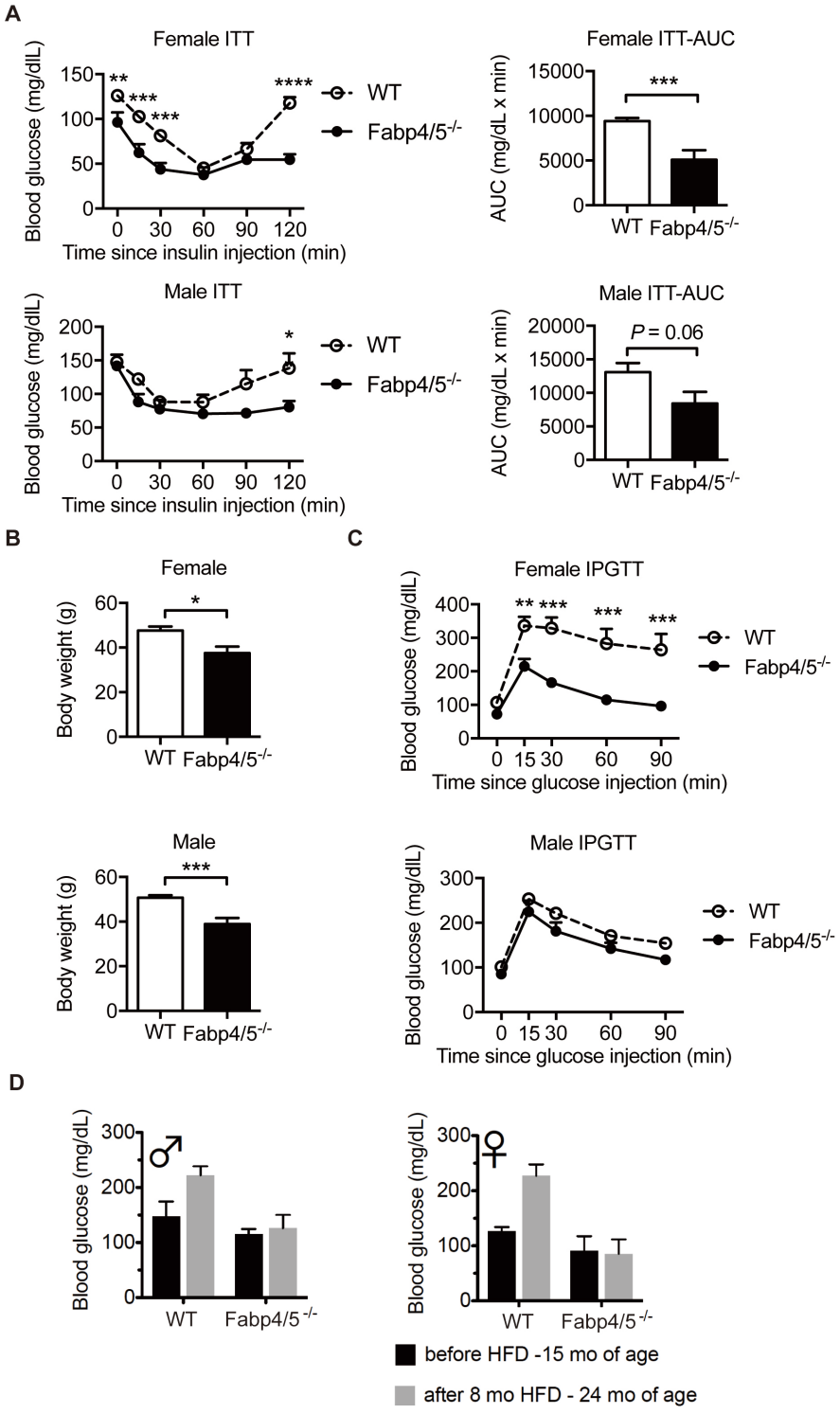
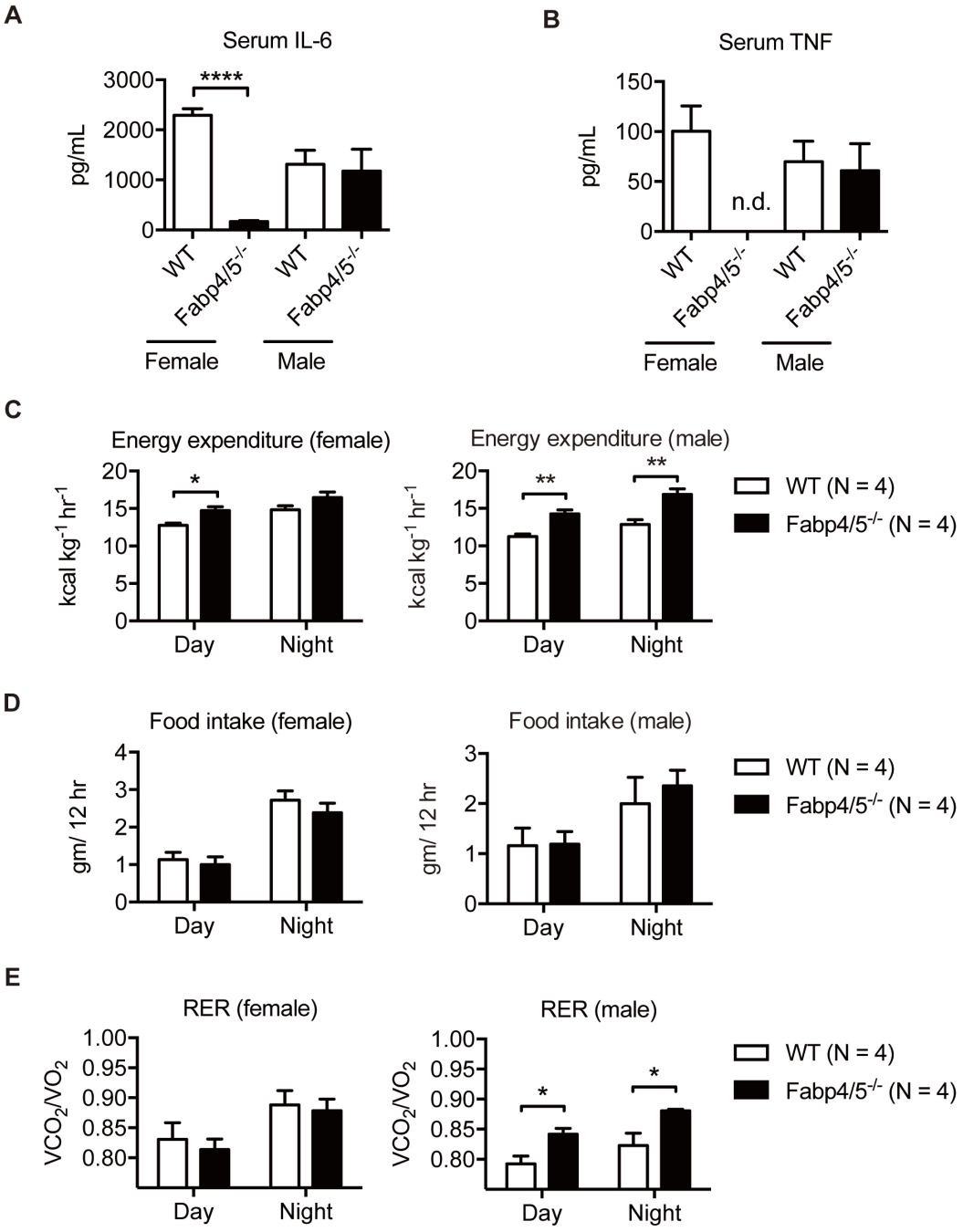
