

Supplementary table

Supplementary table 1. Primers used for transcript quantification by RT-PCR

Gene ^a	Primer sequences (5'-3') ^b
Mus ANP F	TCGGAGCCTACGAAGATCCA
Mus ANP R	GTGGCAATGTGACCAAGCTG
Mus BNP F	GTTTGGGCTGTAACGCACTG
Mus BNP R	TTGTGGCAAGTTTGTGCTCC
Mus β -MHC F	CTTACTTGCTACCCTCAGGTGG
Mus β -MHC R	ATGGCTGAGCCTTGGATTCTC
Mus TGF- β F	TGGCCAGATCCTGTCCAAAC
Mus TGF- β R	CATAGATGGCGTTGTTGCGG
Mus Collagen I F	TTCTCCTGGCAAAGACGGAC
Mus Collagen I R	CTCAAGGTCACGGTCACGAA
Mus Collagen III F	CAAGGCTGCAAGATGGATGC
Mus Collagen III R	TGCACCAGAATCTGTCCACC
Mus sGC- β F	ACAGGTGTCTCATGTCTCCA
Mus sGC- β R	GTGCTCCTTGCTTGACACAC
Mus SGLT2 F	GCTGGATTTGAGTGGAATGC
Mus SGLT2 R	CGGTCAGATACTGGCACA
Mus Fis1 F	CAAAGAGGAACAGCGGGACT
Mus Fis1 R	ACAGCCCTCGCACATACTTT
Mus Drp1 F	ATGCCAGCAAGTCCACAGAA
Mus Drp1 R	TGTTCTCGGGCAGACAGTTT
Mus Mfn1 F	GCAGACAGCACATGGAGAGA
Mus Mfn1 R	GATCCGATTCCGAGCTTCCG
Mus Mfn2 F	TGCACCGCCATATAGAGGAAG
Mus Mfn2 R	TCTGCAGTGAAGTGGCAATG
Mus β -actin F	CCTCTATGCCAACACAGTGC
Mus β -actin R	ACATCTGCTGGAAGGTGGAC

^a Mus, mouse; ^b F, forward primer; R, reverse primer.

Supplementary table 2. General and echocardiographic features of db/db mice with or without insulin treatment.

	db/db	db/db+insulin
Body weight (g)	49.67±3.89	51±3.69
Blood glucose (mmol/L)	27.03±2.84	16.40±2.90***

HW/TL (mg/mm)	10.69±1.40	10.34±0.81
EF (%)	54.73±5.28	51.02±4.74
FS (%)	29.58±3.65	27.68±2.93
IVRT (ms)	23.46±2.50	24.92±3.17
DT (ms)	33.54±3.69	35.66±2.86
E/A	1.26±0.22	1.19±0.15

Mice in the db/db+insulin group (n=6) were injected the adjusted dose of insulin glargine (Sanofi-Aventis Pharmaceuticals, NJ) subcutaneously. Mice in the db/db (n=6) group were injected the same volume of normal saline as the db/db+insulin group. Data are presented as mean±SD, n=8 per group. *** $P<0.001$ represents significant differences between db/db and db/db+insulin mice. Abbreviations: DT, deceleration time; E/A, velocity of early mitral flow to velocity of late mitral flow ratio; EF, ejection fraction; FS, fraction shortening; HW/TL, heart weight to tibia length ratio; IVRT, isovolumetric relaxation time.

Supplementary figures

Supplementary figure 1

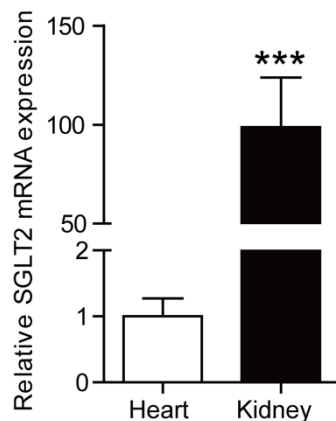


Figure S1. Relative mRNA expression of SGLT2 in heart and kidney. Data are presented as mean±SD, n=6 per group. *** $P<0.001$ represents significant differences between heart and kidney.

