

Supplementary information

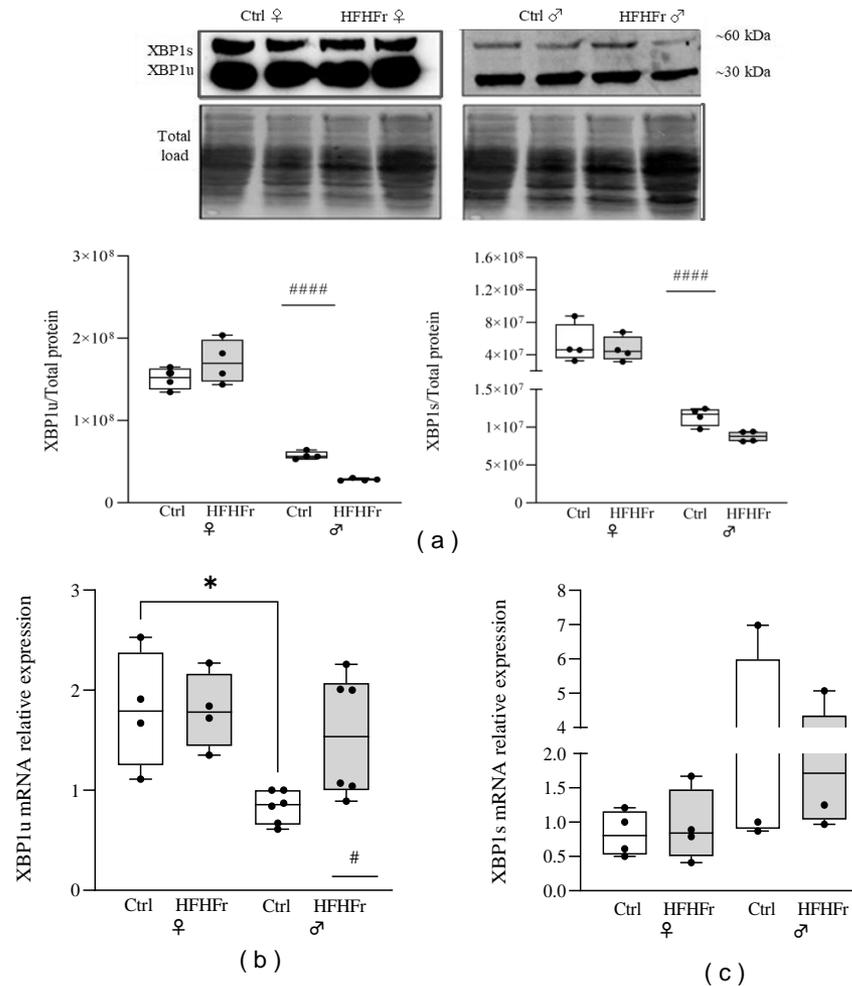
Supplementary Table S1

**Table S1.** Basic characteristics of Sprague Dawley rats after three months of feeding the HFHFr diet

	Female rats		Male rats	
	Ctrl	HFHFr	Ctrl	HFHFr
<b>Final body weight (g)</b>	260 ± 11	268 ± 9	430 ± 14	438 ± 37
<b>Liver weight (g)</b>	7.9 ± 0.6	9.5 ± 1.5 *	15.7 ± 1.5	16.3 ± 1.8
<b>pWAT weight (g)</b>	2.2 ± 0.3	2.5 ± 0.5	4.8 ± 0.9	7.5 ± 2.1*
<b>Blood TG (mg/dL)</b>	118 ± 15	197 ± 65 *	109 ± 19	249 ± 57 ***
<b>Liver TG (mg/g protein)</b>	50.7 ± 11.4	115.3 ± 60.2**	44.7 ± 8.4	59.6 ± 8.7 **
<b>Liver Chol (mg/g protein)</b>	9.9 ± 1.1	11.0 ± 2.1	6.9 ± 1.5	7.3 ± 1.0
<b>Serum AST (U/L)</b>	43 ± 6	37 ± 13	40 ± 16	36 ± 8
<b>Serum ALT (U/L)</b>	26 ± 6	25 ± 6	29 ± 7	14 ± 6***

Data obtained from control and high-fat high-fructose fed male and female rats (n = 7–8 per group) [27,28]. Data are presented as the mean ± SD. \*\*\* p < 0.001, \*\* p < 0.01, \* p < 0.05. ALT: alanine transaminase; AST: aspartate transaminase; Chol: cholesterol; Ctrl: control; pWAT: perigonadal white adipose tissue; TG: triglyceride.

