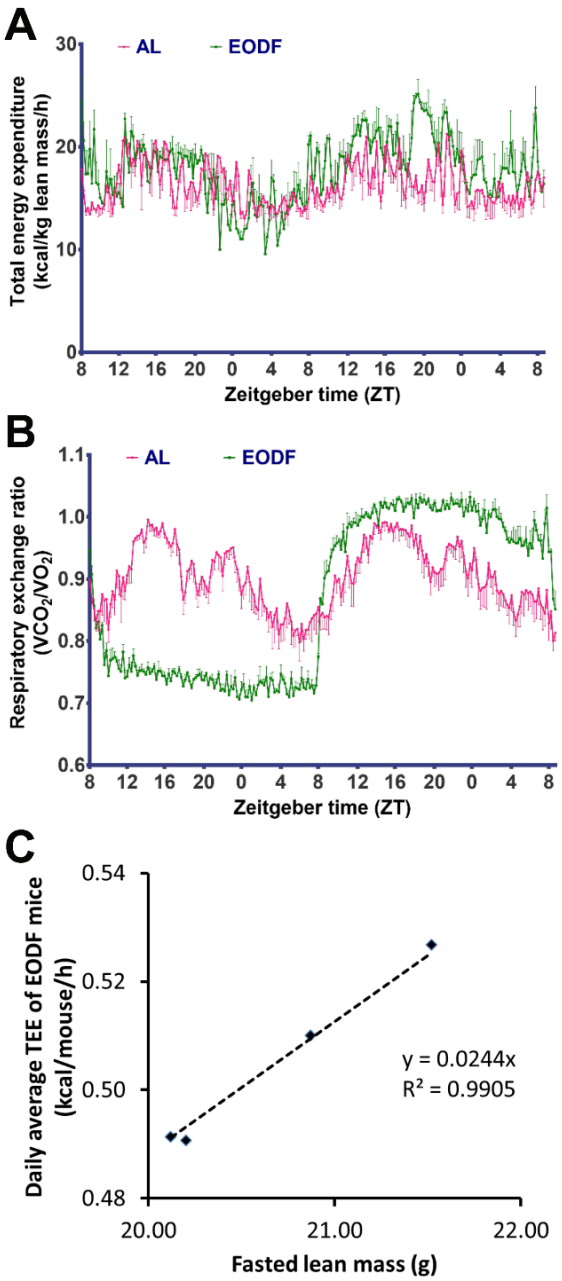
