

SUPPLEMENTARY TABLES

Table S1 List of primers used for quantitative real-time PCR in our study.

| S.No. | Gene | Forward primer (5' to 3') | Reverse primer (5' to 3') | T _a (°C) |
|-------|--|------------------------------|-----------------------------|---------------------|
| 1 | RPL32 | AGATTCAAGGGCCAGATCCT | CGATGGCTTTTCGGTTCTTA | 57 |
| 2 | SIRT1 | TGACTTCAGATCAAGAGATGGT AT | TGGCTTGAGGATCTGGGAGAT | 58 |
| 3 | SIRT3 | GCTGCCAGCAAGGTTCTTAC | CCTTTCCACACCCTGGACTA | 57 |
| 4 | NRF1 | GCTCTTTGAGACCCTGCTTTC | GTGGAGTTGAGTATGTCCGAGT | 56 |
| 5 | NRF2 | AACCAGAAGCACACTGAAGG | CCATTTCCGAGTCACTGAAC | 57 |
| 6 | PGC-1α | ATGTGTCGCCTTCTTGCTCT | ATCTACTGCCTGGGGACCTT | 57 |
| 7 | TFAM | AGCTGATGGGCTTAGAGAAGG | ATTTCCCCTGAGCTGACTCAT | 62 |
| 8 | Mt-ND1 | AAAGAACCATAACGCCCTCT | GGCTCATCCCGATCATAGAA | 57 |
| 9 | Mt-ND2 | AAGCCCACGATCAACTGAAG | GTCAGTAGTGAATGGGGCT | 57 |
| 10 | Mt-ND6 | TACAACCAACATCCCACCCA | GTTGTCTAGGGTTGGCGTTG | 57 |
| 11 | Mt-CO-II | TTCCTCATCAGCTCCCTAGT | GTAGGGAGGGAAGGGCAATT | 57 |
| 12 | Mt-CO-III | ATGACCACTAACAGGAGCCC | GTGGTGGCCTTGGTATGTTT | 57 |
| 13 | Mt-ATP6 | AGCAAACATTACAGCAGGCC | ACAGGCTGACTAGAAGGGTG | 57 |
| 14 | Mt-ATP8 | GCCACAACACTAGACACATCCAC | GGGGTAATGAAAGAGGCAAAT AG | 57 |
| 15 | Mfn1 | GAGGGAAGACCAAATCGACA | CAAAACAGACAGGCGACAAA | 58 |
| 16 | Mfn2 | AGGAAATTGCTGCCATGAAC | GTCTCTTCTCGGTGCAGGTC | 58 |
| 17 | Drp1 | TCCAATTCCATTATCCTTG | TCAATACATCCATGGCATCA | 58 |
| 18 | Opa1 | AAAATCAGAAAAGCCCTTCC | TTTCGGATCCATGATCTGTT | 57 |
| 20 | MMP2 | GGGTGGTGGTCACAGCTATT | CGGTGTGCAGTGAAGATTGT | 57 |
| 21 | MMP9 | CCACCGAGCTATCCACTCAT | GTCCGGTTTCAGCATGTTTT | 57 |
| 22 | COLLAGEN-I | CTCAAGAGCGGAGAATAC | ATCTGTCCACCAGTGCTT | 54 |
| 23 | ANP | AGCGAGCAGACCGATGAAG | AGCCCTCAGTTTGGCTTTTCA | 57 |
| 24 | BNP | GACCAAGGCCCTACAAAAGA | CCCAAAGCAGCTTGAACATATG | 53 |
| 25 | β-MHC | TGGAGCTGATGCACCTGTAG | ACTTCGTCTCATTGGGGATG | 55 |
| 26 | β2-microglobulin | ACTGCTACGTGTCTCAGTTCC | CTCCTTCAGAGTGACGTGTTT | 57 |