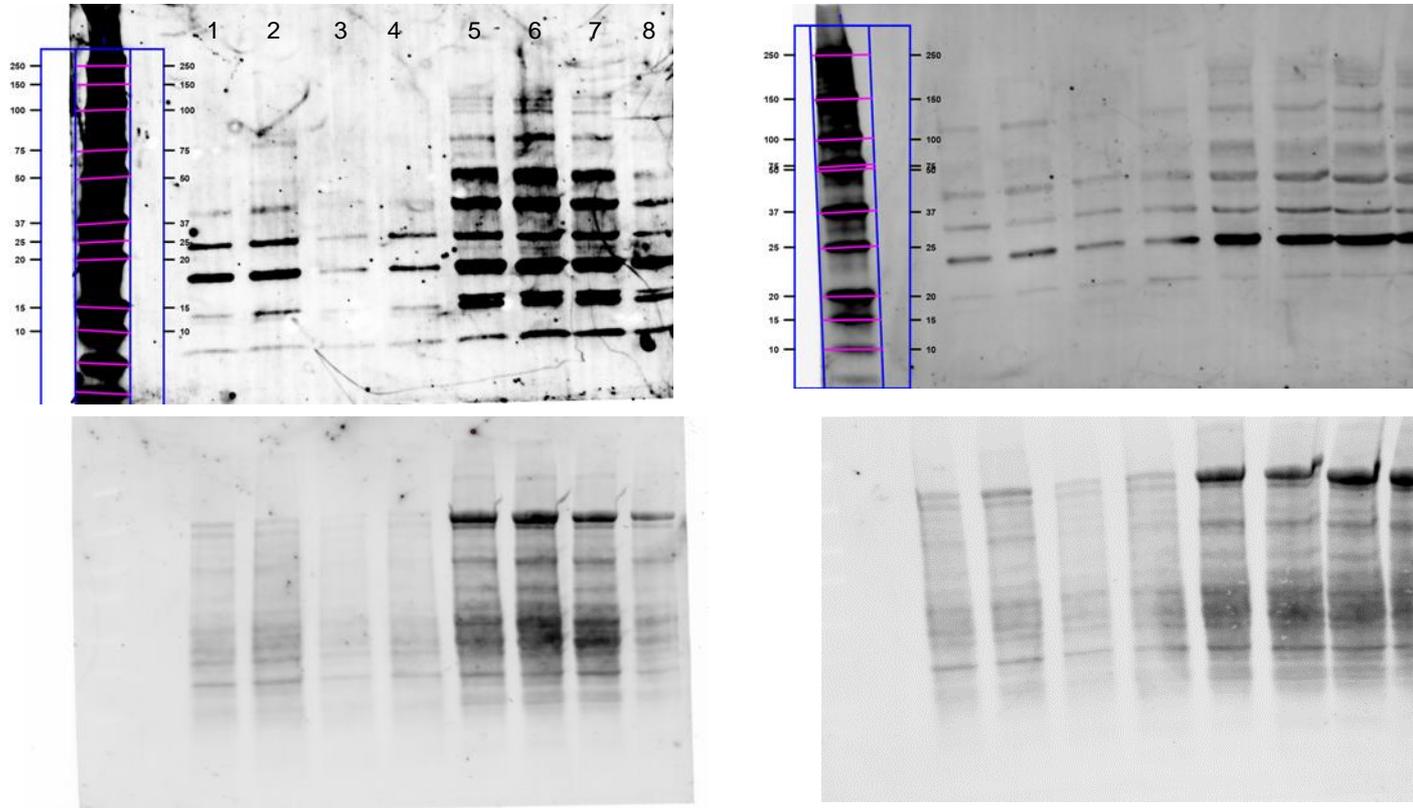
## Supplementary figure S1



**Figure S1. Effect of HFHFr diet on the expression levels of unfolded protein response stress sensor XBP1 in the rat livers.** Western blot representative images and densitometric analysis of (a) XBP1u, and XBP1s, and (b) XBP1u and (c) XBP1s mRNA splicing as analyzed by RT-qPCR on isolated mRNA from liver tissue. A significant main effect of sex was observed when both XBP1 and XBP1s were analyzed with male subjects being characterized by higher protein levels than females (XBP1u, sex:  $F(1, 12) = 248.7$ ;  $p < 0.0001$ ; sex x diet interaction:  $F(1, 12) = 11.11$ ;  $p = 0.0060$ ; XBP1s, sex:  $F(1, 12) = 31.41$ ;  $p = 0.0001$ ; sex x diet interaction:  $F(1, 12) = 0.06543$ ;  $p = 0.8024$ ). Sex differences were also observed at the mRNA level (XBP1u, sex:  $F(1, 