Table S1, related to Figure 1. Effects of deleting βKlotho in nervous system on metabolic parameters.

	Klb$^{fl/fl}$	*Klb*$^{fl/fl}$/Tg	*Klb*^{Camk2a}	*Klb*^{Camk2a}/Tg
Plasma Glucose (mg/dl)	194±22	152±4.4*	172±11	195±16
Plasma Insulin (ng/ml)	46.6±22	2.0±0.3*	30.2±15	48.3±25
Plasma Cholesterol (mg/dl)	303±19	178±13*	256±20	259±20
Plasma Triglyceride (mg/dl)	77.3±1.1	68.6±3.8	83.6±3.2	85.3±5.2
Plasma Leptin (ng/ml)	70.1±9.1	25.8±7.8*	50.3±4.6	65.8±6.8
Hepatic Cholesterol	3.7±0.4	2.5±0.1*	2.9±0.2	3.3±0.3
Hepatic Triglyceride	86.9±17	14.7±2.9*	51.3±9.0	70.0±16

Measurements were made after 3 months on the high fat diet. Data are shown as the mean ± S.E.M. n=8-13/group. *p<0.05 compared to control (*Klb*$^{fl/fl}$ or *Klb*^{Camk2a}).

Figure S1

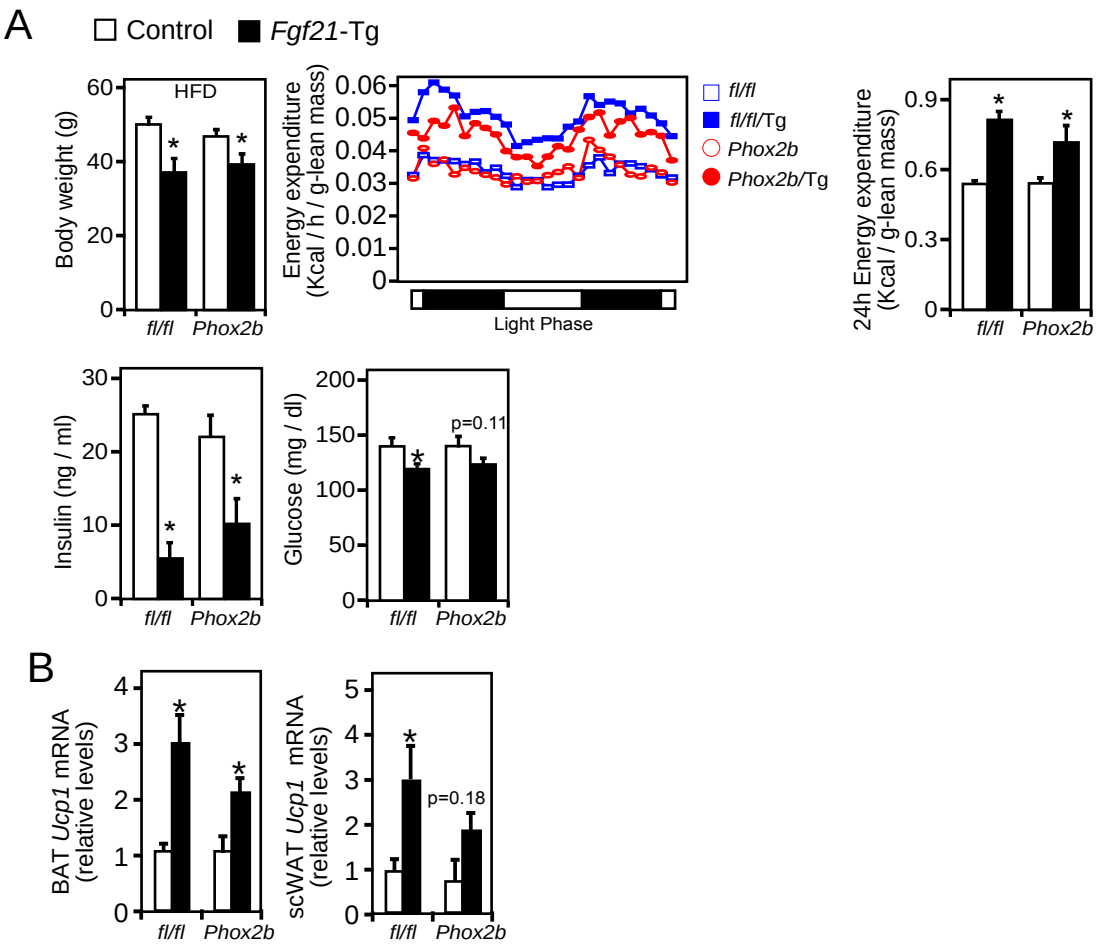
A
Control
Fgf21-Tg
HFD
Body weight (g)
fl/fl
Phox2b
Energy expenditure (Kcal / h / g-lean mass)
Light Phase
fl/fl
fl/fl/Tg
Phox2b
Phox2b/Tg
24h Energy expenditure (Kcal / g-lean mass)
Insulin (ng / ml)
Glucose (mg / dl)
p=0.11
B
BAT Ucp1 mRNA (relative levels)
scWAT Ucp1 mRNA (relative levels)
p=0.18

