

Figure S1. ERR α mediates gender disparity in hepatic VLDL secretion and associated genes. (A) Levels of plasma TG from 12-week-old male and female C57BL/6 mice fasted overnight. (B) VLDL-TG secretion (left panel) and rates (right panel) in 12-week-old C57BL/6 mice fasted overnight followed by intravenous injection with

500 mg/kg body weight of Triton WR-1339. (C) Protein levels of human $ERR\alpha$, ApoB, MTP and PLA2G12B in HepG2 cells treated with different doses of $ERR\alpha$ inverse agonist C29 or XCT790. Densitometry analysis of the western blotting data normalized to the intensity of β -tubulin. (D) mRNA levels of human *PDI*, *DGAT2* and *CIDEB* in HepG2 cells treated as (C) ($n = 3$). Data presented as means \pm SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, two-tailed Student's t test.

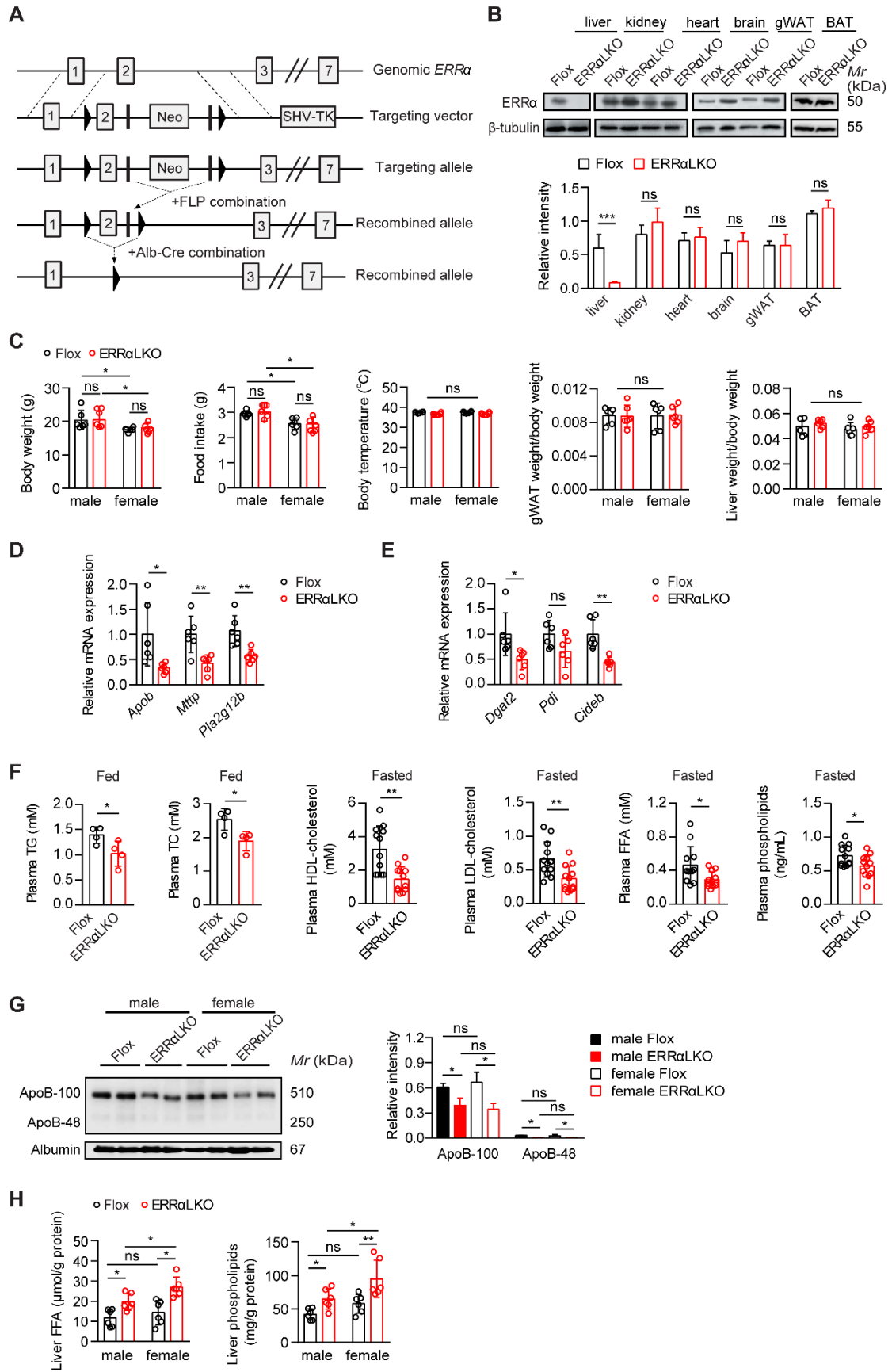


Figure S2. Generation and characterization of liver-specific *ERRα*-deficient mice. (A)

Schematic diagram of the strategy used to generate liver-specific ERR α -deficient mice. (B) Western blotting for ERR α in indicated tissues of control (Flox) and ERR α LKO mice (left panel). Densitometry analysis of the western blotting data normalized to the intensity of β -tubulin (right panel). (C) Body weight, food intake, body temperature, relative liver weight and gonadal white adipose tissue