12) = 6.761$ ;  $p = 0.0232$ ; sex x diet interaction:  $F(1, 12) = 2.364$ ;  $p = 0.1501$ ; XBP1s, sex:  $F(1, 12) = 4.230$ ;  $p = 0.0621$ ; sex x diet interaction:  $F(1, 12) = 0.1677$ ;  $p = 0.6894$ ) with male subjects showing lower levels. Statistical analysis was conducted using two-way ANOVA followed

## Supplementary information

### Supplementary figure S2



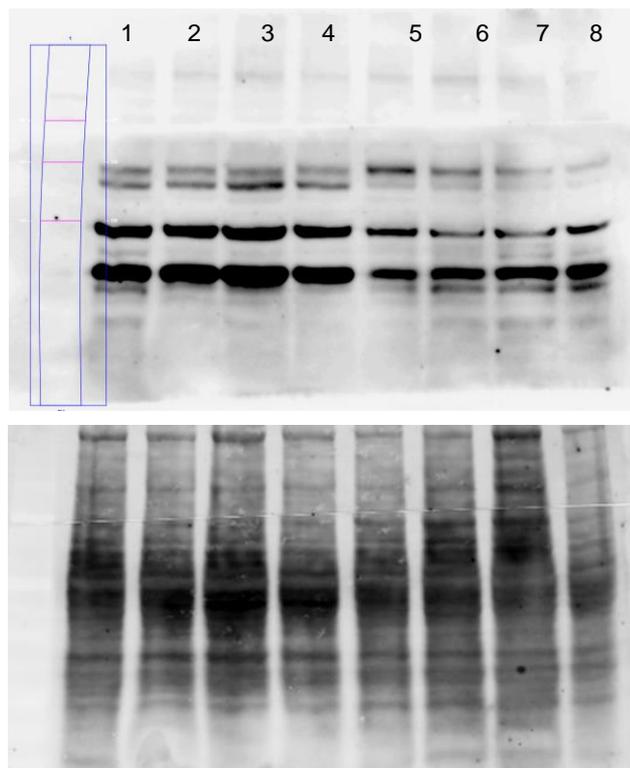
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2: Ctrl ♀ pool 3-4  
3: Ctrl ♀ pool 5-6  
4: Ctrl ♀ pool 7-8  
5: HFHFr ♀ pool 1-2  
6: HFHFr ♀ pool 3-4  
7: HFHFr ♀ pool 5-6  
8: HFHFr ♀ pool 7-8

The full-size original immunoblots for cytosolic NRF2 IB image

1: Ctrl ♂ pool 1-2  
2: Ctrl ♂ pool 3-4  
3: Ctrl ♂ pool 5-6  
4: Ctrl ♂ pool 7-8  
5: HFHFr ♂ pool 1-2  
6: HFHFr ♂ pool 3-4  
7: HFHFr ♂ pool 5-6  
8: HFHFr ♂ pool 7-8

