Supporting Information

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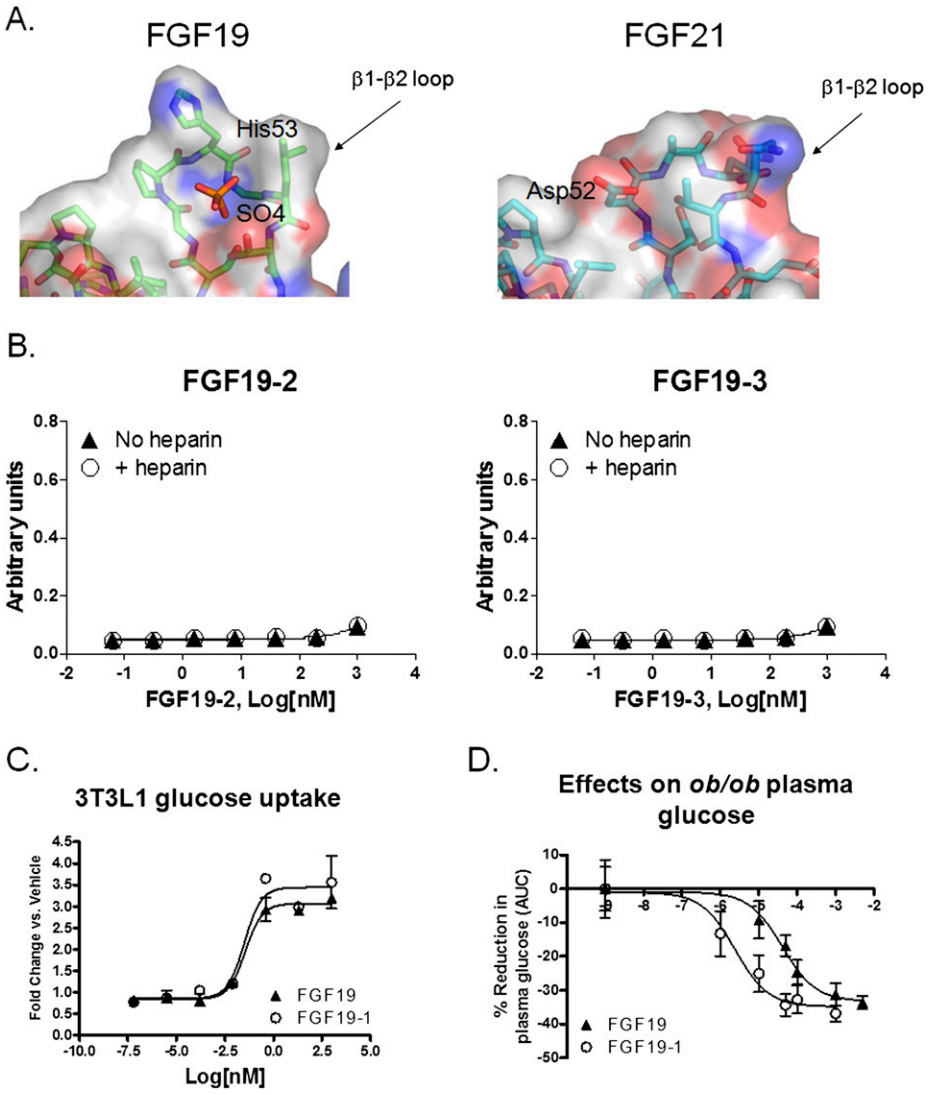

Fig. S1. Heparin-interacting regions of FGF19. (*A*) The β1-β2 loop region in apo-FGF19 structure (PDB code: 1PWA) and in the FGF21 model based on the FGF19 structure. The atomic color scheme is red for oxygen, blue for nitrogen, orange for sulfur, green for carbon in FGF19, and cyan for carbon in FGF21. (*B*) Solid-phase binding assay measuring the interaction between FGFR4 and FGF19-2 or FGF19-3 in the presence or absence of heparin. (*C*) Differentiated 3T3-L1 adipocytes were incubated for 72 h with recombinant FGF19 or FGF19-1 and were assayed for glucose uptake. (*D*) The *ob/ob* mice were injected with recombinant FGF19 ($n = 10$) or FGF19-1 ($n = 10$). Plasma glucose levels were measured between 3 and 7 h after injection and are plotted as area under the curve (AUC) during this time period.

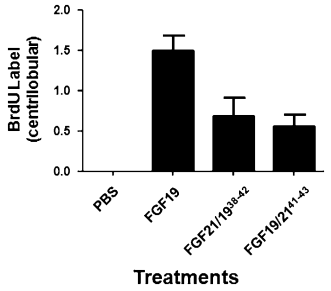

Fig. S2. Semiquantitative analysis of BrdU immunostaining of livers from female FVB mice treated for 6 d with PBS or 2 mg/kg/d recombinant FGF19, FGF21/19$^{38-42}$, or FGF19/21$^{41-43}$. The scores assigned to BrdU incorporation for these animals were based on a semiquantitative scale described in *Materials and Methods*.