Supplementary Figure 1. Urinary ACR in m/m and db/db group (n = 8 in per group). Abbreviation: ACR: albumin-to-creatinine ratio. ***P < 0.001.

Supplementary Figure 2. qRT-PCR analysis showing the mRNA level of Mta2 in the kidneys (A) of m/m and db/db mice (n = 3 per group) and HK-2 cells treated with HG (B) or PA (C). All results are representative of three independent experiments. Values are presented as mean ± standard deviation. **P < 0.01; ***P < 0.001.
**Supplementary Figure 3.** (A) BDH1 protein expression levels after AAV9-Bdh1-GFP injection in all major organs in the mice body were detected. (B) Blood level of βOHB in mice from the indicated groups (n = 5 in m/m group, n = 4 in vector, and AAV-Bdh1-GFP injected db/db group). (C) Plasma TC in mice from the indicated groups (n = 5 in m/m group, n = 4 in vector, and AAV-Bdh1-GFP injected db/db group). (D) Plasma TG in mice from the indicated groups (n = 5 in m/m group, n = 4 in vector, and AAV-Bdh1-GFP injected db/db group). Abbreviations: BDH1: β-hydroxybutyrate dehydrogenase 1; TC: total cholesterol; TG: total triglyceride. **P < 0.01; ***P < 0.001; Abbreviation: ns: no significance.
Supplementary Figure 4. Body weight (A) and fasted blood glucose (B) of mice in the indicated groups (n = 5 in m/m group, n = 4 in vector, and AAV-Bdh1-GFP injected db/db group). Body weight (C) and fasted blood glucose (D) of mice in the indicated groups (n = 5 per group). Body weight (E) and fasted blood glucose (F) of mice in the indicated groups (n = 5 in m/m group; n = 4 in SD and KD groups).
Supplementary Figure 5. (A) Representative WB image showing the protein level of NRF2 protein in the cytoplasm of HK-2 cells transfected with NC siRNA or Bdh1 siRNA. (B) Representative WB images showing the protein level of NRF2 in the cytoplasm of BDH1-overexpressed HK-2 cells treated with HG or PA. (C) Representative WB images showing the protein level of NRF2 in the cytoplasm of βOHB-supplemented HK-2 cells treated with HG or PA. All results are representative of three independent experiments. Values are presented as mean ± standard deviation. Abbreviations: BDH1: β-hydroxybutyrate dehydrogenase 1; βOHB: β-hydroxybutyrate; WB: western blot; HG: high glucose; PA: palmitic acid. * P < 0.05; ** P < 0.01; *** P < 0.001.

Supplementary Figure 6. qRT-PCR analysis showing the NRF2 mRNA levels of βOHB-supplemented HK-2 cells treated with HG (A) or PA (B). All results are representative of three independent experiments. Values are presented as mean ± standard deviation. Abbreviation: ns: no significance.
Supplementary Figure 7. qRT-PCR analysis showing the mRNA levels of Gclm, Gpx4, and Sod2 in mice kidneys. (A) The mRNA levels of Gclm, Gpx4, and Sod2 in the kidneys of m/m group (n = 5), db/db + Vehicle (n = 4), and db/db + βOHB group (n = 4). (B) The mRNA levels of Gclm, Gpx4, and Sod2 in the kidneys of m/m group (n = 5), db/db + SD (n = 4), and db/db + KD group (n = 4). All results are representative of three independent experiments. Values are presented as mean ± standard deviation. Abbreviations: βOHB: β-hydroxybutyrate; SD: standard diet; KD: ketogenic diet. *P < 0.05; **P < 0.01; ***P < 0.001.

Supplementary Figure 8. (A) qRT-PCR analysis showing the mRNA level of Bdh1 in HK-2 cells, SV40-MES cells, and Mpc5 cells. (B) WB analysis showing the protein level of BDH1 in HK-2 cells, SV40-MES cells, and Mpc5 cells. ***P < 0.001.