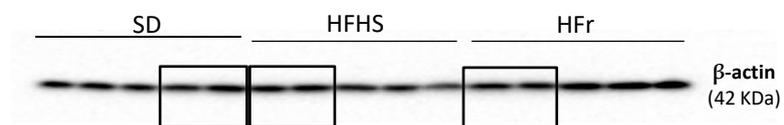
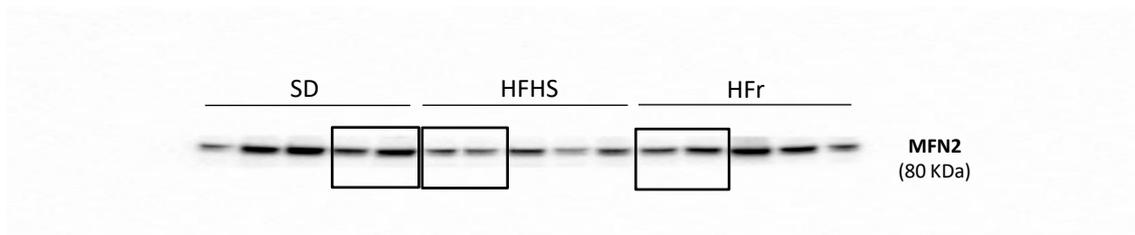


Supplementary Figures file S1:  
Heart



**Supplementary Figure S1a. Representative western blotting for  $\beta$ -actin in mouse heart.**  
Representative whole blots of  $\beta$ -actin protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 5.

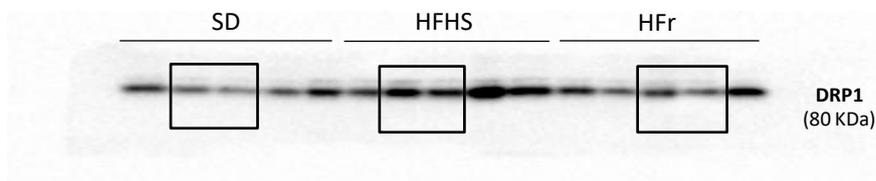


**Supplementary Figure S1b. Representative western blotting for MFN2 in mouse heart.**

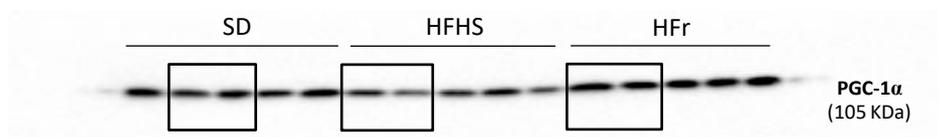
Representative whole blots of MFN2 protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

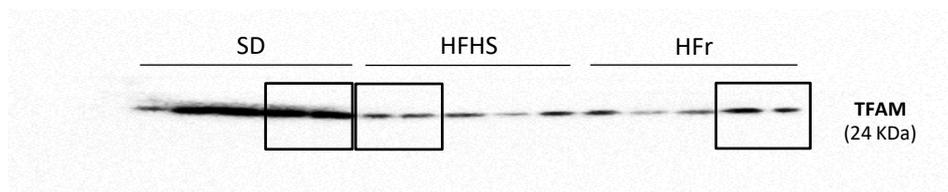
The bands enclosed in the boxes are reported in Figure 8 (A).



**Supplementary Figure S1c. Representative western blotting for DRP1 in mouse heart.**  
Representative whole blots of DRP1 protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 8 (B).



**Supplementary Figure S1d. Representative western blotting for PGC-1 $\alpha$  in mouse heart.**  
Representative whole blots of PGC-1 $\alpha$  protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 7 (A).

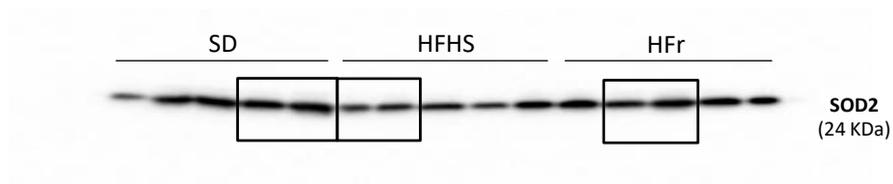


**Supplementary Figure S1e. Representative western blotting for TFAM in mouse heart.**

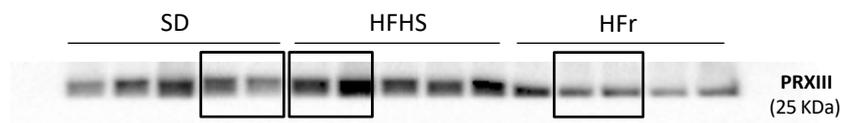
Representative whole blots of TFAM protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 7 (B).



