# Science Advances

### Supplementary Materials for

## Mitochondrial proteostasis stress in muscle drives a long-range protective response to alleviate dietary obesity independently of ATF4

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*Sci. Adv.* **8**, eabo0340 (2022) DOI: 10.1126/sciadv.abo0340

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Figs. S1 to S8 Tables S1 and S2



Fig. S1. Metabolic characterization of mice with skeletal muscle-specific ablation of the Lonp1 gene. (A) Western blot analysis of LONP1 expression in the GC, soleus (Sol), white vastus lateralis (WV) muscles and hearts of WT and LONP1 mKO mice following HFD feeding. (B) Growth curves of indicated mice. n = 8-13 mice per group. (C) Body composition measured to determine lean mass. n = 7-10 mice per group. (D) Lean mass plotted as a percentage of body weight. (E) Top: Representative WGA staining of GC muscle from indicated mice fed either CD or HFD. Scale bar represents 50 µm. Bottom: Cross-sectional areas of GC myofibers were measured by ImageJ. n = 6-7 mice per group. DAPI, blue; Wheat germ agglutinin (WGA), green. (F) Food consumption. n = 7-8 mice per group. (G and H) Oxygen consumption (G) and carbon dioxide production (H) per hour during the light/dark cycle normalized to body weight. n = 8mice per group. Color legend for the panel: red, WT CD; blue: LONP1 mKO CD. (I) Left: Glucose tolerance test (GTT). Right: Area under the curve for GTT is shown. n = 4-8 mice per group. (J) Weight of eWAT and BAT from indicated mice. n = 8-10 mice per group. Color legend for the panel: white, WT CD; gray, LONP1 mKO CD; orange, WT HFD; green, HSA-Cre HFD; diagonal hatch, LONP1 mKO HFD. Values represent the mean  $\pm$  SEM. \* P < 0.05versus corresponding WT controls; # P < 0.05 versus corresponding CD controls. The P values were determined using two-tailed unpaired Student's t test (G and H) or one-way ANOVA and Fisher's least-significant difference (LSD) post hoc test (**B** to **D**, **F**, **I** and **J**).



**Fig. S2. Muscle LONP1 regulates the response of adipose tissue and liver to HFD.** (**A** and **B**) Expression of genes (qRT-PCR) related to macrophages, fibrosis, lipolysis, thermogenesis, and

mitochondrial fatty acid oxidation in the eWAT of the indicated mice following HFD feeding. n = 6 mice per group. (C) Quantification of the UCP1/Tubulin, NDUFB8/Tubulin,

TOM20/Tubulin and TIM23/Tubulin signal ratios in the BAT from CD-fed LONP1 mKO mice was normalized (= 1.0) to the WT controls fed CD. n = 4 mice per group. (**D**) Expression of genes (qRT-PCR) related to amino acid metabolism, one-carbon metabolism and Fgf21 in the BAT from HFD-fed LONP1 mKO mice and WT controls. n = 6 mice per group. (E) Representative western blot analysis of LONP1 protein expression in livers from the indicated mice fed either CD or HFD. n = 4 mice per group. (F) Pictures of livers from the indicated mice fed either CD or HFD. (G) Expression of genes (RT-qPCR) related to fatty acid import, de novo fatty acid lipogenesis, fatty acid oxidation and gluconeogenesis in livers from HFD-fed LONP1 mKO mice and WT controls. n = 6 mice per group. (H) Left: representative western blot analysis of liver lysates for mice of the indicated genotypes using the indicated antibodies. Right: Quantification of the FASN/Tubulin signal ratios normalized (= 1.0) to the WT controls. n = 4mice per group. (I) Expression of genes (qRT-PCR) related to UPR, amino acid metabolism, one-carbon metabolism and Fgf21 in the livers from HFD-fed LONP1 mKO mice and WT controls. n = 6 mice per group. Color legend for the panel: white, WT CD; gray, LONP1 mKO CD; orange, WT HFD; diagonal hatch, LONP1 mKO HFD. Values represent mean ± SEM. \*P < 0.05 versus WT controls. The P values were determined using a two-tailed unpaired Student's ttest.



Genes downregulated in LONP1 mKO (2-week)						
Go_terms_BP	Count	P-value				
muscle system process	18	3.24E-16				
regulation of muscle system process	14	2.71E-14				
heart contraction	13	1.54E-13				
heart process	13	2.77E-13				
muscle contraction	14	4.03E-13				
striated muscle contraction	11	3.40E-12				
cardiac muscle contraction	10	8.29E-12				
regulation of muscle contraction	10	6.15E-11				
transition between fast and slow fiber	5	7.15E-11				
muscle adaptation	9	1.88E-10				

F

Genes upregulated in LONP1 mKO (6-week)

KEGG	Count	P-value
Cardiac muscle contraction	15	6.11E-06
Ribosome	23	6.63E-06
Aminoacyl-tRNA biosynthesis	12	3.00E-05
p53 signaling pathway	12	7.36E-05
MAPK signaling pathway	28	1.25E-04
Biosynthesis of amino acids	12	1.85E-04
Dilated cardiomyopathy	13	2.64E-04
Hypertrophic cardiomyopathy	12	7.02E-04
Thyroid cancer	7	1.10E-03
One carbon pool by folate	5	1.21E-03



G

Go\_terms\_BP

ossification

factor stimulus

extracellular matrix organization

cell-substrate adhesion

muscle cell differentiation

muscle system process

response to wounding

extracellular structure organization

regulation of cellular response to growth

serine/threonine kinase signaling pathway 40

regulation of cell-substrate adhesion

transmembrane receptor protein

Genes downregulated in LONP1 mKO (6-week)

Genes downregulated in LONP1 mKO (6-week)

Count P-value

3.30E-13

3.72E-13

1.64E-12

2.21E-11

2.87E-11

5.19E-11

7.27E-11

8.58E-11

4.14E-10

4.50E-10

39

39

43

44

36

31

44

44

49

KEGG	Count	P-value
Proteoglycans in cancer	32	5.49E-10
Glucagon signaling pathway	21	5.25E-09
AGE-RAGE signaling pathway in		
diabetic complications	18	4.83E-07
Wnt signaling pathway	23	8.98E-07
Ras signaling pathway	28	1.73E-06
Apelin signaling pathway	20	3.01E-06
MAPK signaling pathway	32	3.06E-06
Oxytocin signaling pathway	21	4.67E-06
Melanogenesis	16	8.99E-06
Relaxin signaling pathway	18	1.78E-05