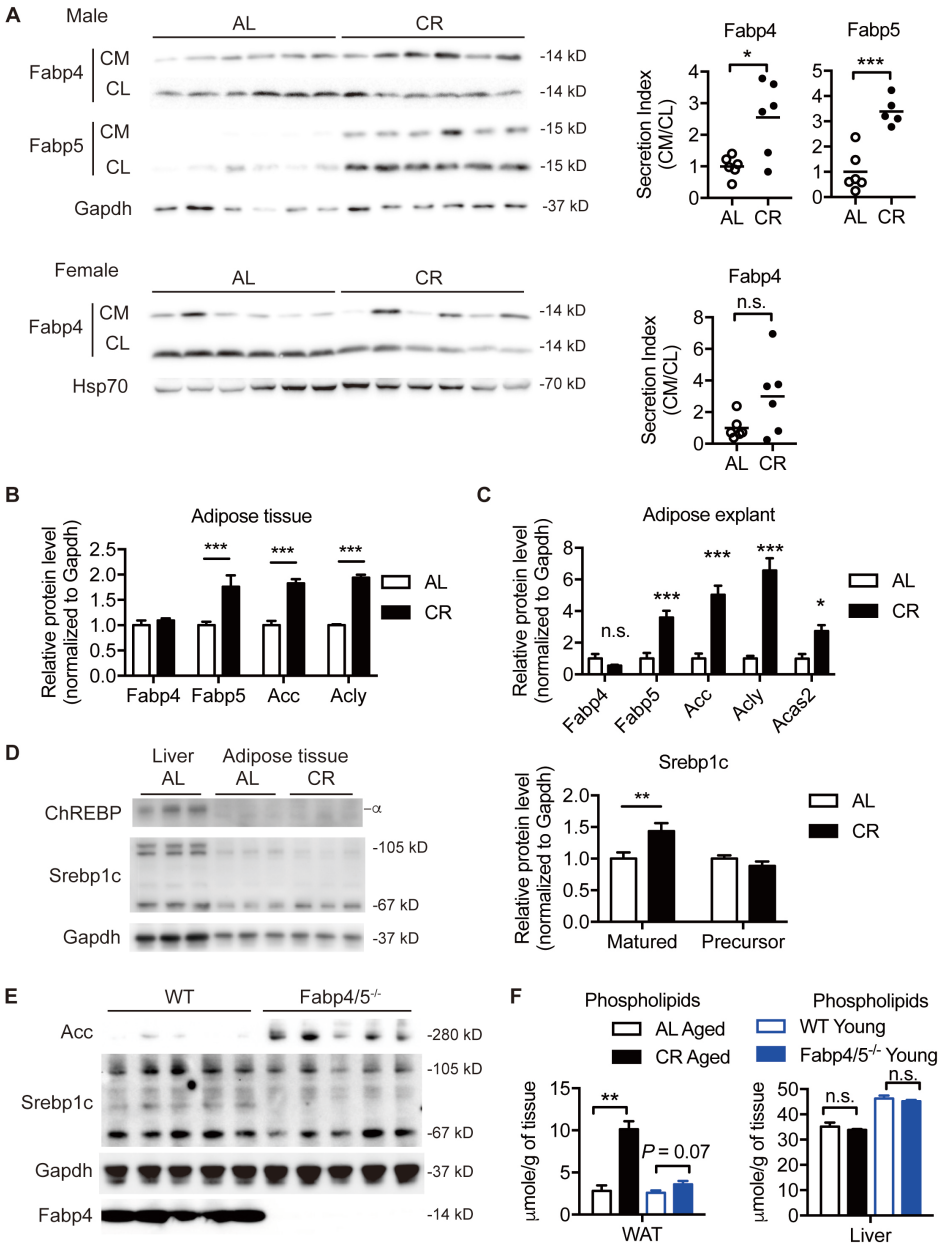