**Supplementary Figure S1f. Representative western blotting for SOD2 in mouse heart.**  
Representative whole blots of SOD2 protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 5 (A).

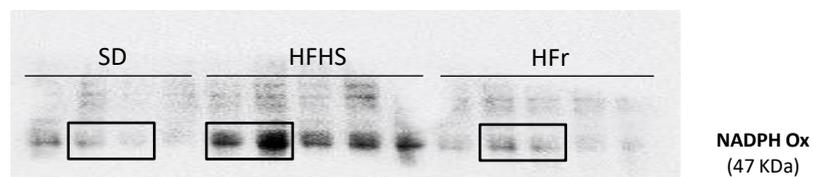


**Supplementary Figure S1g. Representative western blotting for PRXIII in mouse heart.**

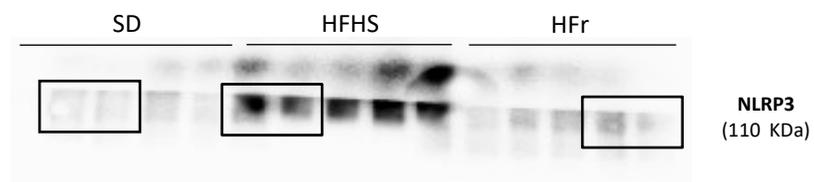
Representative whole blots of PRXIII protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

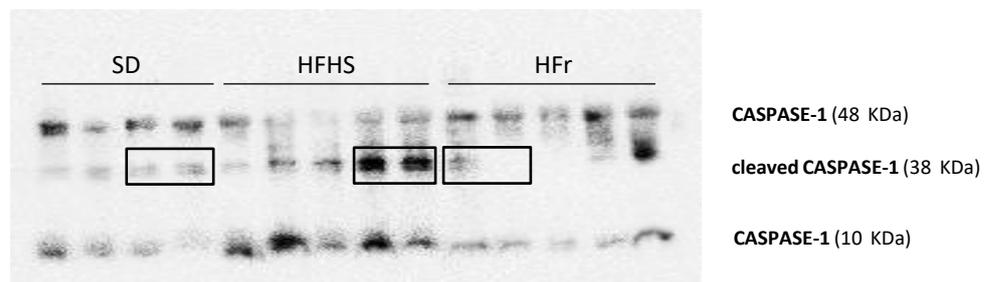
The bands enclosed in the boxes are reported in Figure 5 (B).



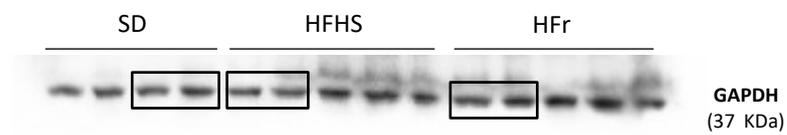
**Supplementary Figure S1h. Representative western blotting for NADPH Ox in mouse heart.**  
Representative whole blots of NADPH Ox protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 3 (C).



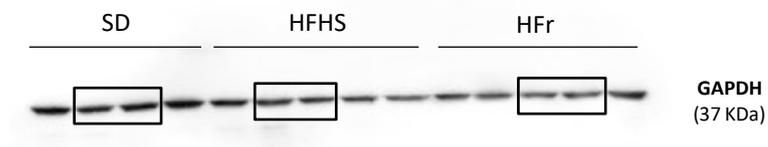
**Supplementary Figure S1i. Representative western blotting for NLRP3 in mouse heart.** Representative whole blots of NLRP3 protein used in manuscript. SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose). The bands enclosed in the boxes are reported in Figure 3 (A).



**Supplementary Figure S1j. Representative western blotting for CASPASE-1 in mouse heart.** Representative whole blots of cleaved CASPASE-1 protein used in manuscript. SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose). The bands enclosed in the boxes are reported in Figure 3 (B).

