SUPPLEMENTARY DATA

Supplementary Table 1. relative to Fig. 1. Candidate hepatokine genes involved in obesity.

Unigene	Symbol	Name	DM/NGT, by SAGE	p value vs. BMI	Correlation coefficient
Hs.73853	BMP2	Bone morphogenetic protein 2	4.54	0.0001	0.63
Hs.512580	LECT2	Leukocyte cell-derived chemotaxin2	2.11	0.0001	0.61
Hs.3416	ADFP	adipose differentiation-rclate4 protein	0.15	0.0020	0.54
Hs.443518	BPAG1	Homo sapiens dystonin (DST), transcript variant leA, mRNA	1.51	0.01	0.49
Hs.173594	SERPINF1	serine (or cysteine) proteinase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1	2.02	0.01	0.47
Hs.157307	GNAS	GNAS complex locus	1.99	0.01	0.47
Hs.324746	AHSG	AHSG alpha2 HS glycoprotein	0.02	0.02	0.42
Hs.10458	CCL 16	chemokine (C-C motif) ligand 16	6.82	0.02	0.42
Hs.168718	AFM	afamin	0.57	0.02	0.42
Hs.241257	LTBP1	LTBP1 latent transforming growth factor beta binding protein 1	0.05	0.02	0.42
Hs.1012	C4BPA	complement component 4 binding protein, alpha	0.29	0.03	0.41
Hs.234734	LYZ	lysozyme (renal amyloidosis)	0.45	0.03	0.4
Hs.2 12581	MMP24	MMP24 matrix metalloproteinase 24 (membrane inserted)	0.05	0.03	0.4
Hs.4 06455	PSAP	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	2.47	0.03	0.4
Hs. 1498	ERG	histidine-rich glycoprotein	8.49	0.04	0.39
Hs.9914	FST	FST follistatin	0.02	0.04	0.38
Hs.119651	GPC3	glypican 3	67.75	0.04	-0.38
Hs.512001	GPLD1	glycosylphosphatidy linositol specific phospholipase D1	2.27	0.04	0.38
Hs.75615	APOC2	Apolipoprotein C-II	2.02	0.04	0.37
Hs.515258	GDF15	GDF15 growth differentiation factor 15	0.03	0.04	0.37
Hs. 31439	SPINT2	SPINT2 serine protease inhibitor Kunitz type 2	0.02	0.04	0.37

Hs.159	TNFRSF1A	TNFRSF1A tumor necrosis factor receptor superfamily member 1A	0.05	0.05	0.36

BMI, body mass index.

