

Expanded View Figures

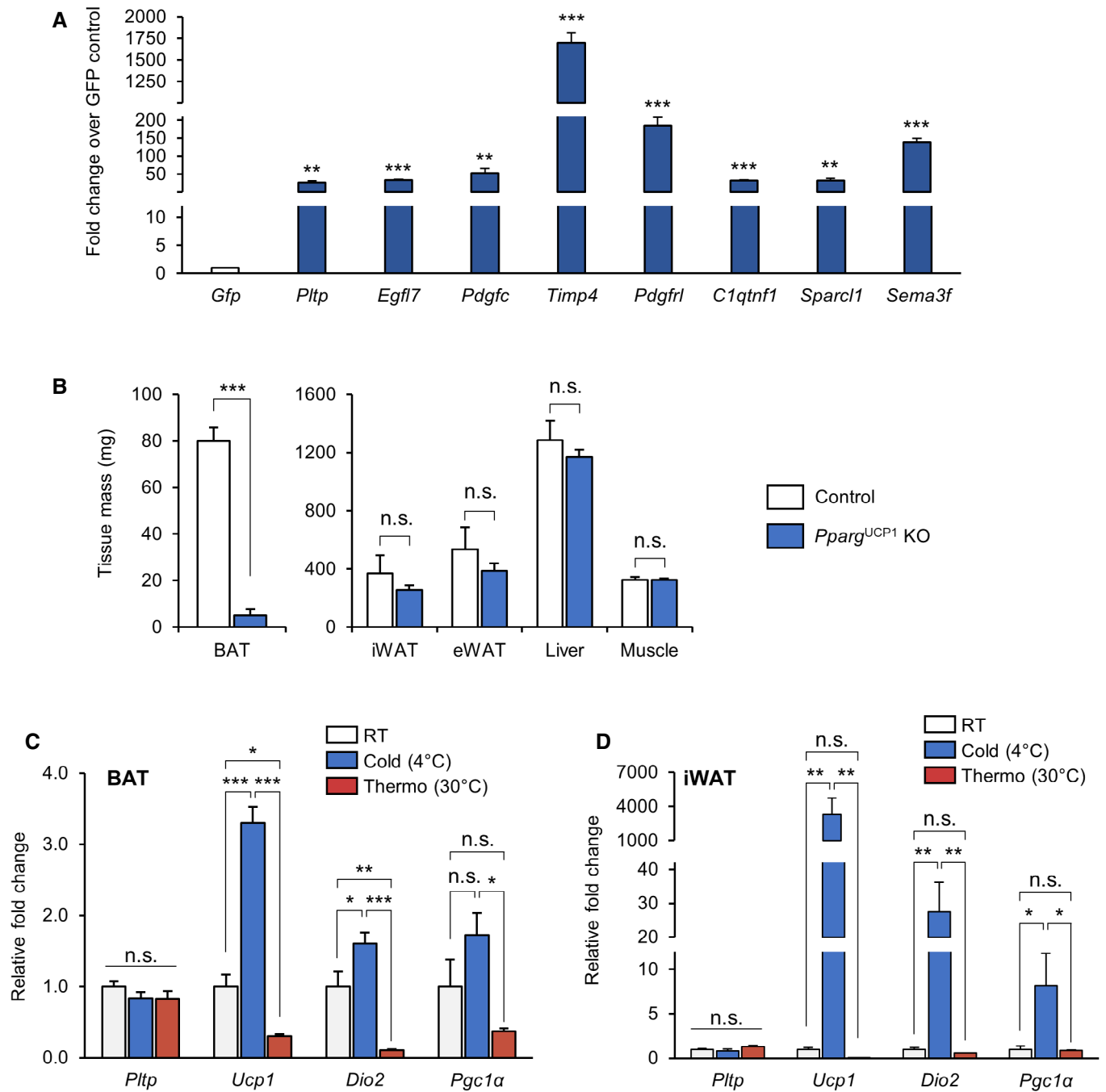


Figure EV1.

