SUPPLEMENTAL DATA

Supplemental methods

Animals and diets

All procedures involving animals were approved by the Institutional Animal Care and Use Committees at Temple University and Columbia University. The mice were maintained under appropriate barrier conditions in a 12h light-dark cycle and received food and water *ad libitum*. Male C57BL/6 (6 weeks), *db/db* (6 weeks) and *Ppara*$^{-/-}$ (8 weeks) mice were obtained from the Jackson Laboratory and fed on chow diet supplemented with tesaglitazar or combination of tesaglitazar and resveratrol. The *aMHC-Sirt1*$^{-/-}$ (6 weeks; male) mice have been previously described (1). All diets were purchased from Bio-Serv and they were stored at 4^{o}C. C57BL/6 mice aMHC-*Sirt1*$^{-/-}$ mice were fed with the rodent grain-based standard chow diet that contained 0.2mg/kg of food pellet tesaglitazar or both 0.2mg/kg of food pellet tesaglitazar and 0.067% resveratrol. *Ppara*$^{-/-}$ mice were also fed with rodent grain-based standard chow diet and chow diet supplemented with 0.2mg/kg of food pellet tesaglitazar. For the experiments with injections, C57BL/6 mice were administered daily with tesaglitazar (0.5μmol/kg body weight) or combination of tesaglitazar and resveratrol (100mg/kg body weight). C57BL/6 mice were fed with high-fat diet (HFD; fat calories - 60%, Table S8), that contained 0.2mg/kg of food pellet tesaglitazar. Plasma triglycerides were measured with enzymatic assay kit (Infinity, Louisville) and blood glucose levels were assessed by glucometer. Prior to 2D-echocardiography or euthanasia mice were anesthetized by isofluorane inhalation. Mouse hearts were harvested, flash frozen and stored at -80°C until further use.

RNA purification and gene expression analysis

RNA purification was performed with the TRIzol reagent (Invitrogen) according to the instructions of the manufacturer. RNA was treated with DNase (Invitrogen) and cDNA was synthesized using the ProtoScript® II First Strand cDNA Synthesis Kit (New England Biolabs) and analyzed with

quantitative real-time PCR that was performed with Brilliant II SYBR Green QPCR Reagents (Agilent Technologies). Incorporation of the SYBR green dye into the PCR products was monitored in real time with an Mx3000 sequence detection system (Stratagene). Samples were normalized against murine *18S* or *36b4* or human *Rps13* (Table S7).

Quantitation of mitochondrial DNA

Mitochondrial DNA was quantified by calculating the ratio of mitochondrial gene copy number (*CoxII*) to nuclear gene copy number (*b-globin*). Cardiac DNA was extracted from frozen tissue. Specifically, cardiac tissue was added in DNA buffer (0.5% SDS, 0.1M NaCl, 0.05M Tris, pH8.0, 3mM EDTA) with Proteinase K (100μg/ml) and incubated at 60^{o}C overnight. 75μl 8M potassium acetate and 500μl chloroform were added and samples were centrifuged at 9,500 rpm for 5 min. DNA was precipitated from the aqueous phase by addition of 100% ethanol and centrifugation and washed twice with 75% ethanol. The DNA pellet was diluted in ddH2O. 100ng of DNA were used for PCR analysis. Real time quantitative PCR was performed with SYBR Select Master Mix by Applied Biosystems. After an initial 10min activation step at 95 ^{o}C, 40 circles of 95 ^{o}C for 30sec, annealing at 60^{o}C for 30sec and elongation at 72^{o}C for 45sec, were followed. PCR products were further analyzed for quality purposes with the use of melting curve. Real-time qPCR was performed in Applied Biosystem Step-one thermocycler.