Table S2 List of antibodies used for western blotting in our study

| S.No. | Name of the antibody | Cat. No. | Dilution |
|-------|----------------------|----------|----------|
| 1 | Sirt1 | 9475S | 1:1000 |
| 2 | Sirt3 | Ab189860 | 1:1000 |
| 3 | PGC-1 α | Ab191838 | 1:1000 |
| 4 | TFAM | Ab131607 | 1:2500 |
| 5 | NRF1 | 69432S | 1:1000 |
| 6 | NRF2 | Ab137550 | 1:1000 |
| 7 | SOD2 | 13141S | 1:2500 |
| 8 | Ac-SOD2 | Ab137037 | 1:1000 |
| 9 | Catalase | Ab52477 | 1:1000 |
| 10 | OXPPOS | Ab110413 | 1:250 |

| | | | |
|----|----------------|----------|--------|
| 11 | Mfn1 | Ab104274 | 1:1000 |
| 12 | Mfn2 | Ab50838 | 1:1000 |
| 13 | Drp1 | 8570S | 1:1000 |
| 14 | Opa1 | 80471S | 1:1000 |
| 15 | GAPDH | 8884S | 1:5000 |
| 16 | β -Actin | Ab8227 | 1:5000 |

Table S3 Shown the composition of diets used in the study.

| S.No. | Name of the ingredient | Quantity in Corn starch diet | | Quantity in High fructose diet | |
|-------|------------------------|------------------------------|------|--------------------------------|------|
| | | Gm | Kcal | Gm | Kcal |
| 1 | Casein | 200 | 800 | 200 | 800 |
| 2 | DL-Mthionine | 3 | 12 | 3 | 12 |
| 3 | Corn Starch | 650 | 2600 | 0 | 0 |
| 5 | Fructose | 0 | 0 | 650 | 2600 |
| 6 | Cellulose, BW200 | 50 | 0 | 50 | 0 |
| 7 | Corn oil | 50 | 450 | 50 | 450 |
| 8 | Mineral Mix S1001 | 35 | 0 | 35 | 0 |
| 9 | Vitamin Mix V1001 | 10 | 40 | 10 | 40 |
| 10 | Choline bitartarate | 2 | 0 | 2 | 0 |
| 11 | FD&C Blue dye#1 | 0.2 | 0 | 0 | 0 |
| 12 | FD& Red dye#40 | 0 | 0 | 0.2 | 0 |