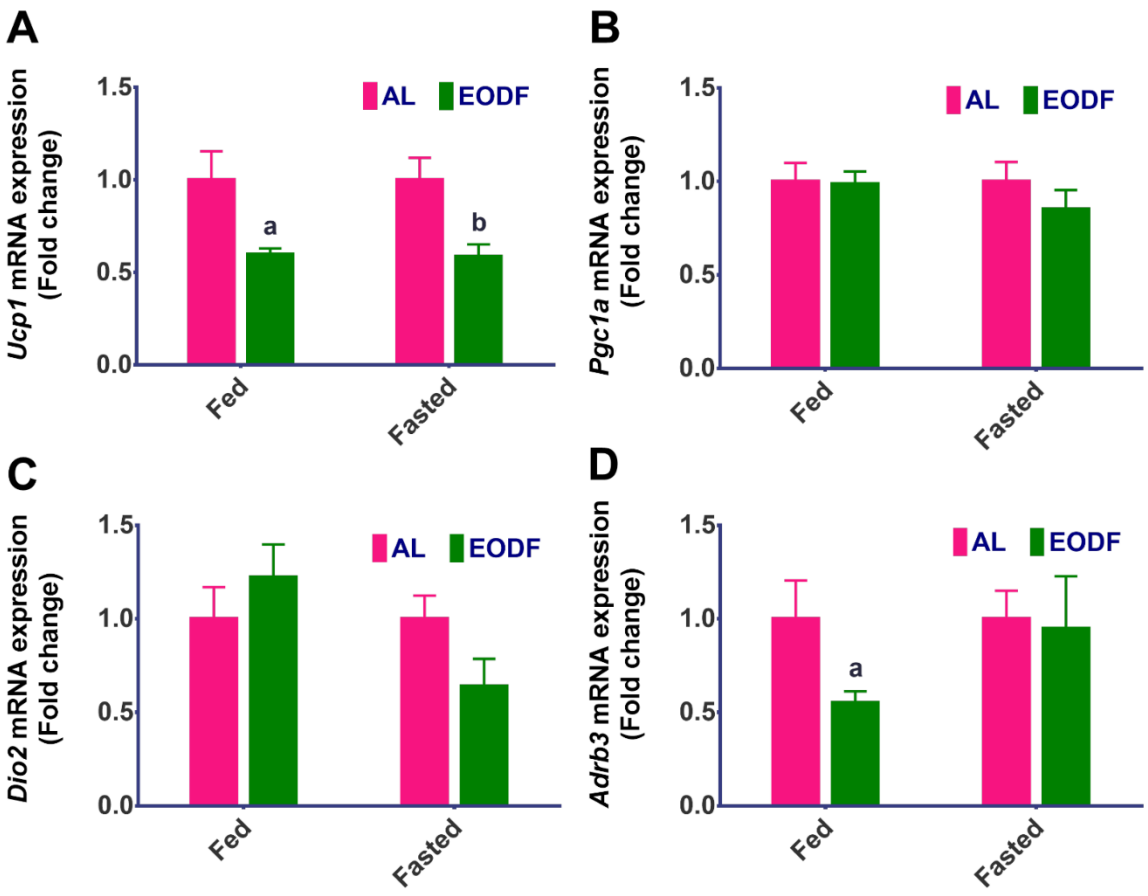
Supplemental Document