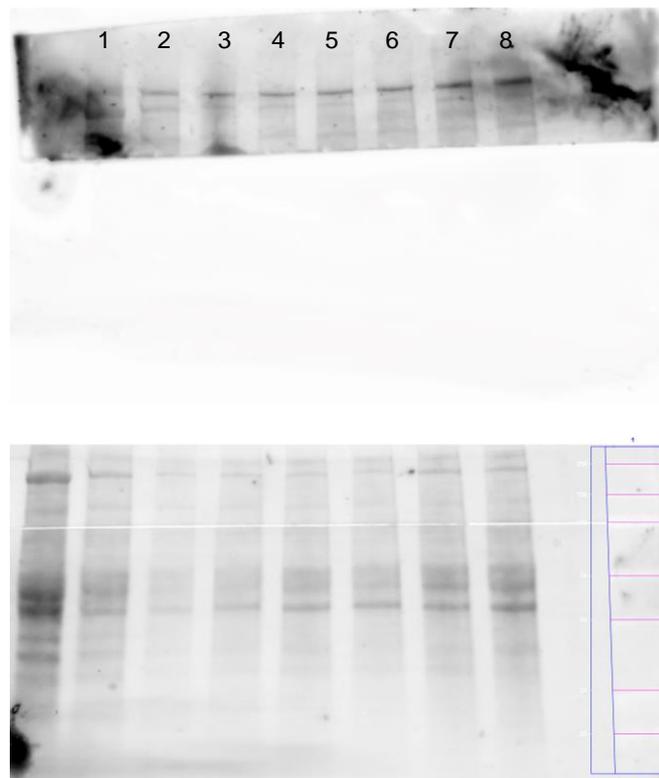
## Supplementary information

### Supplementary figure S3



- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: Ctrl ♀ pool 5-6
- 4: Ctrl ♀ pool 7-8
- 5: HFHFr ♀ pool 1-2
- 6: HFHFr ♀ pool 3-4
- 7: HFHFr ♀ pool 5-6
- 8: HFHFr ♀ pool 7-8

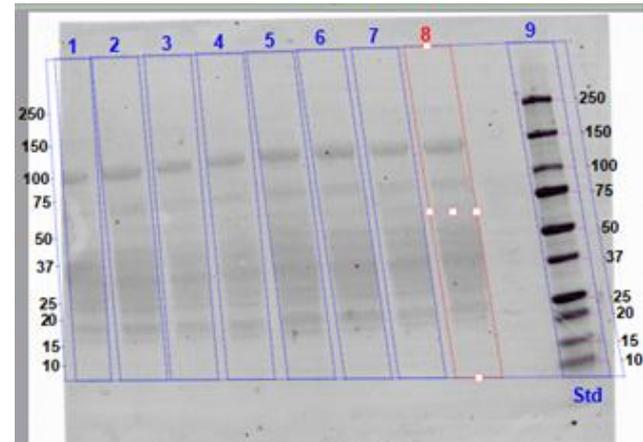
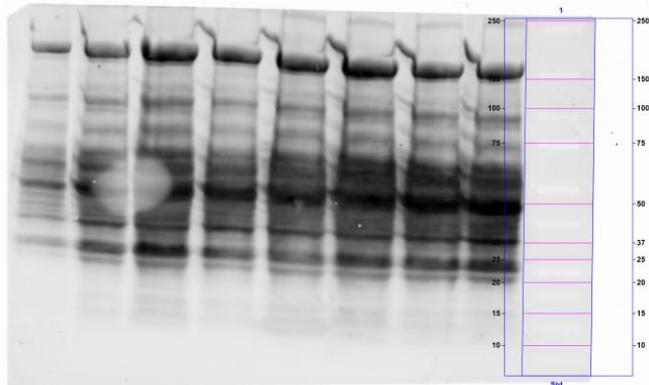
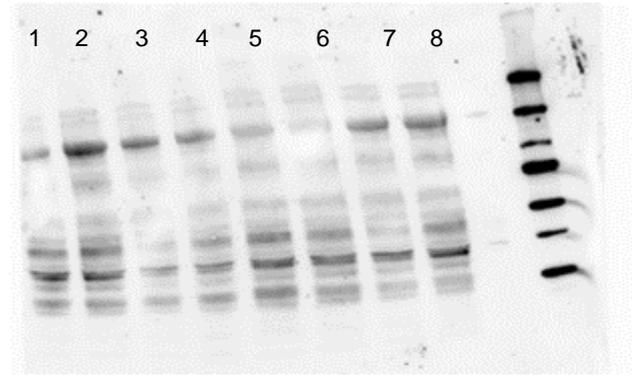
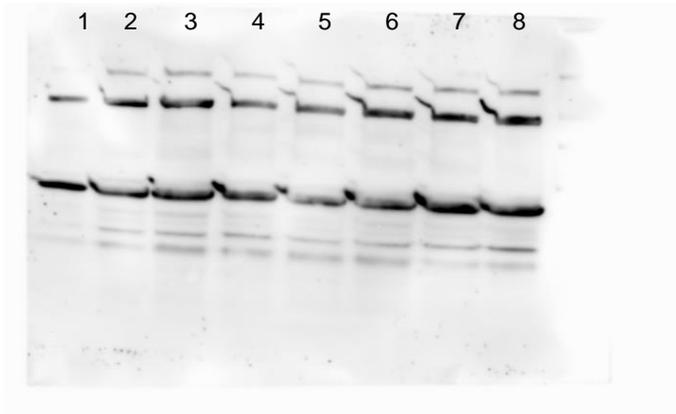
The full-size original immunoblots for nuclear NRF2 IB image