weight of male and female ERR α LKO mice compared with Flox littermates at 9 week of age ($n = 6$ mice per condition and sex). (D) mRNA levels of genes related to VLDL secretion (*Apob*, *Mttp* and *Pla2g12b*) in the livers of Flox and ERR α LKO mice ($n = 6$ mice per group). (E) mRNA levels of genes related to VLDL secretion (*Dgat2*, *Pdi* and *Cideb*) in the livers of Flox and ERR α LKO mice ($n = 6$ mice per group). (F) Levels of plasma TG, TC under fed condition and plasma HDL-cholesterol, LDL-cholesterol, FFA, phospholipids in Flox and ERR α LKO mice under fasting condition ($n = 4$ mice per group for fed condition and $n = 12$ mice per group for fasting condition). (G) Western blot showing plasma levels of ApoB protein from Flox and ERR α LKO male and female mice (left panel). Densitometry analysis of the western blotting data normalized to the intensity of Albumin (right panel). (H) FFA and phospholipids levels from liver of Flox and ERR α LKO mice under fasting condition ($n = 6$ mice per condition and sex). Data presented as means \pm SD. * $P < 0.05$, ** $P < 0.01$, two-tailed Student's t test for paired groups (B, D-F) or one-way ANOVA followed by Tukey's post hoc analysis (C, G and H). Abbreviations: gWAT, gonadal white adipose tissue; BAT, brown adipose tissue; FFA, free fatty acids; TG, triglyceride; TC, total cholesterol.