Supplemental Figure 1. Total energy expenditure and respiratory exchange ratio in a cycle of EODF. Related to Figure 1.

(A-B) Total energy expenditure (A) and respiratory exchange ratio (B) from two continued days of EODF experiment. On day first day (Fasted), EODF mice were on fasting state while AL mice were on feeding state, and on second day (Fed), both groups of mice were on feeding state. n=4 mice/group.

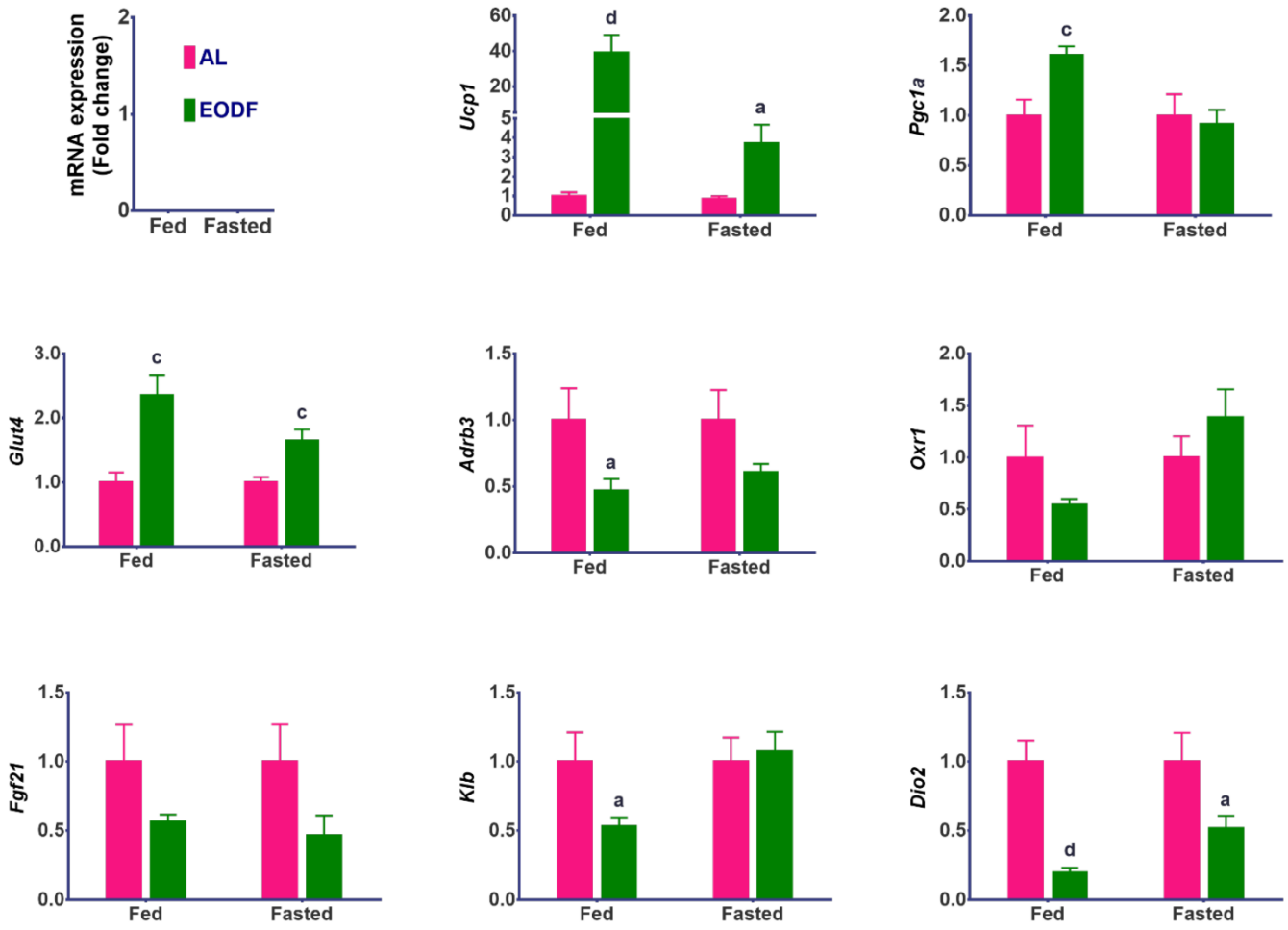
(C) Linear correlation of daily average total energy expenditure (TEE) and lean mass in mice synchronized with food intake. Since the TEE of mice is linearly correlated with fasted lean mass (R^2=0.9905) when synchronized with food intake, the TEE data were normalized to the lean mass.



Supplemental Figure 2. Effect of EODF on thermogenic gene expression in interscapular BAT. Related to Figure 1.

(A-D) qPCR analysis of *Ucp1* (A), *Pgc1a* (B), *Dio2* (C), and *Adrb3* (D) mRNA in interscapular brown fat after normalized against AL.

