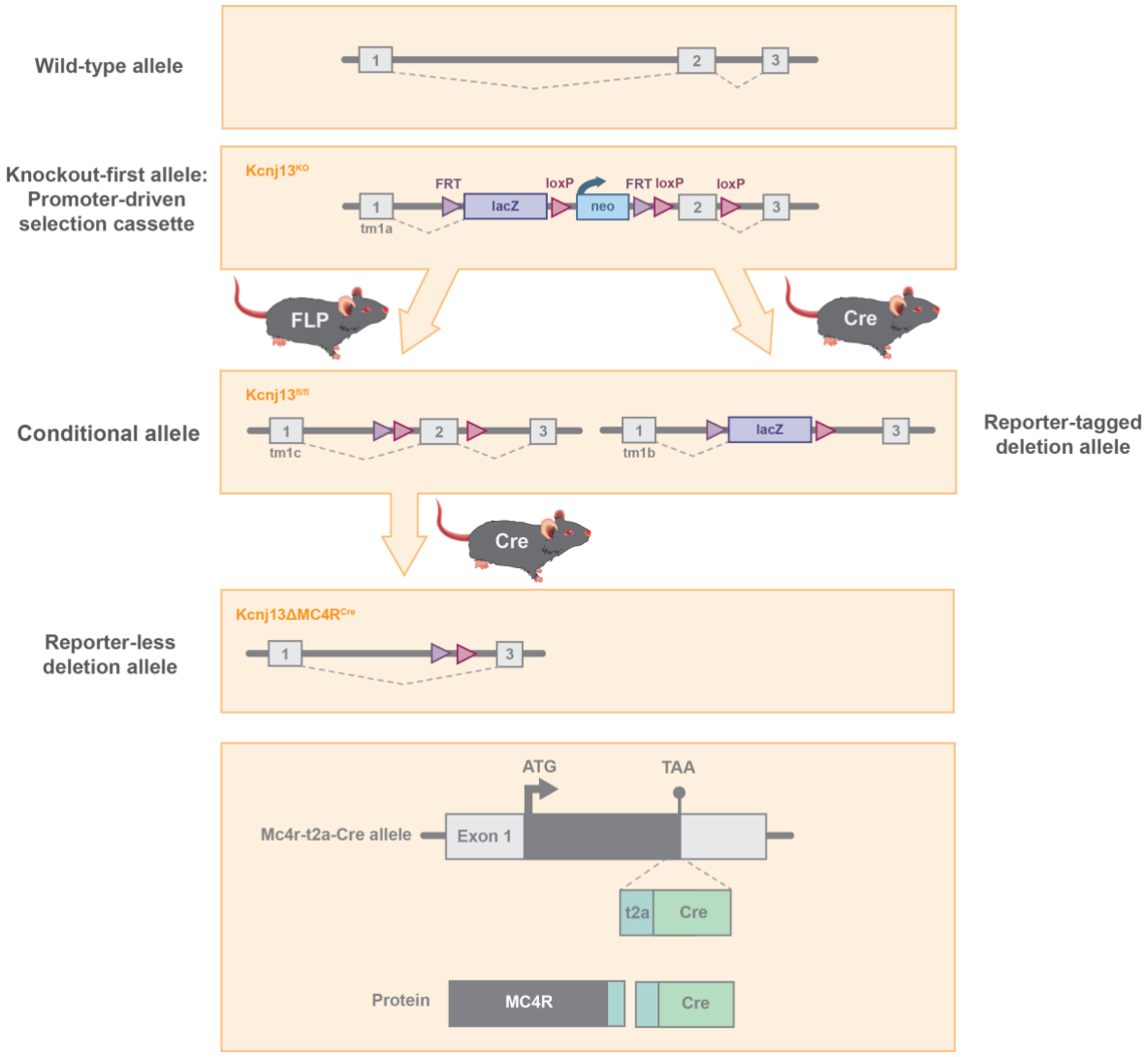
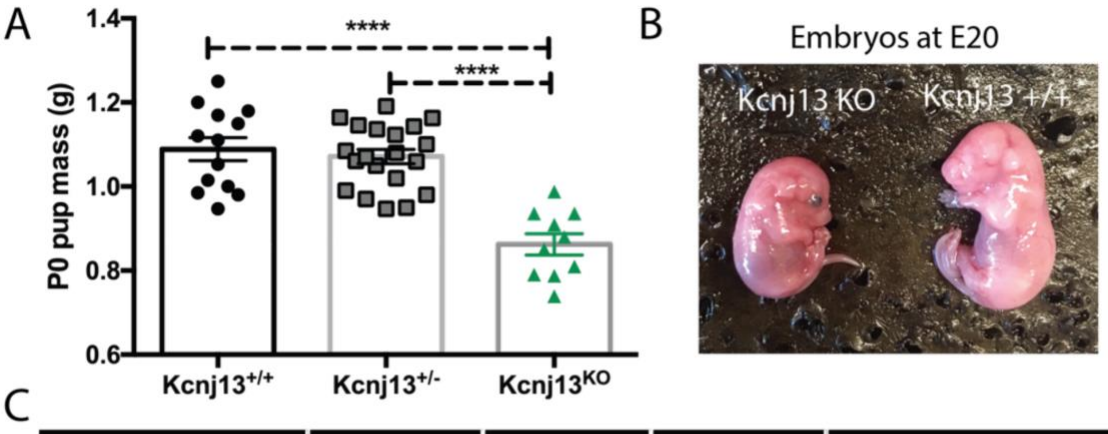


Figure S1 Creation of global and tissue-specific *Kcnj13* knockout mice.
Transgene construct and breeding strategy for promoter-driven, knockout-first, *Kcnj13* targeted germline transmissible line (*Kcnj13*^{KO}), crossed with Flp recombinase transgenic mice (FLP) and then with MC4R-t2a-Cre recombinase mutant mice (Cre) to generate a MC4R-Cre site-specific *Kcnj13* knockout (*Kcnj13ΔMC4R*^{Cre}) line.



