

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: Conditional knockout of *Cept1* in murine endothelium. A) *Cept1Lp* allele contains engineered *LoxP* sequences (black triangles) flanking exon 3 (E3) of *Cept1* to facilitate *Cre*-mediated recombination. Primers P1, 2, and 3 are used to confirm successful recombination of E3. B) Representative PRC gel using primers P1 and P2. 1) *Cept1*^{+/+} mouse, 2) *Cept1*^{+/+}, *VE-cadherin-CreERT2* (*Cre*⁺) mouse, and 3) *Cept1Lp/Lp*, *VE-cadherin-CreERT2* (*Cre*⁺) mouse. C) *Cept1* recombination in organs using PCR primers P1 and P3, demonstrating successful recombination of *Cept1* in heart, aorta, and lung tissue of *Cept1Lp/LpCre*⁺ mouse.

Supplemental Figure 2: *Ppara*, *Acox1*, and *Cpt1a* expression in peripheral arterial tissue. Maximally (Max) diseased arterial segments have mildly higher levels of *Ppara* (A) and *Cpt1a* (B), and significantly higher levels of *Acox1* (C). * $p < 0.05$

Supplemental Figure 3: CEPT1 protein content in *db/db* and *+/+* mouse aortic and skeletal muscle tissue. A) Representative Western blot of CEPT1 in aorta and skeletal muscle tissue of *db/db* and *+/+* mice. B) Quantitative assessment of relative CEPT1 content in *db/db* and *+/+* aortic tissue. * $p < 0.05$

Supplemental Figure 4: Summary of absolute quantities of independent phosphatidylcholine (PC) and phosphatidylethanolamine (PE) species evaluated in MLECs isolated from *Cept1Lp/LpCre*⁻ and *Cept1Lp/LpCre*⁺ mice. A) 54 independent PC

species were evaluated in *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* MLECs. B) 23 independent PE species were evaluated in *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* MLECs.

Supplemental Figure 5: Acute knockdown of *Cept1* decreases endothelial migration.

Representative images of mouse heart endothelial cell (MHEC) monolayers demonstrate reduced scratch gap closure over 16 hours following transfection with *Cept1* esiRNA.

Supplemental Figure 6: Bodyweights and blood glucose of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice following treatment with Fenofibrate or STZ.

A) Bodyweights (grams) of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice that received a Fenofibrate diet, and pre- and post-TMX treatment for conditional knockout of *Cept1* in the endothelium. B) Bodyweights of mice that received STZ to induce a diabetes-like phenotype, and pre- and post-TMX treatment. C) Blood glucose of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice following STZ treatment in maintained on a regular diet. D) Blood glucose of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice following STZ treatment in maintained on a Fenofibrate diet.

Supplemental Figure 7: Collateral vessel density in ischemic hind-limbs of

***Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice.** A) Representative angiograms of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice maintained on a regular diet that underwent unilateral HLI. 14 days post-HLI post-mortem peripheral angiograms were performed to evaluate density of adductor segment hind-limb arterial collaterals (inserts 2.5x magnification). B) Comparative analysis demonstrated no significant difference between

Cept1Lp/LpCre⁻ (n = 11) and *Cept1Lp/LpCre⁺* (n = 9) ischemic hind-limb adductor arterial collaterals.

Supplemental Figure 8: PPAR α , CPT1a, and ACOX1 protein content in ischemic and non-ischemic hind-limbs of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice. A) Representative Western blots of CPT1a, ACOX1, and PPAR α in ischemic and non-ischemic hind-limb muscle tissue from *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice maintained on a regular diet. Caveolin1 blots were used as blot loading controls. B) Representative Western blots from *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice pre-treated with STZ and maintained on a regular diet. C) Representative Western blots from *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice maintained on a fenofibrate diet. D) Representative Western blots from *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* mice pre-treated with STZ and maintained on a fenofibrate diet.

Supplemental Figure 9: Effect of Fenofibrate on MLEC tubule formation. A) Representative images of *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* MLEC formation of tubules after 6 hours of incubation on Matrigel with growth media supplemented with 25 μ M Fenofibrate. B) *Cept1Lp/LpCre⁻* and *Cept1Lp/LpCre⁺* MLEC tubule formation over 6 hours following treatment with or without 25 μ M Fenofibrate (n = 3 per condition). * $p < 0.05$

Supplemental Figure 10: Impact of 18:0/18:2 and 16:0/18:1 phospholipids on phospho-PPAR α and CPT1a. Representative Western blots of CPT1a, phospho-PPAR α ,

PPAR α , and Caveolin1 from HUVECs that were pre-treated with esiRNA *Gfp* or *Cept1*, and either PC 14:0, 18:0/18:2, or 16:0/18:1.

Supplemental Figure 11: Hind-paw Doppler perfusion in *Ppara*^{-/-} and *Cept1Lp/LpCre+Ppara*^{-/-} mice that received regular or fenofibrate diet. A) Hind-paw Doppler perfusion recovery at Day 0, 3, and 7 post-HLI in *Ppara*^{-/-} mice that received regular (n = 4) and Fenofibrate (n = 12) diets. B) Hind-paw Doppler perfusion recovery post-HLI in *Cept1Lp/LpCre+Ppara*^{-/-} mice that received regular (n = 4) and fenofibrate (n = 12).