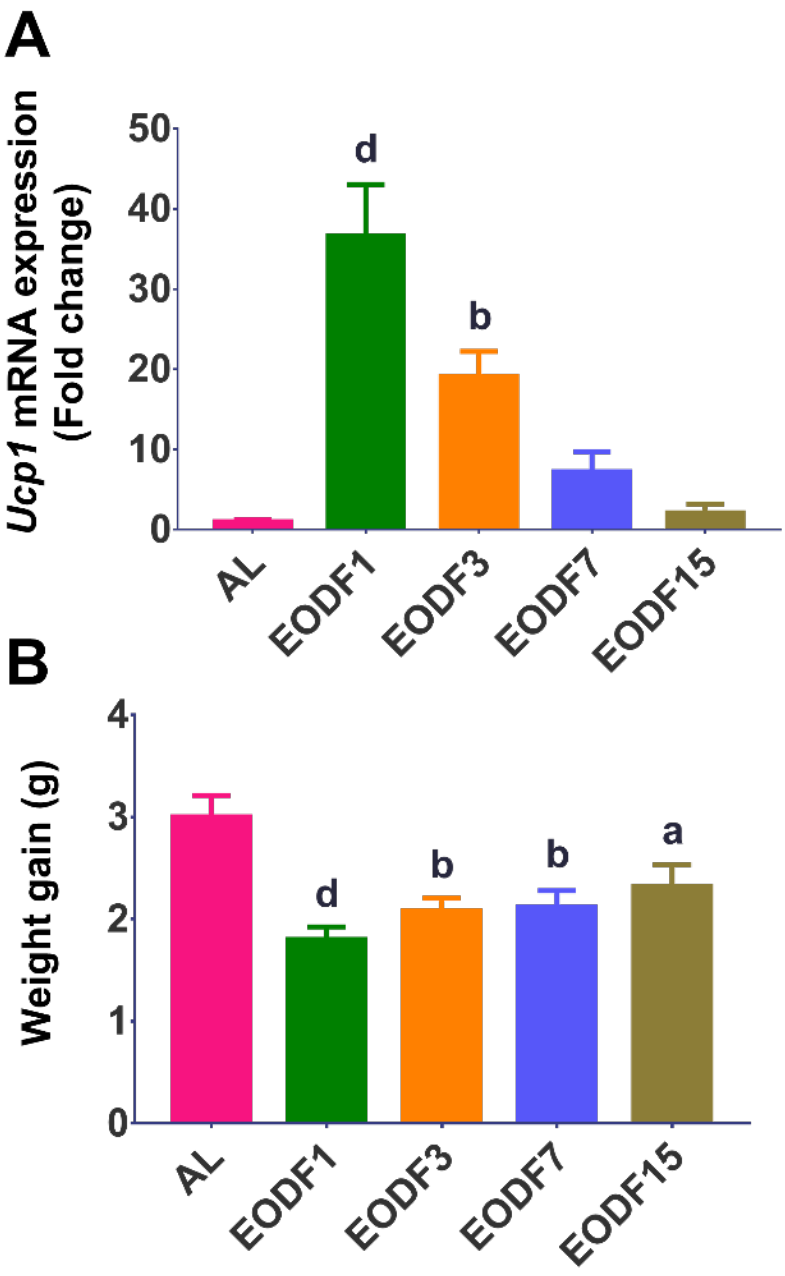
Data are presented as mean ± SEM (n = 6–8 in each group). Different lowercase letters indicate different statistical significance by two-tailed unpaired *t*-test, a, $p < 0.05$ and b, $p < 0.01$ vs AL.



Supplemental Figure 3. **Effect of EODF on thermogenic gene expression in inguinal WAT. Related to Figure 1.**

Differentiated mRNA levels of beige fat thermogenic genes in subcutaneous inguinal WAT from EODF mice (n=8) and AL mice (n=7) under fed and fasted states.

Data are presented as mean ± SEM. Different lowercase letters indicate different statistical significance by two-tailed unpaired *t*-test, a, $p < 0.05$; c, $p < 0.005$; and d, $p < 0.001$ versus AL.