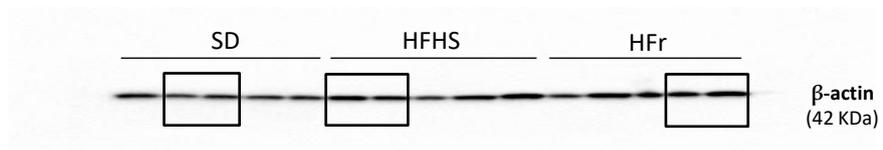


**Supplementary Figure S1k. Representative western blotting for GAPDH in mouse heart.**  
Representative whole blots of GAPDH protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 3 (A) and 3 (C).



**Supplementary Figure S11. Representative western blotting for GAPDH in mouse heart.**  
Representative whole blots of GAPDH protein used in manuscript.  
SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).  
The bands enclosed in the boxes are reported in Figure 3 (B).

Supplementary Figures file S2:  
Tibialis anterior  
skeletal muscle

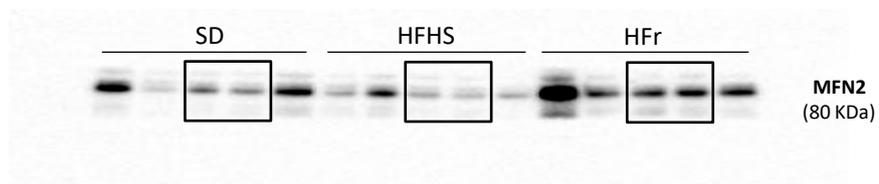


**Supplementary Figure S2a. Representative western blotting for  $\beta$ -actin in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of  $\beta$ -actin protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 5.

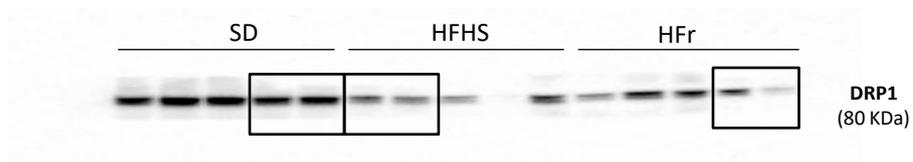


**Supplementary Figure S2b. Representative western blotting for MFN2 in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of MFN2 protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 8 (A).

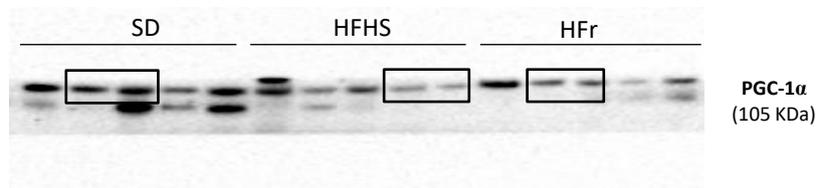


**Supplementary Figure S2c. Representative western blotting for DRP1 in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of DRP1 protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 8 (B).

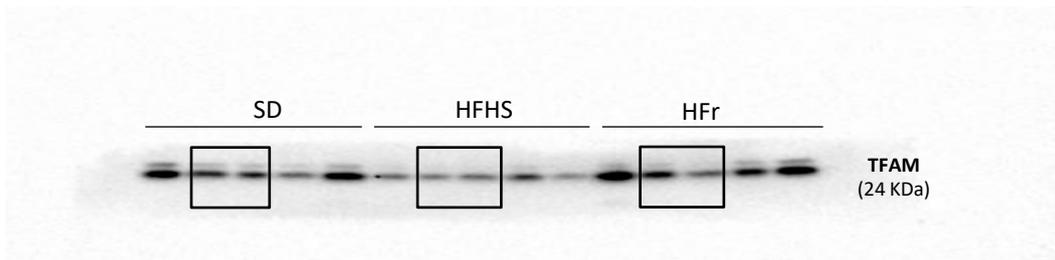


**Supplementary Figure S2d. Representative western blotting for PGC-1 $\alpha$  in mouse Tibialis Anterior muscle.**

Representative whole blots of PGC-1 $\alpha$  protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 7 (A).

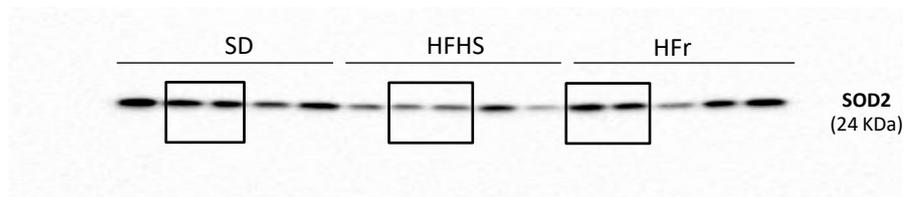


**Supplementary Figure S2e. Representative western blotting for TFAM in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of TFAM protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 7 (B).

