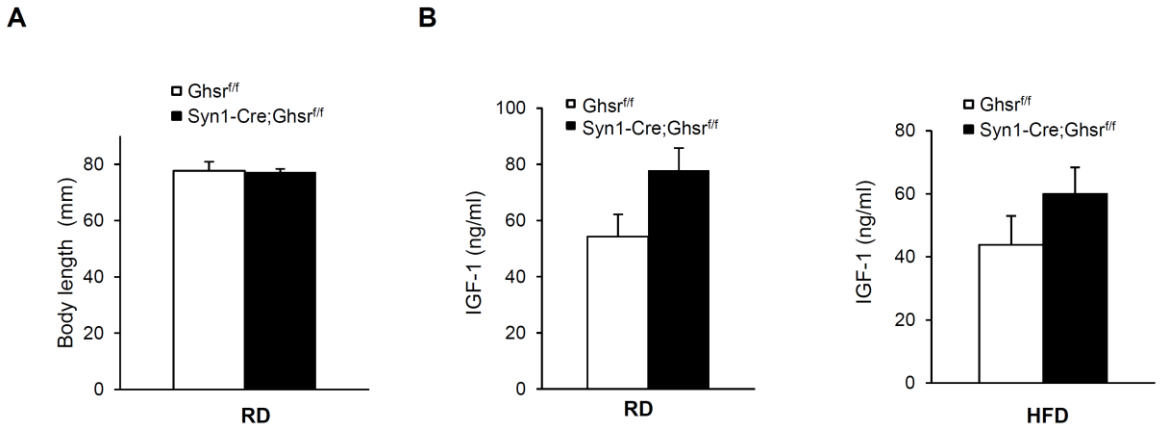
SUPPLEMENTARY DATA

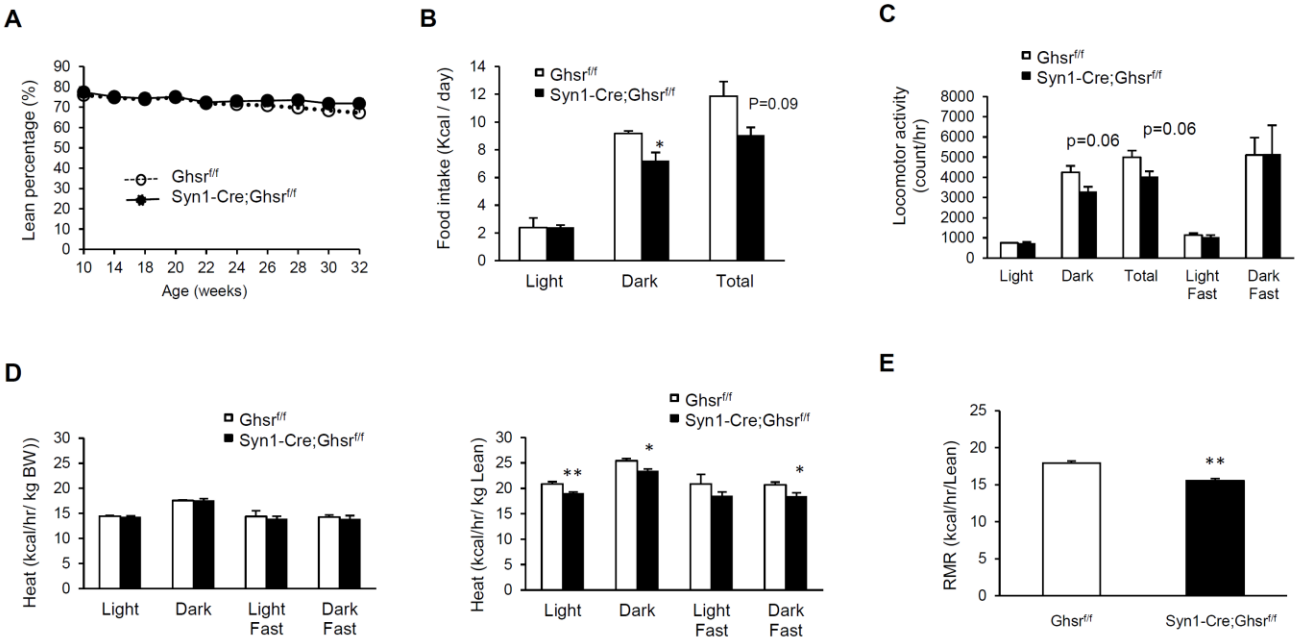
Supplementary Figure 1.