Supplementary figure 2

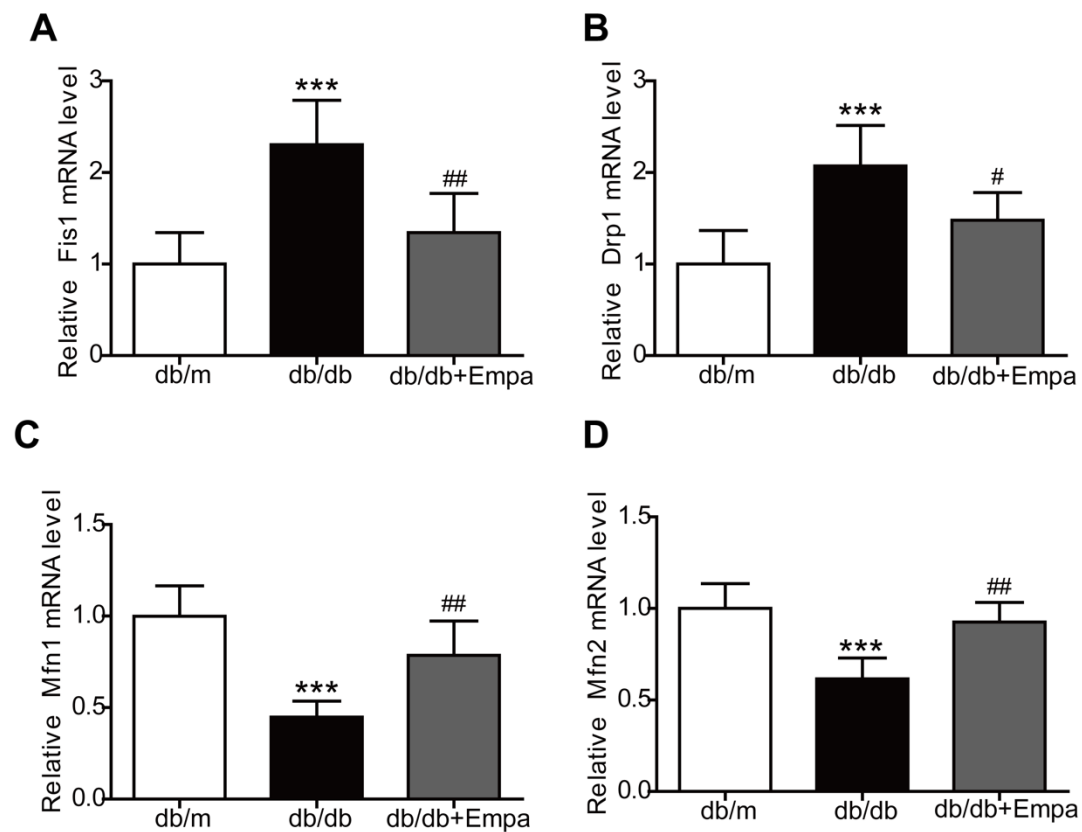


Figure S2. Changes in proteins related to mitochondrial dynamics. (A-D) mRNA expression of Fis1, Drp1, Mfn1 and Mfn2 was measured by quantitative RT-PCR, n=6 per group. *** $P < 0.001$ represents significant differences between db/m and db/db mice; ## $P < 0.01$ and # $P < 0.05$ represent significant differences between db/db and db/db+Empa. Abbreviations: Drp1, Dynamin related protein 1; Fis1, fission; Mfn1, mitofusin 1; Mfn2, mitofusin 2.

