) Cornmeal, 5.0% (w/v) Baker's yeast extract (#212750 BactoTM Yeast Extract, B.D. Diagnostic Systems, Sparks, MD), 5% (w/v) Sucrose, 0.46% (w/v) Agar, 1% (v/v) Acid mix. To prepare the media, Cornmeal (86 g), Sucrose (50 g), Yeast extract (50 g) and Agar (4.6 g) were mixed in a liter of water and brought to boil with constant stirring. The media was allowed to cool down to 60°C, before 10 ml of acid mix was added and mixed in the media. The media was then poured in vials (~5 ml/vial) and allowed to cool down before storing at 4°C for later usage.

DR media: The DR media contained 8.6% (w/v) Cornmeal, 0.5% (w/v) Baker's yeast extract (#212750 BactoTM Yeast Extract, B.D. Diagnostic Systems, Sparks, MD), 5% (w/v) Sucrose, 0.46% (w/v) Agar, 1% (v/v) Acid mix. To prepare the media, Cornmeal (86 g), Sucrose (50 g), Yeast extract (5 g) and Agar (4.6 g) were mixed in a liter of water and brought to boil with constant stirring. The media was allowed to cool down to 60°C, before 10 ml of acid mix was added and mixed in the media. The media was then poured in vials (~5 ml/vial) and allowed to cool down before storing at 4°C for later usage.

AL or DR media with RU486: For induction of gene switch (GS) GAL4 drivers, we used AL or DR media with additional RU486 mixed in the media. RU486 was added in the cooling media at the same time as acid mix. RU486 was dissolved in 95% ethanol and was used at a final concentration of 100 μM (the media is then referred as (+) or 'with RU486'). The control AL or DR media contained the same volume of 95 % ethanol and is referred to as media (-) or 'without RU486'.

Fly Rearing

Genetic crosses: To set up the crosses, 10-12 young virgin females, carrying a GAL4 driver or control (w^{1118}) were kept with 3-5 young male flies, carrying the UAS construct to be specifically expressed, in new stock bottles. For example, male flies carrying UAS-sug are crossed to virgin females from the RU486 inducible *5966-GS-GAL4* driver stocks. Flies were kept in the stock bottles for four days, after which the parents were removed and the larvae were allowed to develop in standard lab conditions (25°C temperature, 60% humidity and 12 hr day and 12 hr night).

The newly eclosed flies from six independent crosses/populations were allowed to mate for 2-3 days, to complete development post-eclosion, before they were sorted into females and males under light CO2 anesthesia. Sorted females were then transferred to the appropriate media for survival analyses, to a total of 25 per vial, 6 different vials per condition and cross, from six independent crosses/populations (bottles).

Survival Analysis: All longevity survival assays were carried out on AL or DR media as described previously (Katewa et al., 2012; Zid et al., 2009). Adult female flies were transferred within 2-3 days of eclosion to DR or AL media and were maintained at 25 ºC temperature, 60% humidity and 12 hrs light and 12 hrs dark conditions for their entire lifespan. 25 mated females were maintained per vial and living flies were transferred every 2-3 days onto fresh vials and death occurrences recorded. 6 independent mating bottles were used per condition, resulting in n=150 per replicate/condition.

Dissection of guts for mRNA preparation and RT-qPCR: Flies were dissected in chilled PBS on a hollow glass dish and guts were placed immediately in cooled Trizol in eppendorfs which were snap frozen in liquid nitrogen. 10-12 guts were collected per replicate from the same vial, and different vials (each replicate vial originates from an individual mating bottle) were used for each replicate. Total RNA was extracted using Direct-zol RNA MiniPrep kit (Zymo Research). 500 ng of total RNA was used per sample and cDNA was synthesized using iScript Reverse Transcription Supermix for RT-qPCR (Bio-Rad). The qPCR reactions were performed with at least 3 independent biological replicates using SensiFAST SYBR No-ROX Kit (BIOLINE). Data was analysed using the 2^(-DDCT) method and values for each replicated are plotted normalized to the gene *rp49*. Primers are available in this Supplemental Data.