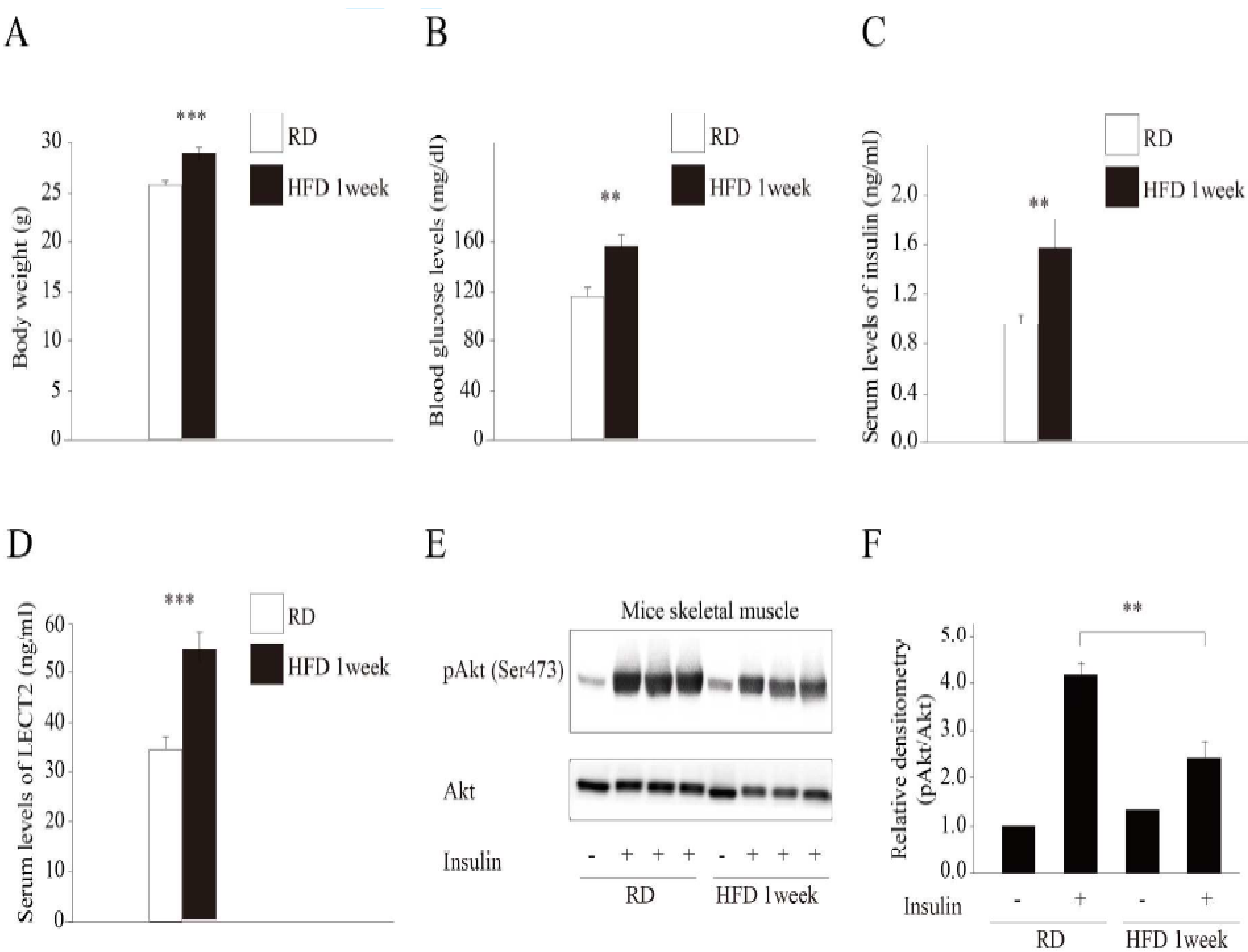
Supplementary Table 2. relative to Fig.1. Clinical characteristics of the human subjects whose blood was sampled.

N	200
Age (years)	55±11
Sex (M/F)	118/82
Body mass index (kg/m^2)	22.9±3.1
Waist circumstance (cm)	81.0±9.0
Fasting plasma glucose (mg/dl)	97±11
HOMA-IR	1.4±0.9
HbA1c (%)	5.7±0.4
Systolic blood pressure (mmHg)	124±18
Selenoprotein P (μg/ml)	6.0±0.8