Neuronal *Ghsr* ablation does not affect the body length. (**A**), Body length, n=3-4. **(B)** Plasma IGF-1 in RD- and HFD-fed mice measured after overnight fasting. n=6-7.



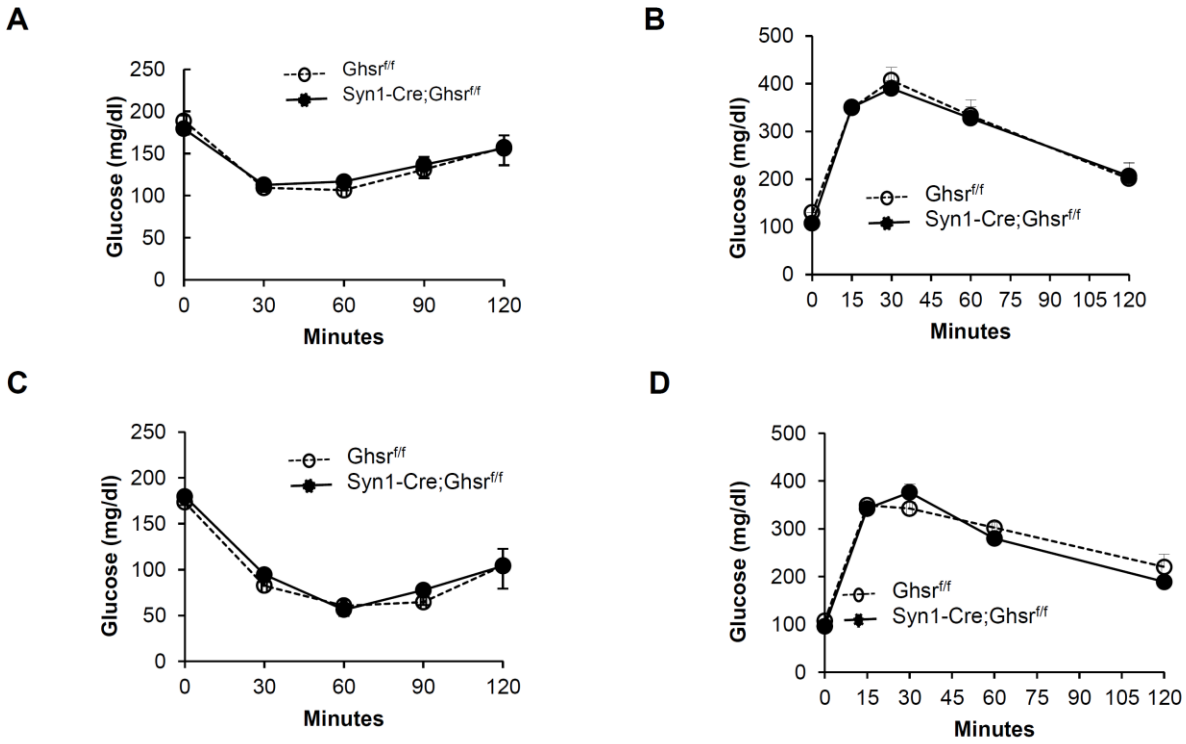
Supplementary Figure 2.

