

Supplemental Figure Legends

Figure S1 eWAT histology of ad-cav1KO mice on a high fat diet. **A**, Control or ad-cav1KO mice were put on a high fat diet and the body weight was tracked over the indicated timepoints. **B**, eWAT histology control, ad-cav1KO and whole body cav1KO mice. Data are presented as mean \pm s.e.m. * $P < 0.05$

Figure S2 RNA seq analysis of ad-cav1KO sWAT reveal a strong inflammatory response and loss of mitochondrial function. **A**, significantly upregulated pathways in ad-cav1KO mice compared to control mice. **B**, significantly downregulated pathways in ad-cav1KO mice compared to control mice. **C**, Heat maps to demonstrate the changes in specific mitochondria and mitochondria-regulating genes.

Figure S3 TCA cycle intermediates accumulate in eWAT depleted of cav1. TCA cycle intermediates were quantified by mass spectrometry in eWAT following 4 weeks of high fat feeding. Data are presented as mean \pm s.e.m. *** $P < 0.001$.

Figure S4 Ad-cav1KO mice display shifts in whole body metabolism on a chow diet. Chow-fed mice, 12-15 weeks of age were subjected to several metabolic physiology tests: **A-B**, a intraperitoneal glucose tolerance test (IPGTT) where serum glucose (**A**) and insulin (**B**) were quantified at the indicated timepoints after glucose injection, **C**, an insulin tolerance test (ITT), where serum glucose was quantified at the specified timepoints following insulin injection, **D**, a pyruvate tolerance test (PTT), where hepatic glucose production was estimated by measuring blood glucose at the indicated timepoints following an i.p. injection of pyruvate, **E**, an arginine tolerance test (ArgTT) where serum insulin was measured at the indicated timepoints following arginine injection, **F**, a triglyceride (TG) clearance test where serum TG was quantified at various timepoint following TG gavage, and **G**, a $\beta 3$ agonist sensitivity test where non-esterified fatty acid (NEFA) and glycerol release into the blood was measured following injection of CL-316, 243 compound. **H-J**, Mice were analyzed in metabolic cages and the RER trace (**H**) and activity trace (**I**) is shown. **J**, Food intake was measured in the light and dark cycles of the day. Data are presented as mean \pm s.e.m. * $P < 0.05$, ** $P < 0.01$.

Figure S5 Whole body cav1 knockout mice display impaired glucose metabolism. Wild-type, cav1KO and cav1HET were placed in a high fat diet for 4 weeks, after which several metabolic physiology tests were conducted: **A-B**, Intraperitoneal glucose tolerance test (IPGTT) where serum glucose (**A**) and insulin (**B**) were quantified at the indicated timepoints after glucose injection, **C**, insulin tolerance test (ITT), where serum glucose was quantified at the specified timepoints following insulin injection and **D**, and arginine tolerance test (argTT) where serum insulin was measured at the indicated timepoints following arginine injection. **E**, IPGTT was conducted on control and ad-cav1KO mice following 16 weeks of high fat feeding. **F**, ^{14}C -labeled 2-deoxyglucose (2DG) was injected i.v. into mice on a HFD for 4 weeks and tissues were harvested 30 minutes after injection for quantification radioactive glucose uptake rate. Data are presented as mean \pm s.e.m. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Figure S6 sEV characterization. **A**, nanoparticle analysis of isolated AT-sEV size distribution. **B**, Electron micrograph of isolated AT-sEVs. **C**, Western blot analysis of the EV marker flotillin-1 and general cell marker histone H3.

Figure S7 Biodistribution of AT-sEVs. Isolated AT-sEV membranes were labeled with DiR dye injected into WT mice. Mice were euthanized 16 hours later and tissues were harvested for detection of DiR.