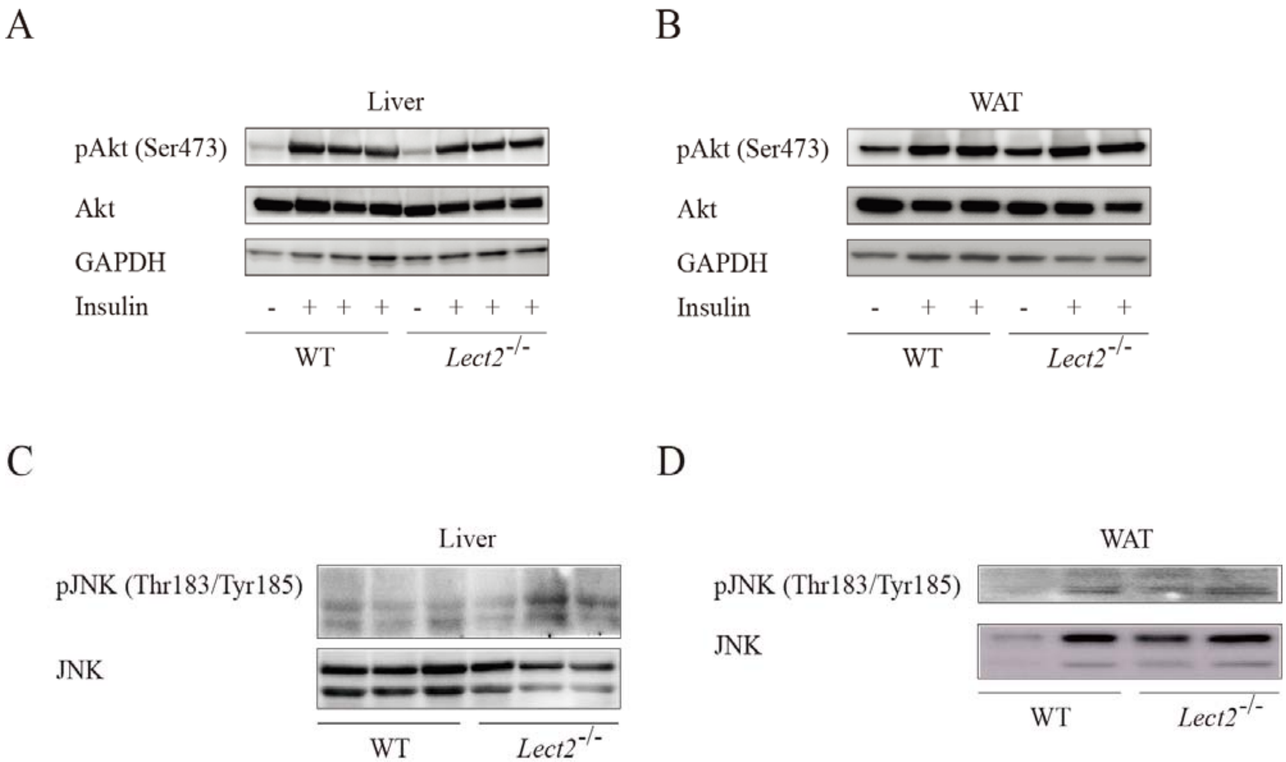
HOMA-IR, homeostasis model assessment for insulin resistance; HbA$_{1c}$, hemoglobin A$_{1c}$. Blood was sampled following overnight fasting.

