SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1. GH, IGF-1 and GHRH expression levels of the wild-type, Irs1-floxed, Nestin-Cre, NIrs1KO, Synapsin-Cre and Syn-Irs1KO mice. (A) GH mRNA expression levels in the pituitary in the wild-type, Irs1-floxed, Nestin-Cre and NIrs1KO mice (n = 9-10 at 12 weeks). (B) IGF-1 mRNA expression levels in the liver in the wild-type, Irs1-floxed, Nestin-Cre and NIrs1KO mice (n = 9-10 at 12 weeks). (C) GHRH mRNA expression levels in the hypothalamus in the wild-type, Irs1-floxed, Nestin-Cre and NIrs1KO mice (n = 10 at 12 weeks). (D) GH mRNA expression levels in the pituitary in the wild-type, Irs1-floxed, Synapsin-Cre and Syn-Irs1KO mice (n = 10 at 10 weeks). (E) IGF-1 mRNA expression levels in the liver in the wild-type, Irs1-floxed, Synapsin-Cre and Syn-Irs1KO mice (n = 10 at 10 weeks). (F) GHRH mRNA expression levels in the hypothalamus in the wild-type, Irs1-floxed, Synapsin-Cre and Syn-Irs1KO mice (n = 10 at 10 weeks). Data are expressed as means ± SEM. Statistical significance is depicted as * ($P < 0.05$) and ** ($P < 0.01$). n.s.: not significant

Supplemental Figure 2. Phenotypes of the Nestin-Cre and NIrs1KO mice. (A) Food intake in the Nestin-Cre and NIrs1KO mice at 8 weeks (n = 6). (B) POMC, AgRP and NYP

mRNA expression levels in the hypothalamus of the Nestin-Cre and NIrs1KO mice at 16 weeks (n = 5). (C) Body temperature of the Nestin-Cre and NIrs1KO mice at 10 weeks (n = 13-14). Data are expressed as means ± SEM. n.s.: not significant

Supplemental Figure 3. Plasma GH and IGF-1 levels in the Syn-Irs1KO mice. (A) Plasma GH concentrations in the Synapsin-Cre and Syn-Irs1KO mice at 10 weeks (n=16-21). (B) Plasma IGF-1 concentrations in the Synapsin-Cre and Syn-Irs1KO mice at 10 weeks (n=16-21). Data are expressed as means ± SEM. Statistical significance is depicted as * ($P < 0.05$) and ** ($P < 0.01$). n.s.: not significant

Supplemental Figure 4. Immunohistochemistry for GHRH and Irs1. (A) Fluorescence immunohistochemistry for Irs1 (upper left) and GHRH (upper right) of the hypothalamus of the wild-type mice at 12 weeks. Merged image of GHRH and Irs1 staining in the serial section of the hypothalamus (bottom). (B) GHRH staining in sections of the hypothalamus of the wild-type mice at 10 weeks. A primary antibody against GHRH (LS-C482423) was used for this staining. (C) Immunohistochemical staining of hypothalamus of the wild-type mice at 12 weeks performed without the primary antibody of either GHRH or Irs1 demonstrated no immunoreactivity. (D) Immunohistochemical

staining for Irs1 in the liver of the wild-type and LIrs1KO mice at 12 weeks. Immunoreactivity was observed in the wild-type mice (left), but not in the LIrs1KO mice (right).