Supplementary figure 3

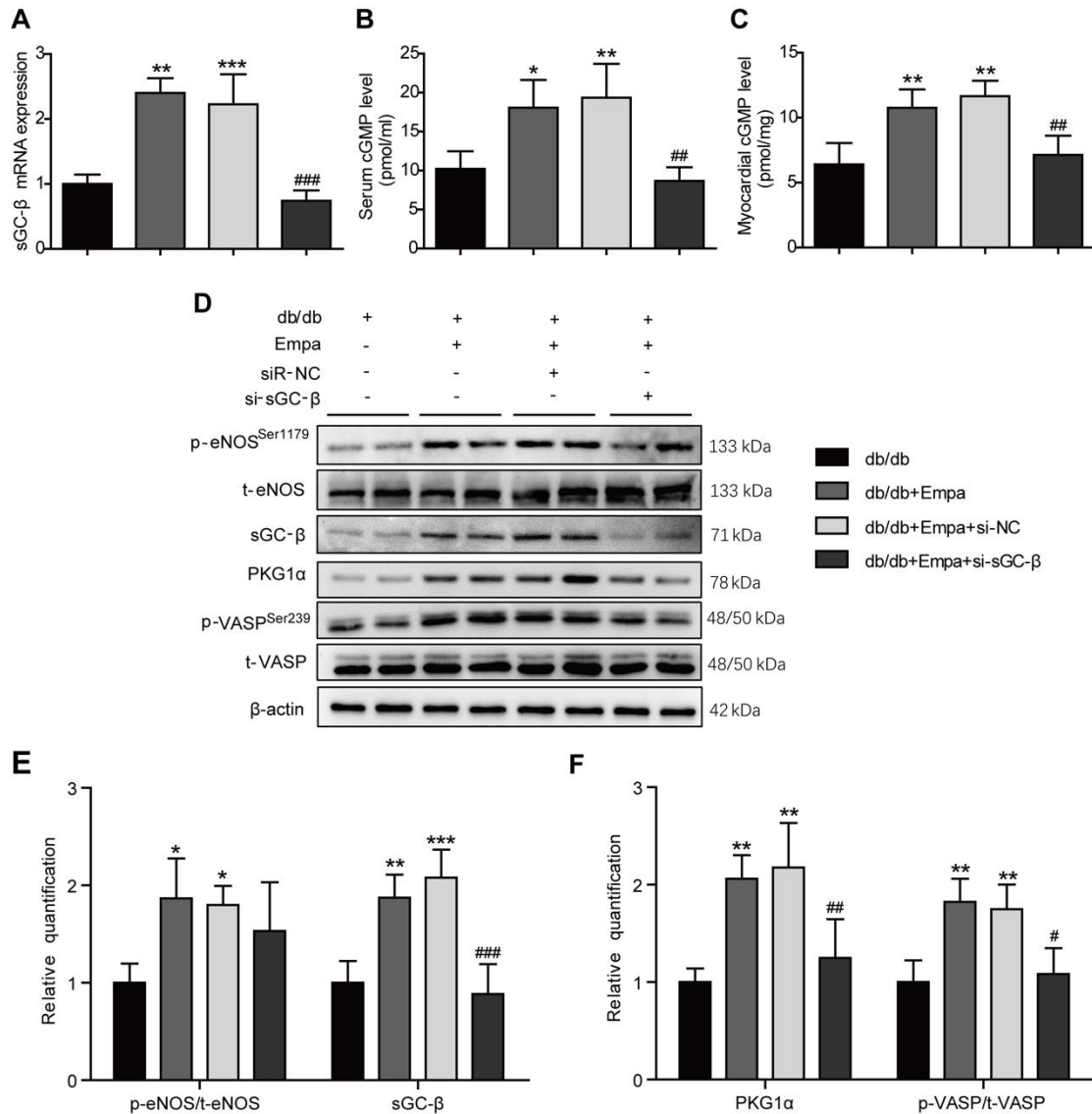


Figure S3. Downregulation of sGC-β undermined the effect of empagliflozin on diabetic heart. (A) mRNA expression of sGC-β was measured by quantitative RT-PCR after transfection in different groups, n=6 per group. (B-C) Representative levels of cGMP in serum and myocardium were evaluated by Elisa, n=4 per group. (D) Protein expression of p-eNOS, t-eNOS, sGC-β, PKG1α, p-VASP and t-VASP in myocardium were determined by western blot. (E-F) Quantitative analysis of p-eNOS/t-eNOS, sGC-β, PKG1α and p-VASP/t-VASP for western blot, n=4 per group. Data are presented as mean±SD. *** $P < 0.001$, ** $P < 0.01$ and * $P < 0.05$ represent significant differences between db/db and db/db+Empa mice; ### $P < 0.001$,

$P < 0.01$ and # $P < 0.05$ represent significant differences between db/db+Empa+si-NC and db/db+Empa+si-sGC- β .