**FIGRURE LEGENDS**

**Figure S1. Hepatic-specific knockout of HIF-2α had no impact on the body weight, glucose homeostasis in HFD-induced NAFLD mice.** Experiments were conducted after 12 weeks of HFD. (A) The body weight trends over a 12-week period. (B) Food intake of mice. (C) Glucose tolerance (GTT, with AUC) in HIF-2α *ALB cre* mice and HIF-2α *fl/fl* mice. (D) Insulin sensitivity (ITT, with AUC) in HIF-2α *ALB cre* mice and HIF-2α *fl/fl* mice. (E)) The epididymal fat-pad weight. (F) The inguinal fat weight. (G) Western Blot analysis of HIF-2α in the liver. (H) Western Blot analysis of HIF-2α in the muscle. (I)Western Blot analysis of HIF-2α in the intestine.

**Figure S2. Validation of HIF-2α overexpression.** (A) Western Blot analysis of HIF-2α. (B) Relative mRNA level of HIF-2α.

**Figure S2. Western Blot analysis of PI3K 110α and 110β.**