Fig. S3. Analysis of genes regulated in LONP1 mKO muscles. (A) Percentage of mitochondrial area per muscle fiber area in Figure 3A was quantified from the indicated genotypes. (B) Results of quantitative PCR to determine mitochondrial DNA levels in GC muscles from CD or HFD-fed LONP1 mKO mice and WT controls using primers for NADH dehydrogenase (Nd1, mitochondria-encoded) and lipoprotein lipase (Lpl, nuclear-encoded). Nd1 levels were normalized to Lpl DNA content and expressed relative to WT (=1.0) muscles. n = 6mice per group. (C) Representative western blot analysis of muscle lysates from the indicated mice fed either CD or HFD. n = 4-5 mice per group. (**D** and **E**) GO enrichment analysis of downregulated gene transcripts in LONP1 mKO muscles at the ages of 2 weeks and 6 weeks, with the top ten terms shown. (F and G) KEGG pathway analysis of gene transcripts upregulated (F) or downregulated (G) in LONP1 mKO muscles at the age of 6 weeks. (H) Volcano plot showing fold changes versus P values for the regulated myokine genes in GC muscles from 6week-old male LONP1 mKO mice compared to WT controls. Significantly upregulated genes are represented by red dots, whereas downregulated genes are represented by blue dots. Color legend for the panel: white, WT CD; gray, LONP1 mKO CD; orange, WT HFD; diagonal hatch, LONP1 mKO HFD. Values represent mean  $\pm$  SEM.

#### Fig. S4

Α

#### В

Genes	unregulated	in	MCK-AOTC
Genes	upregulateu		MCK-DOTC

Genes downregulated in MCK-ΔOTC					
Go_terms_BP	Count	P-value			
muscle system process	47	6.49E-23			
muscle cell development	31	1.95E-18			
muscle contraction	36	2.04E-18			
striated muscle cell development	29	2.29E-17			
striated muscle cell differentiation	36	3.03E-17			
muscle cell differentiation	40	3.19E-17			
striated muscle contraction	26	1.48E-16			
striated muscle tissue development	41	4.86E-16			
muscle tissue development	41	2.73E-15			
myofibril assembly	17	4.48E-14			

KEGG	Count	P-value
Protein processing in endoplasmic reticulum	29	4.17E-09
Aminoacyl-tRNA biosynthesis	16	7.78E-08
RNA transport	24	8.85E-06
Ribosome biogenesis in eukaryotes	18	2.59E-05
Steroid biosynthesis	6	2.93E-04
Apoptosis	17	3.45E-04
Ferroptosis	8	6.11E-04
NF-kappa B signaling pathway	14	9.43E-04
Epstein-Barr virus infection	23	1.03E-03
Arginine and proline metabolism	9	1.14E-03

C Genes downregulated in M	ΙCK-ΔΟΤΟ	;	D		
KEGG	Count	P-value	<sup>5</sup> 1	::	♦ Up
Glucagon signaling pathway	15	2.71E-08			Down     Non
Adrenergic signaling in cardiomyocy	tes 17	1.49E-07	4		
Calcium signaling pathway	19	3.65E-07	ne	· · · ·	
Glycolysis / Gluconeogenesis	11	5.37E-07	- C 🗧	12	
GnRH signaling pathway	12	1.65E-06	ظ	• • • • •	
Oxytocin signaling pathway	15	4.39E-06	<b>ວັ</b> 2 -		Gdf15
Hypertrophic cardiomyopathy	11	1.18E-05	우	<b>31</b>	Faf21
HIF-1 signaling pathway	12	1.99E-05	1		
Fructose and mannose metabolism	7	2.11E-05			
Amphetamine addiction	9	4.06E-05	0 <b> </b>	<u> </u>	_
			-10	-5 0 5	10
				Log <sub>2</sub> (fold change)	

Fig. S4. Analysis of genes regulated in MCK- $\Delta$ OTC muscles. (A) GO enrichment analysis of gene transcripts downregulated in MCK- $\Delta$ OTC muscles. (B and C) KEGG pathway analysis of gene transcripts upregulated (B) or downregulated (C) in MCK- $\Delta$ OTC muscles. (D) Volcano plot showing fold changes versus *P* values for the regulated myokine genes in GC muscles from MCK- $\Delta$ OTC mice compared to NTG controls. Significantly upregulated genes are represented by red dots, whereas downregulated genes are represented by blue dots.



Fig. S5. Muscle-specific overexpression of  $\Delta$ OTC confers resistance to diet-induced obesity. (A) Body weight of the indicated 6-week-old mice fed normal chow diet. n = 12-14 mice per group. (B) Mitochondrial respiration rates were determined on mitochondria isolated from muscles of the indicated mice using succinate as substrate. Succinate/rotenone (Suc/Rot)-stimulated, ADP-dependent respiration, and oligomycin (oligo)-induced respiration are shown. n

= 6 mice for CD and n = 4 mice for HFD. (C) Increase in body weight following HFD feeding. n = 12-14 mice per group. (**D**) Representative pictures of the indicated mice fed a HFD for 12 weeks. (**E**) Food consumption. n = 5-6 mice per group. (**F**) Physical activity. n = 5-6 mice per group. (**G**) Representative pictures of eWAT, iWAT and BAT from HFD-fed MCK- $\Delta$ OTC mice and NTG controls. (**H**) Weight of eWAT, iWAT and BAT from the indicated mice fed a HFD for 12 weeks. n = 11-14 mice per group. (**I**) Expression of genes (qRT-PCR) related to macrophage and fibrosis in the eWAT from HFD-fed MCK- $\Delta$ OTC and WT controls. n = 6 mice per group. (**J**) Masson's trichrome staining in the eWAT of the indicated HFD-fed mice. The scale bar represents 50 µm. n = 5-6 mice per group. Color legend for the panel: white, NTG CD; gray, MCK- $\Delta$ OTC CD; orange, NTG HFD; diagonal hatch, MCK- $\Delta$ OTC HFD. Values represent mean ± SEM. \**P* < 0.05 versus NTG controls. The *P* values were determined using a two-tailed unpaired Student's *t* test.



Fig. S6. ATF4-dependent and -independent reprogramming of muscle metabolism by
LONP1. (A) Genome browser tracks of RNA-seq data were visualized in IGV. (B and C)
Principal component analysis (PCA) (B) and Heatmap analysis (C) of muscle metabolites.
Capillary electrophoresis-mass spectrometry (CE-MS) based metabolite analysis were performed

with GC muscles from the indicated mice. n = 7 mice per group. Red represents relative increase in abundance, blue represents relative decrease. (**D**) One-carbon metabolism and associated pathways in WT, LONP1 mKO and LONP1/ATF4 DmKO muscles. Colored text, red, increase in LONP1 mKO muscle; blue, decrease in LONP1/ATF4 DmKO muscle. Circled metabolites changed in LONP1/ATF4 DmKO muscles compared to LONP1 mKO mice; red, increase; blue, decrease.

