Supplemental Figure Legends

Supplemental Figure 1. Naringenin treatment stimulates Fgf21 mRNA expression and increases plasma FGF21 concentrations in Ldlr<sup>−/−</sup> mice.

Ldlr<sup>−/−</sup> mice, n = 12/group, were fed a chow diet, or a high-fat diet (HFD) alone or supplemented with naringenin (3%) for 4 weeks. Liver Fgf21 mRNA abundance by qRT-PCR from mice fasted for 6 hours (A). Plasma FGF21 concentration was determined by ELISA in animals fasted overnight (16 hours) (B). Values are the mean ± SEM. Different letters indicate statistical significance (P <0.05).

Supplemental Figure 2. Prevention of diet-induced weight gain in WT and Fgf21<sup>−/−</sup> mice by naringenin.

Male WT and Fgf21<sup>−/−</sup> mice were fed a chow diet, a high-fat diet (HFD), or a HFD supplemented with 3% naringenin for 16 weeks (n=6-7/group). A: Weight gain (g) over 16 weeks. B: Caloric intake expressed as kcal/mouse/day. C: Mean adipocyte diameter (µm) in epididymal adipose tissue. Values are the mean ± SEM. Different upper case letters indicate statistical significance among WT animals (P <0.05). Different lower case letters indicate statistical significance among Fgf21<sup>−/−</sup> mice (P <0.05). Asterisk (*) indicates statistical significance between genotypes (WT vs. Fgf21<sup>−/−</sup>) fed the same diet (P <0.05).

Supplemental Figure 3. Gene expression profiling in white adipose tissue of WT and Fgf21<sup>−/−</sup> mice.

mRNA abundance was measured in epididymal adipose tissue depots collected from male WT and Fgf21<sup>−/−</sup> mice fed a chow diet, a high-fat diet (HFD) or a HFD supplemented with 3% naringenin for 16 weeks (n=6-7/group). Values are the mean ± SEM (n=6-7/group) and are normalized to Actb, beta actin. Different upper case letters indicate statistical significance among WT animals (P <0.05). Different lower case letters indicate statistical significance among Fgf21<sup>−/−</sup> mice (P <0.05). Asterisk (*) indicates statistical significance between genotypes (WT vs. Fgf21<sup>−/−</sup>) fed the same diet (P <0.05).

Supplemental Figure 4. Gene expression profiling in livers of WT and Fgf21<sup>−/−</sup> mice.

mRNA abundance was measured in liver collected from male WT and Fgf21<sup>−/−</sup> mice fed a chow diet, a high-fat diet (HFD) or a HFD supplemented with 3% naringenin for 16 weeks (n=6-7/group). Values are the mean ± SEM (n= 6-7/group) and are normalized to Actb, beta actin. Different upper case letters indicate statistical significance among WT animals (P <0.05). Different lower case letters indicate statistical significance among Fgf21<sup>−/−</sup> mice (P <0.05).
Asterisk (*) indicates statistical significance between genotypes (WT vs. Fgl21<sup>−/−</sup>) fed the same diet ($P < 0.05$).
Supplemental Figure 1

A  
**Fgf21 mRNA**

![Bar graph showing Fgf21 mRNA levels across different dietary conditions.](image)

B  
**Plasma FGF21**

![Bar graph showing Plasma FGF21 levels across different dietary conditions.](image)
Supplemental Figure 2

A. Weight Gain over 16 weeks (g)

- Chow
- HFD
- HFD + Naringenin

B. Caloric Intake (Kcal/mouse/day)

- Chow
- HFD
- HFD + Naringenin

C. Mean Adipocyte Diameter (μm)

- Chow
- HFD
- HFD + Naringenin

* indicates statistical significance

WT vs. Fgf21−/−
Supplemental Figure 3

A  WAT Klb (β-klotho)

Gene expression (ratio to β-actin)

WT  Fgf21−/−

Chow  HFD  HFD + Naringenin

B  WAT Fgfr1

Gene expression (ratio to β-actin)

WT  Fgf21−/−

Chow  HFD  HFD + Naringenin

C  WAT Fgfr2

Gene expression (ratio to β-actin)

WT  Fgf21−/−

Chow  HFD  HFD + Naringenin

a, b, * denote statistical significance.
Supplemental Figure 4

A. Hepatic Klb (β-klotho)

- WT
- Fgf21−/−

Chow: A
HFD: A
HFD + Naringenin: a

B. Hepatic Fgfr1

- WT
- Fgf21−/−

Chow: A
HFD: a
HFD + Naringenin: AB

C. Hepatic Fgfr2

- WT
- Fgf21−/−

Chow: A
HFD: a
HFD + Naringenin: AB