Lipid analysis

Measurement of triglyceride and free fatty acid content (TG): triglyceride and free fatty acid were measured using a commercially available kit (Stanbio labs, Boerne, TX). Flies from 3 independent matting bottles that were fed AL or DR diet for 10 days were separated in at least 12 batches of 4-5 and snap frozen in liquid nitrogen. Heads were removed to avoid interference of the red eye pigment with the signal produced by the reaction, at the wavelength measured (500 mm). Frozen flies were then homogenized in PBS for measurement of triglyceride and free fatty acid as per the instructions of the manufacturer. Total protein was measured by the Bradford assay and used for normalization.

Oil Red O (ORO) staining and quantification: guts were dissected in PBS and fixed in 4% formaldehyde/PBS for 20 min. Guts were then washed twice with PBS and incubated in a fresh Oil Red O solution (6 ml of 0.5% Oil Red O in isopropanol and 4 ml of demineralized water, passed by a 0.45um filter) for 30 min, without agitation. Guts were then rinsed twice in distilled water and mounted in Mowiol mounting media. Quantification of the ORO signal was performed in the anterior half of the midguts as described in (Mehlem et al., 2013), using ImageJ. Briefly, images were converted to 8bit and a constant minimum threshold applied to the entire image for the red channel. The area above the threshold was then measured in the anterior midgut, to estimate the amount of local neutral lipids.

Lipid synthesis assay: After 14 days feeding on regular AL and DR media, 150 flies were transferred to AL or DR media with ^{14}C labeled glucose. The media was prepared as follows: 30 µl of freshly prepared 5% sucrose (with 2 µCi of ^{14}C labeled glucose (Perkin Elmers, Waltham, MA)) was added on top of the AL or DR media (5 ml food) and allowed to air dry for 3 hrs. After which the flies were transferred onto this media. After 36 hrs of feeding, the flies were snap-frozen in liquid nitrogen. The frozen samples (~20 mg/replicate) were homogenized in chloroform-methanol (2:1) and total lipid was extracted by the Folch method (Folch et al., 1957). Total lipid was resuspended

in 600 µl of chloroform, of which 200 µl was taken and mixed with 4 ml of scintillation fluid and counted in a scintillation counter. The *de novo* synthesis of lipids is expressed as the amount of ^{14}C radioactivity incorporated in lipids extracted from 1 mg of fly wt.

Immunostaining and Microscopy: Intact guts were fixed at room temperature for 45 min in 100 mM glutamic acid, 25 mM KCl, 20 mM $MgSO_4$, 4 mM sodium phosphate, 1 mM $MgCl_2$, and 4% formaldehyde. All subsequent incubations were done in PBS, 0.5% BSA, and 0.1% Triton X-100 at 4ºC. The following primary antibodies were used in overnight incubations: rabbit anti-pH3 (phosphorylated histone H3, Upstate, 1:1000), mouse anti-armadillo (Developmental Studies Hybridoma Bank, 1:100). Fluorescent secondary antibodies were obtained from Jackson Immunoresearch. DAPI was used to stain DNA. Confocal images were collected using a Zeiss LSM700 confocal system and processed using ImageJ and Adobe Illustrator.

Polysome Immunoprecipitation: To prepare FLAG antibody conjugated beads, 200 µg of monoclonal ANTI-FLAG M2 antibody (Sigma-Aldrich #F1804) was conjugated to 12.5 mg of 1.00 µm Polybead Carboxylate Microspheres (Polysciences #08226) using the PolyLink Protein Coupling Kit (Polysciences #24350) as instructed. Immunoprecipitation was performed on ice or at 4°C. FLAG antibody conjugated beads were equilibrated three times, 10 minutes with 2 ml of equilibration buffer. The beads were then equilibrated once with 2 ml of equilibration buffer with 2 mg/ml yeast tRNA, 2 mg/ml BSA and 100U RNasin Plus for 10 minutes. Approximately 100 female flies were homogenized with 2ml of homogenization buffer, incubated on ice for 10 minutes and spun down at 14,000 X g for 10 minutes. Supernatant was then added to the equilibrated beads and incubated for 3 hours with rotation. After incubation, the mixture was spun down and the supernatant was discarded (or saved for further analysis). Beads were then washed four times with 2ml of ice-cold wash buffer for 10 minutes each. Bound ribosome and mRNA were eluted with either the elution buffer for 30 minutes, or with ice cold Trizol-LS (Invitrogen #10296-028) for 10 minutes. The eluted ribosome and mRNA were collected for RNA extraction.