#### Fig. S7

	Go terms BP Cluster II	C	ount	<i>P</i> -value			Go terms BP	Cluster IV	Count	Pavalue
1	cellular respiration	20	)	3.62E-13		1			oount	/ Value
	respiratory electron transport chain	14	Ļ	1.07E-11			energy derivation by oxidat	tion of organic	45	1 01E 14
	antigen processing and presentation of						compounds		45	1.01E-14
Ħ	exogenous antigen	10	)	1.23E-11	t	Ĕ	ATP metabolic process		44	1.04E-14
<del>a</del>	electron transport chain	14		2.12E-11	Ż	ğ	generation of precursor me	etabolites and energy	57	1.42E-14
e	generation of precursor metabolites and	energy 27		2.2/E-11		be	muscle cell differentiation		56	1.01E-13
ğ	exogenous pentide antigen	9		4 29E-11	5	ge	striated muscle contraction	1	32	2.25E-12
4	ATP synthesis coupled electron transpor	t 12	)	6.65E-11		Ē	muscle system process		53	5.06E-12
Ľ.	energy derivation by oxidation of organic	-			- ji	1	positive regulation of ion tra	ansport	46	1.26E-11
₹	compounds	21		1.81E-10		<	ducose metabolic process		33	4 22E-11
	mitochondrial ATP synthesis coupled ele	ectron					stricted annuals call differen	, 	33	9.000 44
	transport	11		5.23E-10			striated muscle cell differen	itiation	44	0.20E-11
	NADH dehydrogenase complex assemb	ly 10	)	7.41E-10			extracellular matrix organiz	ration	40	1.00E-10
В	Asns Aldh18a1 Adh112 Pycr1 Sic3a2 Sic7a1 Sic7a2 Sic7a5 Sic7a1 Sic6a9 Sic6a9 Sic22a4 Rbp4 Gars Lars Nars Lars Nars Cars Cars Cars Cars Cars Cars Cars C			C 5 4 4 3 2 -10 -10		-5	0 5 Log <sub>2</sub> (fold change)	• <i>Fgf21</i> • Up • Dow • <i>Gdf15</i>	n	

**Fig. S7. ATF4-dependent and -independent reprogramming of muscle gene expression by LONP1.** (**A**) GO enrichment analysis of Cluster II (ATF4-dependent) and IV (ATF4independent) genes, with the top ten terms shown. (**B**) Heat-map analysis of ATF4-dependent genes involved in muscle amino acids and one-carbon metabolism. Red represents relative increase in abundance, blue represents relative decrease. (**C**) Volcano plot showing fold changes versus *P* values for the ATF4-independent regulated myokine genes by LONP1 deficiency.

Significantly upregulated genes are represented by red dots, whereas downregulated genes are represented by blue dots.



Fig. S8. Mitochondrial proteostasis stress in skeletal muscle directs a long-range metabolic response to alleviate dietary obesity independent of ATF4. (A) Pictures of eWAT, iWAT, and BAT from the indicated mice fed HFD. (B) Mitochondrial respiration rates were determined from the BAT of the indicated genotypes using succinate as substrate. Succinate/rotenone (Suc/Rot)-stimulated, ADP-dependent respiration, and antimycin-induced respiration are shown. n = 5-7 mice per group. (C) Expression of genes (qRT-PCR) related to UPR in the BAT from indicated mice. n = 5-6 mice per group. (D) Pictures of livers from the indicated mice fed HFD.

(E) Liver triglyceride levels from the indicated mice. n = 5-10 mice per group. Color legend for the panel: white, WT HFD; orange, LONP1 mKO HFD; gray, ATF4 mKO HFD; diagonal hatch, LONP1/ATF4 DmKO HFD. Values represent mean  $\pm$  SEM. \* *P* < 0.05 versus WT controls. The *P* values were determined using one-way ANOVA and Fisher's least-significant difference (LSD) post hoc test.

#### Table S1.

Genes commonly upregulated (1.5-fold change and P < 0.05) by both LONP1 deficiency and  $\Delta OTC$  overexpression in skeletal muscle.

~		Fold change	Fold change (vs. Control)			
Gene symbol	Description	LONP1 mKO	ΜСК-ΔΟΤС			
Gdf15	growth differentiation factor 15	320.3	634.2			
Cdsn	corneodesmosin	290.9	115.7			
Fgf21	fibroblast growth factor 21	276.7	713.8			
Soat2	sterol O-acyltransferase 2	234.6	231.9			
Trib3	tribbles pseudokinase 3	84.6	172.6			
S100a8	S100 calcium binding protein A8	76.1	54.3			
Psat1	phosphoserine aminotransferase 1	72.1	21.6			
Asns	asparagine synthetase (glutamine-hydrolyzing)	66.4	52.2			
Arhgap33	Rho GTPase activating protein 33	64.5	15.5			
P2rx3	purinergic receptor P2X 3	63.2	7.9			
Dlg2	discs large MAGUK scaffold protein 2	62.6	46.7			
Tenm4	teneurin transmembrane protein 4	60.3	16.8			
Mthfd2	<i>methylenetetrahydrofolate dehydrogenase</i> ( <i>NADP</i> + <i>dependent</i> ) 2, <i>methenyltetrahydrofolate</i> <i>cyclohydrolase</i>	54.6	25.1			
Slc7a5	solute carrier family 7 member 5	29.5	21.6			
Trim66	tripartite motif containing 66	26.5	10.2			
Slc7a11	solute carrier family 7 member 11	24.3	71.3			
Sox11	SRY-box transcription factor 11	19.7	2.8			
Myl4	myosin light chain 4	15.6	4.8			
Mt2	metallothionein 1X	15.3	19.6			
Slc1a4	solute carrier family 1 member 4	14.9	3.8			
Chrng	cholinergic receptor nicotinic gamma subunit	14.8	2.1			
Ankrd1	ankyrin repeat domain 1	14.4	12.0			
Sesn2	sestrin 2	13.7	18.3			
Mthfd11	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1 like	12.9	6.7			
<i>Reep6</i>	receptor accessory protein 6	12.9	11.0			
Myh8	myosin heavy chain 8	12.5	2.4			
Nrcam	neuronal cell adhesion molecule	12.2	3.6			
Cth	cystathionine gamma-lyase	11.8	22.6			
Zp2	zona pellucida glycoprotein 2	11.7	6.9			
Zfp365	zinc finger protein 365	11.7	2.6			
Kcnk2	potassium two pore domain channel subfamily K member 2	10.8	3.0			
Aldh18a1	aldehyde dehydrogenase 18 family member A1	10.4	6.2			
Slc7a1	solute carrier family 7 member 1	10.3	5.7			

