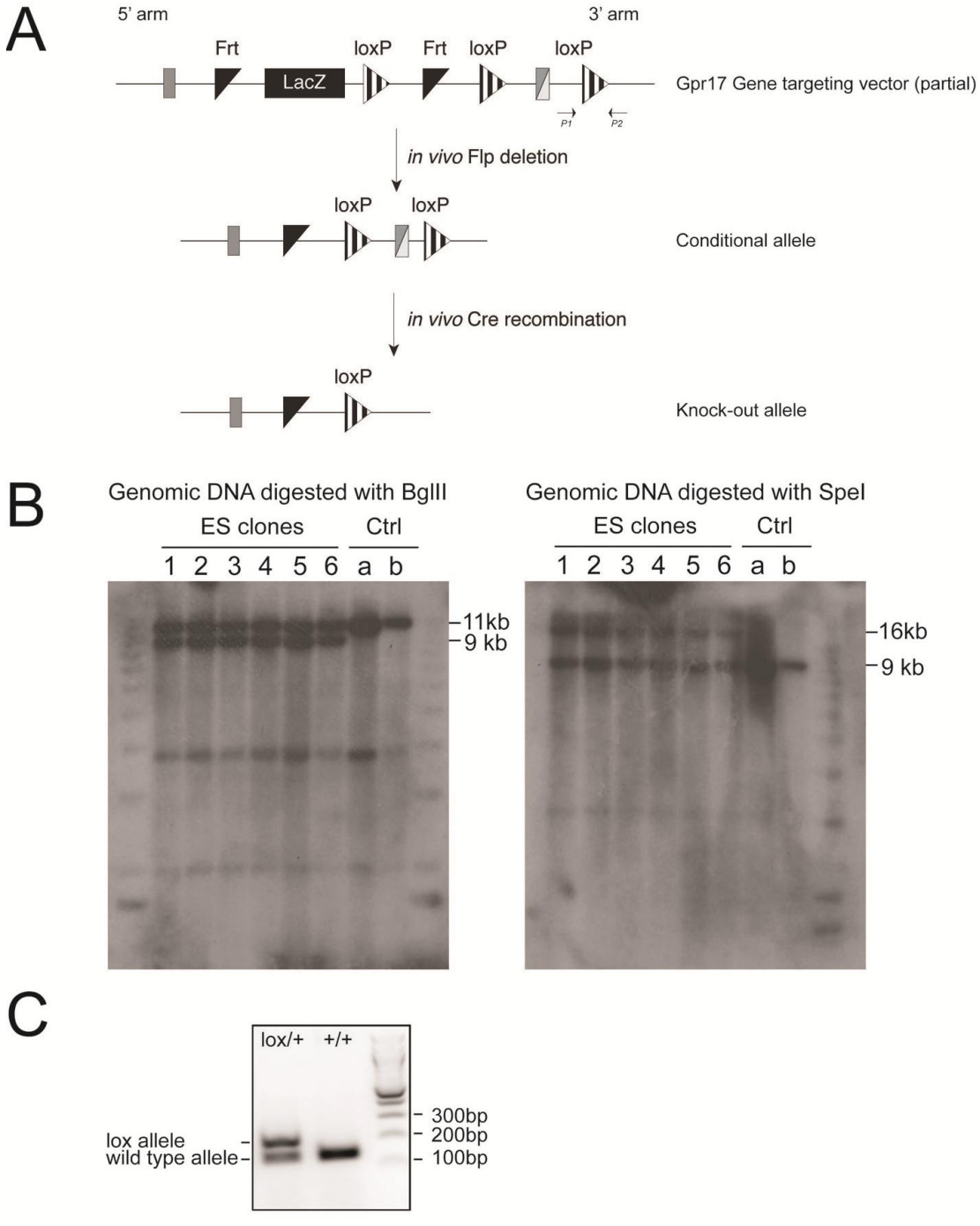
SUPPLEMENTARY DATA

Supplementary Figure S1. Generation of Gpr17 Mutant Mice

(A) Schematic diagram depicting the general structure of targeting vector and Cre-mediated deletion of Gpr17. (B) Southern blots confirming the 5' and 3' integration of the targeting vector. (C) Genotyping strategy to detect wild type and targeted mutant allele.

