



Supplementary information, Figure S6. MID1 mediates TFEB activity. (A) siRNA library screening for E3 ligases that modulate the activity of TFEB (measured by 4×CLEAR-Luc activity) in HepG2 cells. (B) Immunoblots showing the levels of UBR5, ASB3 and ubiquitinated MID1 in liver extracts from *Fgf21*^{+/+} and *Fgf21*^{-/-} mice fed or fasted for 24 h. (C) qPCR results showing relative hepatic levels of *Mid1* isoform 1 and isoform 2 in wildtype mice fed with a regular diet. (D) qPCR results in liver extracts from *Fgf21*^{+/+} and *Fgf21*^{-/-} mice fed or fasted for 24 h. (E-I), Immunoblots (E), qPCR results (F), LAMP1 staining (G) and quantification (H), and hepatic triglyceride content (I) showing the effect of *Mid1* knockdown in *Fgf21*^{-/-} mice fasted for 24

h. Scale bar, 10 μm . Data are shown as mean \pm s.e.m. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, n = 8 mice or 5 replicates for HepG2 cells per group.