Figure S1. Transfection efficiency of AAV9-shPFKFB3 and AAV-PFKFB3 in db/m mice. Protein levels of PFKFB3 in db/m, db/m + shPFKFB3 and db/m + PFKFB3 groups by (A) western blotting, with (B) semi-quantitative analyses (n=6). Data represent the mean ± SD from three independent experiments. **P<0.01 vs. db/m group by t-test. AAV, adeno-associated virus; sh, short hairpin; PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3.

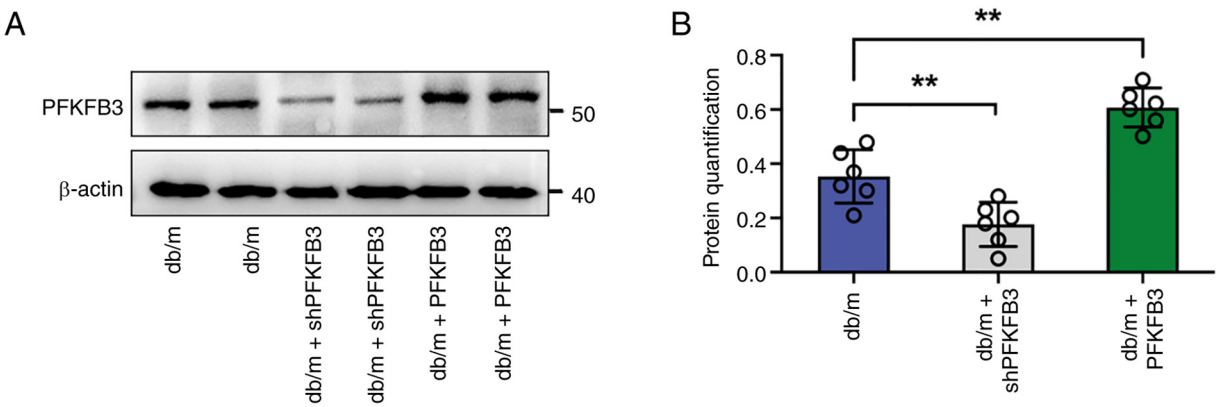

Figure S2. Overexpression of PFKFB3 promotes renal fibrosis in db/db mice. (A) Schematic illustration of PFKFB3 overexpression administration in the db/db group. Protein levels of α-SMA and FN in db/m, db/db and db/db + PFKFB3 groups by (B) western blotting, with (C) semi-quantitative analyses (n=6). (D) Representative images of Masson staining, Sirius red and IHC staining (α-SMA and FN level; scale bar, 50 $\mu$m) in db/m, db/db and db/db + PFKFB3 groups (n=6). Data represent the mean ± SD from three independent experiments. $^{**}$P<0.01 vs. db/db group by one-way ANOVA. PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3; α-SMA, α-smooth muscle actin; FN, fibronectin IHC, immunohistochemistry.

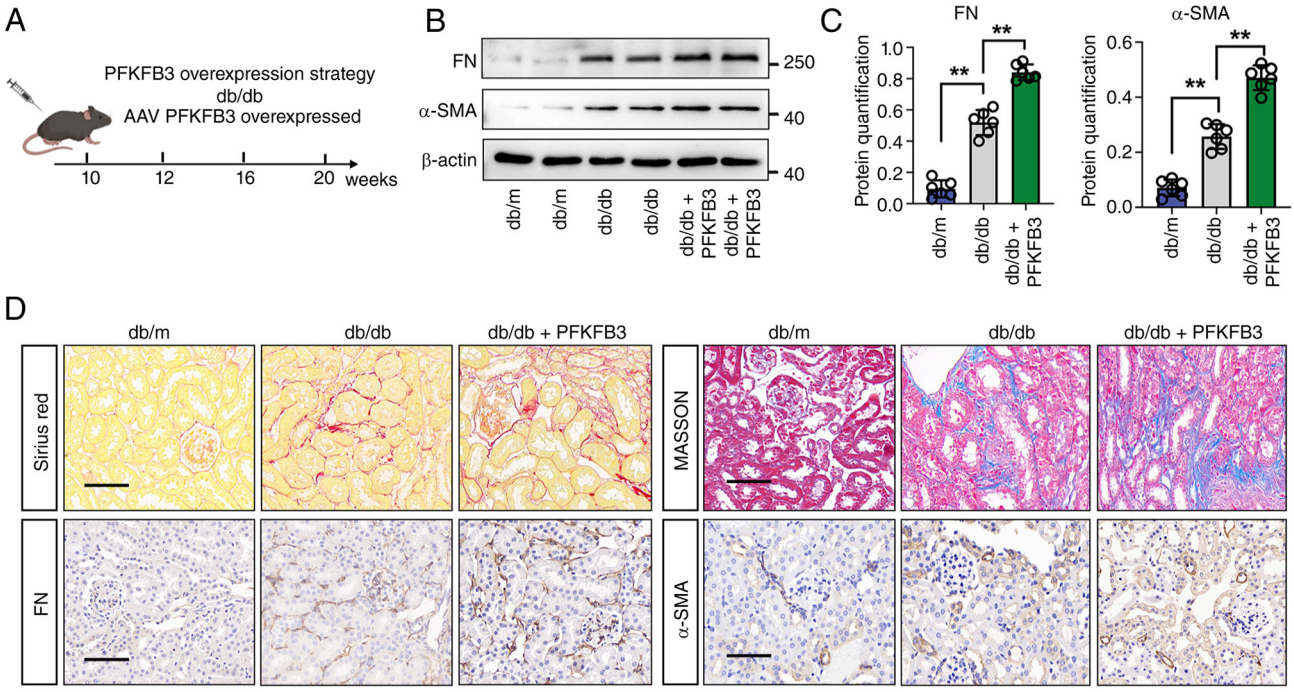

Figure S3. PFKFB3 mediated lactate accumulation in db/db mice. The lactate concentration in db/m, db/db, db/db + shPFKFB3 and db/db + PFKFB3 groups (n=8). Data represent the mean ± SD from three independent experiments. **P<0.01 vs. db/db or db/db+PFKFB3 group by one-way ANOVA. PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3.

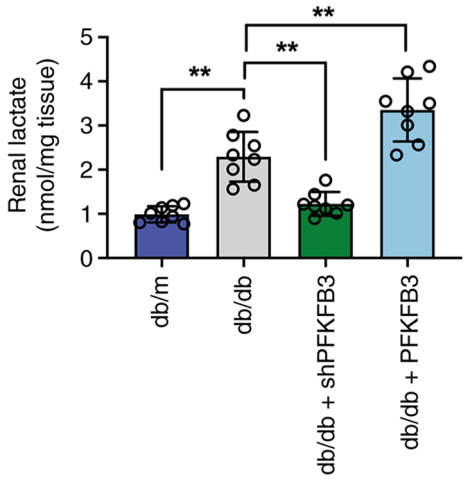

Figure S4. Transfection efficiency of siPFKFB3 in HK-2 cells under normal glucose condition. Protein levels of PFKFB3 in NG and NG + siPFKFB3 groups by (A) western blotting, with (B) semi-quantitative analyses (n=3). Data represent the mean ± SD from three independent experiments. **P<0.01 vs. NG group by t-test. PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3; si, small interfering; NG, normal glucose.