

**Supplemental Table S3.** Cardiac Parameters in ND-Fed Rats versus HFD-Fed Rats

Heart parameter	ND	HFD	P value
Cardiac function at week 12			
LVEF, %	84.67±0.88	78.83±1.70	0.0124
%FS	49.2±1.06	42.5±1.64	0.0142
E/A ratio	1.34±0.10	1.31±0.05	NS
LF/HF ratio	0.15±0.02	0.16±0.02	NS
Mitochondrial function at week 28			
Mitochondrial ROS level (arbitrary unit)	605.00±39.00	540.70±45.51	NS
Mitochondrial membrane potential change	1.18±0.07	1.32±0.12	NS
Normalized mitochondrial absorbance at $\lambda$ 540 nm (ratio at 30 min to baseline)	0.92±0.02	0.93±0.01	NS
Mitochondrial metabolism at week 28			
CPT1 protein expression	0.40±0.03	0.57±0.04	0.0053
PGC-1 $\alpha$ protein expression	0.67±0.03	0.73±0.04	NS
p-AMPK/Total AMPK protein expression	2.43±0.36	1.39±0.07	0.0167
Insulin signaling at week 28			
p-IRS/Total IRS protein expression	0.60±0.05	0.45±0.04	0.0462
p-AKT/Total AKT protein expression	0.93±0.04	0.74±0.03	0.0019
Mitochondrial respiration at week 28			
State 3 respiration rate, pmol/min	98.20±37.75	296.50±21.95	<0.0001
State 4 respiration rate, pmol/min	21.34±5.33	44.59±5.56	0.0057
Oxygen consumption rate (OCR)	4.73±0.53	7.34±0.92	0.0305
Complex I protein expression	0.31±0.02	0.19±0.02	0.0014
Complex II protein expression	1.79±0.08	1.58±0.04	0.0290
Complex III protein expression	1.13±0.06	0.85±0.13	0.0004
Complex IV protein expression	0.89±0.04	0.57±0.03	<0.0001
Complex V protein expression	1.19±0.06	1.24±0.04	NS
Mitochondrial dynamics at week 28			
MFN1 protein expression	0.78±0.04	0.82±0.04	NS
MFN2 protein expression	1.84±0.08	1.78±0.03	NS
OPA1 protein expression	0.60±0.03	0.85±0.03	<0.0001
Mitochondrial DRP1 protein expression	0.73±0.03	0.67±0.04	NS
Cytosolic p-DRP1 <sup>ser616</sup> /total DRP1 protein expression	0.87±0.03	0.87±0.02	NS
Mitophagy at week 28			
Mitochondrial PINK1/Parkin protein expression	2.18±0.24	1.90±0.31	0.0033
Cytosolic PINK1/Parkin protein expression	0.30±0.04	0.82±0.14	0.0023
Autophagy at week 28			
Beclin-1 protein expression	0.69±0.05	0.89±0.03	0.0109
LC3-II protein expression	0.88±0.07	1.17±0.06	0.0080
p62 protein expression	0.85±0.06	1.32±0.10	0.0013

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**Supplemental Table S3.** Continued

Heart parameter	ND	HFD	P value
Apoptosis at week 28			
Cytosolic/Mitochondrial cytochrome c protein expression	0.58±0.07	0.58±0.04	NS
Bax/Bcl-2 protein expression	0.70±0.03	0.63±0.02	NS
Cleaved caspase 3/Procaspase 3 protein expression	0.51±0.05	0.47±0.04	NS
Antioxidant at week 28			
GPX4 protein expression	0.57±0.04	0.66±0.06	NS
SOD2 protein expression	1.71±0.07	1.37±0.06	0.0048
Lipid peroxidation at week 28			
MDA level, mmol/g protein	296.02±16.98	295.72±25.09	NS
Inflammation at week 28			
TNF-α protein expression	0.53±0.05	0.84±0.06	0.0022
p-NFκB/Total NFκB protein expression	1.83±0.10	1.69±0.04	NS
Anti-aging marker at week 28			
sRAGE protein expression	1.18±0.03	0.91±0.04	0.0011
Cardiac function at week 28			
LVEF, %	86.48±1.57	81.38±1.49	0.0185
%FS	51.83±1.86	45.77±1.53	0.0221
E/A ratio	1.21±0.03	1.34±0.03	0.0101
LF/HF ratio	0.14±0.03	0.26±0.04	0.0264

Values are expressed as mean±standard error of the mean ( $n=8$  per group). Week 12, baseline; Week 28, follow-up. All protein expressions are normalized to the expression of housekeeping proteins.

ND, normal diet-fed rats; HFD, high-fat diet-fed rats; LVEF, left ventricular ejection fraction; FS, fractional shortening; E/A, early to late ventricular filling velocity; NS, no significance; LF/HF, lower frequency/high frequency; ROS, reactive oxygen species; CPT1, carnitine palmitoyltransferase I; PGC-1α, peroxisome proliferator-activated receptor gamma coactivator-1α; p-AMPK, phosphorylated-activated protein kinase; AMPK, activated protein kinase; p-IRS, phosphorylated-insulin receptor substrate 1; IRS, insulin receptor substrate 1; MFN1, mitofusin 1; MFN2, mitofusin 2; OPA1, optic atrophy 1; DRP1, dynamin-related protein 1; p-DRP1<sup>ser616</sup>, phosphorylated-dynamin-related at serine<sup>616</sup>; PINK1, PTEN-induced kinase 1; LC3-II, light chain 3-II; Bax/Bcl, Bcl-2-associated X protein/B-cell lymphoma; GPX4, glutathione peroxidase 4; SOD2, superoxide dismutase 2; MDA, malondialdehyde; TNF-α, tumor necrosis factor-α; p-NFκB, phosphorylated-nuclear factor kappa-light-chain-enhancer of activated B cells; NFκB, nuclear factor kappa-light-chain-enhancer of activated B cells; sRAGE, soluble-receptor for advanced glycation end product.