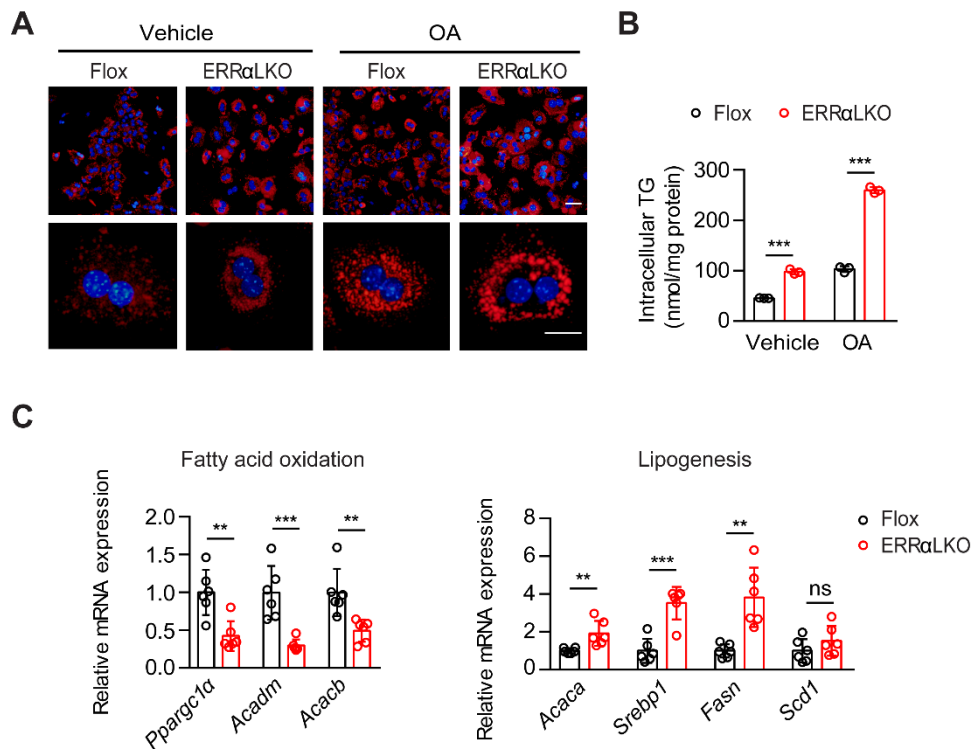


Figure S3. ERR α governs expression of essential genes involved in lipid metabolism.

(A) Representative fields of primary hepatocytes from male Flox and ERR α LKO mice with or without OA treatment. Lipid droplets (LDs) were labeled with Nile Red (red). (B) Intracellular TG contents from Flox and ERR α LKO hepatocytes ($n = 3$). (C) mRNA levels of genes related to fatty acid oxidation (*Ppargc1a*, *Acadm* and *Acacb*) and genes related to lipogenesis (*Acaca*, *Srebp1*, *Fasn* and *Scd1*) in the livers of Flox and ERR α LKO mice ($n = 6$ mice per group). Data presented as means \pm SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, two-tailed Student's t test. Abbreviations: OA, oleic acid; TG, triglyceride.

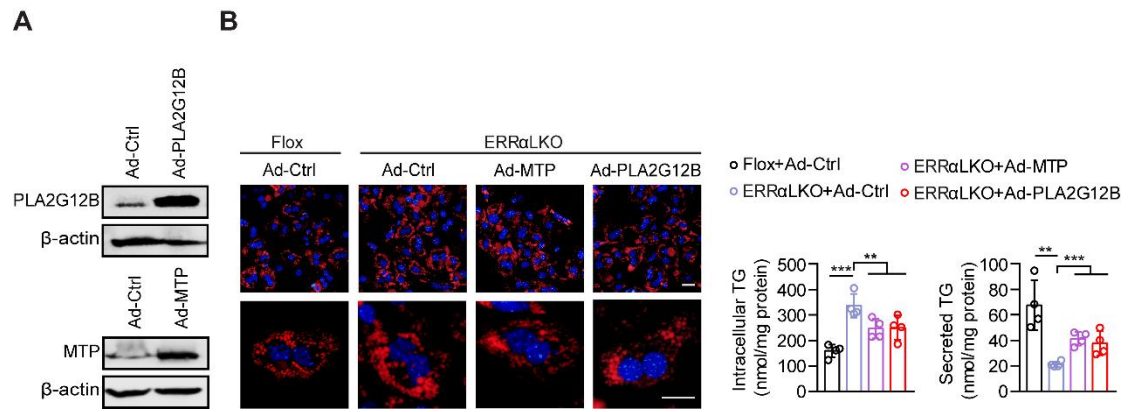


Figure S4. Restoration of MTP or PLA2G12B expression rescues VLDL-TG secretion in ERRαLKO hepatocytes. (A) Western blot showing the levels of MTP and PLA2G12B proteins in hepatocytes infected with adenovirus expressing MTP (Ad-MTP) or PLA2G12B (Ad-PLA2G12B). (B) Representative fields of male Flox and ERRαLKO hepatocytes infected with Ad-MTP, Ad-PLA2G12B or Ad-Ctrl. Lipid droplets (LDs) were labeled with Nile Red (red). Scale bar, 20 μm. Intracellular TG contents and secreted TG from hepatocytes infected with Ad-MTP, Ad-PLA2G12B or Ad-Ctrl as indicated ($n = 4$). Data presented as means \pm SD. ** $P < 0.01$, *** $P < 0.001$, two-tailed Student's t test.

