



**Fig. S1.** (Related to **Figs. 2, 4 & 6**) Energy expenditure, food intake, blood glucose, serum leptin concentrations and Lepr localization in *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice. (A) Total body weight is higher in 10-week old female *Rpgrip11*<sup>+/-</sup> compared with *Rpgrip11*<sup>+/+</sup> mice fed regular chow (LFD). (B) Energy intake during the light cycle of 19-week old male *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice having been fed a high fat diet (HFD) for 3 days. Energy expenditure (C) and total movement counts (D) of 19-week old male *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice having been fed HFD for 3 days. Serum leptin concentration (E) and serum leptin adjusted for fat mass (F) of *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice having been fed the high-fat diet for 7 days before they were sacrificed. (G) Blood glucose concentrations of 19-week old male mice having been fed HFD for 7 days, or fed HFD for 6 days and subsequently fasted for 24h. Energy expenditure (H, J) and total movement counts (I, K) of 4-week old and 5-week old male *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice fed regular chow (LFD) or HFD for one week, respectively. (L) Overlap of fluorescent signal (green) specific to the anti-Lepr antibody and tomato (tm)-positive neurons (red) expressing Lepr-b in the arcuate (ARC) and ventromedial (VMH) hypothalamus of compound heterozygous *Lepr-b*<sup>cre/+</sup>, *Gt(ROSA)26Sor*<sup>tm2Sho/+</sup> mice (Leshan et al., 2006). (M) Co-localization of Lepr and Tgn46 in arcuate cells with polarized (red dashed-line circle) or scattered (white dashed-line circle) Lepr localization. (N) Relative *Adcy3* (encodes AcIII) mRNA levels in the whole hypothalamus of 19-week old *Rpgrip11*<sup>+/-</sup> and *Rpgrip11*<sup>+/+</sup> mice fed HFD. Error bars represent SEM.

**Movie S1.** (Related to **Figure 4B**) Localization of Lepr in the vicinity of the cilium *in vivo*. Z-stack of an arcuate neuron from an *Rpgrip11*<sup>+/-</sup> mouse administered leptin intraperitoneally that convenes Lepr (red) in the vicinity of the cilium (green).

**Movie S2.** (Related to **Figure 4B**) Diffuse Lepr localization *in vivo*. Z-stack of an arcuate neuron from an *Rpgrip11*<sup>+/-</sup> mouse administered leptin intraperitoneally that displays a diffuse Lepr (red) localization with respect to the cilium (green).

**Movie S3.** (Related to **Figure 6B**) Co-localization of Lepr and Rpgrip11 *in vivo*. Z-stack demonstrating co-localization of Lepr (red) and Rpgrip11 (green).