SUPPLEMENTARY DATA

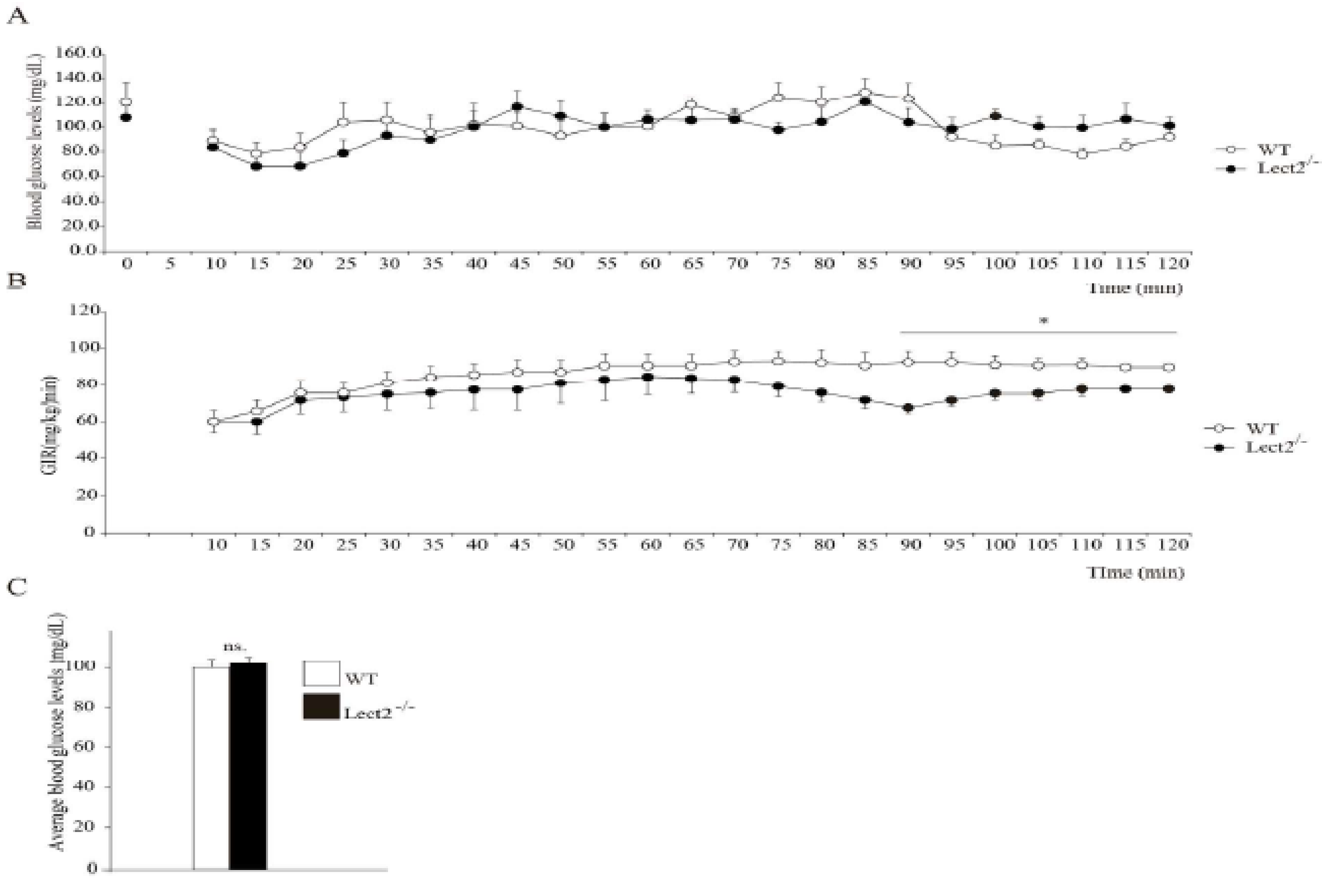
Supplementary Figure 1. Insulin resistance in mice fed a 60% high fat diet for 1 week.(A) Body weight of C57BL6J mice fed a high fat diet (HFD; *n* = 8) or regular diet (RD; *n* = 8). Five-week-old male mice were fed a HFD for 1 week. (B) Blood glucose levels of C57BL6J mice fed a HFD or a RD for 1 week (*n* = 8). (C) Serum levels of insulin in C57BL6J mice fed a HFD or a RD for 1 week (*n* = 8). (D) Serum levels of LECT2 in C57BL6J mice fed HFD (*n* = 8) or RD (*n* = 8). (E) and (F) Western blot analysis and quantification of the bands of phosphorylated Akt in skeletal muscle of C57BL6J mice fed a HFD or a RD after a 12-h fast (*n* = 3). Mice were injected with insulin intraperitoneally (10 units/kg body weight). At 15 min after insulin administration, mice were anesthetized and hind-limb muscle samples were removed for analysis. Data in (A-D) and (F) represent the means ± SEM. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.