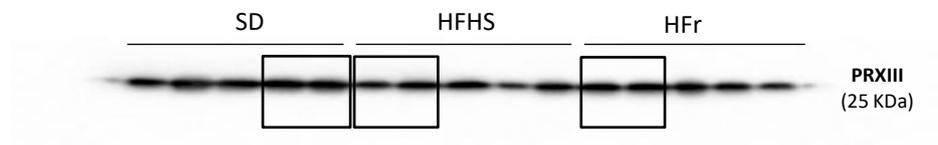


**Supplementary Figure S2f. Representative western blotting for SOD2 in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of SOD2 protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 5 (A).

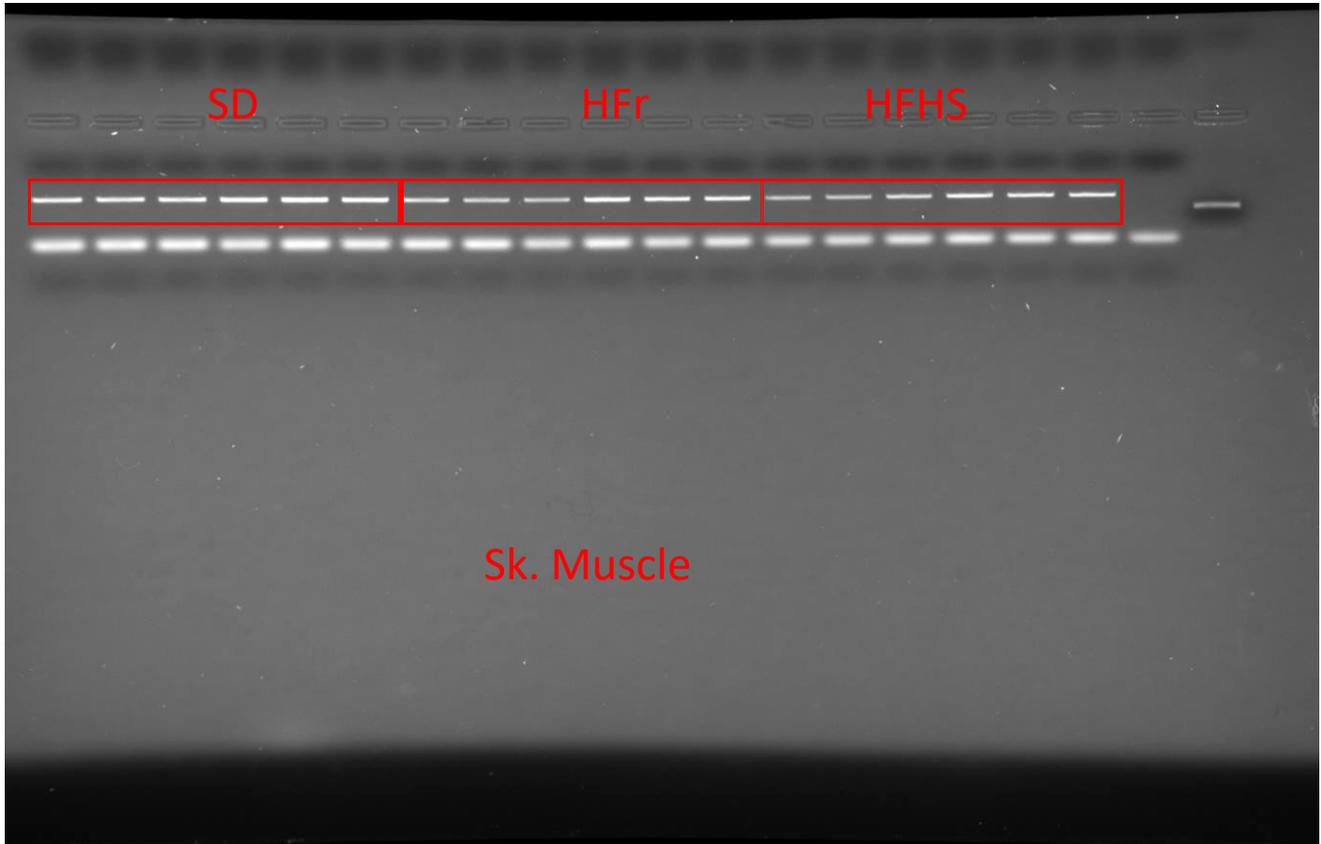


**Supplementary Figure S2g. Representative western blotting for PRXIII in mouse Tibialis Anterior skeletal muscle.**

Representative whole blots of PRXIII protein used in manuscript.

SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose).

The bands enclosed in the boxes are reported in Figure 5 (B).



**Supplementary Figure S2h. Representative agarose gel for amplicons in mouse TibialisAnterior skeletal muscle.**

Representative agarose gel showing amplicons obtained from Fpg-treated and untreated total DNA. SD (Standard Diet, controls), HFHS (High-Fat High-Sucrose) and HFr (High-Fructose). The bands enclosed in the boxes are reported in Figure 6 (C).

## List of Abbreviations

<b>AGEs</b>	Advanced Glycation End products
<b>AUC</b>	Area Under Curve
<b>CML</b>	N $\epsilon$ -(carboxymethyl)-lysine
<b>CVD</b>	Cardiovascular Diseases
<b>DNL</b>	De novo Lipogenesis
<b>DRP1</b>	Dynamin Related Protein 1
<b>ECL</b>	Enhanced Chemiluminescence
<b>ELISA</b>	Enzyme-Linked Immunosorbent Assay
<b>F.I.</b>	Fusion Index
<b>FPG</b>	Formamidopyrimidine/8-oxoguanine DNA N-glycosylase
<b>GAPDH</b>	Glyceraldehyde-3-phosphate Dehydrogenase
<b>GOLD</b>	6-{1-[(5S)-5-ammonio-6-oxido-6-oxohexyl]imidazolium-3-yl}-L-norleucine/glyoxylderived Lysine Dimer
<b>HbA1c</b>	Hemoglobin A1c
<b>HF</b>	High Fat
<b>HFHS</b>	High Fat High Sucrose diet
<b>HFr</b>	High Fructose diet
<b>HRP</b>	Horseradish Peroxidase
<b>IL-1<math>\beta</math></b>	Interleukin-1 $\beta$
<b>IL-6</b>	Interleukin-6
<b>IL-18</b>	Interleukin-18
<b>ITT</b>	Insulin Tolerance Test
<b>LDH</b>	Lactate Dehydrogenase
<b>MQC</b>	Mitochondrial Quality Control
<b>MFN2</b>	Mitofusin 2
<b>MOLD</b>	6-{1-[(5S)-5-ammonio-6-oxido-6-oxohexyl]-4-methyl-imidazoli/methylglyoxal-Lysine Dimer
<b>MS</b>	Metabolic Syndrome
<b>mtDNA</b>	Mitochondrial DNA
<b>NADPHox</b>	Nicotinamide Adenine Dinucleotide Phosphate Hydrogen oxidase
<b>NAFLD</b>	Non-alcoholic Fatty Liver Disease
<b>NLRP3</b>	Nucleotide-binding domain, Leucine-Rich-containing family, Pyrin domain-containing-3
<b>OGTT</b>	Oral Glucose Tolerance Test
<b>OH8dG</b>	8-hydroxydeoxyguanosine
<b>OXPHOS</b>	Oxidative Phosphorylation
<b>PGC-1<math>\alpha</math></b>	Peroxisome proliferator-activated receptor-Gamma Coactivator 1alpha
<b>PRXIII</b>	Peroxiredoxin 3
<b>PVDF</b>	Polyvinylidene Difluoride
<b>qRT-PCR</b>	Quantitative Real-Time Polymerase Chain Reaction
<b>RAGE</b>	Receptor for Advance Glycation End-products
<b>ROS</b>	Reactive Oxygen Species
<b>SD</b>	Standard Diet
<b>SDS-PAGE</b>	Sodium Dodecyl Sulphate - Polyacrylamide Gel Electrophoresis
<b>SEM</b>	Standard Error of Mean
<b>SOD2</b>	Superoxide Dismutase 2
<b>T2D</b>	Type 2 Diabetes
<b>TA</b>	Tibialis Anterioris
<b>TFAM</b>	Transcription Factor A, mitochondrial
<b>UHPLC</b>	Ultra-High-Performance Liquid Chromatography
<b>WT</b>	Wild Type