SUPPLEMENTARY FIGURES

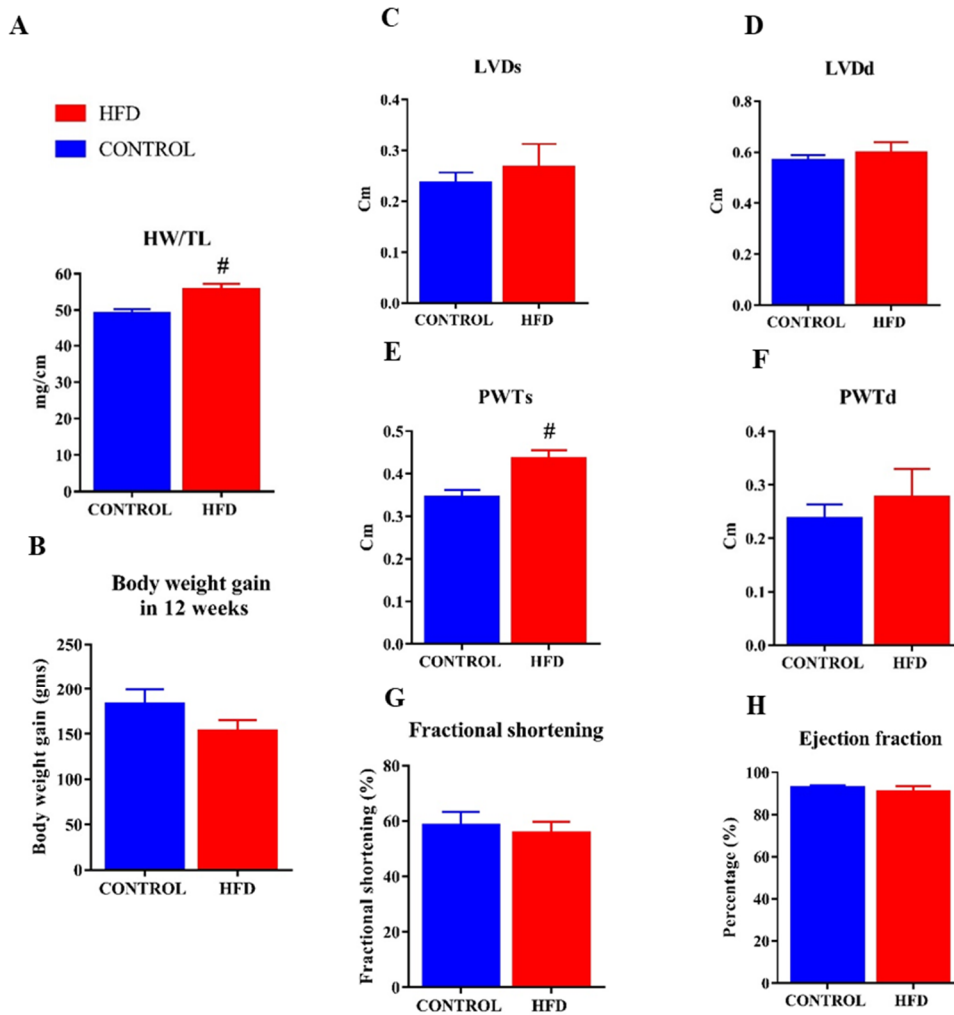


Figure S1. Twelve weeks of high fructose diet feeding induces cardiac hypertrophy without affecting cardiac functional parameters. **A** Heart weight to body weight ratio. **B** Body weight change. **C** Left ventricular internal diameter during systole (LVD_s). **D** Left ventricular internal diameter during diastole (LVD_d). **E** Posterior wall thickness during systole (PWT_s). **F** Posterior wall thickness during diastole (PWT_d). **G** Fractional shortening. **H** Ejection fraction. Data was represented as Mean ± SEM, #p<0.05 vs Control, ##p<0.01 vs Control, (N=5).

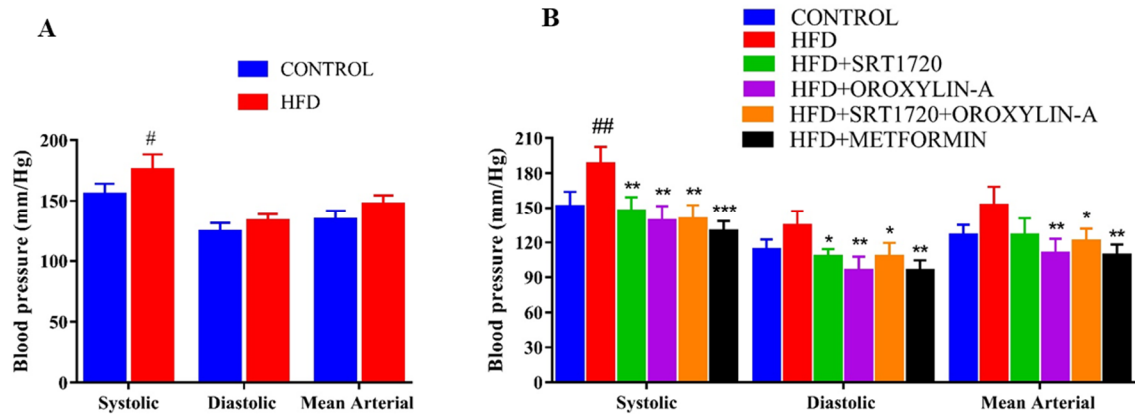


Figure S2 Sirtuin activation reduces high fructose diet-induced blood pressure in rats. A Systolic, diastolic, and mean arterial blood pressure at 12 weeks of high fructose feeding. **B** Systolic, diastolic and mean arterial blood pressure after 8 weeks of treatment with sirtuin activators. Data was represented as Mean \pm SEM, [#] $p < 0.05$ vs Control, ^{##} $p < 0.01$ vs Control, ^{*} $p < 0.05$ vs HFD, ^{**} $p < 0.01$ vs HFD, ^{***} $p < 0.001$ vs HFD, (N=5).