The following buffers were used for immonoprecipitation. 1). Equilibration buffer: 50 mM Tris-HCl, pH 7.4, 300 mM NaCl, 1mM EGTA, 10 mM MgCl2, 0.2 mg/ml heparin, 1 mM DTT, 10% glycerol, 1% Triton-X 100. 2). Homogenization buffer: equilibration buffer + 0.5 mg/ml cycloheximide, 1X mini cOmplete, Mini, EDTA-free protease inhibitor cocktail, 0.1% sodium deoxycholate, 200U/ml SuperaseIN, 200U/ml RNasin Plus. 3). Wash buffer: equilibration buffer + 0.5 mg/ml cycloheximide, 1X mini cOmplete, Mini, EDTA-free protease inhibitor cocktail, 50U/ml SuperaseIN, 50U/ml RNasin Plus. 4). Elution buffer: equilibration buffer + 0.5 mg/ml cycloheximide, 1X mini cOmplete, Mini, EDTA-free protease inhibitor cocktail, 200U/ml SuperaseIN, 200U/ml RNasin Plus, 200 µg/ml 3X FLAG peptide.

Primers Used for RT-qPCR analysis of gene expression

Gene Name	Primer Forward (5' -> 3')	Primer Reverse (5' -> 3')
RP49	TCCTACCAGCTTCAAGATGAC	CACGTTGTGCACCAGGAACT
IRE1	TGACAATCTGAAGCGACAGG	TTGCGGATCCTTGTGTATCA
Sugarbabe	AGTCCGTGATCATGAAGGCT	AGCGGCAATAGTAGAGTCCG
CG6277	CAGCTACAACAAGCCCAACA	CATGGTTCCGAAGTTGTCCT
CG6271	AGTGCGGAGACTACGAGGAA	GAAGTCACCCTCGACCATGT
CG6283	CTCTTCCGTTCTGGCTGTTC	CGGGCTTATCGTAGCTGAAG
CG15533	GTGGTTCCTGGAGTACGAGT	TCTCGCTCGGAATTGATGGT

Statistical analysis of ORO staining or gene expression (qPCR) by two-way ANOVA with Bonferroni's post-hoc test is shown, as well as significance of interaction between genetic manipulation (RU486) and diet (AL and DR) – relates to all figures – performed using GraphPad Prism software v5.0.

Fig 1B		
ANOVA table	**F (DFn, DFd)**	**P value**
Interaction Between Diet and RNAi	F (1, 52) = 15.51	0.0002
IRE1 RNAi	F (1, 52) = 35.25	< 0.0001
Diet	F (1, 52) = 21.51	< 0.0001

Fig 1C		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RNAi	F (1, 42) = 6.555	P = 0.0141
IRE1 RNAi	F (1, 42) = 31.53	P < 0.0001
Diet	F (1, 42) = 0.3449	P = 0.5602

Fig 1D		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RNAi	F (1, 20) = 10.07	P = 0.0048
IRE1 RNAi	F (1, 20) = 201.6	P < 0.0001
Diet	F (1, 20) = 0.5224	P = 0.4782