The phenotype of *Syn1-Cre;Ghsr$^{f/f}$* mice fed regular diet (RD). Lean percentage (**A**), food intake (**B**), locomotor activity (**C**), energy expenditure (Heat) adjusted by body weight (BW) or lean mass (**D**), and resting metabolic rate (RMR) normalized by lean mass (**E**). n=6-7. *, p<0.05 **, p<0.001, *Ghsr$^{f/f}$ vs.* *Syn1*-Cre;*Ghsr$^{f/f}$*.



SUPPLEMENTARY DATA

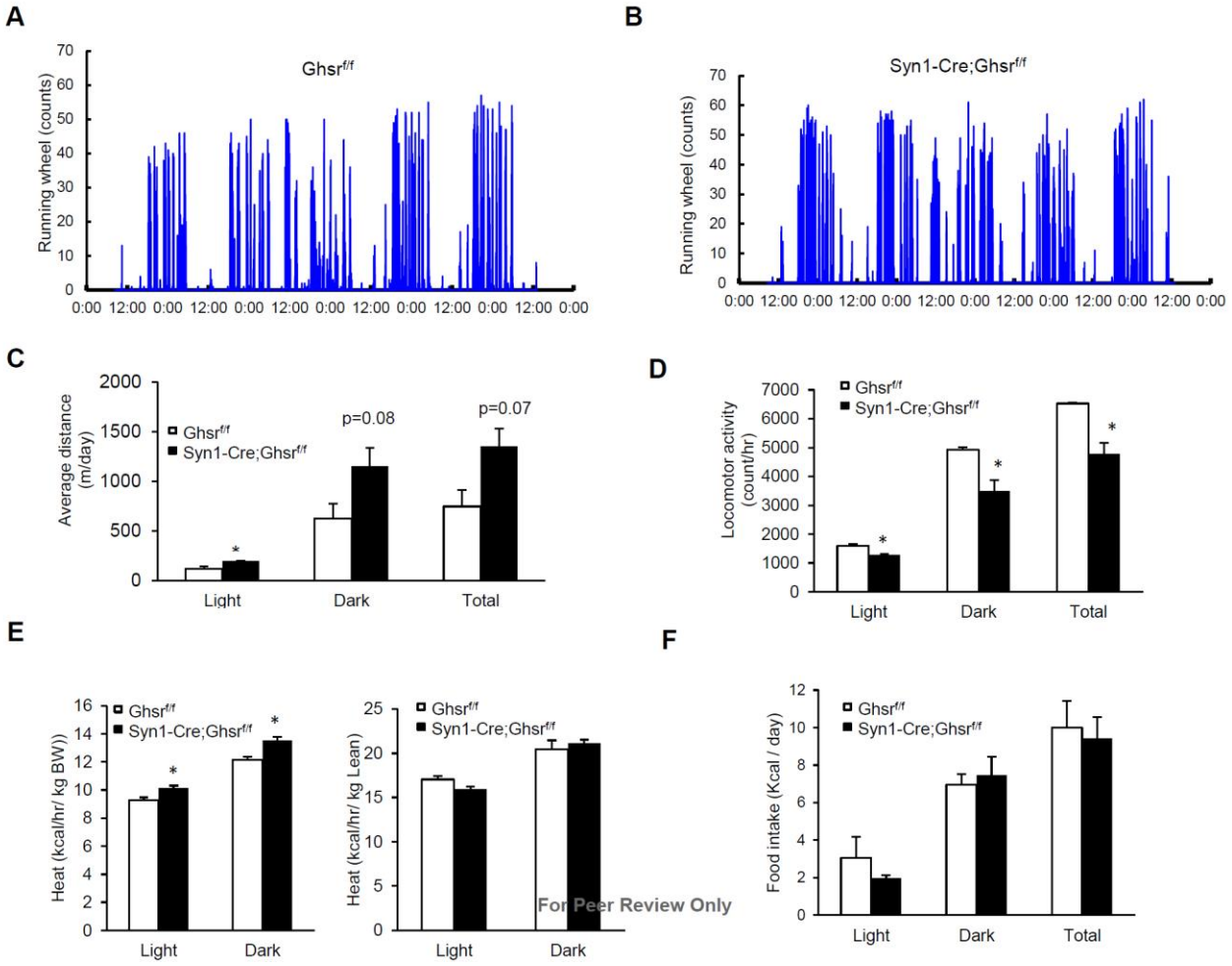
Supplementary Figure 3.
Neuronal *Ghsr* deletion does not affect insulin sensitivity under RD. ITT (**A**) and GTT (**B**) of mice fed RD for 22 weeks. ITT (**C**) and GTT (**D**) of mice fed RD for 44 weeks. n=5-7.