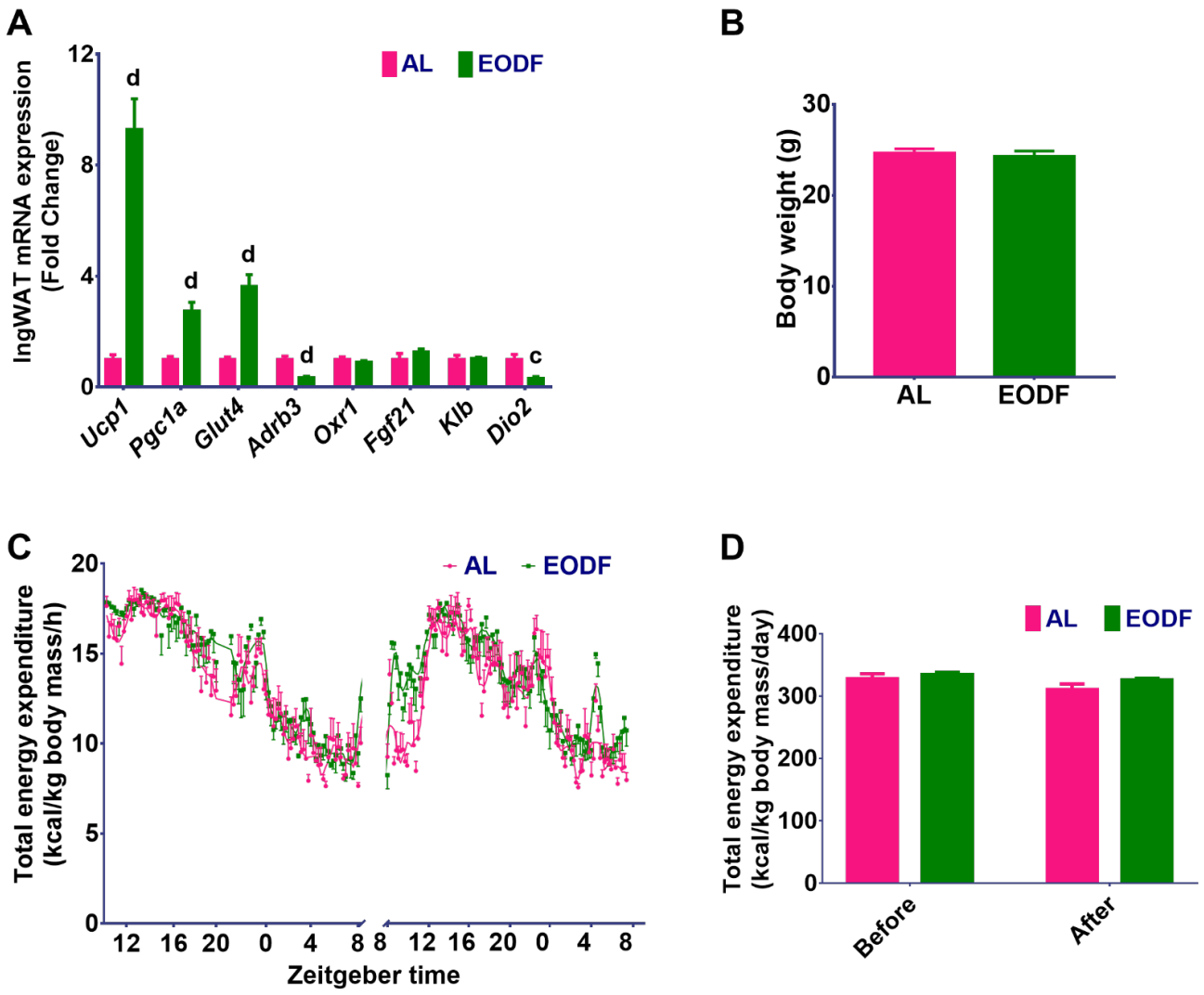


Supplemental Figure 4. Time course of weight gain and *Ucp1* expression in inguinal WAT of EODF mice after returning to the AL feeding. Related to Figure 1.

(A) *Ucp1* mRNA expression (fold change versus AL) of inguinal WAT in EODF mice after returning to the AL feeding for 1 (EODF1), 3 (EODF3), 7 (EODF7) and 15 (EODF15) days. n= 6 mice/group.

(B) Body weight gain. n= 6 mice/group.

Data are presented as mean ± SEM. Different lowercase letters indicate statistical significance by one-way ANOVA with Bonferroni posttest, a, $p < 0.05$; b, $p < 0.01$ and d, $p < 0.001$ versus AL.



Supplemental Figure 5. Effect of short term EODF on inguinal WAT beiging, body weight and energy expenditure. Related to Figure 1.

