Supplementary Materials for

An adipo-biliary-uridine axis that regulates energy homeostasis

Yingfeng Deng, Zhao V. Wang, Ruth Gordillo, Yu An, Chen Zhang, Qiren Liang, Jun Yoshino, Kelly M. Cautivo, Jef De Brabander, Joel K. Elmquist, Jay D. Horton, Joseph A. Hill, Samuel Klein, Philipp E. Scherer*

*Corresponding author. Email: philipp.scherer@utsouthwestern.edu

Published 17 March 2017, *Science* **355**, eaaf5375 (2017)
DOI: 10.1126/science.aaf5375

This PDF file includes:

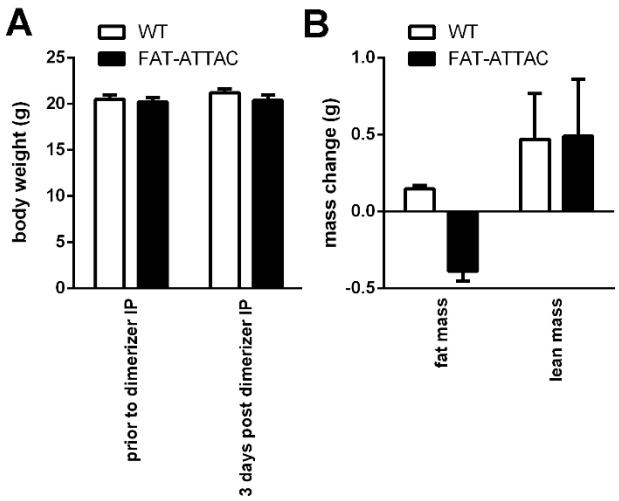

Fig. S1. FAT-ATTAC mice body weight, fat mass and lean mass.

(A-B) Prior to and three days after dimerizer injection, male WT and FAT-ATTAC mice were measured for body weight, fat mass and lean mass using NMR. The change in fat mass and lean mass was calculated for each mouse (n = 6 per group). Values are means ± SEM.

Fig. S2. The uridine *de novo* synthesis pathway in fat depots.

(**A-C**) Fasting-induced (24 hours) transcriptional changes of the two additional enzymes for pyrimidine biosynthesis in epididymal fat (eWAT), subcutaneous fat (sWAT) and brown fat (BAT) from male WT mice (n = 5 per group). Values are means ± SEM.

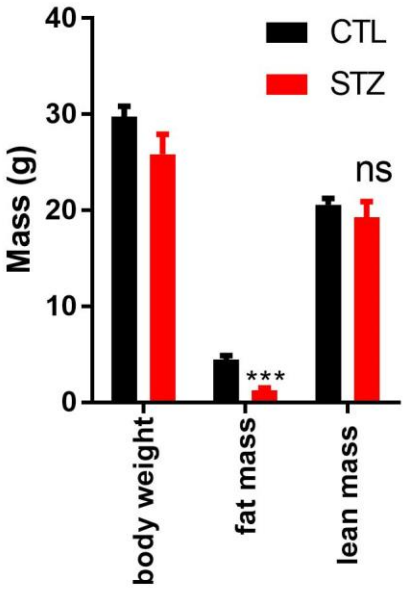

Fig. S3. STZ reduces fat mass, but not lean mass in C57 mice

Male WT mice were measured for body weight, fat mass and lean mass using NMR 7 weeks after STZ treatment (n = 6 per group). Values are means ± SEM. Data were analyzed with two-tail Student's *t* test. ***, $p < 0.001$.

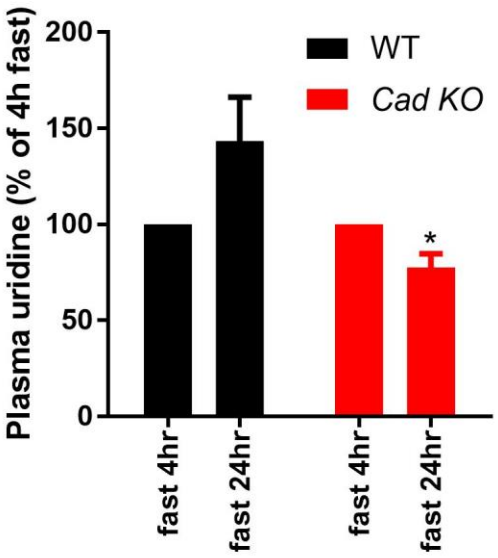

Fig. S4. Plasma uridine levels are not increased in adipocyte specific Cad knockout mice after 24 hours of fasting.

Relative plasma uridine levels in male WT and adipocyte specific Cad KO mice (9~12 weeks old) were determined in a fasting/refeeding study (n = 4 per group). Values are means ± SEM. Data were analyzed with two-tail Student's *t* test. *, $p < 0.05$. To obtain an adipocyte-specific Cad knockout mouse, we generated a Cad floxed ($Cad^{f/f}$) mouse using an ES clone from KOMP (UC Davis). We bred mice to obtain the inducible adipocyte-specific Cad knockout mice of the genotype: adiponectin promoter-rtTA, TRE-Cre, $Cad^{f/f}$. We induced Cad deficiency with doxycycline (Dox)-containing food.

Table S1. Subject characteristics (all subjects were female)

Age (years)	46.7 ± 7.4
Body mass index (kg/m^2)	28.3 ± 1.6
Fat-free mass (kg)	49.3 ± 6.4
Total body fat (%)	41.1 ± 4.9
Visceral adipose tissue volume (cm3)	670 ± 324
Intrahepatic triglyceride content (%)	3.37 ± 3.11
Glucose (mg/dl)	90.8 ± 5.6
Insulin (mU/l)	7.2 ± 3.0
HOMA-IR	1.74 ± 0.87
Triglyceride (mg/dl)	91 ± 37
HDL-cholesterol (mg/dl)	57 ± 5
LDL-cholesterol (mg/dl)	124 ± 38

Values are means ± SD. HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance.

Table S2. Primer sequences

Gene	Primer
18s	AGGGTTCGATTCCGGAGAGG
	CAACTTTAATATACGCTATTGG
Cad	ATGAGTGGCTGCAACAGCGT
	AGGCCACAATCCAGAGCACA
Dhodh	GGATGCTGCTGCAGACTATG
	CAATGTCCTCCTTGTCCTGG
Umps	TGGCTGAGGAGCACTGTGAA
	CGGTTAGCCGCTGCAAGTAT