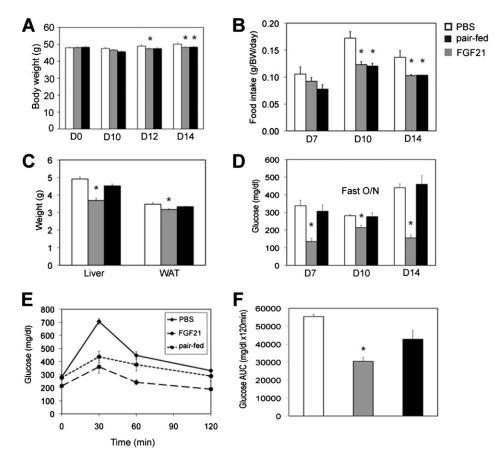
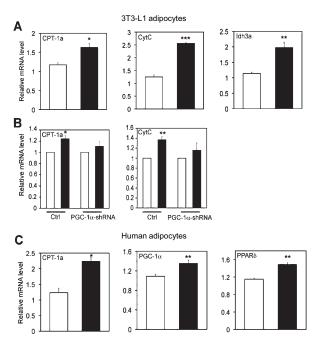
## **Supporting Information**

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**Fig. S1.** For 14 d, *ob/ob* mice (n = 8 animals/group) were treated with PBS (white bars) or 60 µg fibroblast growth factor 21 (FGF21) (gray bars) or were paired-fed (black bars). (A) Body weights of *ob/ob* mice. (B) Daily food intake normalized to body weight in treated animals. (C) Liver and epididymal fat (white adipose tissue, WAT) weights in *ob/ob* mice. (D) Daily blood glucose levels in *ob/ob* mice. (E) Plasma glucose levels of PBS-treated (solid line, diamonds), FGF21-dosed (dashed line, squares), and body weight-matched (small dashed line, circles) animals during oral glucose-tolerance test (OGTT). (F) Glucose area under the curve (AUC) above basal during OGTT. \*P < 0.05 (Student's *t* test).



**Fig. S2.** Effects of FGF21 on 3T3-L1 and human adipocyte gene expression. 3T3-L1 or human adipocytes were treated with PBS or FGF21 (4.0  $\mu$ g/mL) for 72 h. (A) Changes for gene expression were determined for *CPT-1a*, *CytC*, and *Idh3a* in 3T3-L1 cells. (B) Gene expression of *CPT-1a* and *CytC* in 3T3-L1 adipocytes transduced with adenovirus overexpressing shRNA against PGC-1a (alpha symbol). (C) Gene expression changes for *CPT-1a*, *PGC-1a* (alpha symbol), and *PPARd* (delta symbol) in human adipocytes. Data shown are from quantitative RT-PCRs, normalized to the housekeeping gene, TATA box binding protein. Data are averages of three independent experiments. \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001 (Student's *t* test).

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