C

Pup Genotype (P0)	Kcnj13 KO	Kcnj13+/-	Kcnj13+/+	Total Pups (10 litters)
Number	22	44	20	86
Ratio	0.26	0.51	0.23	

Figure S2 P0 lethality from homozygous deletion of Kir7.1 in mice
(A) Mass of P0 pups with genotypes *Kcnj13*$^{+/+}$, *Kcnj13*$^{+/-}$, and *Kcnj13*^{KO} (B) Representative gross pathology of *Kcnj13*^{KO} and *Kcnj13*$^{+/+}$ E20 embryos (C) Genotype distribution of offspring from *Kcnj13*$^{+/-}$ intercrosses examined by PCR (n = 10-20, ****P<0.0001, one-way ANOVA with Tukey's multiple comparisons test).

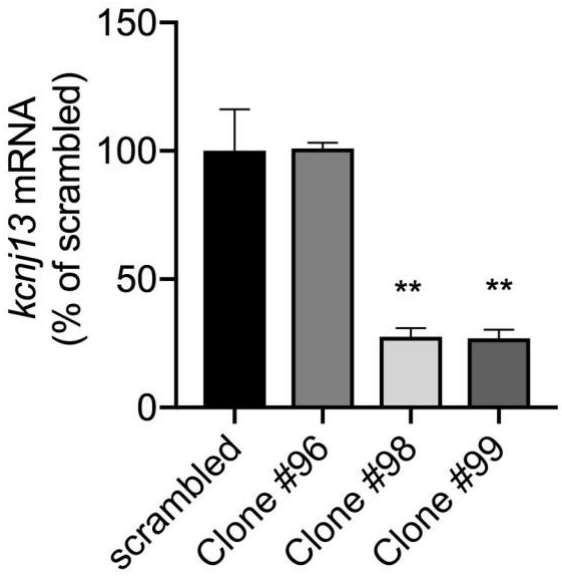


Figure S3 Validation of a lentiviral mouse *Kcnj13* shRNA vector. Lentiviral vectors were validated using HEK 293 cells transfected with a mouse *Kcnj13* expression vector. *Kcnj13* mRNA expression was measured in cells infected with three different *Kcnj13* shRNA viruses, and a control scrambled shRNA virus by qRTPCR, and normalized to β-actin mRNA levels. Data show the mean and SEM for 3 infections (unpaired t-test, **$p<0.01$). The clone #99 virus was used for all *Kcnj13 in vivo* knockdown experiments.

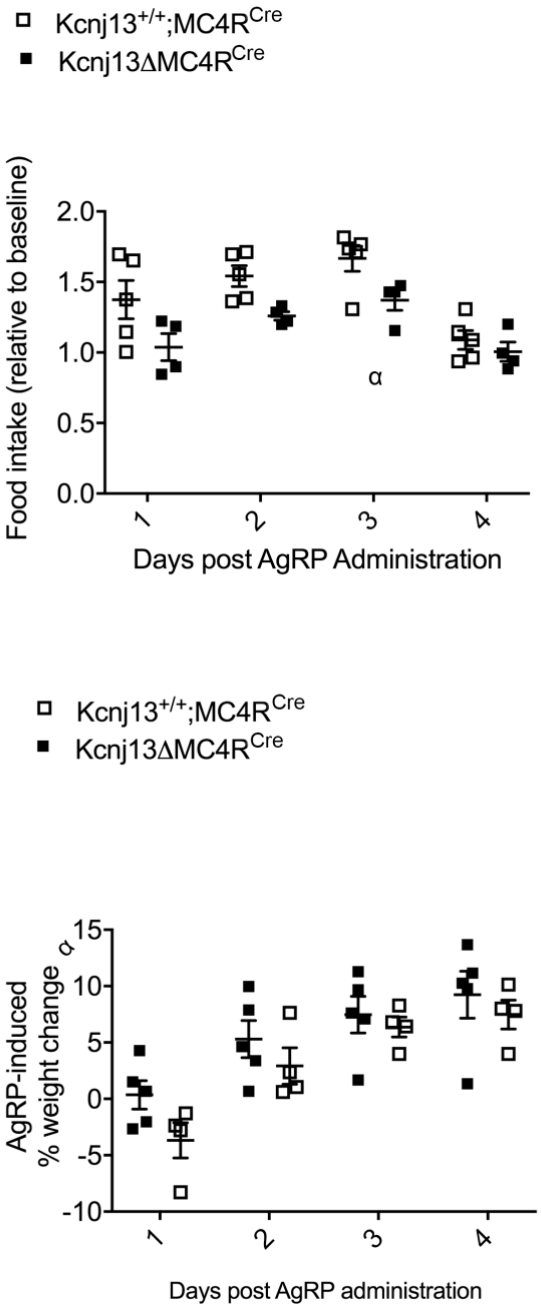


Figure S4 Normal orexigenic response to AgRP in *Kcnj13ΔMC4R^{Cre}* mice.
Change in chow consumption (top) and change in body weight (bottom) following intracerebroventricular administration of AgRP at a dose of 2nmol on day 0. Consumption on days "-2 and -1" were useds to calculate basal intake. AgRP increased intake, but no effect of geneotype was seen. (B) Weight gain was also observed, with no effect of geneotype on the effect. (n = 4-5/group, 2-way ANOVA with multiple comparions test).