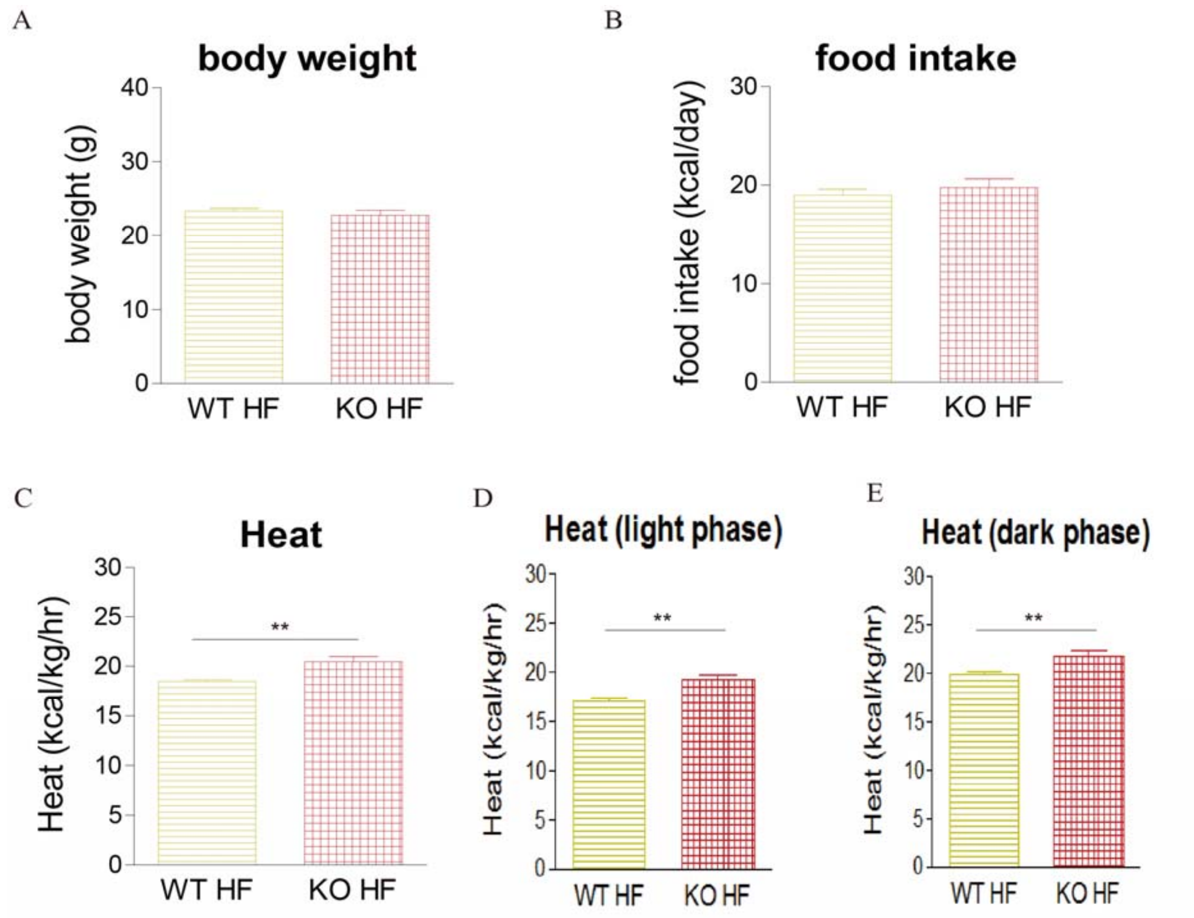
Supplementary Figure 2. Insulin signalling and JNK phosphorylation in the liver and adipose tissue of *Lect2*-deficinet and wild-type mice. (A) and (B) Western blot analysis of phosphorylated Akt in liver and white adipose tissue of *Lect2*-deficient and wild-type mice. Mice were stimulated with insulin intraperitoneally (10 units/kg body weight). At 15 min after insulin administration, mice were sacrificed and liver and epididymal white adipose tissue samples were removed for analysis. (C) and (D) Western blot analysis of phosphorylated JNK in liver and white adipose tissue of *Lect2*-deficient and wild-type mice fed a normal chow.