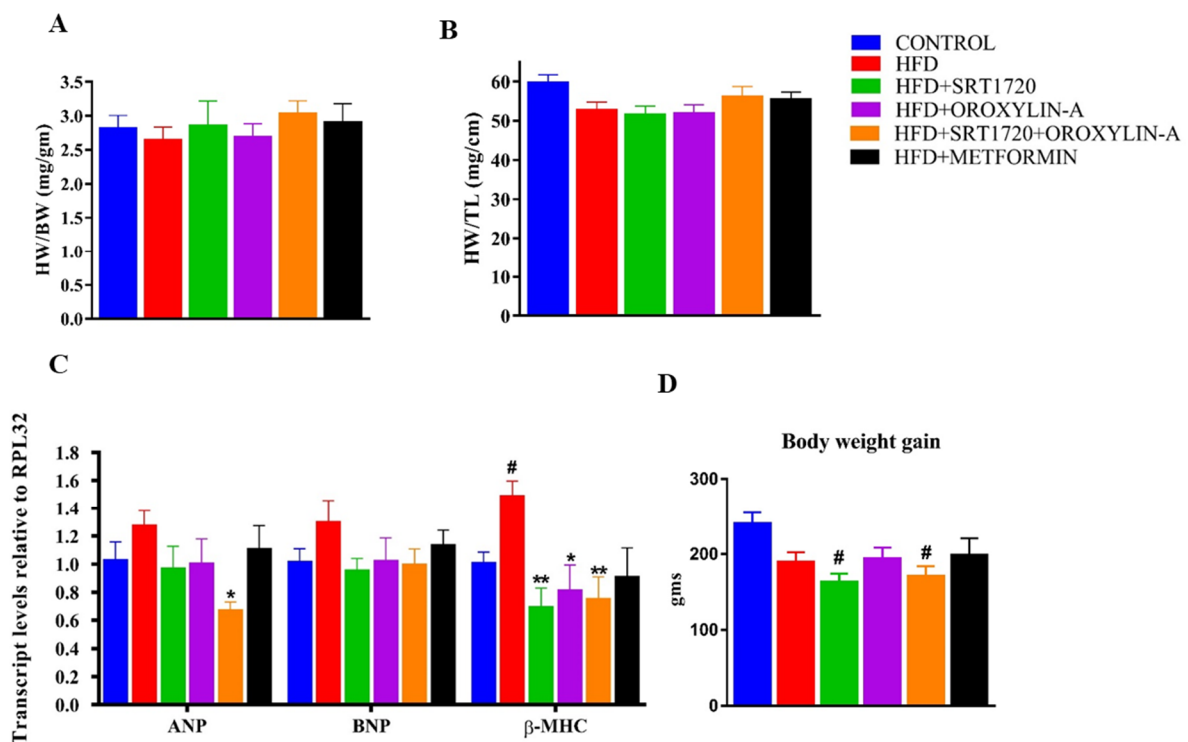


Figure S3 Sirtuin activation ameliorates high fructose diet-induced cardiac hypertrophy in rats. A Heart weight to body weight ratio. **B** Heart weight to tail length ratio. **C** Fetal hypertrophic gene transcripts levels. **D** Body weight change. Data were represented as Mean \pm SEM, [#] $p < 0.05$ vs Control, ^{*} $p < 0.05$ vs HFD, ^{**} $p < 0.01$ vs HFD, (N=5).