Pck2	phosphoenolpyruvate carboxykinase 2, mitochondrial	10.2	6.8
Kcnk3	potassium two pore domain channel subfamily K member 3	9.8	2.2
Gabrr2	gamma-aminobutyric acid type A receptor subunit rho2	9.3	1.8
Smpdl3b	sphingomyelin phosphodiesterase acid like 3B	9.0	7.0
Myog	myogenin	8.4	2.6
Tbc1d31	TBC1 domain family member 31	8.1	8.5
Fam171b	family with sequence similarity 171 member B	7.9	3.6
Lgals3	galectin 3	7.5	40.6
Phgdh	phosphoglycerate dehydrogenase	7.2	6.9
Aldh1l2	aldehyde dehydrogenase 1 family member L2	7.2	4.5
Gadd45a	growth arrest and DNA damage inducible alpha	7.2	4.5
Slc38a1	solute carrier family 38 member 1	7.1	4.9
Uchl1	ubiquitin C-terminal hydrolase L1	7.1	3.1
Pycr1	pyrroline-5-carboxylate reductase 1	7.0	5.3
Arsg	arylsulfatase G	6.7	5.3
Fads3	fatty acid desaturase 3	6.7	6.4
Rassf7	Ras association domain family member 7	6.5	2.8
Slc6a9	solute carrier family 6 member 9	6.4	9.8
Mt1	metallothionein 1A	6.3	10.0
Igfbp2	insulin like growth factor binding protein 2	6.2	3.5
Cpne2	copine 2	6.0	4.5
Arhgdig	Rho GDP dissociation inhibitor gamma	6.0	1.9
Fgf7	fibroblast growth factor 7	5.8	4.6
Arhgef2	Rho/Rac guanine nucleotide exchange factor 2	5.8	2.4
Ttc9	tetratricopeptide repeat domain 9	5.7	1.8
Tubb2b	tubulin beta 2B class IIb	5.6	3.1
Nog	noggin	5.5	14.1
Chrnd	cholinergic receptor nicotinic delta subunit	5.4	4.4
N4bp2l1	NEDD4 binding protein 2 like 1	5.4	5.2
Ostn	osteocrin	5.2	4.9
G0s2	G0/G1 switch 2	5.1	1.9
Gm13889	chromosome 11 open reading frame 96	5.0	4.1
Ncam1	neural cell adhesion molecule 1	5.0	1.7
Atf5	activating transcription factor 5	4.9	5.2
Stc2	stanniocalcin 2	4.9	2.1
Cbx4	chromobox 4	4.8	2.6
Gdf9	growth differentiation factor 9	4.8	2.7
Cdkn1a	cyclin dependent kinase inhibitor 1A	4.7	5.2
Ddit3	DNA damage inducible transcript 3	4.7	5.4
Rin1	Ras and Rab interactor 1	4.6	2.6

Snhg12		4.5	5.8
Zfp52		4.4	1.6
Runx1	RUNX family transcription factor 1	4.4	2.7
Bid	BH3 interacting domain death agonist	4.4	9.4
Dclk1	doublecortin like kinase 1	4.4	2.3
LOC106740	PHD finger protein 10	4.4	4.5
Aldh1b1	aldehyde dehydrogenase 1 family member B1	4.3	1.8
Acot2	acyl-CoA thioesterase 1	4.3	8.1
Cyb5r1	cytochrome b5 reductase 1	4.3	3.5
Slc17a7	solute carrier family 17 member 7	4.2	5.0
Usp11	ubiquitin specific peptidase 11	4.1	3.0
Osbpl3	oxysterol binding protein like 3	4.0	2.3
Eif4ebp1	eukaryotic translation initiation factor 4E binding protein 1	4.0	4.0
Ern1	endoplasmic reticulum to nucleus signaling 1	3.9	4.1
Masp1	mannan binding lectin serine peptidase 1	3.8	2.5
Chka	choline kinase alpha	3.8	3.0
Arl14ep	ADP ribosylation factor like GTPase 14 effector protein	3.8	2.1
Ctsl	cathepsin V	3.7	7.3
Tmem82	transmembrane protein 82	3.6	2.0
Rnf185	ring finger protein 185	3.6	4.6
Erdr1		3.6	1.6
Nacad	NAC alpha domain containing	3.6	3.7
Snd1	staphylococcal nuclease and tudor domain containing 1	3.6	3.5
Tmeff1	MSANTD3-TMEFF1 readthrough	3.6	4.8
Ero11	endoplasmic reticulum oxidoreductase 1 alpha	3.5	3.4
Vat11	vesicle amine transport 1 like	3.5	4.5
Rrad	RRAD, Ras related glycolysis inhibitor and calcium channel regulator	3.5	5.7
Lgi2	leucine rich repeat LGI family member 2	3.5	2.4
Agpat9	glycerol-3-phosphate acyltransferase 3	3.5	3.3
Eda2r	ectodysplasin A2 receptor	3.4	7.0
Мус	MYC proto-oncogene, bHLH transcription factor	3.4	2.3
Eeflal	eukaryotic translation elongation factor 1 alpha 1	3.4	2.3
Nol8	nucleolar protein 8	3.4	1.7
Gas5	growth arrest specific 5	3.4	1.7
Tbx6	T-box transcription factor 6	3.4	2.8
Slc3a2	solute carrier family 3 member 2	3.4	5.3
Nupr1	nuclear protein 1, transcriptional regulator	3.4	3.7
Emb	embigin	3.3	7.6
Slc24a3	solute carrier family 24 member 3	3.3	3.6