Fig 1E				
	F (DFn, DFd)	**P value**		
Interaction Between Diet and RNAi	F (3, 67) = 7.858	P = 0.0001		
IRE1 RNAi	F (3, 67) = 22.39	P < 0.0001		
Diet	F (1, 67) = 7.372	P = 0.0084		
Bonferroni's multiple comparisons test	**Mean Diff.**	**95% CI of diff.**	**Significant ?**	**Summary**
no sucrose				
ctrl:AL vs. ctrl:DR	-22.41	-36.08 to -8.735	Yes	***
ctrl:AL vs. RNAi:AL	8.553	-5.730 to 22.84	No	ns
ctrl:AL vs. RNAi:DR	8.244	-6.038 to 22.53	No	ns
ctrl:DR vs. RNAi:AL	30.96	17.29 to 44.64	Yes	****
ctrl:DR vs. RNAi:DR	30.65	16.98 to 44.33	Yes	****
RNAi:AL vs. RNAi:DR	-0.3086	-14.59 to 13.97	No	ns
+ 5% sucrose				
ctrl suc:AL vs. ctrl suc:DR	-1.808	-7.511 to 3.896	No	ns
ctrl suc:AL vs. RNAi suc:AL	4.031	0.1858 to 7.876	Yes	*
ctrl suc:AL vs. RNAi suc:DR	4.259	0.3280 to 8.190	Yes	*
ctrl suc:DR vs. RNAi suc:AL	5.839	0.2662 to 11.41	Yes	*
ctrl suc:DR vs. RNAi suc:DR	6.066	0.4346 to 11.70	Yes	*
RNAi suc:AL vs. RNAi suc:DR	0.2278	-3.510 to 3.966	No	ns

Fig 2A		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RNAi	F (1, 34) = 5.473	P = 0.0253
XBP1 RNAi	F (1, 34) = 5.463	P = 0.0255
Diet	F (1, 34) = 5.422	P = 0.0260

Fig 3D		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RNAi	F (1, 24) = 1.626	P = 0.2145
IRE1 RNAi	F (1, 24) = 5.551	P = 0.0270
Diet	F (1, 24) = 7.802	P = 0.0101

Fig 3E		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RNAi	F (1, 8) = 0.5417	P = 0.4827
XBP1 RNAi	F (1, 8) = 23.74	P = 0.0012
Diet	F (1, 8) = 4.409	P = 0.0690

Fig 3F		
	F (DFn, DFd)	**P value**
Interaction Between Diet and UAS-XBP1s	F (1, 8) = 13.67	P = 0.0061
UAS-XBP1s RNAi	F (1, 8) = 16.82	P = 0.0034
Diet	F (1, 8) = 198.0	P < 0.0001

Fig 4B		
	F (DFn, DFd)	**P value**
Interaction Between Diet and sug RNAi	F (1, 28) = 5.704	P = 0.0239
sug RNAi	F (1, 28) = 8.602	P = 0.0066
Diet	F (1, 28) = 6.828	P = 0.0143

Fig S1P (ORO for 5966 x w1118 +/-RU486)		
	F (DFn, DFd)	**P value**
Interaction Between Diet and RU486	F (1, 26) = 1.591	P = 0.2184
RU486	F (1, 26) = 2.427	P = 0.1313
Diet	F (1, 26) = 75.88	P < 0.0001

Fig S2C (ORO for 5966; IRE1 RNAi x UAS-GFP)		
	F (DFn, DFd)	**P value**
Interaction Between Diet and IRE1 RNAi	F (1, 29) = 4.029	P = 0.0541
IRE1 RNAi	F (1, 29) = 11.70	P = 0.0019

Diet	F (1, 29) = 34.61	P < 0.0001

Fig S2E (ORO for 5966 x UAS-XBP1s)		
	F (DFn, DFd)	**P value**
Interaction Between Diet and UAS-XBP1s	F (1, 31) = 0.2049	P = 0.6540
UAS-XBP1s	F (1, 31) = 0.1797	P = 0.6746
Diet	F (1, 31) = 12.96	P = 0.0011

Cox proportional hazards analysis for all survival curves (relates to all figures) were made using the R package "Survival". Here we report the probability that B1,2=0, from fitting the formula phenotype=B1*variable1+B2*variable2+B1,2*(variable1*variable2), as well as testing if the proportionality assumption is met by testing for a non-zero slope in a generalized linear regression of the scaled Schoenfeld residuals on functions of time.