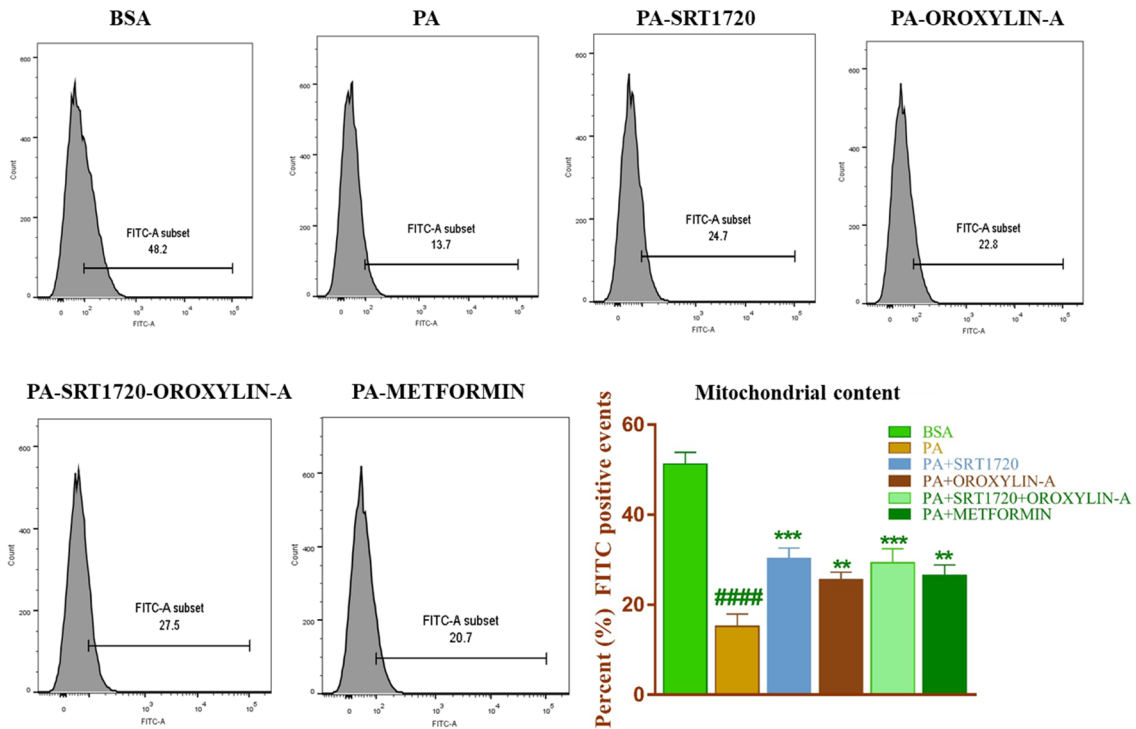


Figure S4 Sirtuin activation enhances mitochondrial content in palmitate-induced insulin resistant cardiomyoblast (H9c2) cells. Effect of sirtuin modulation on mitochondrial content. ### $p < 0.001$ vs BSA, ** $p < 0.01$ vs PA, *** $p < 0.001$ vs PA, (n=3).

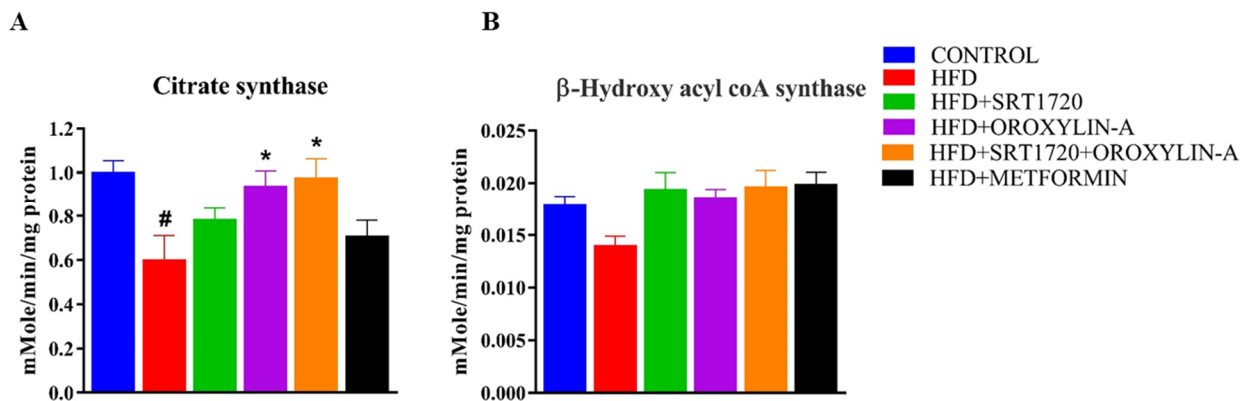


Figure S5 Sirtuin activation ameliorates high fructose diet-induced perturbation of mitochondrial enzymatic activity in diabetic rat heart. **A** Citrate synthase activity. **B** β -hydroxy acyl CoA dehydrogenase activity. Data was represented as Mean \pm SEM, # $p < 0.05$ vs Control, * $p < 0.05$ vs HFD, (N=5).

