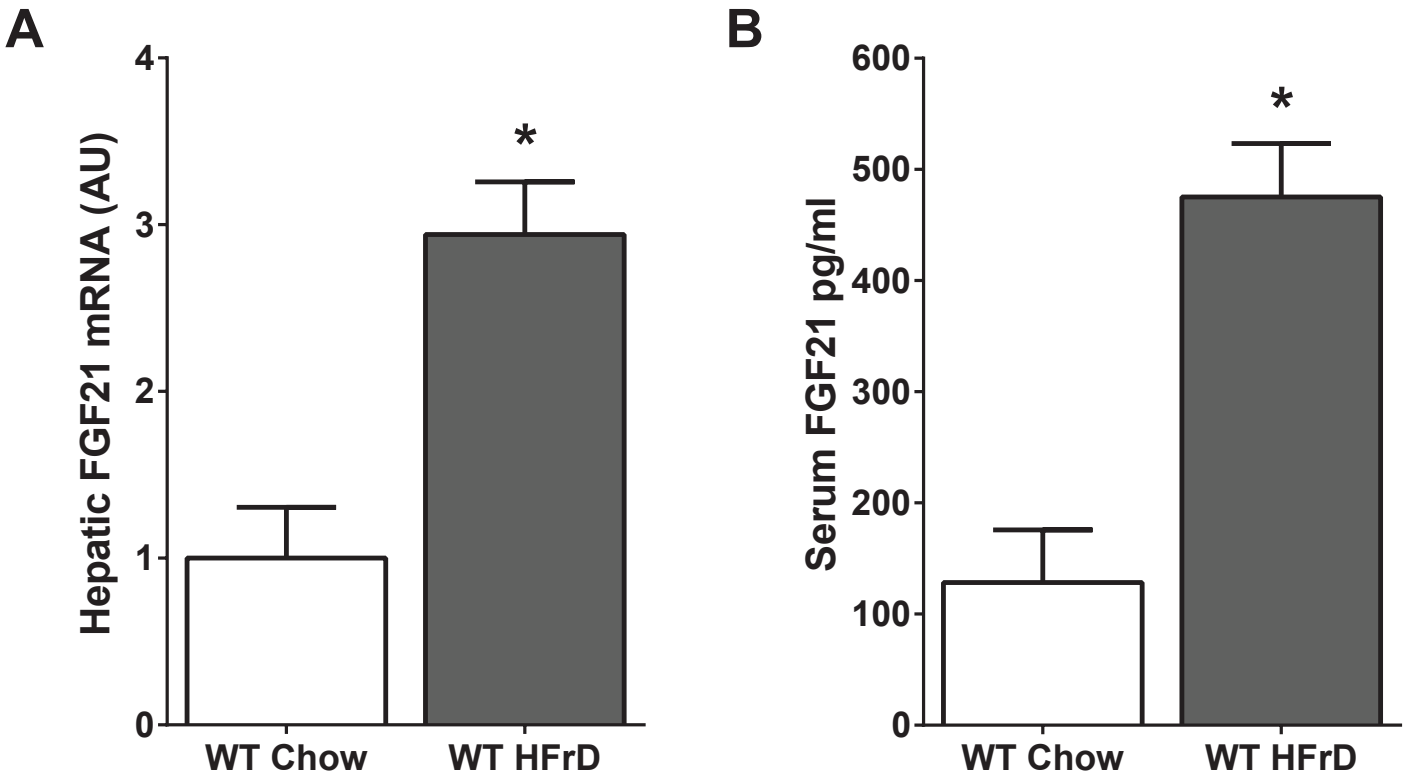
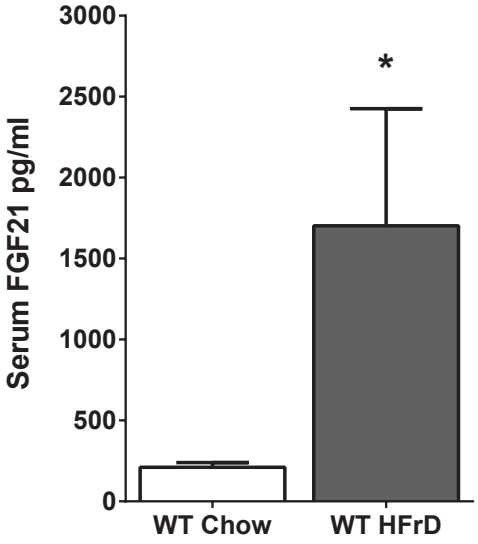
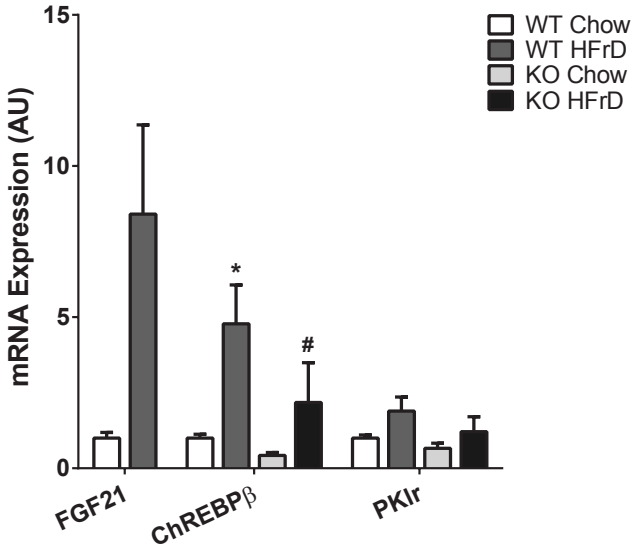
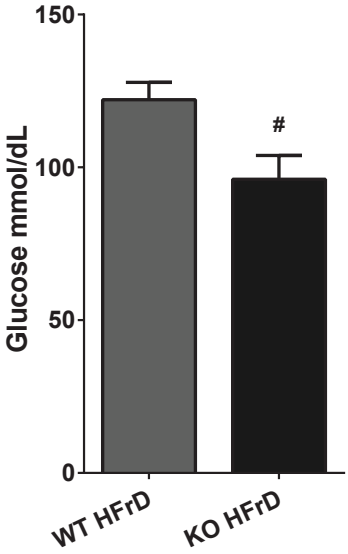


