Extended Data Figure Legends

Extended Data Figure 1. EHMT1 regulates endogenous PRDM16 protein expression *in vivo.*

a, The putative BAT was micro-dissected from wild-type and *Ehmt1*^{myf5} KO embryos. mRNA expression of *Prdm16* was measured by qRT-PCR. Data are presented as mean and s.e.m.; n=8-10. **b,** Western blotting to detect endogenous EHMT1, PRDM16, UCP1, and MHC in BAT from wild-type and *Ehmt1*^{myf5} KO embryos. α-tublin protein was shown as a loading control.

Extended Data Figure 2. Ectopic activation of skeletal muscle-selective genes and reduction of BAT-selective genes in the BAT from *Ehmt1*^{adipo} KO mice.

a, Western blotting for endogenous EHMT1in BAT and liver from wild-type and *Ehmt1*^{adipo} KO mice. β-actin protein was shown as a loading control. **b,** mRNA expression levels of BAT, skeletal muscle, white fat and beige-fat selective genes in BAT from *Ehmt1*^{adipo} KO mice. Values were normalized to those in wild-type mice. The mRNA levels were visualized by a heat-map using Multi Experiment Viewer. **c,** Venn diagram shows the overlapped genes between *Ehmt1*^{myf5} KO and *Ehmt1*^{adipo} KO mice. RNA-sequencing and GO analyses identified 33 genes that were similarly dysregulated both in the *Ehmt1*^{myf5} KO BAT and the *Ehmt1*^{adipo} KO BAT. The mRNA expression values were normalized to wild-type mice for each KO model and visualized by a heat-map using Multi Experiment Viewer. The color scale shows the mRNA levels of the genes in blue (low)-white (no change)-red (high) scheme.

Extended Data Figure 3. EHMT1 is required for beige/brite cell development.

a, The b3-AR agonist, CL316,243 at a dose of 0.5 mg/kg or saline were administered to wild-type (WT) or *Ehmt1*^{adipo} KO mice for 7 days. Inguinal WAT was harvested for gene expression analysis. mRNA expression levels of BAT and beige-fat selective genes (as indicated) were measured by qRT-PCR. n= 3-6. †, significant between saline and CL316,243 in WT mice. **b,** Immunohistochemistry for UCP1 in a. Scale bar, 100 μm. Nuclei were stained with DAPI. **c,** To test a cell-autonomous requirement for EHMT1 in beige/brite cell development, the stromal vascular (SV) fraction were isolated from the inguinal WAT of *Ehmt1*$^{flox/flox}$ mice. Cells were infected with adenovirus expressing GFP or Cre. The SV cells were differentiated in the

presence or absence of rosiglitazone (Rosi) at 0.5 μM. mRNA expression levels of BAT-selective genes (as indicated) were measured by qRT-PCR. Deletion of *Ehmt1* was confirmed by qRT-PCR (right graph). n=3; data are presented as mean and s.e.m.; * $P< 0.05$, ** $P <0.01$, *** $P <0.001$.