Figure EV1. Expression of batokine candidates and regulation of PLTP expression.

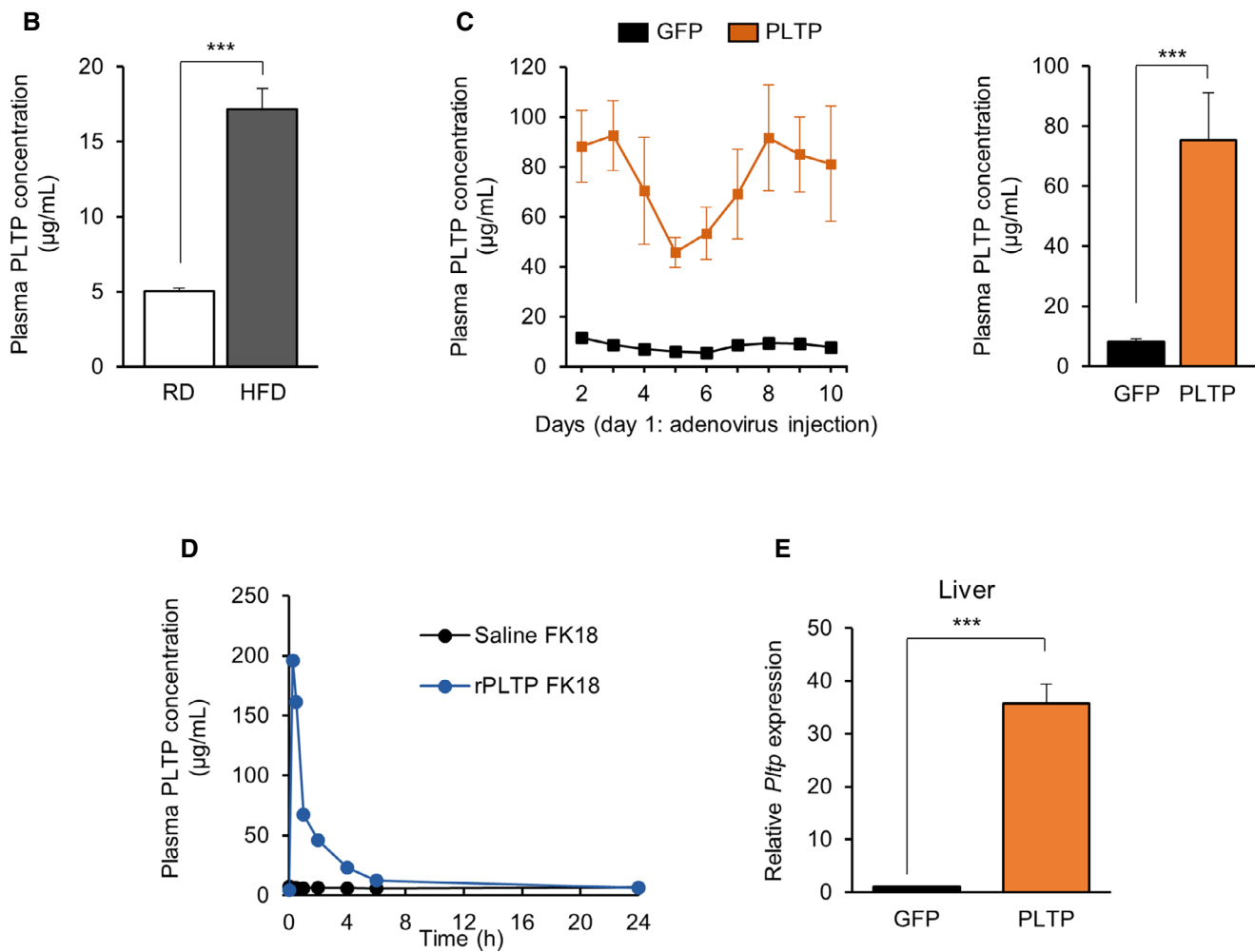
- A Hepatic expression of batokine candidates in mice that received adenovirus expressing indicated genes. $n = 5$ for all groups. $**P < 0.01$, $***P < 0.001$ relative to GFP by Student's t -test.
- B Tissue mass of $Pparg^{UCP1}$ KO mice and control mice. $n = 3$ for control, $n = 4$ for $Pparg^{UCP1}$ KO. $***P < 0.001$ relative to control by Student's t -test. N.S., not significant.
- C Relative gene expression of thermogenic genes in the interscapular BAT from C57Bl/6 mice housed at room temperature (RT), cold (4°C), or thermoneutrality (30°C) for 2 weeks. $18s$ was used as an internal control. $n = 5$ for all groups. ANOVA followed by Tukey's test. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. N.S., not significant.
- D Relative gene expression of thermogenic genes in the iWAT from C57Bl/6 mice housed at room temperature (RT) exposure to cold (4°C) and thermoneutrality (30°C) for 2 weeks. $18s$ was used as an internal control. $n = 5$ for all groups. ANOVA followed by Tukey's test. $*P < 0.05$, $**P < 0.01$. N.S., not significant.