Supplemental Figure 1. FGF21 levels in wild type mice fed adlib fed a HFrD for 4 weeks. A) Hepatic FGF21 mRNA expression and B) circulating FGF21 levels are concomitantly increased. *P<0.05, Chow vs Fructose. n = 5-7 per group.

Supplemental Figure 2







Supplemental Figure 2. Acute response to HFrD in WT and FGF21 KO mice. Chow fed mice were fasted overnight and refed HFrD for 4 hours. A) Serum FGF21 levels were significantly elevated during this prandial phase. B) The induction of *ChREBP-β* was significantly attenuated in FGF21 KO mice. C) Fed serum glucose levels were significantly lower in FGF 21 KO mice consuming HFrD. *P<0.05, Chow vs Fructose for each genotype. #P<0.05, Fructose WT vs Fructose KO. n = 6 per group.

Human Subjects Data	
Subjects (M/F)	14 (9/5)
Age (Years)	36 ± 12
Waist circumference (cm)	89 ± 8
Body mass index (kg/m^2)	25.8 ± 3.1
Total cholesterol (mg/dL)	158 ± 17
LDL-C (mg/dL)	90 ± 22
HDL-C (mg/dL)	48 ± 17
Triglycerides (mg/dL)	114 ± 100
Apolipoprotein B (mg/dL)	77 ± 10
LDL size (mm)	21.1 ± 0.8
Fasting glucose (mg/dL)	86 ± 6
2 h OGTT glucose (mg/dL)	101 ± 26
Insulin (U/mL)	5.1 ± 5.5
HbA1C (%)	5.2 ± 0.4
hs-CRP (mg/L)	0.66 ± 0.06
FGF21 (pg/mL)	133 ± 104

Supplementary Table 1. Characteristics of human subjects. Values are shown as mean ± SD