Adult Mouse Cardiomyocyte Isolation

Adult mouse cardiomyocytes (ACMs) were isolated from ventricles of C57BL/6 mice treated with chow diet containing tesaglitazar or combination of tesaglitazar and resveratrol. Hearts from heparinized mice (90USP; ip) were cannulated through the aorta. Hearts were perfused with perfusion buffer (120.4mM NaCl, 14.7mM KCL, 0.6mM NaH_2PO_4, 0.6mM KH_2PO_4, 1.2mM $MgSO_4$, 10mM Hepes, 4.6mM $NaHCO_3$, 30mM taurine, 10mM BDM, 5.5mM glucose; pH 7.4) for 3min followed by digestion with perfusion buffer containing 19250 units collagenese type II (Worthington), 5-6mg trypsin and 1mM $CaCl_2$ for 7min. Ventricles were gently teared in small

pieces, perfusion buffer containing 5mg/ml BSA and 0.125mM $CaCl_2$ was added and filtered with 100um nylon strainer. The filtrate was pelleted by gravity for 5min, centrifuged for 30sec at 700rpm and the pellet resuspended in perfusion buffer containing 5mg/ml BSA and 0.225mM $CaCl_2$. The cells were pelleted by gravity for 10min, centrifuged for 30sec at 700rpm and the pellet resuspended in perfusion buffer containing 5mg/ml BSA and 0.525mM $CaCl_2$. The cells were pelleted by gravity for 10min, centrifuged for 30sec at 700rpm and the pellet was resuspended in perfusion buffer containing 5mg/ml BSA and 1.025mM $CaCl_2$.

MitoTracker Red staining

Cells were plated in sterile glass chamber slides (Thermo Scientific, Nunc, 177380) that had been pre-coated with fibronectin/gelatin or laminin when ACMs were used. Cells were exposed to MitoTracker Red (200nM/well) per manufacturer's instructions (Molecular Probes). Hoechst (Thermo Fisher) was used as nuclear stain at 1:1000. Imaging was performed using Nikon Eclipse TI-RCP (20x objective; excitation 550nm, emission 570nm). Images were analyzed with ImageJ software. Corrected Total Cell Fluorescence (CTCF) (analyzed particles / total area) was calculated and expressed as fluorescence arbitrary units (AU).

Protein purification and analysis

Cells were homogenized in RIPA buffer containing protease inhibitors (1mM benzamidine, 1mM phenylmethylsulfonyl fluoride, 10μg/ml leupeptin, 10μg/ml aprotinin, 5mM ethylene glycol tetraacetic acid, 2mM ethylene diamine tetraacetic acid - SIGMA), as well as 1mM dithiothreitol and phosphatase inhibitors (Halt phosphatase inhibitor cocktail – Thermo Scientific). 30-40ug of total protein extracts were analyzed with SDS-PAGE and transferred onto PVDF membranes with Trans-Blot-Turbo BioRad System for Western Blotting. Table S6 contains information about the antibodies we used for this study.

Transient transfection and luciferase assay

For transfection and luciferase assay analyses human *Ppargc1a* promoter was cloned into a pGL3 basic vector (pGL3-BV, Promega). The deletion fragments of *Ppargc1a* promoter were amplified from the human genomic sequence using the common reverse primer +120R combined with -1631F, -1386F, -1012F and -210F *PPARGC1A* primers that introduced KpnI and XhoI restriction sites in the 5´ and 3´ ends of the amplified fragment (Table S7). After amplification, the fragments were purified through electrophoresis followed by gel extraction using the StrataPrep DNA Gel Extraction kit (Agilent Technologies). Purified *PPARGC1A* promoter fragments were digested with KpnI and XhoI and cloned to the respective sites of the pGL3-BV plasmid. Sequencing of final GL3BV-*PPARGC1A*-1631, pGL3BV-*PPARGC1A*-1386, pGL3BV-*PPARGC1A*-1012, and pGL3BV-*PPARGC1A*-210 plasmidswas performed to confirm proper sequence (GeneWiz).