Data information: All the data were represented as mean \pm SEM.

Source data are available online for this figure.

A Mouse recombinant PLTP sequence:

1 ELPGCKIRVT SAALELVKQE GLR **FLEQELETITIPDVYGA**KGHFYFNISD VRVTQLHLIS SELHFQPDQDLLNINSNASL
 81 GLHFRRQLLYWFLYDGGYINASAEGVSI RT GLQLSQDSSGRIKVS NVSCEASVSKMMAF GGTFRRMYNF FSTFITSGMR
 161 FLLNQQICPVLYHAGTVLLN SLLDTPVRS SVDDL VGIDY SLLKDPVVSNGNLDMEFRGA FFPLKEDNWSLPNRAVEPQL
 241 EDDERMVYVAFSEFFFD SAMESYFQAGALQLTLVGDVKVPS DLDMLLRATYFGSIVLLSPTVINSPLKLEATSPPRCTI
 321 KPSGTTISITASVTITLAPPMLPEVELSKMIMEGRLSAKL TLRGKALRVKLDLRRFQIYS NQSALESAL IPLQAPLKT
 401 LQIGVMPLLNERTWRGVQIPLPEGINFVRE VVTNHAGFVT VGADLHFAKGLREVIDKNRPADVAASHVPPPSAAAA

**Figure EV2. Plasma PLTP levels following virally induced or recombinant PLTP administration.**

- A Mouse PLTP coding sequence (<https://www.ncbi.nlm.nih.gov/gene> (gene ID:18830). Amino acid sequence of peptide FK18 (for mass spectrometry quantification) is highlighted.
- B Plasma PLTP concentration of mice on regular chow diet (RD) and high-fat diet (HFD). $n = 4$ for both groups. $***P < 0.001$ by Student's t -test.
- C Plasma PLTP concentration of mice that received adenovirus expressing GFP or PLTP. PLTP protein levels were determined every day throughout 10 days. $n = 4$ for GFP and $n = 5$ for PLTP. Average bar graph of 10 days is shown in the right graph. $***P < 0.001$ by Student's t -test.
- D Plasma PLTP concentration of rPLTP-treated mice. PLTP protein levels were determined during 24 h following i.v. injection of rPLTP at 360 µg per mouse. $n = 1$ for both groups.
- E Liver *Pltp* mRNA expression in mice that received AAV GFP or PLTP. *Tbp* was used as an internal control. $n = 4$ for GFP and $n = 6$ for PLTP. $***P < 0.001$ relative to GFP by Student's t -test.

Data information: All the data were represented as mean \pm SEM.