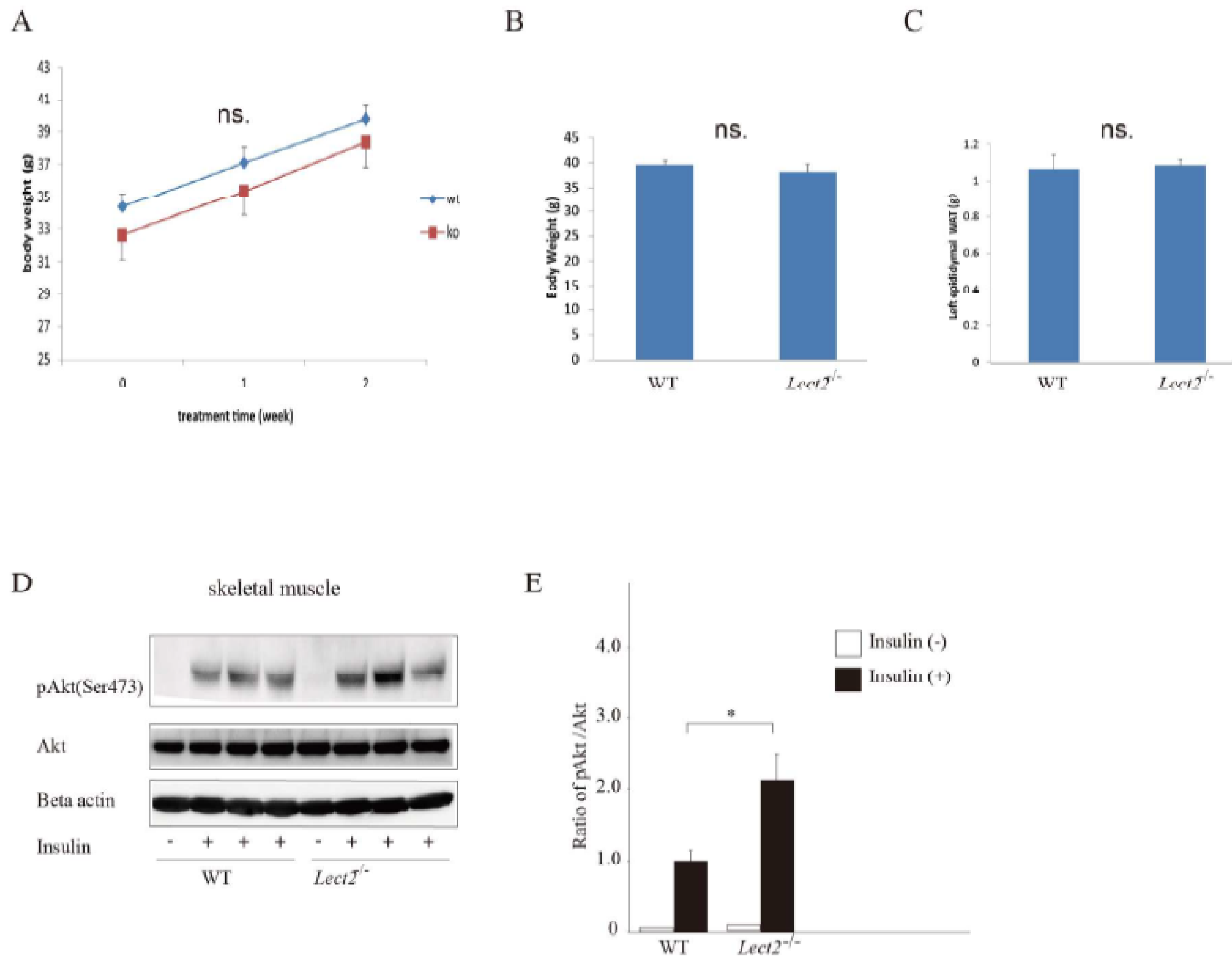
Supplementary Figure 3. Glucose levels during hyperinsulinemic-euglycemic clamp. (A) Time course of blood glucose levels during hyperinsulinemic-euglycemic clamp in wild-type and *Lect2*-deficient mice (n = 6-7). (B) Time course of glucose infusion rate during hyperinsulinemic-euglycemic clamp in wild-type and *Lect2*-deficient mice (n = 6-7). (C) Average of blood glucose levels at the last 30 min (90min, 105min and 120min) in wild-type and *Lect2*-deficient mice (n = 6-7). Data in (A)- (C) represent the means ± SEM. *$P < 0.05$ *versus* the wild-type mice.