Figure S2

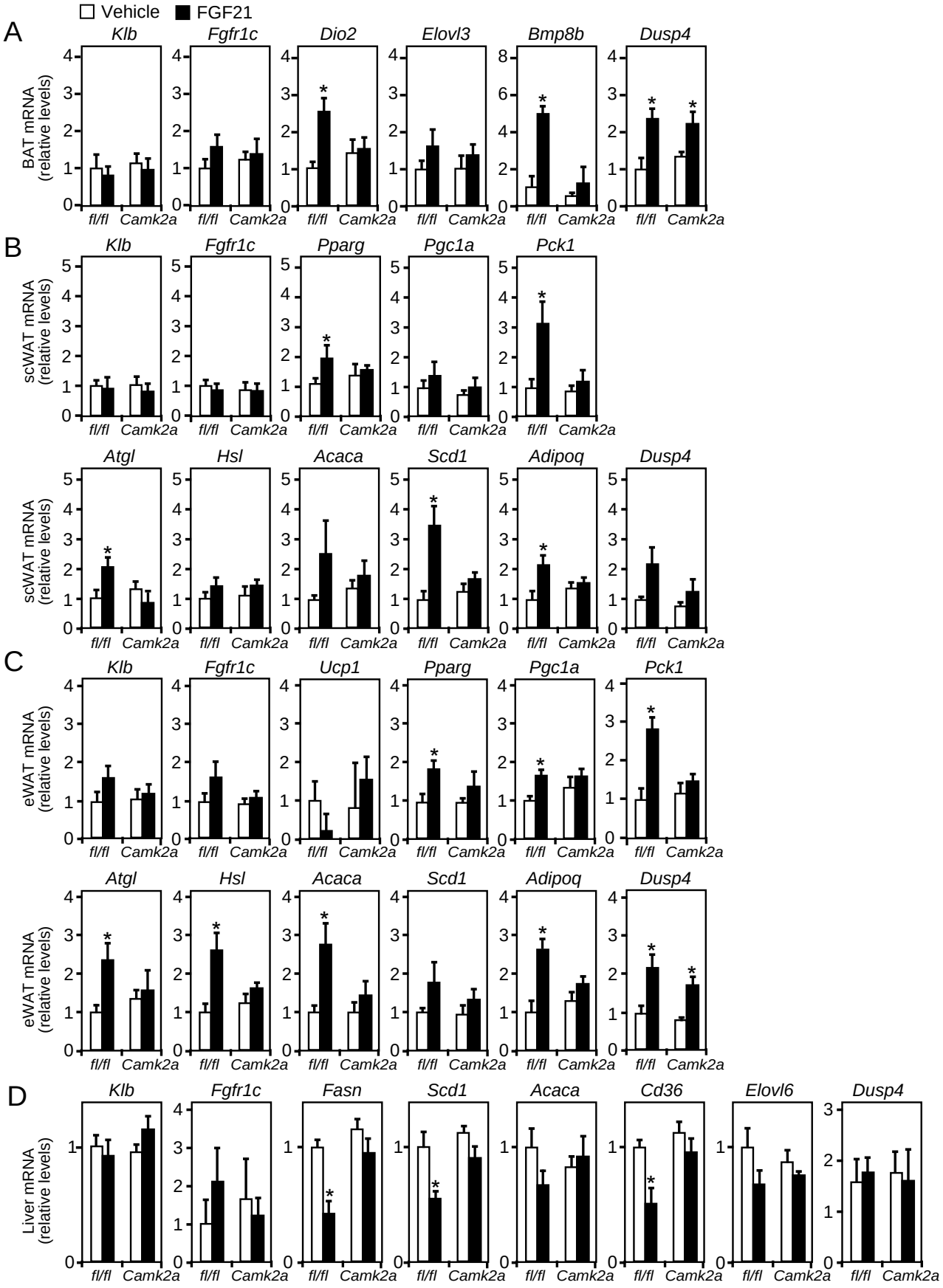
Vehicle
FGF21
A
Klb
Fgfr1c
Dio2
Elovl3
Bmp8b
Dusp4
BAT mRNA (relative levels)
B
Klb
Fgfr1c
Pparg
Pgc1a
Pck1
scWAT mRNA (relative levels)
Atgl
Hsl
Acaca
Scd1
Adipoq
Dusp4
C
Klb
Fgfr1c
Ucp1
Pparg
Pgc1a
Pck1
eWAT mRNA (relative levels)
Atgl
Hsl
Acaca
Scd1
Adipoq
Dusp4
D
Klb
Fgfr1c
Fasn
Scd1
Acaca
Cd36
Elovl6
Dusp4
Liver mRNA (relative levels)
fl/fl
Camk2a

Figure S1, related to Figure 1. FGF21 does not affect metabolic parameters in *Klb*^{Phox2b} mice.

(A) Body weight was measured in groups of *Klb*$^{fl/fl}$, *Klb*$^{fl/fl}$/Tg, *Klb*^{Phox2b} and *Klb*^{Phox2b}/Tg mice after 3 months on high fat diet (HFD). 24 hour heat production was measured starting 24 hours after switching mice to the HFD. Plasma insulin and glucose concentrations were made after 3 months on the HFD.

(B) Uncoupling protein 1 (*Ucp1*) gene expression was measured by QPCR in brown adipose tissue (BAT) and subcutaneous white adipose tissue (scWAT) in groups of *Klb*$^{fl/fl}$, *Klb*$^{fl/fl}$/Tg, *Klb*^{Phox2b} and *Klb*^{Phox2b}/Tg mice after 3 months on the HFD.

Data are the mean ± S.E.M. n=6-7/group. *p<0.05 compared to control.

Figure S2, related to Figure 3. *Klb* expression in the nervous system is required for the effects of recombinant FGF21 on gene expression in diet-induced obese mice.

(A-D) Gene expression was analysed by QPCR in (A) brown adipose tissue (BAT), (B) subcutaneous (sc) white adipose tissue (WAT), (C) epididymal (e) WAT, and (D) liver of *Klb*$^{fl/fl}$ and *Klb*^{Camk2a} mice administered either recombinant FGF21 (0.8 mg/kg/day) or vehicle by osmotic minipump for 2 weeks.

Data are the mean ± S.E.M. n=5-6/group. *p<0.05 compared to vehicle.