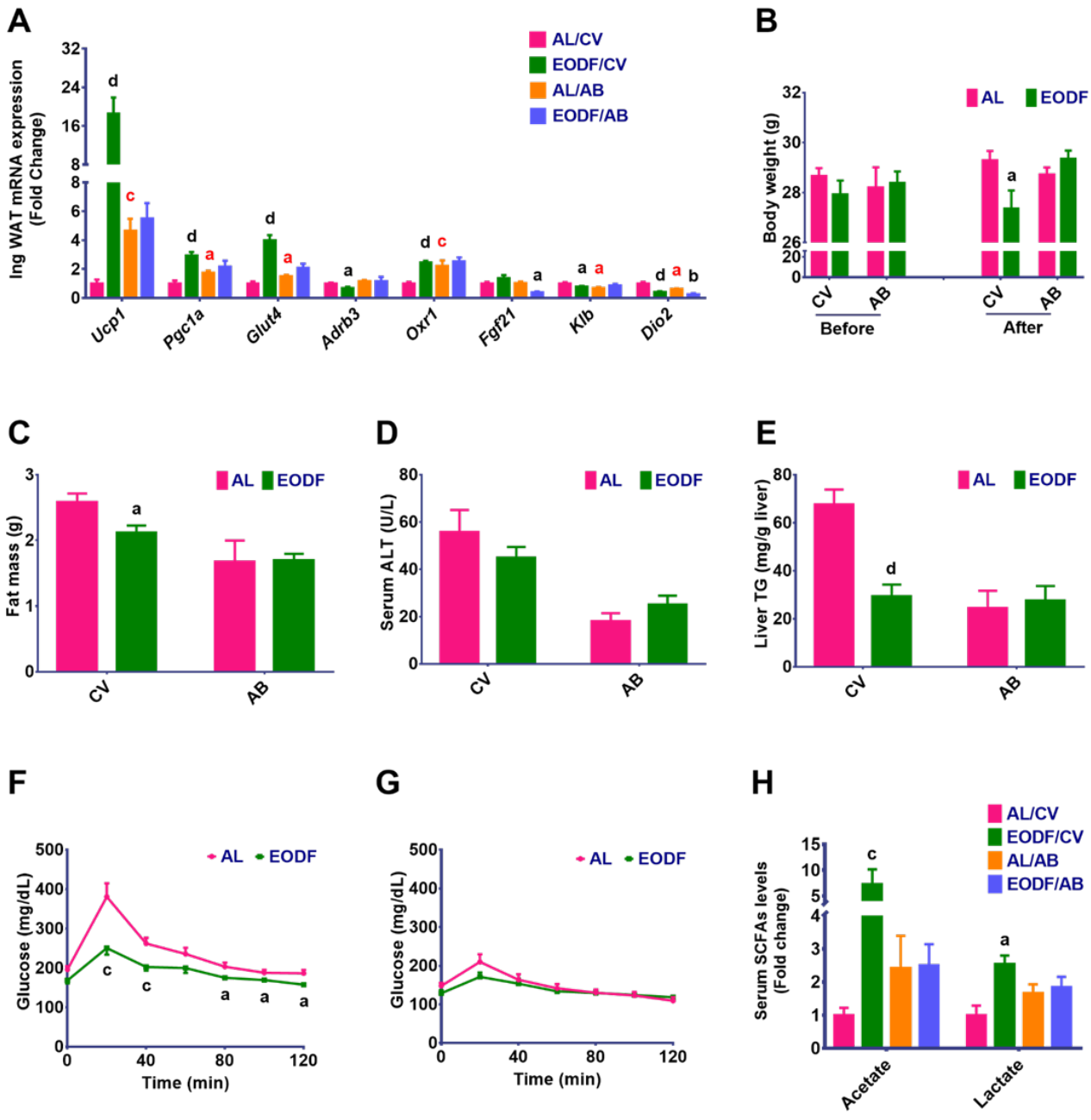
(A) Average mRNA expression of thermogenic genes in inguinal WAT of EODF (3 cycles) and AL mice in the feeding state after normalization against AL. n= 10 mice/group.