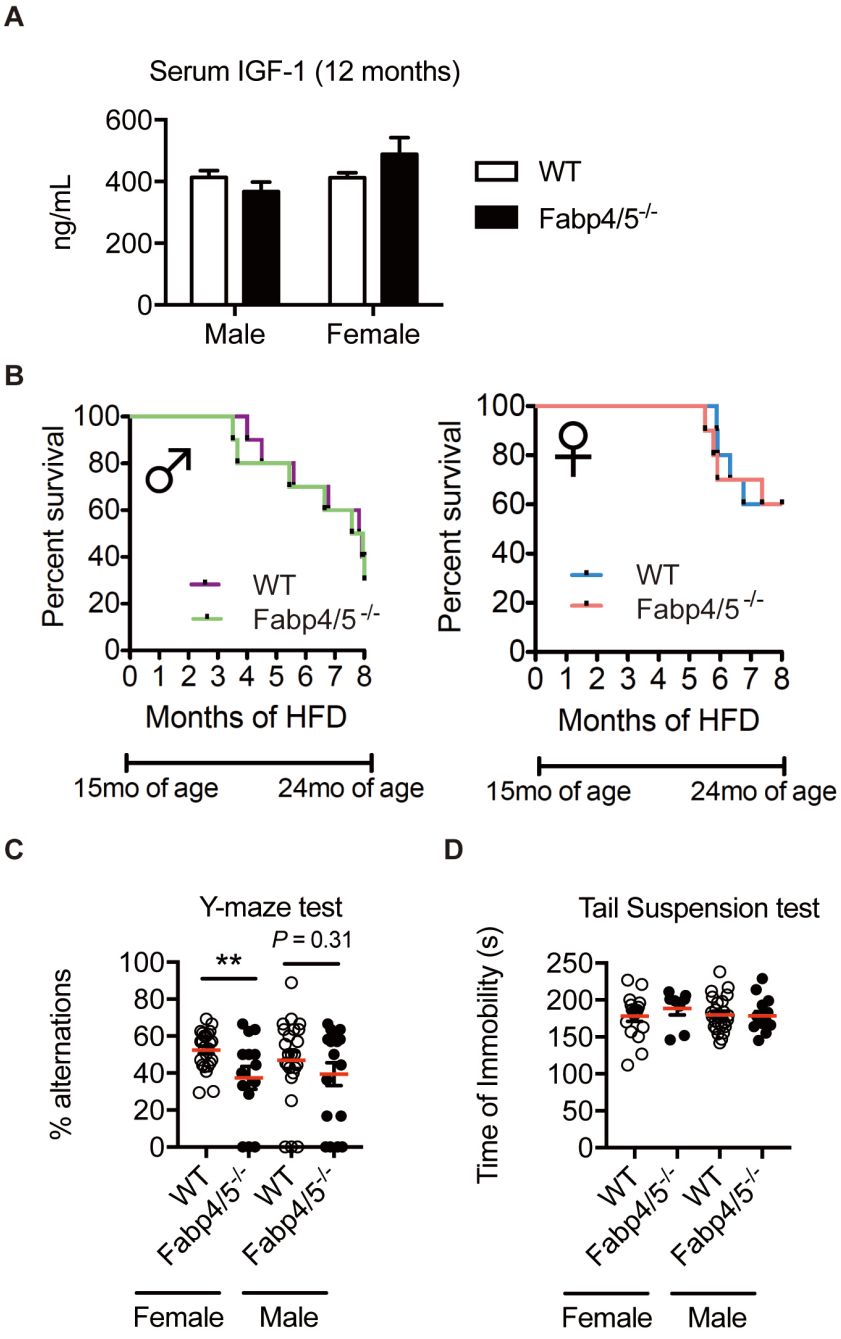
Supplementary Figure 1 related to Figure 1. Middle-aged (11~12-month old) mice of both sexes were investigated for metabolic phenotypes (N = 7-8 female, N = 6 male). A. Insulin tolerance test. Open circle, WT; closed circle, Fabp4/5$^{-/-}$. Areas under the curve (AUC) were plotted on the right. Late-middle-aged (15-month old) mice of both sexes (N = 8 female, N = 10 male) were investigated for metabolic phenotypes (B-D). B. Body weight. C. Intraperitoneal glucose tolerance test. D. Levels of blood glucose in male and female after 6-hour daytime food withdrawal. At 15-16 months of age, mice were placed on high-fat diet (HFD) for 8 months.