Table S1. The primers used to genotype the liver-specific ERR α -deficient mice.

Primer name	Sequence 5'---3'
<i>Esrra-P1</i>	CTGGAGAAAACCTGAGGAGAGGA
<i>Esrra-P2</i>	ATGCTCCTAGTTCCATTCCAAA
<i>Cre-P1</i>	TGCAAACATCACATGCACAC
<i>Cre-P2</i>	TTGGCCCCTTACCATAACTG
<i>Cre-P3</i>	GAAGCAGAAGCTTAGGAAGATGG

Table S2. Mouse primers for quantitative real-time PCR detection.

Primer name		Sequence 5'---3'
<i>Apob</i>	F	GCCCATTGTGGACAAGTTGATC
	R	CCAGGACTTGGAGGTCTTGGA
<i>Mttp</i>	F	CAAGCTCACGTACTCCACTGAAG
	R	TCATCATCACCATCAGGATTCCT
<i>PLa2g12b</i>	F	CCAGCAATGACCAAGTGTTG
	R	GAGAATCACAGGCTGCTTCC
<i>Acadm</i>	F	AGGGTTTAGTTTTGAGTTGACGG
	R	CCCCGCTTTTGTTCATATTCCG
<i>Acaca</i>	F	GATGAACCATCTCCGTTGGC
	R	GACCCAATTATGAATCGGGAGTG
<i>Acacb</i>	F	CGCTACCAACAGTAAGGTGG
	R	GCTTGGCAGGGAGTTCCTC
<i>Srebfl</i>	F	GCAGCCACCATCTAGCCTG
	R	CAGCAGTGAGTCTGCCTTGAT
<i>Fasn</i>	F	GGCATCATTGGGCACTCCTT
	R	GCTGCAAGCACAGCCTCTCT
<i>Scd1</i>	F	TTCTTGCGATACTCTGGTGC
	R	CGGGATTGAATGTTCTTGTTCGT
<i>Actin</i>	F	GGCTGTATTCCCCTCCATCG
	R	CCAGTTGGTAACAATGCCATGT
<i>Ppargc1a</i>	F	TATGGAGTGACATAGAGTGTGCT
	R	CCACTTCAATCCACCCAGAAAG
<i>Dgat2</i>	F	GCGCTACTTCCGAGACTACTT
	R	GGGCCTTATGCCAGGAAACT
<i>Pdi</i>	F	AAAGCTGCCGCAAACTGAAG
	R	GCAGTGTGACAGAGGGTTGTA
<i>Cideb</i>	F	CAATGGCCTGCTAAGGTCAGT
	R	TTCAGACCCTACGGCTTAAC

Table S3. Human primers for quantitative real-time PCR detection

Primer name		Sequence 5'---3'
<i>ESRRA</i>	F	AGGGTTCCTCGGAGACAGAG
	R	TCACAGGATGCCACACCATAG
<i>ApoB</i>	F	CGGGCTCGTTACCACATGAAG
	R	GCGTAGAGACCCATCACATGATA
<i>MTTP</i>	F	AGCTCACGTA TCCACTGAAG
	R	CCTCCATAGTAAGGCCACATCC
<i>PLA2G12B</i>	F	TGGGCATTCCAGCAATGACAA
	R	GATCGAGTGGAGACACCATCG
<i>ACTIN</i>	F	CATGTACGTTGCTATCCAGGC
	R	CTCCTTAATGTCACGCACGAT
<i>DGAT2</i>	F	GCTGACCACCAGGA ACTATATC
	R	CATTGCCACTCCCATTCTTTG
<i>PDI</i>	F	GGTGCTGCGGAAAAGCAAC
	R	ACCTGATCTCGGAACCTTCTG
<i>CIDEB</i>	F	CAGTGA CT TACTCAGGTCAGTATC
	R	TTAGCACTCCATT CAGCAGTAG