SUPPLEMENTARY DATA

Supplementary Figure 4.

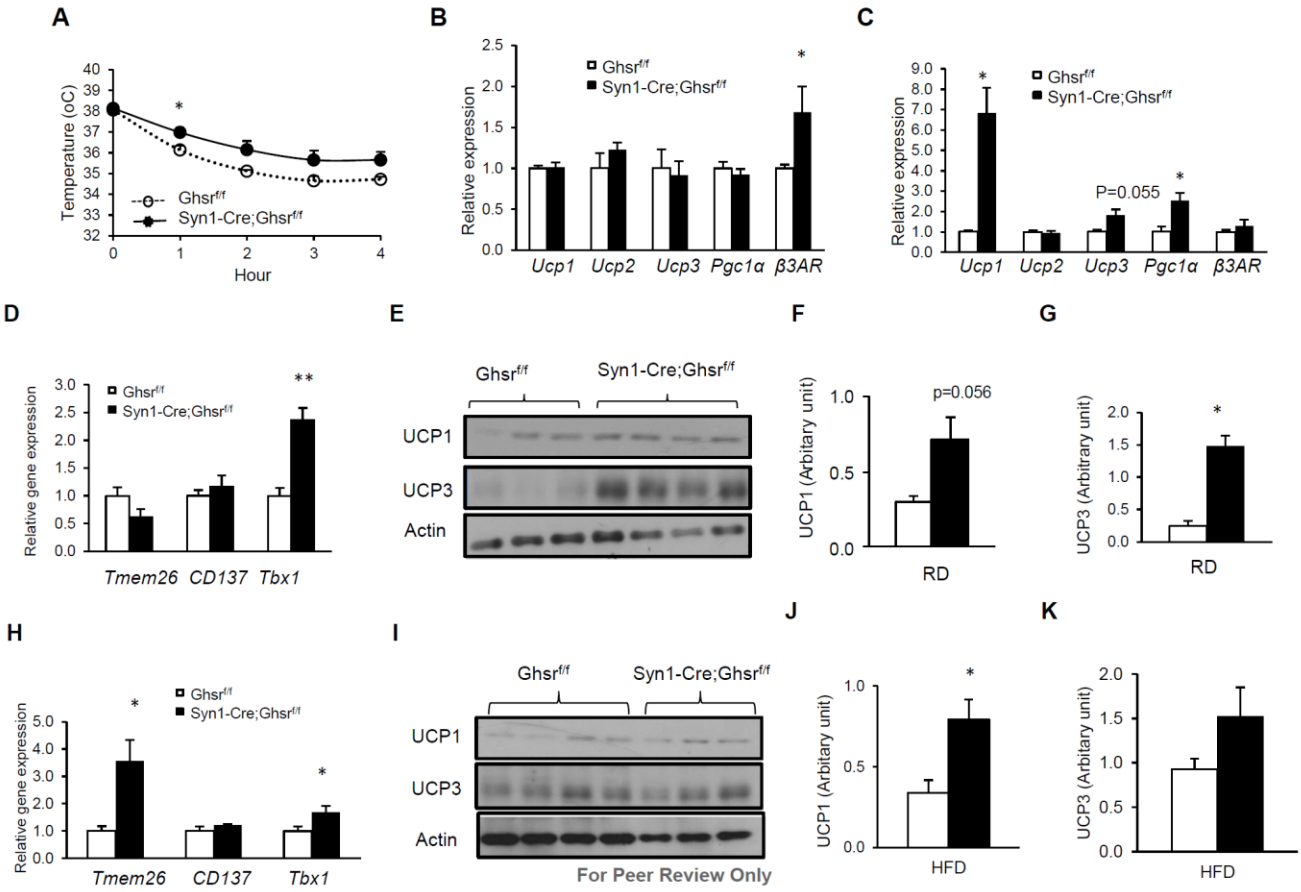
Neuronal *Ghsr* ablation increases voluntary physical activity in mice fed RD. Metabolic profile of RD-fed Syn1-Cre;*Ghsr*$^{f/f}$ mice with running wheels. Five day recording of wheel rotations of *Ghsr*$^{f/f}$ mice (**A**) and Syn1-Cre;*Ghsr*$^{f/f}$ mice (**B**). Average daily running distance (**C**), locomotor activity (**D**), energy expenditure (Heat) adjusted by body weight (BW) or lean mass (**E**), and food intake during wheel running test (**F**). n=5-7,*, p<0.05,*Ghsr*$^{f/f}$ *vs*. Syn1-Cre;*Ghsr*$^{f/f}$.