Supplementary Figure 2 related to Figure 2. A-B. Circulating levels of proinflammatory cytokines IL-6 (A) and TNF (B) in middle-aged WT and Fabp4/5$^{-/-}$ mice (N = 6). C-E. Energy balance measurements by the Columbus Instruments Comprehensive Lab Animal Monitoring System (CLAMS) in middle-aged (12-month old) mice (N = 4 per sex per genotype). C. Energy expenditure. D. Food intake. E. Respiratory exchange ratio (RER). Data were presented as mean ± SEM, and analyzed by unpaired two-way Student's t-Test, ****$P < 0.0001$, n.d., not detected.



Supplementary Figure 3 related to Figure 3. A. FABP secretion assay. Adipose tissue explants were dissected from short-term CR mice and ad libitum control mice (N = 6, upper panel: male mice; lower panel: female mice). CM, conditioned medium. CL, cell lysate. 12.5 µg of proteins isolated from tissue homogenates were loaded per lane. The load of CM samples was adjusted as conditioned from the load of CL. Secretion capacity is measured by the secretion index, which is the ratio of the density of CM sample over that of CL sample. B. Density analysis of Western blot graphs in Figure 3B (N = 3). C. Density analysis of lipogenic enzymes and FABP in adipose explants described in Panel A Upper Panel. D. Western blotting analysis of lipogenic transcription factors in subcutaneous adipose tissue from 4-week CR mice and ad libitum control mice (N = 3). Liver samples from 4-week AL mice served as positive control for Chrebpα and Srebp1c (precursor and cleaved forms). E. Western blotting analysis of epididymal adipose tissue from 3-4 month-old Fabp4/5$^{-/-}$ mice and WT mice (N = 5). F. Levels of phospholipids from epididymal white adipose tissue (WAT) and liver samples from calorie restricted (CR Aged) mice and ad libitum (AL Aged) control mice were analyzed by lipidomics (N = 6). Data were presented as mean ± SEM, and analyzed by multiple comparison t-Test adjusted by Holm-Sidak method (Panels B, D), and unpaired two-way Student's t-Test (Panels A, C, F), n.s., not significant, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.