Phf10	PHD finger protein 10	3.3	4.8
Hhipl1	HHIP like 1	3.3	3.0
Stard5	StAR related lipid transfer domain containing 5	3.3	4.4
Phyhd1	phytanoyl-CoA dioxygenase domain containing 1	3.3	4.0
Napb	NSF attachment protein beta	3.3	2.4
Stbd1	starch binding domain 1	3.3	2.1
Dctd	dCMP deaminase	3.2	1.8
Crym	crystallin mu	3.2	4.7
Cxadr	CXADR Ig-like cell adhesion molecule	3.2	4.1
Glce	glucuronic acid epimerase	3.2	2.4
Aph1c	aph-1 homolog B, gamma-secretase subunit	3.2	5.6
Gars	glycyl-tRNA synthetase 1	3.2	4.8
Ccdc136	coiled-coil domain containing 136	3.2	1.8
Mtbp	MDM2 binding protein	3.2	1.8
Chrna1	cholinergic receptor nicotinic alpha 1 subunit	3.2	1.9
Plekhh1	pleckstrin homology, MyTH4 and FERM domain containing H1	3.1	2.0
Lcn2	lipocalin 2	3.1	46.2
Dennd4a	DENN domain containing 4A	3.1	3.0
Ddit4	DNA damage inducible transcript 4	3.1	1.8
Cbx2	chromobox 2	3.1	2.0
Ciart	circadian associated repressor of transcription	3.1	6.4
Lhfpl2	LHFPL tetraspan subfamily member 2	3.0	2.6
Ghitm	growth hormone inducible transmembrane protein	3.0	2.5
Rundc3a	RUN domain containing 3A	3.0	1.9
Gramd1b	GRAM domain containing 1B	3.0	1.6
Gsto1	glutathione S-transferase omega 1	3.0	9.1
Lars	leucyl-tRNA synthetase 1	2.9	3.8
Map1b	microtubule associated protein 1B	2.9	3.2
Card9	caspase recruitment domain family member 9	2.9	2.4
Lrrc8d	leucine rich repeat containing 8 VRAC subunit D	2.9	3.8
Sncg	synuclein gamma	2.9	2.1
Tubb6	tubulin beta 6 class V	2.9	3.6
Sergef	secretion regulating guanine nucleotide exchange factor	2.9	1.8
Cd68	CD68 molecule	2.8	5.0
Trp53inp1	tumor protein p53 inducible nuclear protein 1	2.8	2.2
Gpnmb	glycoprotein nmb	2.8	6.5
Eif3c	eukaryotic translation initiation factor 3 subunit C like	2.8	4.1
Spag5	sperm associated antigen 5	2.8	2.3
Nlrc3	NLR family CARD domain containing 3	2.7	2.7

Gnmt	glycine N-methyltransferase	2.7	4.6
Atp6v1h	ATPase H+ transporting V1 subunit H	2.7	4.5
Tsga10	testis specific 10	2.7	2.0
Sh3bgrl2	SH3 domain binding glutamate rich protein like 2 2.7		2.3
Aif11	allograft inflammatory factor 1 like	2.7	1.7
Taf15	TATA-box binding protein associated factor 15	2.7	2.7
Pmm1	phosphomannomutase 1	2.6	1.9
Gm11974	small nucleolar RNA host gene 15	2.6	1.9
Htatip2	HIV-1 Tat interactive protein 2	2.6	3.5
Sik1	salt inducible kinase 1B (putative)	2.6	1.7
Igf2bp2	<i>insulin like growth factor 2 mRNA binding protein</i> 2	2.6	1.9
Nradd	neurotrophin receptor associated death domain, pseudogene	2.6	3.3
Prune2	prune homolog 2 with BCH domain	2.6	2.2
Slc19a2	solute carrier family 19 member 2	2.6	2.6
Ubxn11	UBX domain protein 11	2.6	2.3
Osbpl8	oxysterol binding protein like 8	2.6	1.6
Flnc	filamin C	2.5	1.9
Clic4	chloride intracellular channel 4	2.5	2.1
Lilrb4a	leukocyte immunoglobulin like receptor B4	2.5	2.6
Xpot	exportin for tRNA	2.5	3.0
Osbp2	oxysterol binding protein 2	2.5	5.2
Dsn1	DSN1 component of MIS12 kinetochore complex	2.5	1.7
Atf6	activating transcription factor 6	2.5	3.2
Slc2a1	solute carrier family 2 member 1	2.5	3.1
Avil	advillin	2.5	6.8
Bbc3	BCL2 binding component 3	2.4	3.2
Snhg1		2.4	2.4
Rnd1	Rho family GTPase 1	2.4	2.0
Cebpg	CCAAT enhancer binding protein gamma	2.4	1.9
Ankrd32	SMC5-SMC6 complex localization factor 1	2.4	1.6
Extl1	exostosin like glycosyltransferase 1	2.4	3.6
Tlr4	toll like receptor 4	2.4	1.6
Trim46	tripartite motif containing 46	2.4	3.3
Sars	seryl-tRNA synthetase 1	2.4	2.7
Adig	adipogenin	2.4	4.5
Тгаррсба	trafficking protein particle complex 6A	2.4	1.5
Zfp385b	zinc finger protein 385B	2.4	1.6
Ticam2		2.4	36.3
Wfs1	wolframin ER transmembrane glycoprotein	2.4	3.3
Rcc2	regulator of chromosome condensation 2	2.4	1.9

Lrrc58	leucine rich repeat containing 58	2.4	1.6
Nop58	NOP58 ribonucleoprotein	2.3	1.8
Lcorl	ligand dependent nuclear receptor corepressor like	2.3	2.1
Angptl6	angiopoietin like 6	2.3	4.0
Gtpbp2	GTP binding protein 2	2.3	3.3
Mnd1	meiotic nuclear divisions 1	2.3	2.0
Hmgb2	high mobility group box 2	2.2	2.0
Spg21	SPG21 abhydrolase domain containing, maspardin	2.2	4.5
Slc25a33	solute carrier family 25 member 33	2.2	1.9
Tgif1	TGFB induced factor homeobox 1	2.2	6.1
Leprotl1	leptin receptor overlapping transcript like 1	2.2	3.1
Trmt10a	tRNA methyltransferase 10A	2.2	1.8
Tspyl4	TSPY like 4	2.2	2.6
Slc22a4	solute carrier family 22 member 4	2.2	2.0
Tmed5	transmembrane p24 trafficking protein 5	2.2	1.6
Spg20	spartin	2.2	4.0
Hspb7	heat shock protein family B (small) member 7	2.2	1.6
Mamdc2	MAM domain containing 2	2.2	1.9
Fam175a	abraxas 1, BRCA1 A complex subunit	2.2	2.7
Ifrd1	interferon related developmental regulator 1	2.1	1.8
Atxn2l	ataxin 2 like	2.1	1.8
Bex1	brain expressed X-linked 2	2.1	2.9
Shmt2	serine hydroxymethyltransferase 2	2.1	2.6
Prodh	proline dehydrogenase 1	2.1	1.7
Sclt1	sodium channel and clathrin linker 1	2.1	1.5
Ptrh1	peptidyl-tRNA hydrolase 1 homolog	2.1	1.7
Odf2	outer dense fiber of sperm tails 2	2.1	1.6
Zfp945		2.1	2.5
Stap2	signal transducing adaptor family member 2	2.1	3.2
Ddx51	DEAD-box helicase 51	2.1	5.8
Mtm1	myotubularin 1	2.1	2.7
Rhbdd1	rhomboid domain containing 1	2.1	3.3
Dhrs7	dehydrogenase/reductase 7	2.1	1.8
Sfn	stratifin	2.1	1.9
Mid1ip1	MID1 interacting protein 1	2.0	4.5
Dkc1	dyskerin pseudouridine synthase 1	2.0	1.5
Hsp90aa1	heat shock protein 90 alpha family class A member 1	2.0	1.7
Eprs	glutamyl-prolyl-tRNA synthetase 1	2.0	2.6
Scpep1	serine carboxypeptidase 1	2.0	3.4
Adck4	coenzyme Q8B	2.0	1.8