SUPPLEMENTARY DATA

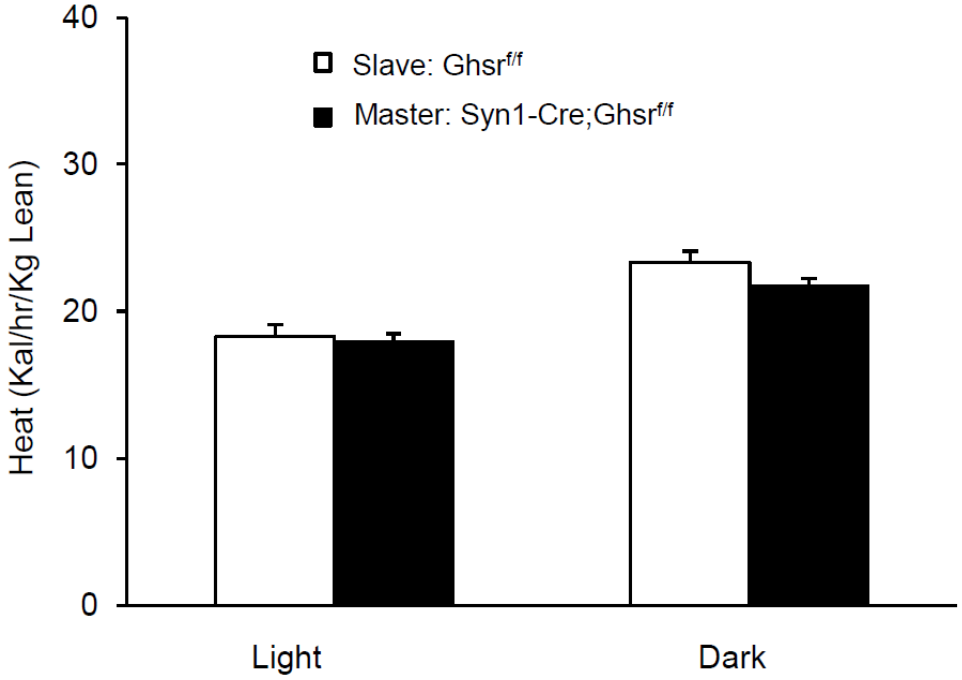
Supplementary Figure 5.