- 1: Ctrl ♂ pool 1-2
- 2: Ctrl ♂ pool 3-4
- 3: Ctrl ♂ pool 5-6
- 4: Ctrl ♂ pool 7-8
- 5: HFHFr ♂ pool 1-2
- 6: HFHFr ♂ pool 3-4
- 7: HFHFr ♂ pool 5-6
- 8: HFHFr ♂ pool 7-8

Supplementary information

Supplementary figure S4



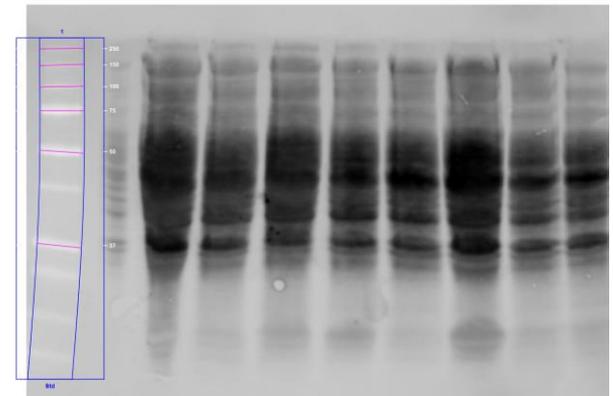
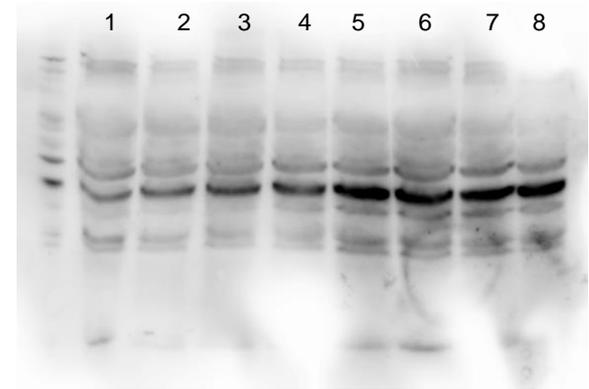
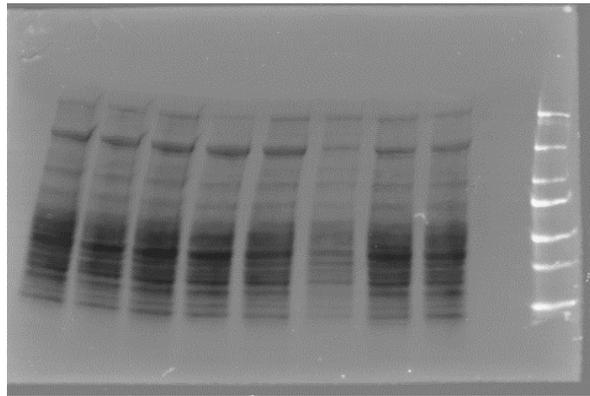
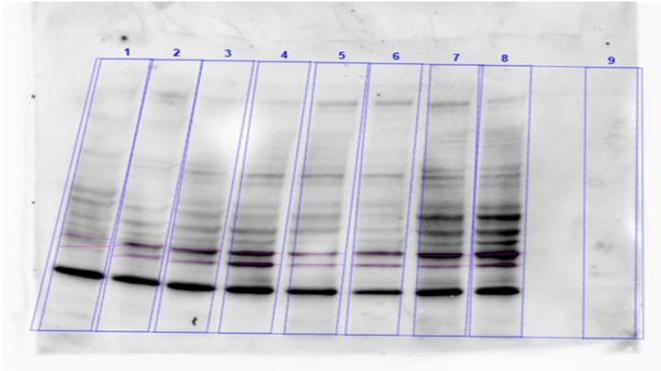
- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: Ctrl ♀ pool 5-6
- 4: Ctrl ♀ pool 7-8
- 5: HFHFr ♀ pool 1-2
- 6: HFHFr ♀ pool 3-4
- 7: HFHFr ♀ pool 5-6
- 8: HFHFr ♀ pool 7-8