Source data are available online for this figure.

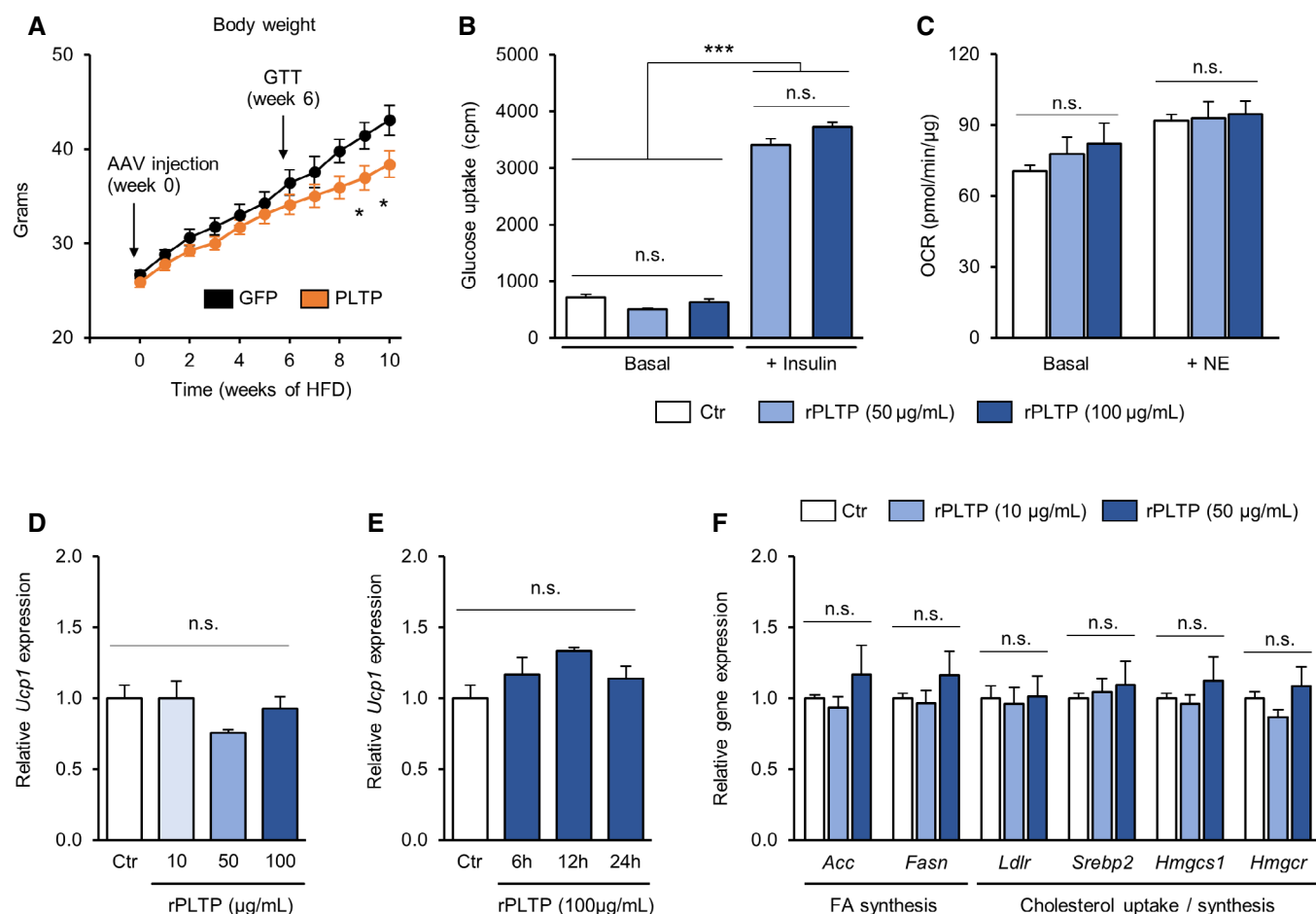


Figure EV3. The systemic vs cell-autonomous effects of PLTP on energy metabolism.