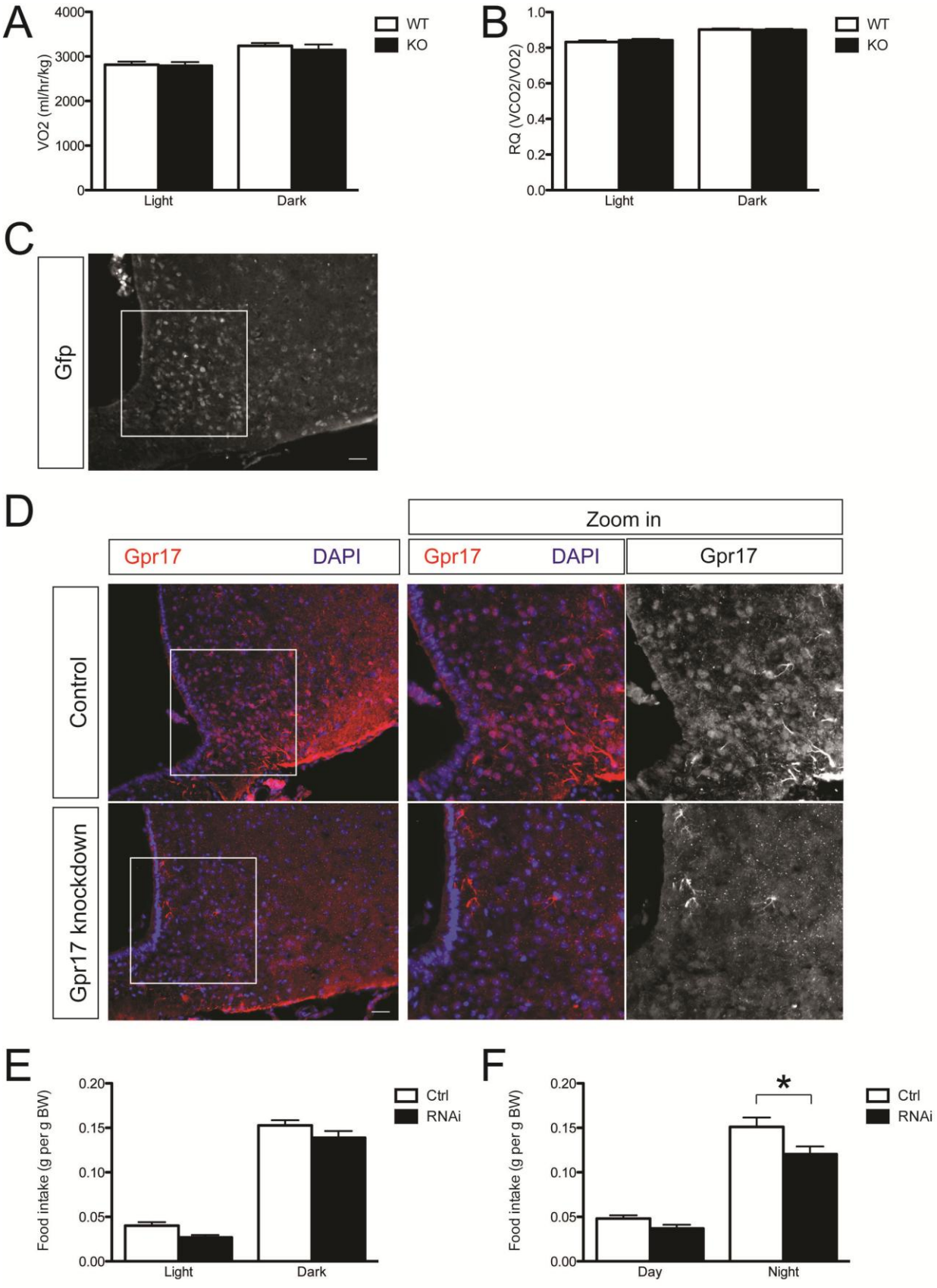


SUPPLEMENTARY DATA

Supplementary Figure S2. Energy Balance in *Agrp-Gpr17*$^{-/-}$ Mice

(A-B) O_2 consumption (VO_2) (A) and respiratory quotient (RQ) (B) measured in *ad libitum*-fed mice (n=8 for each genotype). (C) Representative Gfp staining demonstrating the correct targeting of AgRP neurons after adenovirus injection into the ARH in *Agrp-irs-Cre* mice. (D) Representative Gpr17 staining demonstrating the efficient knockdown of Gpr17 by Cre-dependent siRNA expression after adenoviral injection. Scale bar 50μm. (E) Food intake during light and dark phases of the light cycle in mice before injection of the control virus or Gpr17 RNAi virus (n=5 for each group). (F) Average food intake during light and dark phases of the light cycle in mice during the 5 days following virus injection. (n=5 for each group). We present data as means ± SEM. * = P <0.05 (2way ANOVA with Bonferroni Post-tests or unpaired t-test).