Wbscr27	methyltransferase like 27	2.0	2.9
Parp4	poly(ADP-ribose) polymerase family member 4	2.0	2.6
Pvr	PVR cell adhesion molecule	2.0	1.8
Gyk	glycerol kinase	2.0	2.1
Synj2	synaptojanin 2	2.0	1.7
Agap1	ArfGAP with GTPase domain, ankyrin repeat and PH domain 1	2.0	2.2
Acot6	acyl-CoA thioesterase 6	2.0	1.9
Tfcp2l1	transcription factor CP2 like 1	2.0	8.9
Me2	malic enzyme 2	2.0	2.4
Mks1	MKS transition zone complex subunit 1	2.0	1.5
Ankzfl	ankyrin repeat and zinc finger peptidyl tRNA hydrolase 1	2.0	1.8
Chac1	ChaC glutathione specific gamma- glutamylcyclotransferase 1	2.0	5.0
Baz1a	bromodomain adjacent to zinc finger domain 1A	2.0	1.7
Faap20	FA core complex associated protein 20	2.0	1.7
Shb	SH2 domain containing adaptor protein B	2.0	2.1
Tor3a	torsin family 3 member A	2.0	1.9
Ece2	endothelin converting enzyme 2 2.0		2.7
Cdk20	cyclin dependent kinase 20	2.0	2.5
Hspa9	heat shock protein family A (Hsp70) member 9	2.0	2.2
Maff	MAF bZIP transcription factor F	2.0	1.6
Rpl3	ribosomal protein L3	2.0	2.3
Ncl	nucleolin	1.9	1.9
Gbe1	1,4-alpha-glucan branching enzyme 1	1.9	2.4
Mvd	mevalonate diphosphate decarboxylase	1.9	1.7
Derl1	derlin 1	1.9	2.7
Slc39a11	solute carrier family 39 member 11	1.9	2.4
Plk3	polo like kinase 3	1.9	2.1
Arhgap22	Rho GTPase activating protein 22	1.9	5.3
Ak4	adenylate kinase 4	1.9	1.5
Trmt61a	tRNA methyltransferase 61A	1.9	3.0
Tars	threonyl-tRNA synthetase 1	1.9	1.9
Elmsan1	mitotic deacetylase associated SANT domain protein	1.9	1.7
Hebp1	heme binding protein 1	1.9	2.1
Slc25a5	solute carrier family 25 member 5	1.9	1.7
Nars	asparaginyl-tRNA synthetase 1	1.9	2.7
Zfp568	zinc finger protein 568	1.9	1.6
Iars	isoleucyl-tRNA synthetase 1	1.9	2.5
Ciapin1	cytokine induced apoptosis inhibitor 1	1.9	2.7
Tmem205	transmembrane protein 205	1.9	1.7

Tmem62	transmembrane protein 62	1.9	2.1
Cstb	cystatin B	1.9	3.7
Gpc4	glypican 4	1.9	1.5
Mars	methionyl-tRNA synthetase 1		2.3
Rab27a	RAB27A, member RAS oncogene family	RAB27A, member RAS oncogene family1.9	
Esrrg	estrogen related receptor gamma	1.9	4.3
Mustn1	musculoskeletal, embryonic nuclear protein 1	1.8	2.3
Irak2	interleukin 1 receptor associated kinase 2	1.8	1.9
Dusp14	dual specificity phosphatase 14	1.8	1.8
Llph	<i>LLP homolog, long-term synaptic facilitation factor</i>	1.8	2.0
Garem	GRB2 associated regulator of MAPK1 subtype 1	1.8	1.8
Bri3bp	BRI3 binding protein	1.8	1.8
Arl15	ADP ribosylation factor like GTPase 15	1.8	1.8
Ttc12	tetratricopeptide repeat domain 12	1.8	1.5
Junb	JunB proto-oncogene, AP-1 transcription factor subunit	1.8	2.3
Sh3bp2	SH3 domain binding protein 2	1.8 2.6	
Rabggtb	Rab geranylgeranyltransferase subunit beta	1.8 1.5	
Eif2s2	<i>ukaryotic translation initiation factor 2 subunit</i> 1.8 1.9 <i>eta</i>		1.9
Art5	ADP-ribosyltransferase 5	1.8	1.7
Cx3cl1	C-X3-C motif chemokine ligand 1	1.8	1.7
BC048403	chromosome 12 open reading frame 66	1.8	1.8
B4galt6	beta-1,4-galactosyltransferase 6	1.8	1.5
Tubb2a	tubulin beta 2A class IIa	1.8	1.6
Fam83g	family with sequence similarity 83 member G	1.8	8.4
Zw10	zw10 kinetochore protein	1.8	1.9
Timm8a1	translocase of inner mitochondrial membrane 8A	1.8	1.5
Slc15a2	solute carrier family 15 member 2	1.8	1.5
Srm	spermidine synthase	1.8	1.9
Nfkb2	nuclear factor kappa B subunit 2	1.8 3.4	
Cars	cysteinyl-tRNA synthetase 1	1.7 2.1	
Otulin	OTU deubiquitinase with linear linkage specificity	1.7 1.7	
Snrnp48	small nuclear ribonucleoprotein U11/U12 subunit 48	1.7	1.9
Slc16a1	solute carrier family 16 member 1	1.7 2.1	
Atf4	activating transcription factor 4	1.7	2.5
Dnajb9	DnaJ heat shock protein family (Hsp40) member1.73.0B9		3.0
Fbxo30	F-box protein 30	1.7	2.1
Lrrc2	leucine rich repeat containing 2 1.7		1.5
Bhlhb9	ARMCX5-GPRASP2 readthrough1.7		1.6

