SUPPLEMENTAL DATA

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Supplemental Figure 1. Characterization of BATp85αKO model. Representative microphotographs and quantifications of immunohistochemistry against p85α to assess the presence or absence of this regulatory subunit in BAT and gWAT from BATp85αKO and Control mice. Image magnification: x10. Negative controls without the primary antibody were included to check for nonspecific staining. Results are expressed as mean ± SEM. Statistical significance was performed by two-tailed unpaired *t*-test by comparison *vs*. Control mice (*p<0.05).

Supplemental Figure 2. Effect of the lack of p85α in the body weight and adiposity in BATp85αKO model at 6 and 12 months of age. Body weight, BAT/Body weight ratio and ratios of different compartments of WAT/Body weight in Control and BATp85αKO mice at **(A)** 6 and **(B)** 12 months of age. Results are expressed as mean ± SEM. Statistical significance was performed by two-tailed unpaired *t*-test by comparison *vs*. 6-month-old Control mice (*p<0.05). 6-month-old Control (n=4); 6-month-old BATp85αKO (n=7); 12-month-old Control (n=10); 12-month-old BATp85αKO (n=6).

Supplemental Figure 3. Analysis of adipocyte size in BATp85αKO model at 6 months of age. Representative microphotographs (upper panels) and their quantifications of the adipocyte size (graphs) of hematoxylin and eosin staining in BAT, gWAT and iWAT from Control and BATp85αKO mice at 6 months of age. Image magnification: x20. Results are expressed as mean ± SEM. Statistical significance was assessed by two-tailed unpaired *t*-test by comparison *vs*. 6-month-old Control mice (*p<0.05). 6-month-old Control (n=4); 6-month-old BATp85αKO (n=4).

Supplemental Figure 4. Analysis of glucose metabolism alterations in BATp85αKO model at 6 and 12 months of age. (A) Glucose plasma levels of fasted mice by automatic monitor. **(B)** Glucose and **(C)** Insulin tolerance tests performed in

Control and BATp85αKO mice at 6 and 12 months of age. Results are expressed as mean ± SEM. Statistical significance was carried out by two-tailed unpaired *t*-test by comparison *vs*. 6-month-old Control mice (*p<0.05 and ***p<0.001); *vs*. 6-month-old BATp85αKO mice (†p<0.05). 6-month-old Control (n=4); 6-month-old BATp85αKO (n=7); 12-month-old Control (n=10); 12-month-old BATp85αKO (n=6).

Supplemental Figure 5. Analysis of obesity and glucose metabolism in BATp85αKO model under HFD. (A) Body weight and **(B)** Body weight gain after 10 weeks on HFD in Control and BATp85αKO HFD mice. **(C)** Food intake per week of Control HFD and BATp85αKO HFD mice. **(D)** Insulin tolerance test at 5 weeks on HFD were performed in Control HFD and BATp85αKO HFD. Control HFD (n=8); BATp85αKO HFD (n=7). Results are expressed as mean ± SEM. Statistical significance was performed by two-tailed unpaired *t*-test by comparison *vs*. Control HFD (#p<0.05, ##p<0.01, ###p<0.001 and ####p<0.0001).

Supplemental Figure 6. Expression of pro-inflammatory cytokines in adipose tissues from BATp85αKO mice. *Mcp1, Il1b* or *Il6* mRNA levels were analyzed by qRT-PCR in **(A)** BAT and **(B)** iWAT from Control HFD and BATp85αKO HFD mice. Thus, the amount of target, normalized to endogenous gene and relative to the control is given by qRT-PCR. The value represented in the y axis is the RQ, being: [(RQ) = 2-ΔΔCt; ΔCt (cycle threshold) = Ct (target gene) - Ct (*Gapdh*); ΔΔCt = ΔCt for any sample - ΔCt for the control]. Amplification of *Gapdh* was used in the same reaction of all samples as an internal control. We have used ΔΔCt referred to Control HFD. Results are expressed as mean ± SEM. Statistical significance was performed by two-tailed unpaired *t*-test by comparison *vs*. Control HFD group (#p<0.05). Control HFD (n=8); BATp85αKO HFD (n=7).