Neuronal *Ghsr* ablation improves thermogenesis in BAT and subcutaneous fat tissues under RD feeding. Rectal temperature change of RD-fed mice during 4^{o}C cold challenge (A). Thermogenic gene expression in BAT (**B**) and subcutaneous fat (**C**), tissues were collected immediately after 4^{o}C cold challenge. Beige markers in subcutaneous fat (D) and protein levels of UCP1 and UCP3 (E-G) in RD-fed mice. Beige markers in subcutaneous fat (H) and protein levels of UCP1 and UCP3 (I-K) in HFD-fed mice. n=5-7. *, p<0.05, **, p<0.001, *Ghsr$^{f/f}$ vs. Syn1-Cre;Ghsr$^{f/f}$*.



SUPPLEMENTARY DATA

Supplementary Figure 6.
Neuronal *Ghsr* ablation has no effect on energy expenditure under paired-feeding condition. The paired-feeding study was performed using 40 week-old RD-fed mice, n=4. *Syn1-Cre*;*Ghsr*$^{f/f}$ mice were used as "Master", having free access to food; *Ghsr*$^{f/f}$ mice were used "Slave", limiting their food intake to match that of the "Master" group.



SUPPLEMENTARY DATA

Supplementary Table 1. Real-Time PCR Primer Sequences

18S AGCCTGCGGCTTAATTTGAC CAACTAAGAACGGCCATGCA	**Orexin** GCCGTCTCTACGAACTGTTGC CGCTTTCCCAGATCAGGATA
PGC-1a CATTTGATGCACTGACAGATGGA CCGTCAGGCATGGAGGAA	**Leptin R** TGACCAGTGTAACAGTGCTAACTTCTC CATATTTAACTGAGGGTTGTCTCTGACA
β3-AR TGCCAACTCTGCCTTCAACCCGCTC CGCTCACCTTCATAGCCATCAAACC	**STAT3** CTTGTCTACCTCTACCCCGACAT GATCCATGTCAAACGTGAGCG
UCP1 GTGAAGGTCAGAATGCAAGC AGGGCCCCCTTCATGAGGTC	**DAT** GGAAGCTGGTCAGCCCCTGCTT GAATTGGCGCACCTCCCCTCTG
UCP2 TCACTGTGCCCTTACCATGCT AGGCATGAACCCCTTGTAGAAG	**TH** GGTATACGCCACGCTGAAGG TAGCCACAGTACCGTTCCAGA
UCP3 GAGCGGACCACTCCAGCGTC TGAGACTCCAGCAACTTCTC	**D1R** AACTGTATGGTGCCCTTCTGTGG CATTCGTAGTTGTTGTTGCCCCG
NPY GCTAGGTAACAACGAATGGGG CACATGGAAGGGTCTTCAAGC	**D2R** CACTCCGCCACTTCTTGACATACA TCTCCTCCGACACCTACCCCGA
AgRP GCAGACCGAGCAGAAGAAGT TGCGACTACAGAGGTTCGTG	**BDNF** GGGTCACAGCGGCAGATAAA GCCTTTGGATACCGGGACTT
POMC GGCCCTTCCCCTAGAGTTCA TTGATGATGGCGTTCTTGAA	**SF1** TCCAGTACGGCAAGGAAGAC CTGTGCTCAGCTCCACCTC
CB1 GCTGCAATCTGTTTGCTCAG TTGCCATCTTCTGAGGTGTG	**IR** CAAAAGCACAATCAGAGTGAGTATGAC ACCACGTTGTGCAGGTAATCC
AMPK1α AAGCCGACCCAATGACATCA CTTCCTTCGTACACGCAAAT	**mCD137** CCAGTACCACCATTTCTGTGACTCCA ATGAAGATCAGGGCCAGCAGCA
mTmem26 ACCCTGTCATCCCACAGAG TGTTTGGTGGAGTCCTAAGGTC	**mTbx1** TCGTGAGTGCCT TTGCTCGCT TGCGTAGCGTCGCCGAGC