Original immunoblots for KEAP1 IB image

- 1: CT ♂ pool 1-2
- 2: CT ♂ pool 3-4
- 3: CT ♂ pool 5-6
- 4: CT ♂ pool 7-8
- 5: HFHFr ♂ pool 1-2
- 6: HFHFr ♂ pool 3-4
- 7: HFHFr ♂ pool 5-6
- 8: HFHFr ♂ pool 7-8

Supplementary information

Supplementary figure S5



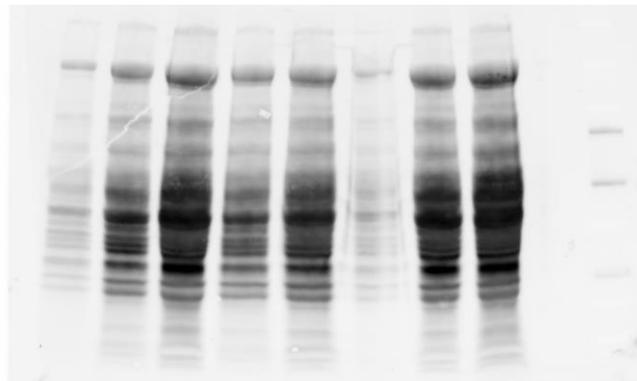
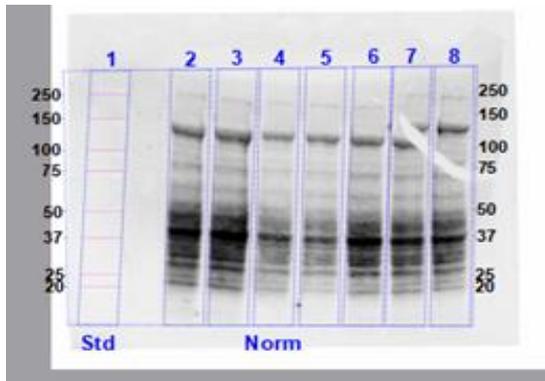
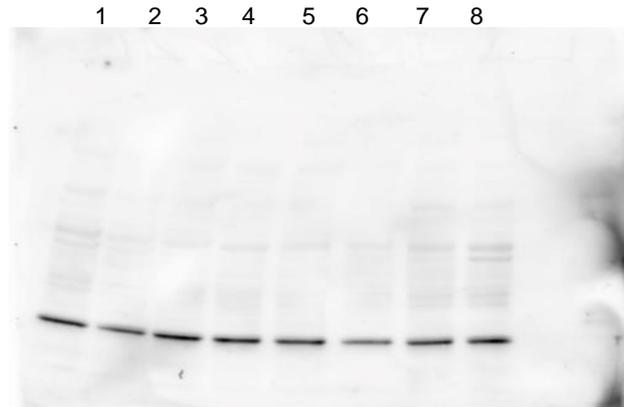
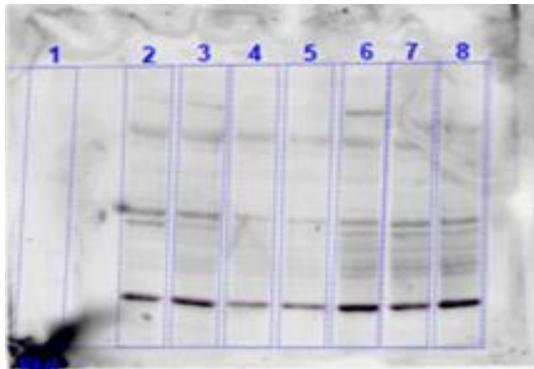
- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: Ctrl ♀ pool 5-6
- 4: Ctrl ♀ pool 7-8
- 5: HFHFr ♀ pool 1-2
- 6: HFHFr ♀ pool 3-4
- 7: HFHFr ♀ pool 5-6
- 8: HFHFr ♀ pool 7-8