		Test proportionality assumption		**Cox regression**	
		ChiSq	**p-value**	**HR**	**p-value**
Fig 1A	**diet**	0.039	8.43E-01	1.5913	<2.00E-16
	RU486	64.126	1.22E-15	2.2153	<2.00E-16
	diet:RU486	1.081	2.98E-01	0.7951	5.90E-07
Fig 1F	**diet**	0.951	0.3294	1.2539	2.10E-06
	RU486	2.834	0.0923	2.0998	<2.00E-16
	diet:RU486	3.701	0.0544	2.1531	<2.00E-16
Fig S1F	**diet**	2.9	0.08878	1.4149	7.10E-13
	RU486	7.51	0.00614	2.2521	<2.00E-16
	diet:RU486	1.22	0.26874	1.8457	<2.00E-16
Fig S1Q	**diet**	3.2897	0.0697	0.3599	<2e-16
	RU486	0.0134	0.9077	1.0593	0.1732
	diet:RU486	0.5066	0.4766	1.1322	0.0034
Fig S1S	**suc**	4.3212	3.76E-02	0.79619	0.00018
	RU486	21.2781	3.97E-06	2.86504	<2.00e-16
	suc:RU486	0.0145	9.04E-01	1.00046	0.99392
Fig S1T	**diet**	2.9	0.08878	1.4149	7.10E-13

	RU486	7.51	0.00614	2.2521	<2.00E-16
	diet:RU486	1.22	0.26874	1.8457	<2.00E-16
Fig S1U	**diet**	9.14	2.50E-03	0.7667	9.50E-10
	RU486	12.99	3.13E-04	1.2619	2.20E-07
	diet:RU486	6.64	9.96E-03	1.1984	4.80E-05
Fig 2B	**diet**	3.79	5.16E-02	0.7434	7.10E-11
	RU486	52.55	4.19E-13	1.6098	<2.00E-16
	diet:RU486	1.31	2.53E-01	1.166	0.00037
Fig 2D	**IRE1i**	1.02	0.311781	1.183	0.0051
	XBP1s	13.45	0.000245	0.5614	<2.00E-16
	IRE1i:XBP1s	7.15	0.007481	0.6839	4.80E-10
Fig S2E	**diet**	2.25	1.34E-01	0.5837	<2e-16
	RU486	23.24	1.43E-06	2.9231	<2e-16
	diet:RU486	5.54	1.85E-02	1.0858	0.15
Fig S2H	**diet**	6.471	0.01097	0.4773	<2e-16
	RU486	0.586	0.44397	1.0439	0.31
	diet:RU486	7.94	0.00484	1.2889	3.10E-09
Fig S2I	**diet**	35.67	2.33E-09	0.7287	1.50E-13
	RU486	10.84	9.93E-04	1.6876	<2e-16
	diet:RU486	4.28	3.86E-02	1.0228	0.6
Fig 4A	**diet**	0.5662	0.452	0.1862	<2e-16
	RU486	0.0282	0.867	2.0545	<2e-16
	diet:RU486	1.1022	0.294	1.1889	0.0025
Fig 4C	**diet**	4.712	0.0299	0.2452	<2e-16
	RU486	0.227	0.6339	0.7927	0.0019
	diet:RU486	1.093	0.2958	1.1847	0.0229
Fig 4D	**IRE1i**	6.12	1.33E-02	1.3345	0.00061
	sug	10.46	1.22E-03	1.1682	0.04414
	IRE1i:sug	11.88	5.67E-04	0.7317	5.70E-05
Fig 4E	**Diet**	1.9	0.16861	0.605	<2e-16
	IRE1i	5.39	0.02022	1.0992	0.0169
	Diet:IRE1i	3.21	0.07329	1.1458	0.0006
Fig 4E	**IRE1i**	1.66E-02	0.8975	1.1909	5.50E-06