(B) Body weight of EODF (3 cycles) and AL mice. n= 10 mice/group.

(C) Circadian total energy expenditure of EODF and AL mice in the feeding state. Indirect calorimetry was performed on the day before and after 3 cycles of EODF treatment. n= 6 mice/group.

(D) Daily total energy expenditure of EODF and AL mice in feeding state on the day before and after 3 cycles of EODF treatment. n= 6 mice/group.

Data are presented as mean ± SEM. Different lowercase letters indicate different statistical significance by two-tailed unpaired *t*-test, c, $p < 0.005$; and d, $p < 0.001$ versus AL.



Supplemental Figure 6. Microbiota depletion abolishes the effect of EODF on WAT beiging and metabolic improvement. Related to Figure 3.

(A) Effect of EODF on mRNA expression of thermogenic genes in inguinal WAT of mice drunk with control vehicle (CV) water or with water added antibiotics cocktail (AB) for 4 weeks. n=6-8 mice/group.

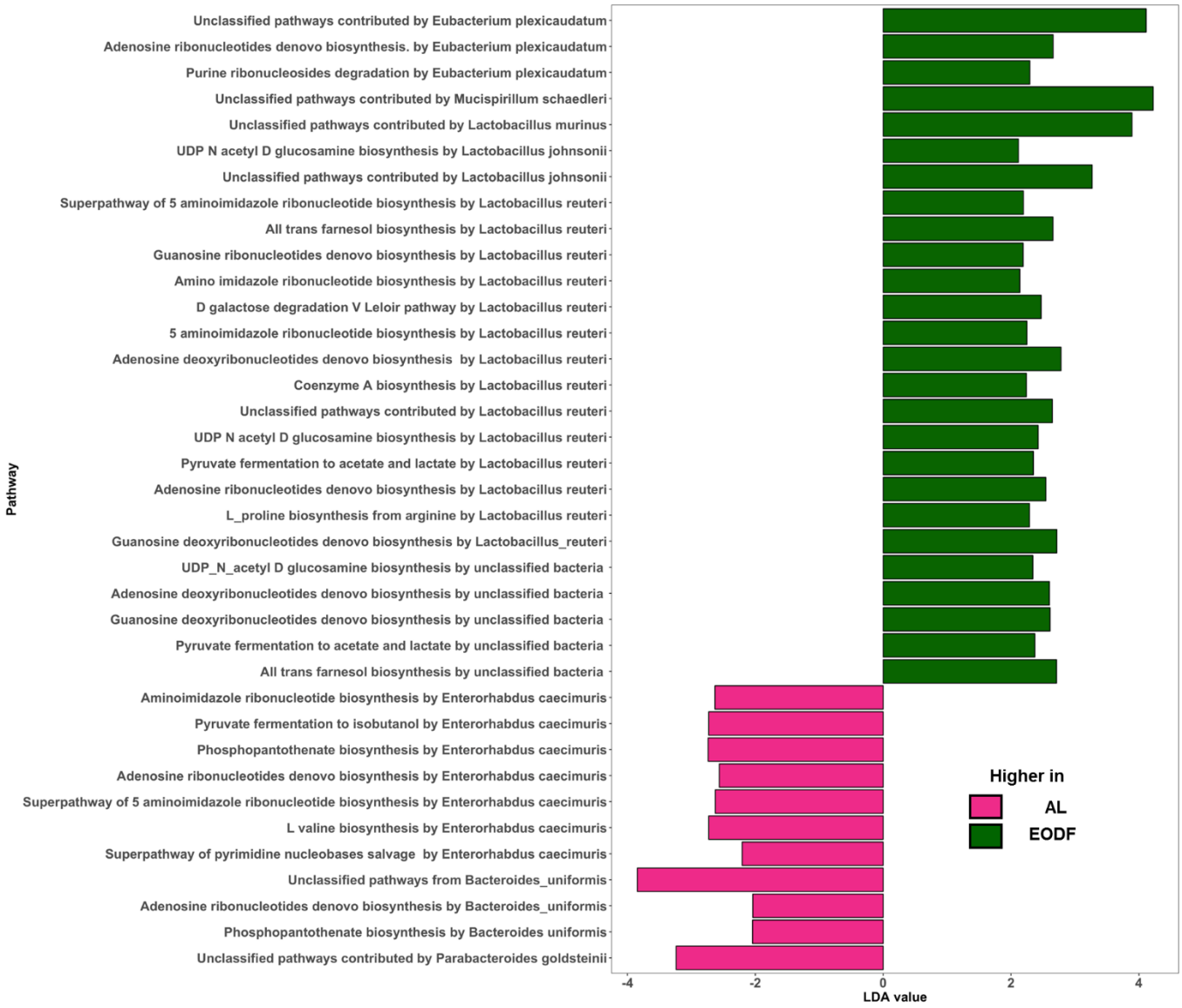
(B) Average body weight of mice before and after EODF treatment. Before EODF treatment, all mice were drunk with CV or AB water for 4 weeks. n=6-8 mice/group.