- A Bodyweight of mice that received AAV GFP (control) or PLTP on HFD. $n = 7$ for GFP and $n = 10$ for PLTP. $*P < 0.05$ relative to GFP by two-way repeated-measures ANOVA followed by Bonferroni's test. Glucose tolerance test was performed at 6 weeks of HFD, and the result is shown in Fig. 3D.
- B Glucose uptake in differentiated brown adipocytes treated with rPLTP. 0.1% BSA was used as a control (Ctr). A subset of cells was treated with insulin to measure insulin-dependent glucose uptake. $n = 3$ for all groups. $***P < 0.001$ by one-way ANOVA followed by Tukey's test. N.S., not significant.
- C OCR in differentiated brown adipocytes treated with rPLTP. OCR was performed at a basal state (without NE stimulation) and NE-stimulated state. $n = 10$ for Ctr, $n = 5$ both for rPLTP 50 and 100 $\mu\text{g/ml}$. One-way ANOVA followed by Tukey's test. N.S., not significant.
- D *Ucp1* mRNA levels in differentiated brown adipocytes treated with rPLTP at indicated doses for 24 h. *Tbp* was used as an internal control. $n = 3$ for all the groups. One-way ANOVA followed by Tukey's test. N.S., not significant.
- E *Ucp1* mRNA levels in differentiated adipocytes treated with rPLTP for indicated time points. *Tbp* was used as an internal control. $n = 3$ for all the groups. One-way ANOVA followed by Tukey's test. N.S., not significant.
- F Cultured hepatocytes were treated with recombinant PLTP protein (10 or 50 $\mu\text{g/ml}$) or vehicle (DMSO) for 24 h. The effect of PLTP on indicated genes was assessed by qRT-PCR. *Tbp* was used as an internal control. $n = 3$ for all groups. One-way ANOVA followed by Tukey's test. N.S., not significant.

Data information: All the data were represented as mean \pm SEM.

Source data are available online for this figure.