The full-size original immunoblots for NQO1 IB image

- 1: HFHFr ♂ pool 1-2
- 2: HFHFr ♂ pool 3-4
- 3: HFHFr ♂ pool 5-6
- 4: HFHFr ♂ pool 7-8
- 5: CT ♂ pool 1-2
- 6: CT ♂ pool 3-4
- 7: CT ♂ pool 5-6
- 8: CT ♂ pool 7-8

## Supplementary information

### Supplementary figure S6



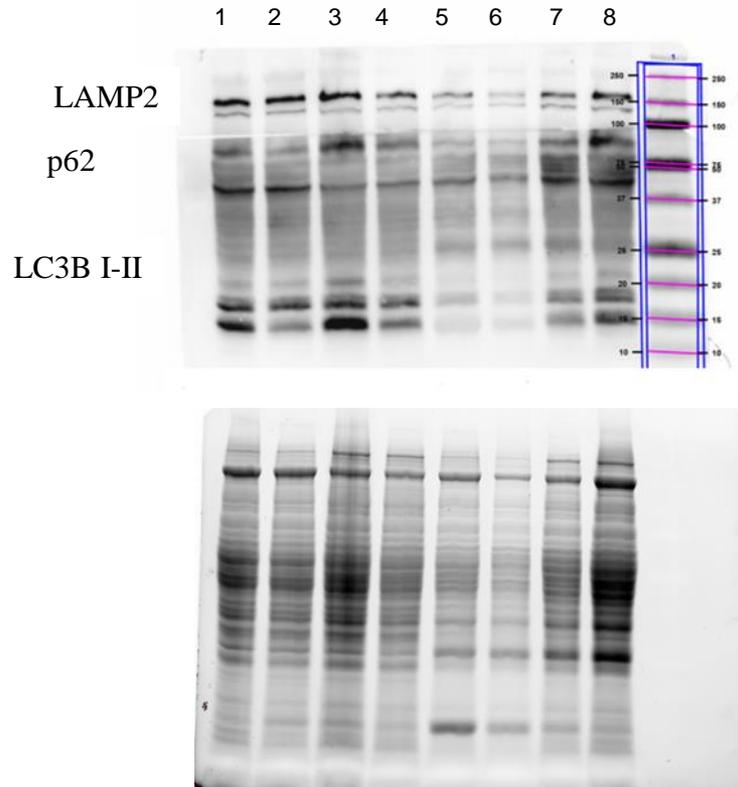
- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: Ctrl ♀ pool 5-6
- 4: Ctrl ♀ pool 7-8
- 5: HFHFr ♀ pool 1-2
- 6: HFHFr ♀ pool 3-4
- 7: HFHFr ♀ pool 5-6
- 8: HFHFr ♀ pool 7-8