96-well-plates were seeded with 50,000 AC16 cells. FuGENE 6 Transfection Reagent (Promega) was used to transfect them with 3µg *PPARGC1A* promoter fragments-containing pGL3-BV plasmid according to manufacturer's protocols. Renilla reporter vector (p-RL-Null, Promega) co-transfection was used for normalization. Cells were treated with rosiglitazone (50µM), WY 14643 (50µM) or combination of rosiglitazone (50µM) and WY-14643 (50µM) 24h post-transfection. Control cells were treated with equivalent volume of dimethyl sulfoxide (DMSO, Sigma-Aldrich). Luciferase activity (Relative Luminescence Units, RLU) was quantified in cell lysates (Dual-Luciferase Reporter Assay System, Promega) by using the Infinite® M1000 PRO plate reader from the aqueous phase by addition of 100% ethanol and centrifugation and washed twice with 75% ethanol.

Chromatin immunoprecipitation

Minced heart tissue was cross-linked with 1 % Formalin (final) for 10 min at room temperature, then homogenized and neutralized with Glycine solution (Cell Signaling). The heart homogenate was lysed with 1 ml Cell lysis buffer [5 mM Hepes pH 8, 85 mM KCl, 0.5 % NP-40, 0.5 mM DTT, protease inhibitor cocktail (Sigma)]. The cell lysates were transferred to 1.5 ml tube and rotated

for 10 minutes at 4 °C. After centrifugation (2,000 x g for 2 minutes), pellet nuclei were suspended with 1ml Nuclear lysis buffer [50 mM Tris pH 8.1, 10 mM EDTA, 1 % SDS, 0.5 mM DTT, protease inhibitor cocktail (Sigma)] and sonicated with Bioruptor sonicator (Power H, 30 seconds on and 30 seconds off cycle for 30 minutes). After centrifuge (16,000 x g for 10 minutes), the supernatant was used as chromatin solution. The chromatin solution (5-10 μg) was diluted with dilution buffer [20 mM Tris, pH 8.1, 2 mM EDTA, 150 mM NaCl, 1% Triton X-100] to reduce SDS concentration to less than 0.1 %. Antibodies was added to the diluted chromatin solution and rotated for overnight at 4 °C. Then, anti-rabbit IgG dynabeads (15μl) was added and rotated for 2 hours at 4 °C. The immunocomplex was washed with 1ml Wash buffer L [0.1% SDS, 1% Triton X-100, 2mM EDTA, 20mM Tris-HCl, pH 8.1, 150mM NaCl], 1 ml Wash buffer H [0.1% SDS, 1% Triton X-100, 2mM EDTA, 20mM Tris-HCl, pH 8.1, 500mM NaCl], 1ml Wash buffer LiCl [0.25M LiCl, 1% NP-40, 1% deoxycholic acid, 1mM EDTA, 10mM Tris, pH 8.1], and 1 ml TE buffer [1mM EDTA pH8, 10mM Tris, pH 7.5]. The immunocomplex was incubated with 150 μl 1 x ChIP elution buffer (Cell Signaling) for 30 minutes at 65°C. One μl proteinase K (New England Biolabs) and 6 μl 5M NaCl were added to the eluted chromatin. After 2 hours incubation at 55 °C, the chromatin fragment was purified with PCR purification kit (Qiagen). The corrected chromatin fragments were validated with quantitative PCR (primers described in Table S7).

Immunoprecipitation (IP)

The protein lysates were purified from homogenized hearts in RIPA buffer after centrifugation at 14,000rpm for 15 mins at 4°C and the protein concentration was measured with a Pierce BCA Protein Assay Kit. Sepharose CL-48 beads (GE Healthcare Life Sciences) were used for the pre-clearing and immunoprecipitation steps. Sepharose beads (30mg) were washed 3 times with distilled water) and finally a 30mg/ml slurry was prepared with IP Mild Lysis Buffer (1% Triton, 20mM Tris-Cl pH=7.5, 125mM NaCl, 1mg $MgCl_2$, 1mM $CaCl_2$, 1% Aprotinin, 1mM PMSF, 50mM NaF, 100μM sodium orthovanadate). In order to reduce non-specific binding, a pre-clearing step was performed as follows: 100μg of protein lysates were treated with resin Sepharose beads in