Supplementary Figure 4. Food intake and heat production in wild-type and *Lect2*-deficient mice fed a HFD for a week **(A)** Body weight of *Lect2*-deficient and wild-type mice fed a HFD for a week (*n* = 7-8). (**B**) Food intake of of *Lect2*-deficient and wild-type mice fed a HFD for a week (*n* = 7-8). (**C**) Heat production of of *Lect2*-deficient and wild-type mice fed a HFD for a week (*n* = 7-8). (**D**) Heat production in light phase of *Lect2*-deficient and wild-type mice fed a HFD for a week (*n* = 7-8). (**E**) Heat production in light phase of *Lect2*-deficient and wild-type mice fed a HFD for a week (*n* = 7-8). Data represent the means ± SEM. ***P* < 0.01.



Supplementary Figure 5. *Lect2* deletion increases muscle insulin sensitivity in mice fed a HFD for 2 weeks. (**A**) Changes of bodyweight of 22 weeks-old *Lect2*-deficient and wild-type mice fed a HFD for 2 weeks (n=7). (**B**) The bodyweight of 22 weeks-old *Lect2*-defeicient and wild-type mice before sacrifice. (n=7). (**C**) The weight of left epididymal adipose tissue of *Lect2*-deficient and wild-type mice (n=7). (**D**) Western blot analysis of phosphorylated Akt in skeletal muscle of *Lect2*-deficient and wild-type mice. Mice were stimulated with insulin (administered through vena cava) at doses of 1 units/kg body weight. At 10 min after insulin administration, hind-limb muscles were removed. (**E**) Quantification of phosphorylated Akt in **D** (n=3). **P*<0.05 (student's *t*-test). Data represent the means ± SEM.



Supplementary Figure 6. Markers of ER stress or inflammation in C2C12 myocytes transfected with pLect2 or in the muscles of *Lect2*-deficient mice. (A) *CHOP* mRNA levels in skeletal muscle of *Lect2*-deficient and wild-type mice fed with normal chow (*n* = 8-9). (B) *CHOP* mRNA levels in C2C12 myotubes transfected with control or *Lect2* expression vector (*n* = 6), mRNA was obtained from the cells differentiated into myotubes for 48 h. (C) Western blot analysis of BiP in in skeletal muscle of *Lect2*-deficient and wild-type mice fed with 60% high fat diet for 15 weeks. (D) Western blot analysis of p-eIF2α in C2C12 myotubes transfected with control or *Lect2* expression vector. (E) *Tnf-α* mRNA levels in skeletal muscle of *Lect2*-deficient and wild-type mice fed a regular diet (*n* = 7-8). (F) *Tnf-α* mRNA levels in C2C12 myotubes transfected with control or *Lect2* expression vector (*n* = 6). mRNA was obtained from the cells differentiated into myotubes for 2 days. (G) Western blot analysis of inflammation-associated proteins in C2C12 myotubes transfected with control or *Lect2* expression vector. Data in (A-B) and (E-F) represent the means ± SEM.*CHOP*, CCAAT/-enhancer-binding protein homologous protein; BiP, Binding immunoglobulin protein; eIF2, Eukaryotic Initiation Factor 2; Tnfa, Tumor necrosis factor α; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; IKK, IκB kinase; IκBα, inhibitor of kappa B.

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