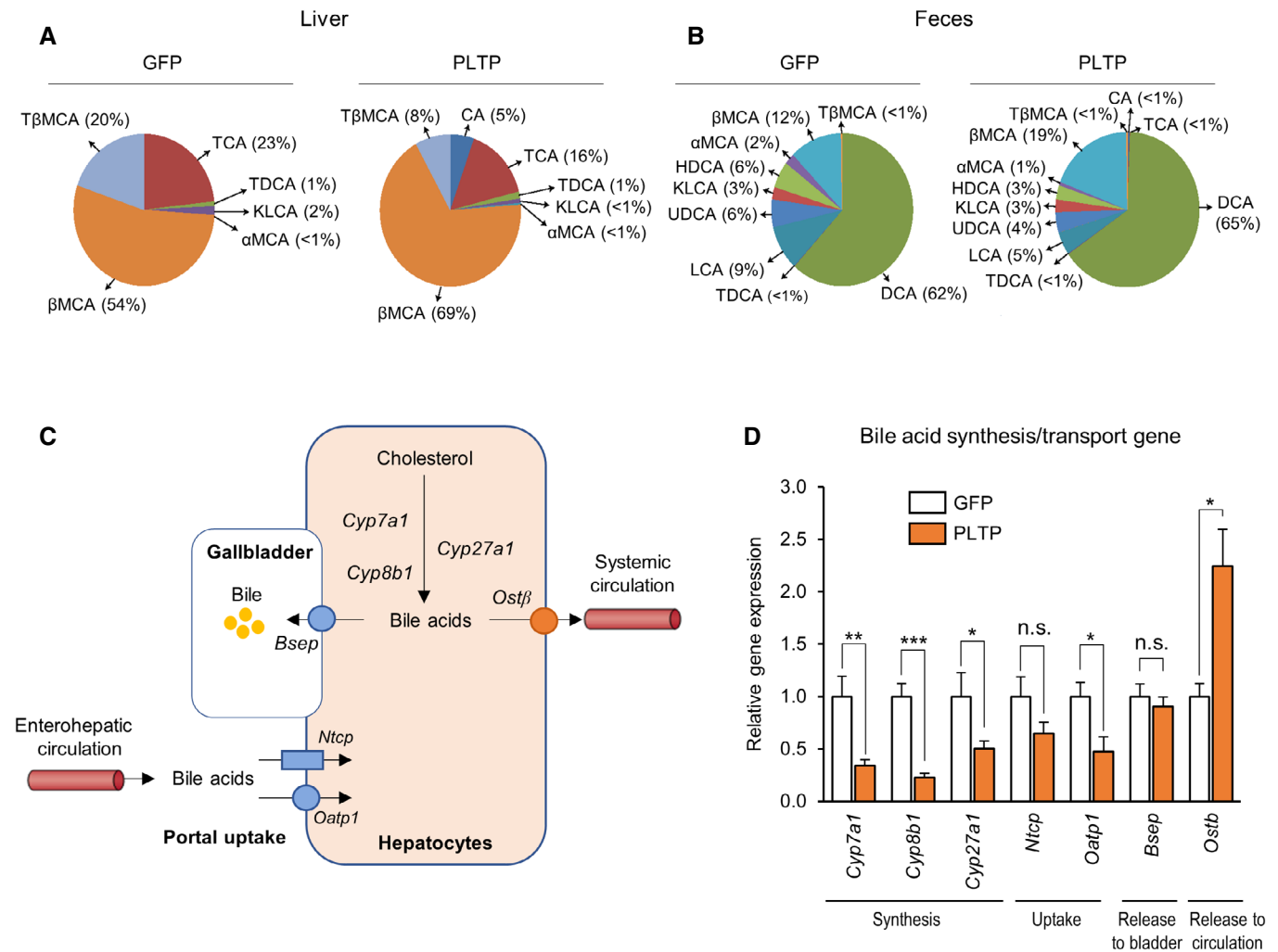


Figure EV4. The effect of PLTP on plasma bile acid composition and liver expression of bile acids synthesis genes.

A Bile acid composition in the liver of mice that received adenovirus expressing GFP (control) or PLTP on HFD. Pooled samples of $n = 5$ for both groups.

B Bile acid composition in the feces of mice in (A). Pooled samples of $n = 5$ for both groups.

C Schematic illustration of the hepatic bile acid synthesis, uptake, and secretion pathway.

D Relative expression of indicated genes involving in the bile acid synthesis, uptake, and secretion in the liver of mice that received GFP control and PLTP on HFD.

Tbp was used as an internal control. $n = 4$ for GFP, $n = 6$ for PLTP except *Ostb* $n = 5$. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ relative to GFP by Student's *t*-test. N.S., not significant.

Data information: All the data were represented as mean \pm SEM.

Source data are available online for this figure.