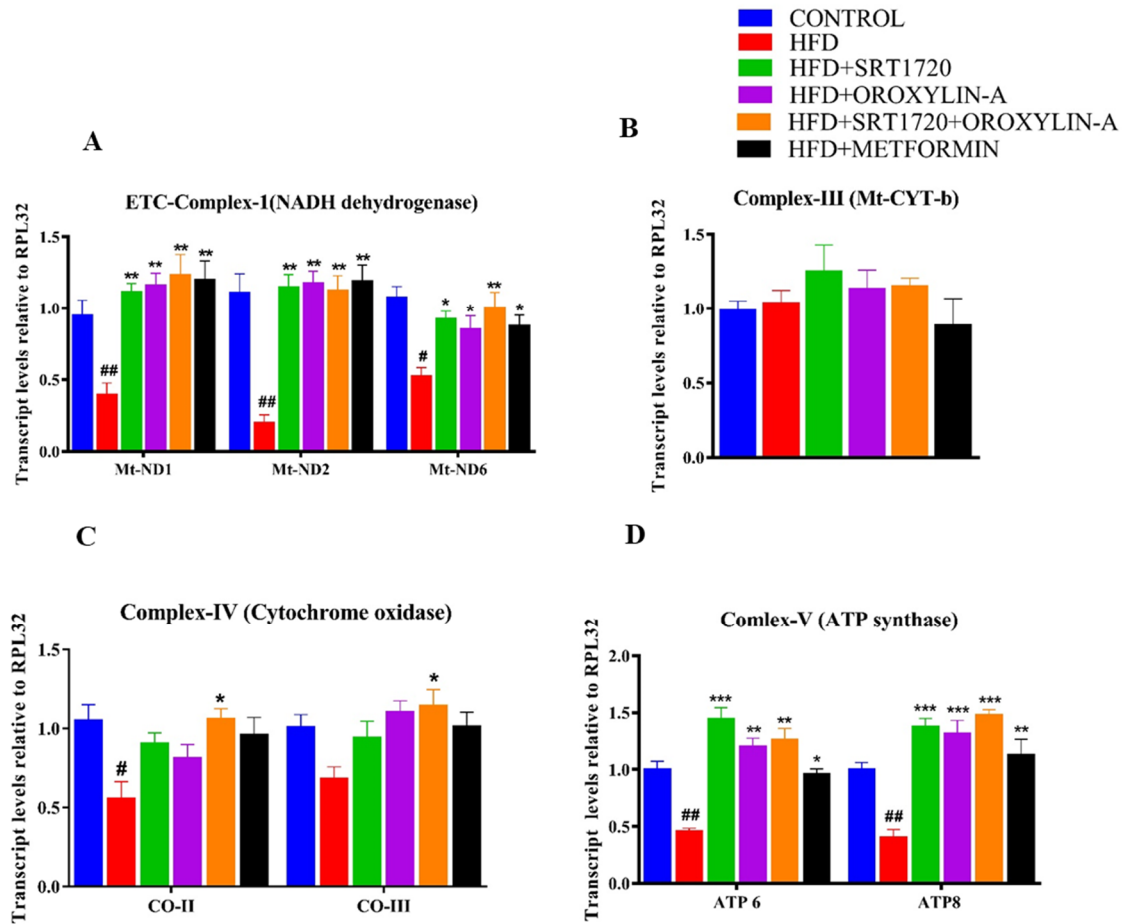


Figure S6 Sirtuin activation enhances mitochondrial DNA-encoded ETC complex gene expression in high fat diet-induced diabetic rats. **A** ETC complex-I (NADH dehydrogenase) subunit mRNA expression (ND1, ND2, ND6). **B** ETC complex-III (cytochrome reductase) subunit mRNA expression (Cyto-b). **C** ETC complex-IV (Cytochrome oxidase) subunit mRNA levels (Cytochrome oxidase-II and III). **D** ETC complex-V (ATP-synthase) subunit (ATP6 and ATP8) mRNA levels. Data was represented as Mean \pm SEM, # p <0.05 vs Control, ## p <0.01 vs Control, * p <0.05 vs HFD, ** p <0.01 vs HFD, *** p <0.001 vs HFD, (N=5).