	sug	9.26E-05	0.9923	0.7977	8.50E-09
	IRE1i:sug	3.52E+00	0.0606	0.8797	0.00078
Fig S4A	**Diet**	3.405	0.065	0.4401	<2e-16
	RU486	0.557	0.455	1.1232	0.0053
	Diet:RU486	0.329	0.566	0.9506	0.2231
Fig S4B	**Diet**	0.809207	0.3684	0.3631	<2e-16
	RU486	4.490467	0.0341	3.403	<2e-16
	Diet:RU486	0.000232	0.9878	0.8942	0.029

Information on all survival experiments (genotype, "n", p-values denote pairwise statistical analysis, and not interaction between both diet and genetic interventions which is address via Cox regression shown above) - relates to all figures - using the GraphPad Prism software v5.0.

Statistical Analysis for Fig 1A							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	203.5	<0.0001	141	137	69	23	-66.7%
Ctrl AL / IRE1 RNAi AL (+RU486)	124.5	<0.0001	137	136	46	23	-50%
IRE1 RNAi DR (+RU486) / IRE1 RNAi AL (+RU486)	6.764	0.0093	137	136	23	23	0%
Ctrl AL / Ctrl DR	143.8	<0.0001	141	137	46	69	50%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig 1F							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	246.5	<0.0001	152	143	67	30	-55.2%
Ctrl AL / IRE1 RNAi AL (+RU486)	0.3713	n.s.	141	143	58	60	3%
IRE1 RNAi AL (+RU486) / IRE1 RNAi	163.8	<0.0001	143	143	60	30	-50.0%

DR (+RU486)							
Ctrl AL / Ctrl DR	57.47	<0.0001	141	152	58	67	15.5%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1A							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	37.33	<0.0001	69	73	72	48	-33.3%

Control flies *(+/+; daughterless-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and ubiquitous IRE1 knockdown (*+/+; daughterless-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1B							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	83.52	<0.0001	54	55	101	47	-53.5%

Control flies *(+/+; tubulin-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and ubiquitous IRE1 knockdown (*+/+; tubulin-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1C							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	1.686	n.s.	94	93	68	72	5.9%

Control flies *(+/+; +/+; elav-GS-GAL4 /IRE1^{39561} RNAi*, without RU486) and head IRE1 knockdown (*+/+; +/+; elav-GS-GAL4 /IRE1^{39561} RNAi*, with RU486)

Statistical Analysis for Fig S1D							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR	3.449	n.s.	74	75	71	71	0%

Control flies *(+/+; mhc-GAL4/+; +/+*) and muscle IRE1 knockdown (*+/+; mhc-GAL4/+; IRE1^{39561} RNAi/+*), background of crossed strains is *w1118*

Statistical Analysis for Fig S1E							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR	0.3613	n.s.	81	100	88	88	0%

Control flies *(+/+; promE(800)-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and oenocyte IRE1 knockdown (*+/+; promE(800)-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1F							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	163.6	<0.0001	142	141	79	48	-65%
Ctrl AL / IRE1 RNAi AL (+RU486)	79.51	<0.0001	149	148	31	26	-16%
IRE1 RNAi AL (+RU486) / IRE1 RNAi DR (+RU486)	145.9	<0.0001	148	142	31	48	+55%
Ctrl AL / Ctrl DR	269.5	<0.0001	149	141	31	79	+155%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39652GD} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39562GD} RNAi/+*, with RU486)

Statistical Analysis for Fig S1Q							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
DR –RU486 / DR +RU486	10.01	0.0016	142	142	85	80	-6%
AL –RU486 / AL +RU486	1.046	0.3064	143	145	69	69	0%
AL +RU486 / DR +RU486	141.0	<0.0001	145	142	69	80	+16%
AL –RU486 / DR –RU486	185.0	<0.0001	143	142	69	85	+23%