Supplementary Figure 4 related to Figure 4. A. Serum levels of IGF-1 in middle-aged (12-month-old) WT (N = 4 female / 5 male) and Fabp4/5$^{-/-}$ (N = 4 female / 5 male). B. Kaplan-Meier survival curves of HFD-fed Fabp4/5$^{-/-}$ and WT mice (N = 8-10) for both sexes. Each data point represents one animal. At 15-16 months of age, mice were placed on high-fat diet (HFD) for 8 months. Survival after initiation of HFD WT male = 40%; Fabp4/5$^{-/-}$ male = 30%; WT female = 60%; Fabp4/5$^{-/-}$ female = 60%. C-D. Healthspan studies of chow-fed aged (30-month-old) mice: (C) Cognitive functions: Y-maze test (WT, N = 24 male and 24 female; Fabp4/5$^{-/-}$, N = 18 male and 14 female). (D) Anti-depressant function: Tail suspension test (WT, N = 24 male and 17 female; Fabp4/5$^{-/-}$, N = 15 male and 8 female). Data were presented as mean ± SEM, and analyzed by unpaired Student's t-Test, *$P < 0.05$, **$P < 0.01$.

Supplementary Table 1. Gait analysis of aged (30-month-old) female mice, Related to Figure 4

	WT (N = 24)	Fabp4/5-/- (N = 14)	*P* value
Belt Speed (cm/s)	11.8 ± 0.1	11.1 ± 0.6	0.12
Stride Length (mm) (FF AVG)	54.20 ± 0.60	54.19 ± 1.80	0.21
Stride Length (mm) (RF AVG)	54.91 ± 0.51	53.22 ± 1.72	0.26
Rear Stance Width (mm)	28.02 ± 0.26	27.32 ± 0.58	0.22
Homolateral Coupling (RR)	0.44 ± 0.01	0.42 ± 0.02	0.23
Homologous Coupling (RR)	0.49 ± 0.01	0.51 ± 0.01	0.10
Diagonal Coupling (RR)	-0.03 ± 0.01	-0.07 ± 0.02	0.05
Print Angle (deg) (RR)	25.06 ± 1.58	23.49 ± 2.32	0.57

Data presented are mean ± SEM.

Supplementary Table 2. Gait analysis of aged (30-month-old) male mice, Related to Figure 4

	WT (N = 25)	Fabp4/5-/- (N = 19)	*P* value
Belt Speed (cm/s)	12.0 ± 0.1	10.6 ± 0.6 *	0.01
Stride Length (mm) (FF AVG)	53.80 ± 0.74	54.55 ± 1.72	0.66
Stride Length (mm) (RF AVG)	54.74 ± 0.75	55.86 ± 1.68	0.51
Rear Stance Width (mm)	26.82 ± 0.30	26.39 ± 0.48	0.43
Homolateral Coupling (RR)	0.41 ± 0.01	0.41 ± 0.02	0.94
Homologous Coupling (RR)	0.50 ± 0.01	0.49 ± 0.02	0.53
Diagonal Coupling (RR)	-0.07 ± 0.01	-0.07 ± 0.02	0.98
Print Angle (deg) (RR)	26.68 ± 1.79	27.83 ± 2.20	0.76

Data presented are mean ± SEM.

Supplementary Table 3. Primer Sequences, Related to Experimental Procedures

Name	**DNA Sequence**
36B4-Forward (F)	CCGATCTGCAGACACACACT
36B4-Reverse (R)	ACCCTGAAGTGCTCGACATC
Acas2-F	GCTGAACTGACACACCTGGA
Acas2-R	AACTTGGCGACAAAGTTGCT
Acly-F	AATGGCCGTCATGTGAGTTT
Acly-R	GTGGCCCCAACTATCAAGAG
Acc-F	GAAGCCACAGTGAAATCTCG
Acc-R	GATGGTTTGGCCTTTCACAT
Fasn-F	GTTGGCCCAGAACTCCTGTA
Fasn-R	GTCGTCTGCCTCCAGAGC
Elovl6-F	AACTTGGCTCGCTTGTTCAT
Elovl6-R	CCAATGGATGCAGGAAAACT
Scd1-F	CAGCCGAGCCTTGTAAGTTC
Scd1-R	GCTCTACACCTGCCTCTTCG