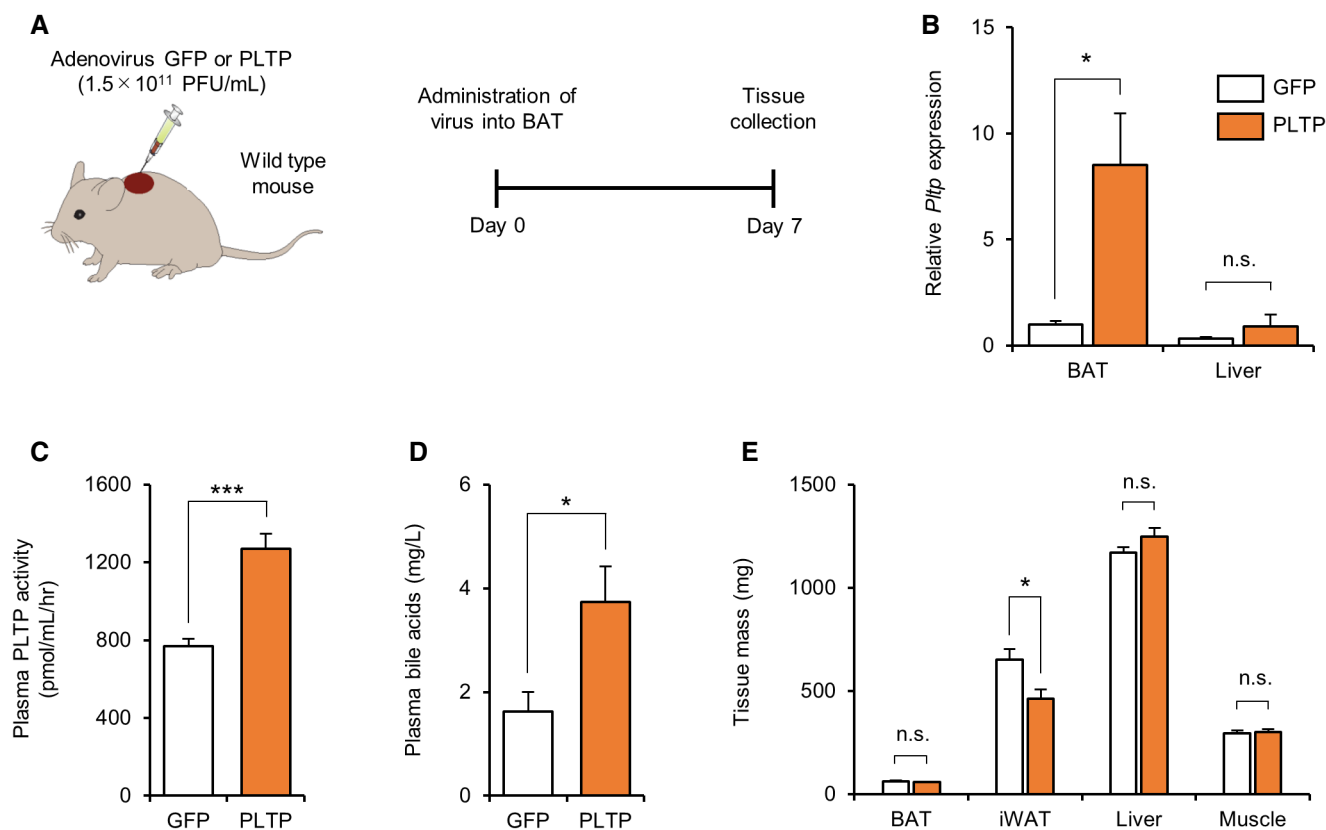


Figure EV5. The effect of BAT-derived PLTP on plasma bile acids and adiposity.

A Schematic illustration of the experiment. Tissues were harvested from mice that received adenovirus expressing GFP (control) or PLTP in the BAT.
 B The expression of *Pltp* in the BAT and liver of mice in (A). *Tbp* was used as an internal control. $n = 6$ for GFP and $n = 7$ for PLTP. * $P < 0.05$ relative to GFP by Student's *t*-test. N.S., not significant.
 C Plasma PLTP activity in (A). $n = 6$ for GFP and $n = 8$ PLTP. *** $P < 0.001$ relative to GFP by Student's *t*-test.
 D Plasma bile acid levels in (A). $n = 5$ for GFP and $n = 7$ PLTP. * $P < 0.05$ relative to GFP by Student's *t*-test.
 E Quantification of indicated tissue mass in (A). $n = 6$ for GFP and $n = 8$ PLTP. * $P < 0.05$ relative to GFP by Student's *t*-test. N.S., not significant.

Data information: All the data were represented as mean \pm SEM.
 Source data are available online for this figure.