Table S4. Primers for promoters

Primer name		Sequence 5'---3'
<i>Apob</i> WT	F	GGGGTACCTCTCAGCATCTTCTCTGCATCC
	R	CCGCTCGAGTGCTTGCTCTACAGGGTCTTC
<i>Apob</i> mA	F	GATGCTAACAATATGCCATGGGCTTCCTCTG
	R	CAGAGGAAGCCCATGGCATATTGTTAGCATC
<i>Apob</i> mB	F	CCGTGCCATTTGGAACCTTTGGCAATTCTCC
	R	GGAGAATTGCCAAAGTTCCAAATGGCACGG
<i>Apob</i> ΔAB	F	GGGGTACCTGGCAATTCTCCTTAAGCCAGC
	R	CCGCTCGAGTGCTTGCTCTACAGGGTCTTC
<i>Mttp</i> WT	F	CCGGGTACCTATATGGCCACCCGGTATCCA
	R	CCGCTCGAGTAACGGAAGCAGAGTAGGAGGA
<i>Mttp</i> mA	F	GGAGGTAAAGTAATTTTCGCCGTTCAATTTTGC
	R	GCAAAATTGAACGGCGAAAATTACCTTAACCTCC
<i>Mttp</i> ΔAB	F	CCGGGTACCGTAGCTCTATTGCTTGCTATC
	R	CCGCTCGAGTAACGGAAGCAGAGTAGGAGGA
<i>Mttp</i> mC	F	GGAGTTTGAATCTGATCGTTCCTATAG
	R	CTATAGGGGAACGATCAGATTCCAACTCC
<i>Mttp</i> ΔABC	F	CCGGGTACCAGATAAACACTGTTGTCGCCGG
	R	CCGCTCGAGTAACGGAAGCAGAGTAGGAGGA
<i>PLa2g12b</i> WT	F	CCGGGTACCGGAGTCCTATGGTTCTGTTCTG
	R	CCGCTCGAGTTTGCACGCACAAGTAGACC
<i>PLa2g12b</i> mA	F	CTGATATGATATCATCAGTTATGGCCCTGGCC
	R	GGCCAGGGCCATAACTGATGATATCATATCAG
<i>PLa2g12b</i> mB	F	CCTCCACGGTTTAAAATTTATAATCTCTAATCGCTCG
	R	CGAGCGATTAGAGATTATAAATTTTAAACCGTGGGAGG
<i>PLa2g12b</i> ΔAB	F	CCGGGTACCGGATCGGCTCCCAGCCTCCA
	R	CCGCTCGAGTTTGCACGCACAAGTAGACC

Table S5. Primers for ChIP real-time PCR detection.

Primer name		Sequence 5'---3'
<i>Esrra</i>	F	CGAACCCAAGCTCAACCTCATCTG
	R	AGAGGTGAGACACGAGCGGACAAA
<i>Apob</i> site A	F	GAAATGACATCCCCCAATGATGC
	R	TTTGAAATGGTTCTGCTTCCCC
<i>Apob</i> site B	F	GCAGTGAGACCACCATCAGATCC
	R	AGGCAGGTACTTGATCCACTGCA
<i>Mttp</i> site A	F	GTATATGGCCACCCGGTATCCACA
	R	GAAAGGTGAAAATTACCTTAACC
<i>Mttp</i> site B	F	GGAAAACACACTTCAAAGGACA
	R	GGAAGTGAGGGTTATTGGGATAT
<i>Mttp</i> site C	F	TGGCCTCACACTCAGAAATCCA
	R	GGGAAAGGTCAGATTCCAAAC
<i>PLa2g12b</i> site A	F	GTGCTCAAGTGTGCTGGAGA
	R	GTTCCCCAGAGGTGGACTTT
<i>PLa2g12b</i> site B	F	CCCGTTTTCTTCTTTTTTG
	R	CTTCTCCCTCCACACATTC