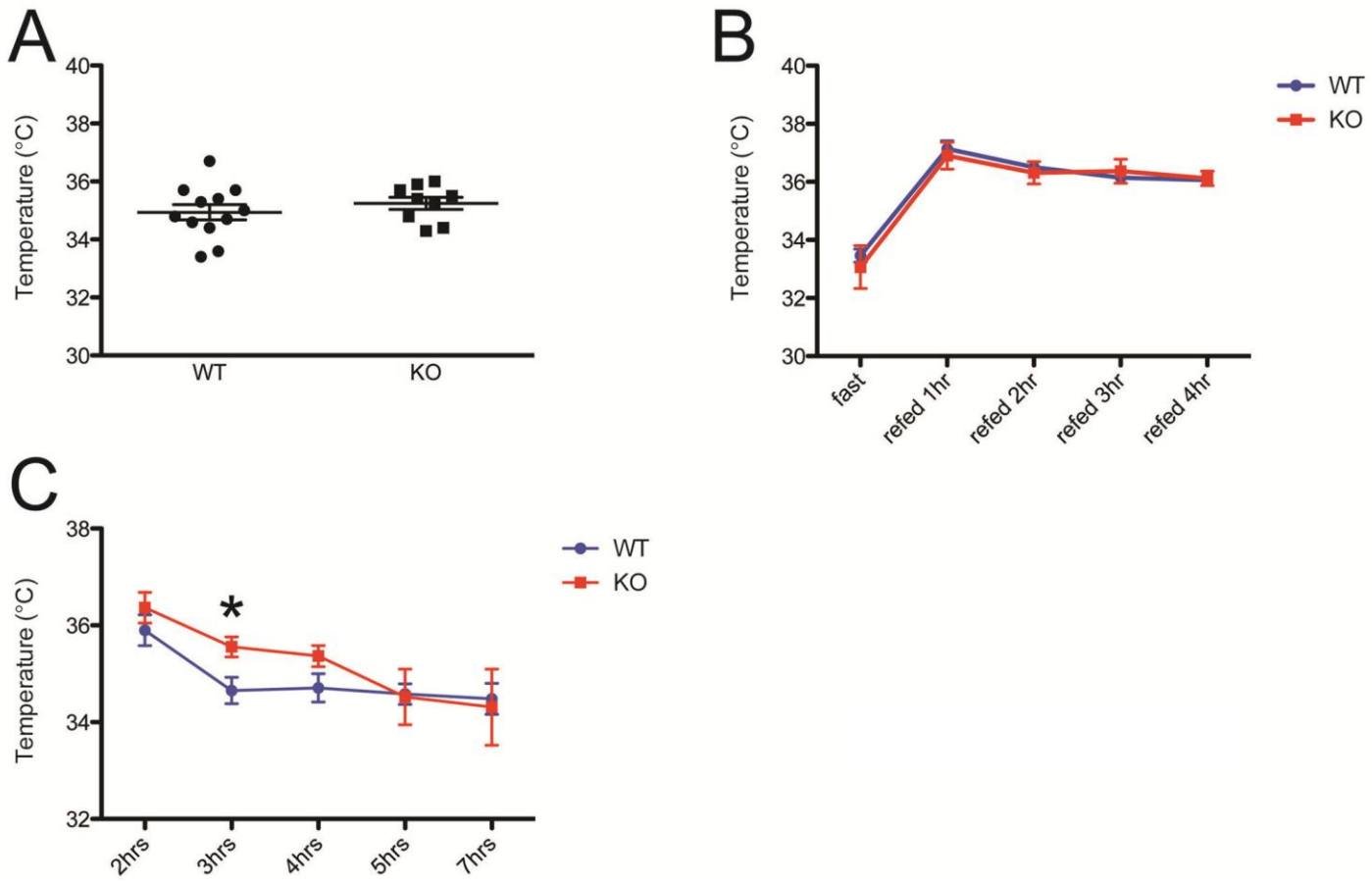
SUPPLEMENTARY DATA



SUPPLEMENTARY DATA

Supplementary Figure S3. Altered Cold Response in *Agrp-Gpr17*$^{-/-}$ Mice

(A) Body temperature in *ad libitum*-fed mice (n=9-12 for each genotype). (B) Time course of body temperature during fasting and refeeding (n=9-11 for each genotype). (C) Time course of body temperature during cold challenge (n=9-11 for each genotype). We present data as means ± SEM. * = P <0.05 (unpaired t-test or 2way ANOVA with Bonferroni Post-tests).



SUPPLEMENTARY DATA

Supplementary Figure S4. Hepatic Gene Expression and Primary Hepatocyte Analyses
(A-F) mRNA levels during *ad libitum* feeding (n=7 for each genotype), after 5-hr fast (n=6-15 for each genotype), after 12-hr fast (n=5-6 for each genotype), after 16-hr fast (n=10-12 for each genotype), after 4-hr refeeding (n=8-9 for each genotype), and after 24-hr refeeding (n=5-6 for each genotype). (G) Liver triglyceride in *ad libitum*-fed (n=7 for each genotype), fasted (n=10-12 for each genotype), 4-hr refed (n=6-7 for each genotype), and 24-hr refed mice (n=6 for each genotype). (H-L) Representative western blotting (H) of protein extracted from isolated primary hepatocytes. Quantitative analysis of phosphorylated mTOR (I), Akt (Ser) (J), Akt (Thr) (K), or GSK (L) content after insulin treatment of primary hepatocytes isolated from WT and KO mice (n=6 for each genotype). (M-N) Glucose production in hepatocytes isolated from control (M) and knockout (N) mice following treatment with vehicle, cAMP, or cAMP and insulin (labeled respectively as V, C, and CI) (n=4). We present data as means ± SEM. * = P <0.05, ** = P <0.01, *** = P <0.001, **** = P <0.0001 (2way ANOVA with Bonferroni Post-tests or unpaired t-test). AU: arbitrary units.

SUPPLEMENTARY DATA