Lrrc51	leucine rich transmembrane and O- methyltransferase domain containing	1.7	2.0
Hax1	HCLS1 associated protein X-1	1.7	2.4
Zfp14	ZFP14 zinc finger protein	1.7	1.5
Etv5	ETS variant transcription factor 5	1.7	1.5
Tmem176b	transmembrane protein 176B	1.7	3.2
Sorbs1	sorbin and SH3 domain containing 1	1.7	1.7
Rb1	RB transcriptional corepressor 1	1.7	1.9
Ninj1	ninjurin 1	1.7	2.7
Snhg8	small nucleolar RNA host gene 8	1.7	2.1
Ppip5k2	diphosphoinositol pentakisphosphate kinase 2	1.7	1.5
Panx1	pannexin 1	1.7	2.2
Noc4l	nucleolar complex associated 4 homolog	1.7	3.6
Pam	peptidylglycine alpha-amidating monooxygenase	1.7	1.7
Ppfibp1	PPFIA binding protein 1	1.7	1.9
Tnip1	TNFAIP3 interacting protein 1	1.7	3.5
Anxa4	annexin A4	1.7	2.1
Eif3a	eukaryotic translation initiation factor 3 subunit A	1.7	1.5
Thnsl2	threonine synthase like 2	1.7	1.6
Litaf	lipopolysaccharide induced TNF factor	1.7	2.0
Hace1	HECT domain and ankyrin repeat containing E3 ubiquitin protein ligase 1	1.7	1.6
Mknk1	MAPK interacting serine/threonine kinase 1	1.7	2.3
Obfc1	STN1 subunit of CST complex	1.7	1.5
Npm1	nucleophosmin 1	1.7	1.9
Slc19a1	solute carrier family 19 member 1	1.6	1.5
Trmt6	tRNA methyltransferase 6	1.6	2.0
Tmem181a	transmembrane protein 181	1.6	1.8
Nfe2l2	nuclear factor, erythroid 2 like 2	1.6	1.7
Slc25a39	solute carrier family 25 member 39	1.6	2.3
Tubalc	tubulin alpha 1c	1.6	2.5
Smim15	small integral membrane protein 15	1.6	1.7
Telo2	telomere maintenance 2	1.6	1.6
Sirpa	signal regulatory protein alpha	1.6	1.9
Ddx10	DEAD-box helicase 10	1.6	1.6
Wars	tryptophanyl-tRNA synthetase 1	1.6	3.8
Utp14a	UTP14A small subunit processome component	1.6	1.8
Zbtb8os	<i>zinc finger and BTB domain containing 8 opposite strand</i>	1.6	3.1
Fubp1	far upstream element binding protein 1	1.6	1.6
Kdm4a	lysine demethylase 4A	1.6	1.5
Herpud1	homocysteine inducible ER protein with ubiquitin like domain 1	1.6	2.4

Aars	alanyl-tRNA synthetase 1	1.6	2.1
Gtf2b	general transcription factor IIB	1.6	1.9
Sdf211	stromal cell derived factor 2 like 1	1.6	2.6
Krcc1	lysine rich coiled-coil 1	1.6	1.8
Mak16	MAK16 homolog	1.6	1.5
Siah1a	siah E3 ubiquitin protein ligase 1	1.6	1.7
D19Bwg1357e	pumilio RNA binding family member 3	1.6	1.7
Dusp4	dual specificity phosphatase 4	1.6	4.1
Slc16a6	solute carrier family 16 member 6	1.6	1.5
Hgh1	HGH1 homolog	1.6	1.5
Slc38a7	solute carrier family 38 member 7	1.6	1.9
Krtcap2	keratinocyte associated protein 2	1.6	2.0
Canx	calnexin	1.6	1.8
Aen	apoptosis enhancing nuclease	1.6	1.8
Eifla	eukaryotic translation initiation factor 1A Y- linked	1.6	1.7
Psph	phosphoserine phosphatase	1.6	1.5
Nubpl	nucleotide binding protein like	1.6	1.6
Tceal	transcription elongation factor A1	1.6	1.9
Msn	moesin	1.5	1.6
Gfod1	glucose-fructose oxidoreductase domain containing 1	1.5	1.7
Slc20a1	solute carrier family 20 member 1	1.5	2.1
Rpl10	ribosomal protein L10	1.5	1.6
Srxn1	sulfiredoxin 1	1.5	4.7
Nfu1	NFU1 iron-sulfur cluster scaffold	1.5	2.1
Cln8	CLN8 transmembrane ER and ERGIC protein	1.5	2.2
Musk	muscle associated receptor tyrosine kinase	1.5	2.9
Hmox1	heme oxygenase 1	1.5	3.8
Manf	mesencephalic astrocyte derived neurotrophic factor	1.5	1.8
Rps18	ribosomal protein S18	1.5	1.6
Erlin1	ER lipid raft associated 1	1.5	2.5
Pacsin2	protein kinase C and casein kinase substrate in neurons 2	1.5	1.5
Wdr46	WD repeat domain 46	1.5	2.0
Bax	BCL2 associated X, apoptosis regulator	1.5	2.2
Yrdc	yrdC N6-threonylcarbamoyltransferase domain containing	1.5	2.1
Ears2	glutamyl-tRNA synthetase 2, mitochondrial	1.5	2.0
Ttll11	tubulin tyrosine ligase like 11	1.5	2.7
Tmem128	transmembrane protein 128	1.5	1.7
Fam129a	niban apoptosis regulator 1	1.5	2.0