The full-size original immunoblots for HO1 IB image

- 1: CT ♂ pool 1-2
- 2: CT ♂ pool 3-4
- 3: CT ♂ pool 5-6
- 4: CT ♂ pool 7-8
- 5: HFHFr ♂ pool 1-2
- 6: HFHFr ♂ pool 3-4
- 7: HFHFr ♂ pool 5-6
- 8: HFHFr ♂ pool 7-8

Supplementary information

Supplementary figure S7

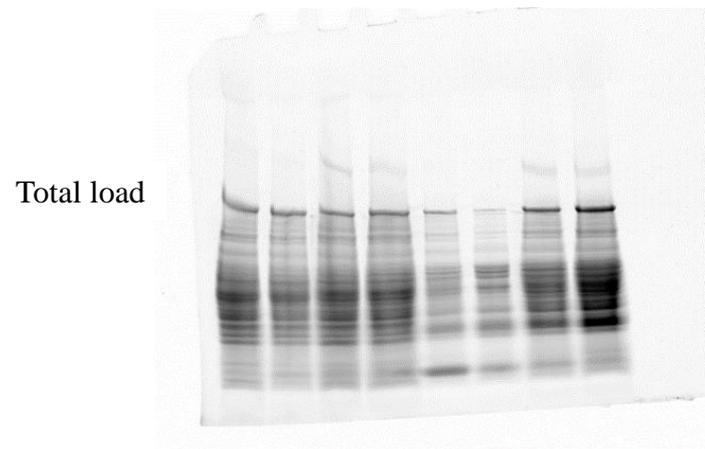
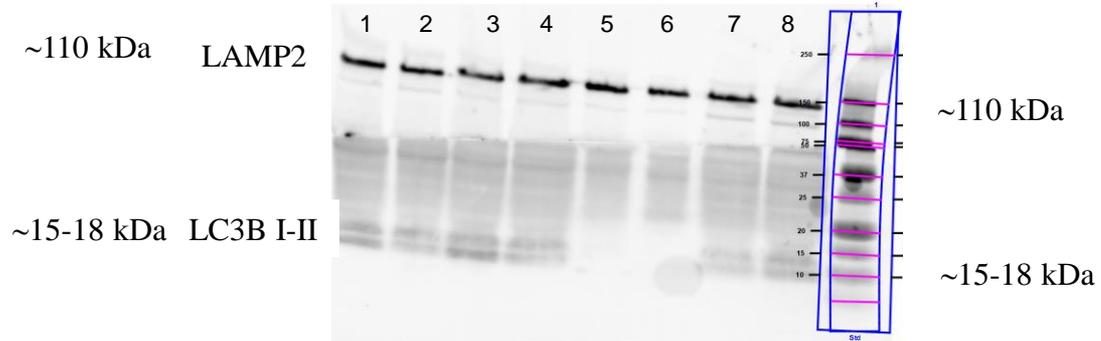


- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: HFHFr ♀ pool 1-2
- 4: HFHFr ♀ pool 3-4
- 5: Ctrl ♂ pool 1-2
- 6: Ctrl ♂ pool 3-4
- 7: HFHFr ♂ pool 1-2
- 8: HFHFr ♂ pool 3-4

The full-size original immunoblots for p62 and LC3B-I and LC3B-II IB images

Supplementary information

Supplementary figure S8



- 1: Ctrl ♀ pool 1-2
- 2: Ctrl ♀ pool 3-4
- 3: HFHFr ♀ pool 1-2
- 4: HFHFr ♀ pool 3-4
- 5: Ctrl ♂ pool 1-2
- 6: Ctrl ♂ pool 3-4
- 7: HFHFr ♂ pool 1-2
- 8: HFHFr ♂ pool 3-4

The full-size original immunoblots for LAMP2\_ images