Supplementary Figure 1. Levels and composition of bile acids in samples. **A**, Ratios of primary to secondary bile acids in the serum and **B**, stool. **C**, The ratios of 12α-OH to non 12α-OH bile acids in serum and **D**, stool. n =135 for Low group, n=28 for High group. Data are shown as the mean ± SEM and analyzed by Wilcoxon signed-rank test.
Supplementary Figure 2

A. KEGG pathway enrichment

| Pathway name                                                                 | Gene count |
|-----------------------------------------------------------------------------|------------|
| Toll-like receptor signaling pathway                                         | 3          |
| TNF signaling pathway                                                       | 4          |
| Terpenoid backbone biosynthesis                                              | 5          |
| Steroid biosynthesis                                                        | 6          |
| Insulin signaling pathway                                                   | 7          |
| Protein digestion and absorption                                            | 8          |
| ECM-receptor interaction                                                    | 9          |
| Butanoate metabolism                                                       | 10         |
| AMPK signaling pathway                                                      | 11         |
| AGE-RAGE signaling pathway in diabetic complications                        | 12         |

B. Body mass (g)

C. Cumulative food intake (kcal/day/mouse)

D. Serum triglyceride (mg/dl)

E. Serum cholesterol (mg/dl)

F. HDL (mg/dl)

G. HDL (mg/dl)

H. ALT (U/L)

I. AST (U/L)

J. Total bile acid (nM)

K. Percent level
Supplementary Figure 2. RNA-seq and biochemical indicators of mice. A, KEGG pathways. B, Body weight. C, Cumulative food intake. D, Serum triglyceride content. E, Serum cholesterol content. F, Serum LDL levels. G, Serum HDL levels. H, Serum ALT and I, AST levels. J, Total bile acids in serum. K-M, Composition of bile acids in serum. (n = 3/group). Data are shown as the mean ± SEM and analyzed by Two-tailed unpaired Student’s t test.
Supplementary Figure 3. Palmitate induces ER stress expression in dose dependent manners. A, p-IRE, p-eIF2α and CHOP expression were measured by western blot. B-D, The statistical graph (n=4/group). All data are presented as the mean ± SEM and analyzed by one-way ANOVA followed by the Bonferroni post hoc test. *P < 0.05, **P < 0.01 vs. control.
Supplementary Figure 4. 

A-D, Composition of bile acids in serum of vehicle, GUDCA or TUDCA treated mice. 

E, Total bile acid in serum. 

F, The mRNA expression of Abcc3, Abcc11 and 

H, Cyp7a1. 

I, Epididymal fat mass. 

J, H&E staining of inguinal adipose tissue (n = 5-8/group). Data are presented as the mean ± SEM and analyzed by one-way ANOVA followed by the Bonferroni post hoc test.
Supplementary Figure 5

(a) p-IRE

(b) p-PERK

(c) p-eIF2α

GAPDH

Tubulin

Tubulin
SERCA2

140kD
114kD

β-actin

43kD
Supplementary Figure 5. Full western blot gel panels. (a, b, c, d, e, f) from which the data in Figure 3A-F were derived. (g) from which the data in Figure 4A were derived. (h) from which the data in Figure 5E were derived. (i) from which the data in Figure 6I were derived. (j) from which the data in Figure 8A were derived. (k) from which the data in Figure 8C were derived. (l) from which the data in Supplementary Figure 3A were derived.
### SUPPLEMENTAL MATERIAL

**Supplementary Table 1. Sequences of the real time PCR primers used in this study**

| Primers        | Forward                        | Reverse                           |
|----------------|--------------------------------|-----------------------------------|
| GAPDH(human)   | CTCAGACACCAGGGGAAGGTGA         | ATGATCTTGAGG CTGGTGTCATA          |
| GAPDH          | AAGGTCACTCCCAGAGCTGAA          | CTGCTTCACCACCTTCTTTGA             |
| CHOP           | CAGATTCCAGTCAAGTTCTAT          | GACCACCTCTGTTCCGTTTCTCT           |
| ATF4           | CCTCTGGGACAAGGGTTTTGTG         | GCACCGTGAAGACATCCCC               |
| sXBP1          | GCCATCAAGGACGTAGCA             | CTTCTCCGAGTAGCGAATCAG             |
| Bip            | TCTGCAGGTCGTCCGACTATTC         | AGGCAGTGCTGTGAGATGC               |
| Abcc3          | ACGGACTTTATCATTTGTGCT          | ATCTGGTGCGTAGTTTCG                |
| Abcc11         | CACCATGCCCTCTTACAA             | CACCATCGCAAGGAACT                 |
| Cyp7a1         | ACAGAAGCATAGACCACCAA           | TGCCAACACGCTTAGAT                 |
| SERCA2(human)  | GATATGCTCATGTGGTGTTG           | AATCTTCTTCAGTCGCTCCA              |
| RyR            | TGGGATTACAGGAAGACG            | ATCGCTCAGAGGAGACACT               |