(C-E) Fat mass (C), serum ALT (D) and liver triglycerides (E) of mice after EODF treatment. Before EODF, all mice were drunk with CV or AB water for 4 weeks. n=6-8 mice/group.

(F-G) Glucose tolerance test in EODF and AL mice drunk CV (F) or AB (G) water. n=6 mice/group.

(H) Serum acetate and lactate levels of EODF and AL mice in the feeding state after

normalization against AL. n= 6 mice/group.
Data are presented as mean ± SEM. Different lowercase letters indicate statistical significance by two-way ANOVA with Sidak multiple comparisons (A, H) or two-tailed unpaired *t*-test (B-G), a, $p < 0.05$; b, $p < 0.01$; c, $p < 0.005$; and d, $p < 0.001$. Black letters show the effects of EODF (EODF versus AL drunk with the same water), red letters the effects of microbiota depletion (AB versus CV within the same feeding regimen). SCFAs, short chain fatty acids.



Supplemental Figure 7. LDA score for the pathways associated with those bacteria in AL and EODF mice. Related to Figure 4.

SUPPLEMENTAL TABLE

Supplemental Table 1. List of primer sequences used in qPCR. Related to the STAR Methods section.

Gene symbol	Gene name	Forward sequence (5' to 3')	Reverse sequence (5' to 3')
18S rRNA	18S ribosomal RNA	ATTGGAGCTGGAATTACCGC	CGGCTACCACATCCAAGGAA
Adrb3	adrenergic receptor, beta 3	GGCCCTCTCTAGTTCCCAG	TAGCCATCAAACCTGTTGAGC
Dio2	Type II iodothyronine deiodinase	AATTATGCCTCGGAGAAGACCG	GGCAGTTGCCTAGTGAAAGGT
Fgf21	Fibroblast growth factor 21	CTGCTGGGGGTCTACCAAG	CTGCGCCTACCACTGTTCC
Glut4	Solute carrier family 2 (facilitated glucose transporter), member 4	GTGACTGGAACACTGGTCCTA	CCAGCCACGTTGCATTGTAG
Klb	Klotho beta	TGTTCTGCTGCGAGCTGTTAC	CCGGACTCACGTACTGTTTTT
Oxr1	Oxidation resistance 1	GATACCACACCCAATGAACTTGT	GCGACAGAGGGCTTACAGG
Pgc1α	Peroxisome proliferator-activated receptor gamma coactivator 1-alpha	TATGGAGTGACATAGAGTGTGCT	CCACTTCAATCCACCCAGAAAG
Mct1	monocarboxylate transporter 1	ATCGCAGGTGGCATTTTAAG	GTCACGCATACTCCGGGC
Ucp1	Uncoupling protein 1	AGGCTTCCAGTACCATTAGGT	CTGAGTGAGGCAAAGCTGATTT