Purpose is to control for effect of RU486 at concentration used on driver-only control flies.
All flies *(+/+; 5966-GS-GAL4/+; +/+*, *w^{1118}* background)

Statistical Analysis for Fig S1S							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	99.93	<0.0001	75	56	55	26	-52.7%
Ctrl DR (+sucrose) / IRE1 RNAi DR (+sucrose +RU486)	145.5	<0.0001	87	74	71	31	-56.3%
IRE1 RNAi DR (+RU486) / IRE1 RNAi DR (+ sucrose +RU486)	10.78	0.0010	56	74	26	31	16.1%
Ctrl DR / Ctrl DR (+sucrose)	15.12	0.0001	75	87	55	71	29%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1T repeat of lifespan v39561							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	197.2	<0.0001	140	184	63	30	-52.3%
Ctrl AL / IRE1 RNAi AL (+RU486)	10.98	0.0009	130	125	57	54	-5.2%
IRE1 RNAi AL (+RU486) / IRE1 RNAi DR (+RU486)	163.7	<0.0001	125	184	54	30	-48.0%
Ctrl AL / Ctrl DR	6.597	0.0102	130	140	57	63	10.5%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39561} RNAi/+*, with RU486)

Statistical Analysis for Fig S1U (second IRE1 RNAi)							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	163.6		141	142	79	48	-40%
Ctrl AL / IRE1 RNAi AL (+RU486)	79.51		149	148	31	26	-17%
IRE1 RNAi AL (+RU486) / IRE1 RNAi DR (+RU486)	145.9		148	142	26	48	+85%
Ctrl AL / Ctrl DR	529.9		149	141	31	79	+155%

Control flies *(+/+; 5966-GS-GAL4/+; IRE1^{39562GD} RNAi/+*, without RU486) and IRE1 knockdown (*+/+; 5966-GS-GAL4/+; IRE1^{39562GD} RNAi/+*, with RU486)

Statistical Analysis for Fig 2B							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / XBP1 RNAi DR (+RU486)	17.33	<0.0001	114	140	31	25	-19%
Ctrl AL / XBP1 RNAi AL (+RU486)	127.5	<0.0001	158	156	31	25	-19%
Ctrl DR / Ctrl AL	1.680	n.s.	112	151	31	31	0%

Control flies *(+/+; 5966-GS-GAL4/+; XBP1^{15347} RNAi/+*, without RU486) and XBP1 knockdown (*+/+; 5966-GS-GAL4/+; XBP1^{15347} RNAi/+*, with RU486)

Statistical Analysis for Fig 2D							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl w1118 DR / w1118; IRE1 RNAi DR (+RU486)	32.18	<0.0001	72	70	71	47	-33.8%
IRE1 RNAi DR (+RU486) / IRE1 RNAi; UAS-XBP1s DR (+RU486)	98.66	<0.0001	70	71	47	95	101%
Ctrl w1118 DR / Ctrl UAS-XBP1s DR	5.089	0.02	72	70	71	74	0.04%

Control flies *(+/+; 5966-GS-GAL4 /UAS-XBP1s; IRE1^{39561} RNAi /+* and *+/+; 5966-GS-GAL4 /+; IRE1^{39561} RNAi/+* without RU486), IRE1 knockdown *(5966-GS-GAL4 /+; IRE1^{39561} RNAi/+* with RU486) and XBP1 rescue of IRE1 depletion (*+/+; 5966-GS-GAL4 /UAS-XBP1s; IRE1^{39561} RNAi/+* with RU486)

Statistical Analysis for Fig S2D							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / UAS-XBP1s DR (+RU486)	5.320	0.021	68	69	71	71	0%

Control flies (*+/+; 5966-GS-GAL4/ UAS-XBP1s; +/+* without RU486) and spliced XBP1 overexpression ((*+/+; 5966-GS-GAL4/ UAS-XBP1s; +/+* with RU486)