Supplemental Table 2 RT-PCR primers			
Mouse		D	
Gene	Forward	Reverse	
36b4	5'-ATCCCTGACGCACCGCCGTGA	5'-TGCATCTGCTTGGAGCCCACGT	
F4/80	5'-TTTCCTCGCCTGCTTCTTC	5'-CCCCGTCTCTGTATTCAACC	
Cd68	5'-GCAGCACAGTGGACATTCAT	5'-TTGCATTTCCACAGCAGAAG	
Cd11c	5'-CAGAACTTCCCAACTGCACA	5'-TCTCTGAAGCTGGCTCATCA	
Hifla	5'-CATGATGGCTCCCTTTTTCA	5'-GTCACCTGGTTGCTGCAATA	
Lox	5'-CAGGCTGCACAATTTCACC	5'-CAAACACCAGGTACGGCTTT	
Tgfβ	5'-TGGAGCAACATGTGGAACTC	5'-GTCAGCAGCCGGTTACCA	
Col3a1	5'-CTCCTGGTGAGCGAGGAC	5'-GACCAGGTTGCCCATCACT	
Col6a1	5'-GGGCATCAAGGTCTTTTCTG	5'-ATGTGTGGGTCTGTGGCAATG	
Pnpla2	5'-CATGATGGTGCCCTATACTC	5'-GTGAGAGGTTGTTTCGTACC	
Lipe	5'-AGCGCTGGAGGAGTGTTTT	5'-CCGCTCTCCAGTTGAACC	
Mgll	5'-GACGGACAGTACCTCTTTTG	5'-AGAAAAGTAGGTTGGCCTCT	
Ppargcla	5'-GGACATGTGCAGCCAAGACTCT	5'-CACTTCAATCCACCCAGAAAGCT	
Prdm16	5'-ACAGGCAGGCTAAGAACCAG	5'-CGTGGAGAGGAGGAGTGTCTTCAG	
Ucpl	5'-GGCCTCTACGACTCAGTCCA	5'-TAAGCCGGCTGAGATCTTGT	
Cidea	5'-TTCAAGGCCGTGTTAAGGA	5'-CCTTTGGTGCTAGGCTTGG	
Ppara	5'-ACTACGGAGTTCACGCATGTG	5'-TTGTCGTACACCAGCTTCAGC	
Dio2	5'-CTGCGCTGTGTCTGGAAC	5'-GGAGCATCTTCACCCAGTTT	
Cpt2	5'-CCAAAGAAGCAGCGATGG	5'-TAGAGCTCAGGCAGGGTGA	
Cox7a	5'-CGAAGAGGGGGGGGGGGGGGCTGACTC	5'-AGCCTGGGAGACCCGTAG	
Atp5a	5'-GCTGAGGAATGTTCAAGCAGA	5'-CCAAGTTCAGGGACATACCC	
Cox4	5'-TACTTCGGTGTGCCTTCGA	5'-TGACATGGGCCACATCAG	
Cptla	5'-CCGATCATGGTTAACAGCAA	5'-TGCAGCAGAGATTTGGCATA	
Cd36	5'-TTGAAAAGTCTCGGACATTGAG	5'-TCAGATCCGAACACAGCGTA	
Scd1	5'-TGGAAATGCCTTTGAGATGG	5'-CCAGCCAGCCTCTTGACTAT	
Fasn	5'-CTCCGTGGACCTTATCACTA	5'-CTGGGAGAGGGTTGTAGTCAG	
Elovl6	5'-CAAAGCACCCGAACTAGGTG	5'-GAGCACAGTGATGTGGTGGT	
Acaca	5'-CCAGGCCATGTTGAGACGCT	5'-ATCACAGAGCGGACGCCATC	
Srebflc	5'-TGCGGCTGTTGTCTACCATA	5'-TGCTGGAGCTGACAGAGAAA	
Dgat2	5'-TCATGGGTGTCTGTGGGTTA	5'-CAGAGTGAAACCAGCCAACA	
Acadl	5'-GCTTATGAATGTGTGCAACTCC	5'-CCGAGCATCCACGTAAGC	
Acadm	5'-AGGTTTCAAGATCGCAATGG	5'-CATTGTCCAAAAGCCAAACC	
<i>G6pc</i>	5'-TCTGTCCCGGATCTACCTTG	5'-GAAAGTTTCAGCCACAGCAA	
G6pd	5'-AGGGAAGAGTTGTACCAAAATGA	5'-CTTCTTCTTGGCCAGGTCAC	
Pepck	5'-GTGCTGGAGTGGATGTTCGG	5'-CTGGCTGATTCTCTGTTTCAGG	
Atf4	5'-AGCAAAACAAGACAGCAGCC	5'-ACTCTCTTCTTCCCCCTTGC	
Atf5	5'-CTGGCTCCCTATGAGGTCCTTG	5'-GAGCTGTGAAATCAACTCGCTCAG	
Ddit3	5'-GCGACAGAGCCAGAATAACA	5'-GATGCACTTCCTTCTGGAACA	
Lonpl	5'-CATTGCCTTGAACCCTCTC	5'-ATGTCGCTCAGGTAGATGG	
Clpp	5'-TGGGCCCGATTGACGACAGTG	5'-TAGATGGCCAGGCCCGCAGT	
TT 11			
Hspd1	S'-GATGCTGTGGGCCGTTACAATG	GTCAATTGACTTTGCAACAGTCACAC	
Hspel	S-GGCCCGAGTTCAGAGTCC	S-IGTCAAAGAGCGGAAGAAACT	
Hspa9	S-CAAGCGACAGGCTGTCACCAAC	S-CAACCCAGGCATCACCATTGG	
Asns	S'-CIGCCICIGCICCACCIT	S'-CACATGCTACAGGCGGACT	
Aldh112	J'-GCATAACTGGATTCGAGGTCA	J-TGAGCCGTAGAAAGTCACCA	

Table S2.RT-PCR primers.

Aldh18a1	5'-AGCGGGAAGAGATCCTGTTAG	5'-GTTTGGACGTGGAGAGGCTA
Slc7a11	5'-GATTCATGTCCACAAGCACAC	5'-GAGCATCACCATCGTCAGAG
Slc6a9	5'-CACAGATGGGGGACACACTTCT	5'-GGTTGTAGTGGGAGCGTAGC
Psatl	5'-CCGGTGGATGTTTCCAAG	5'-TGATGGGCACTCTCTGAGC
Phgdh	5'-GAGAACCCTGCCCAGTCA	5'-AGGCCATTGCTAGAGTCAGG
Shmt2	5'-CCCTGAGATGTGGGAGCTT	5'-CTCGGCTGCAGAAGTTCTCT
Mthfd2	5'-CCTACAGCCCTTCCACCTG	5'-GAGGCCACCCACTCTTCC
Mthfd11	5'-GAGGTGGATATGCTCAGGTCA	5'-ATGTCCCCAGTCAGGTGAAG
Fgf21	5'-TACACAGATGACGACCAAGA	5'-GGCTTCAGACTGGTACACAT
Gdf15	5'-GAGCTACGGGGTCGCTTC	5'-GAGTCCTCTCGGCTCTGGT
Angptl6	5'-ATCTTCTCTGCTGCCCACA	5'-CGTGAGCCTCTGCACAATC
Igfbp2	5'-GCGGGTACCTGTGAAAAGAG	5'-CCTCAGAGTGGTCGTCATCA
Primers for quantification of mtDNA		
mt-Nd1	5'-CCCATTCGCGTTATCTT	5'-AAGTTGATCGTAACGGAAGC
Lpl	5'-GATGGACGGTAAGAGTGATTC	5'-ATCCAAGGGTAGCAGACAGGT