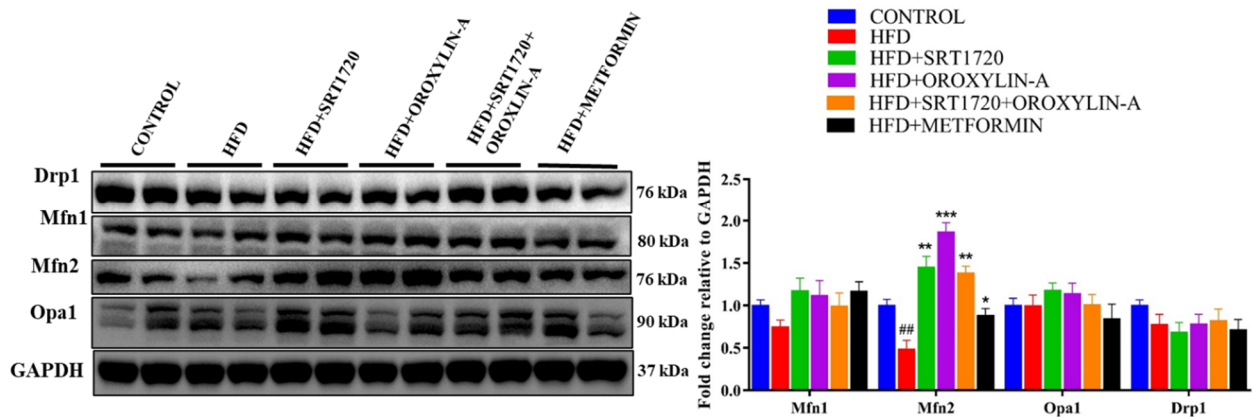


Figure S7 Sirtuin activation ameliorates high fructose diet-induced perturbation of mitochondrial dynamics in diabetic rat heart. A Mitochondrial dynamics-related protein expression. Data was represented as Mean \pm SEM, ### p <0.01 vs Control, * p <0.05 vs HFD, ** p <0.01 vs HFD, *** p <0.001 vs HFD, (N=4), (Blots were developed from different gels due to same molecular weight equal amount of proteins were loaded into gels).

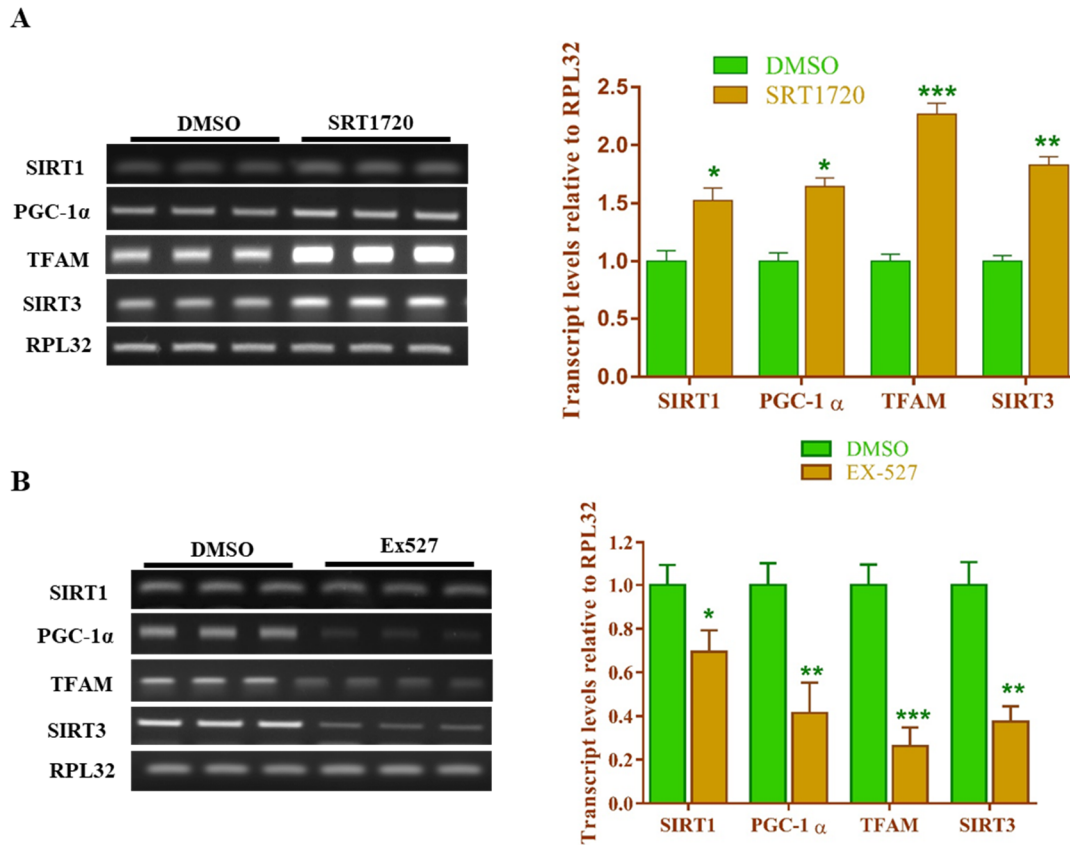


Figure S8 Sirt1 modulation regulates mitochondrial biogenesis-related genes and Sirt3 in rat cardiomyoblast (H9c2). (A) Mitochondrial biogenesis-related gene expression in Sirt1 activation condition. (B) Mitochondrial biogenesis related gene expression in Sirt1 inhibition condition. Data were represented as Mean \pm SEM, * p <0.05 vs DMSO, ** p <0.01 vs DMSO, n=3.