Statistical Analysis for Fig 4A							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / sug RNAi DR (+RU486)	108.5	<0.0001	112	108	99	64	-35.3%
Ctrl AL / sug RNAi AL (+RU486)	65.14	<0.0001	115	118	42	28	-33.3%
Ctrl AL / Ctrl DR	221.0	<0.0001	112	115	42	99	57.5%

Control flies (+/+; *5966-GS-GAL4* /+; *sug*^{27026} *RNAi* / + without RU486) and sugarbabe knockdown (+/+; *5966-GS-GAL4* /+; *sug*^{27026} *RNAi* / + with RU486)

Statistical Analysis for Fig 4C							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / UAS-sug DR (+RU486)	0.9117	n.s.	102	100	96	96	0%
Ctrl AL / UAS-sug AL (+RU486)	12.42	0.0004	90	94	71	71	0%
Ctrl AL / Ctrl DR	79.80	<0.0001	98	100	71	96	35.2%

Control flies (+/+; *5966-GS-GAL4* /*UAS-sug*; +/ + without RU486) and sugarbabe overexpression (+/+; *5966-GS-GAL4* /*UAS-sug*; +/ + with RU486)

Statistical Analysis for Fig 4D							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1 n2		Median Survival Hrs* (MS) Group 1 Group 2		% change in MS
Ctrl DR / IRE1^{39561} RNAi DR (+RU486)	16.03	<0.0001	36	36	119	71	-40.3%
IRE1 RNAi DR (+RU486) / IRE1 RNAi; UAS-sug DR (+RU486)	1.535	n.s.	36	50	71	101	42.3%
Ctrl UAS-sug DR / Ctrl DR	32.70	<0.0001	52	36	119	101	15%

Control flies (+/+; *5966-GS-GAL4* /+; *IRE1*^{39561} *RNAi*/+ and +/+; *5966-GS-GAL4* /*UAS-sug*; *IRE1*^{39561} *RNAi*/+ without RU486), IRE1 knockdown (*5966-GS-GAL4* /+; *IRE1*^{39561} *RNAi*/+ with RU486) and sugarbabe rescue of IRE1 depletion (+/+; *5966-GS-GAL4* /*UAS-sug*; *IRE1*^{39561} *RNAi*/+ with RU486)

Statistical Analysis for Fig 4E							
Group 1/Group 2 (a)	Chi Square (b)	*p* value (b)	# of flies n1	n2	Median Survival (MS) Group 1	Group 2	% change in MS
Ctrl DR / IRE1 RNAi DR (+RU486)	67.47	<0.0001	107	117	76	55	-27.6%
Ctrl UAS-sug DR / IRE RNAi, UAS-sug DR (+RU486)	0.2687	n.s.	131	149	64	69	4.7%
Ctrl AL / IRE1 RNAi AL (+RU486)	0.2723	n.s.	115	120	55	57	3.6%
IRE1 RNAi DR (+RU486) / IRE1 RNAi; UAS-sug DR (+RU486)	19.37	<0.0001	117	149	55	69	25.5%
IRE1 RNAi DR (+RU486) / IRE1 RNAi AL (+RU486)	5.677	0.0172	117	120	55	57	3.6%
Ctrl AL / Ctrl DR	150.9	<0.0001	115	107	55	76	38.2%

Control flies *(+/+; 5966-GS-GAL4 /+; IRE1^{39561} RNAi/+* and *+/+; 5966-GS-GAL4 /UAS-sug; IRE1^{39561} RNAi/+* without RU486), IRE1 knockdown *(5966-GS-GAL4 /+; IRE1^{39561} RNAi/+* with RU486) and sugarbabe rescue of IRE1 depletion (*+/+; 5966-GS-GAL4 /UAS-sug; IRE1^{39561} RNAi/+* with RU486)

(a) Group 1 and Group 2 denote the groups for which the comparison was made
(b) Survival curves were plotted and statistical analyses (Log-rank Mantel-Cox test) were performed using the Graphpad Prism 5 software (Graphpad software, Inc., San Diego, USA)
* mediam starvation survival is in hours (hrs)