a rotating incubator for 1h at 4°C and then centrifugated at 14,000rpm for 2 mins. The Ac-Lysine antibody (2μg) was immobilized on Sepharose beads (30mg) with 500μl of Mild lysis buffer by rotation for 1h at room temperature followed by centrifugation at 1,500rpm for 30 seconds. The supernatant of the pre-cleared protein lysate was transferred to the immobilized antibody (Ac-Lysine) for the IP. The new mixture was incubated with gentle mixing overnight at 4ºC followed by 2 washes with IP Mild Lysis Buffer and 3 washes with RIPA buffer. Between washes, samples were centrifuged at 14,000 rpm for 2min at 4ºC. After final wash and centrifugation pellets were resolved in 50μl of loading buffer (50mM DTT, 62.5mM Tris-Cl pH=6.8, 2% SDS, 10% v/v Glycerol) followed by incubation at 95ºC for 5 min and centrifugation at 4,000rpm for 2 minutes. 15μl of supernatant was analyzed for PGC1α detection by western blotting.

Oxygen consumption rate analysis

Isolated primary ACMs were counted with hematocytometer. Dead cells were detected with Trypan Blue Dye staining. Cells were plated (3000 cells per well) in XF96 Seahorse® plates pre-coated with 20μg/ml laminin (Invitrogen, 23017). In order to assess oxygen consumption rates (OCR) for fatty acid oxidation (FAO) recordings, cells were incubated in substrate limited medium (DMEM containing 10mM Glucose, 1.025mM $CaCl_2$, 0.5mM carnitine, pH=7.4) and assayed with fatty acid oxidation medium as per manufacturer's protocol. Before starting the assay, 0.1mM palmitate conjugated with BSA was added in each well. Drugs used for maximal response during fatty acid oxidation were: oligomycin (3μM) (Sigma, O4875), FCCP (2μM) (Sigma, C2920), and rotenone/antimycin A (0.5μM) (Sigma, A8674) / (Sigma, R8875). The pre-hydrated with XF assay calibrant, XF cartridges were filled with the drugs and the cartridge was calibrated for 30 minutes in Seahorse Analyzer. All experiments were performed at 37ºC. Calculations were made as described in the Seahorse manual and XF Seahorse Mito Stress Test kit user guide. Briefly, basal respiration was calculated with subtraction of non-mitochondrial respiration rate from the last measurement prior to first injection. Maximal respiration was calculated by subtraction of the non-mitochondrial respiration measurement from maximum measurement after FCCP injection. ATP

production-related OCR was obtained indirectly by measuring ATP-linked respiration in the presence of complex V inhibitor (oligomycin). The decrease of oxygen consumption rate that corresponded to the portion of basal respiration, which was used for ATP production, was calculated by subtraction of the minimum measurement following oligomycin injection from the last measurement prior to oligomycin injection. Spare respiratory capacity was equal to (maximum respiration) - (basal respiration).

Lipidomic analysis

Glycerophospholipids and sphingolipids were separated with normal-phase HPLC using an Agilent Zorbax Rx-Sil column (inner diameter 2.1 x 100mm) under the following conditions: mobile phase A (chloroform: methanol: 1M ammonium hydroxide, 89.9:10:0.1, v/v/v) and mobile phase B (chloroform: methanol: water: ammonium hydroxide, 55:39.9:5:0.1, v/v/v); 95% A for 2min, linear gradient to 30% A over 18min and held for 3min, and linear gradient to 95% A over 2min and held for 6min. Quantification of lipid species was accomplished using multiple reaction monitoring (MRM) transitions that were developed in earlier studies (3) in conjunction with referencing of appropriate internal standards: ceramide d18:1/17:0 and sphingomyelin d18:1/12:0 (Avanti Polar Lipids, Alabaster, AL). Values are represented as mole fraction with respect to total lipid (% molarity). For this, lipid mass (in moles) of any specific lipid is normalized by the total mass (in moles) of all the lipids measured (3). In addition, all our results were further normalized by protein content.

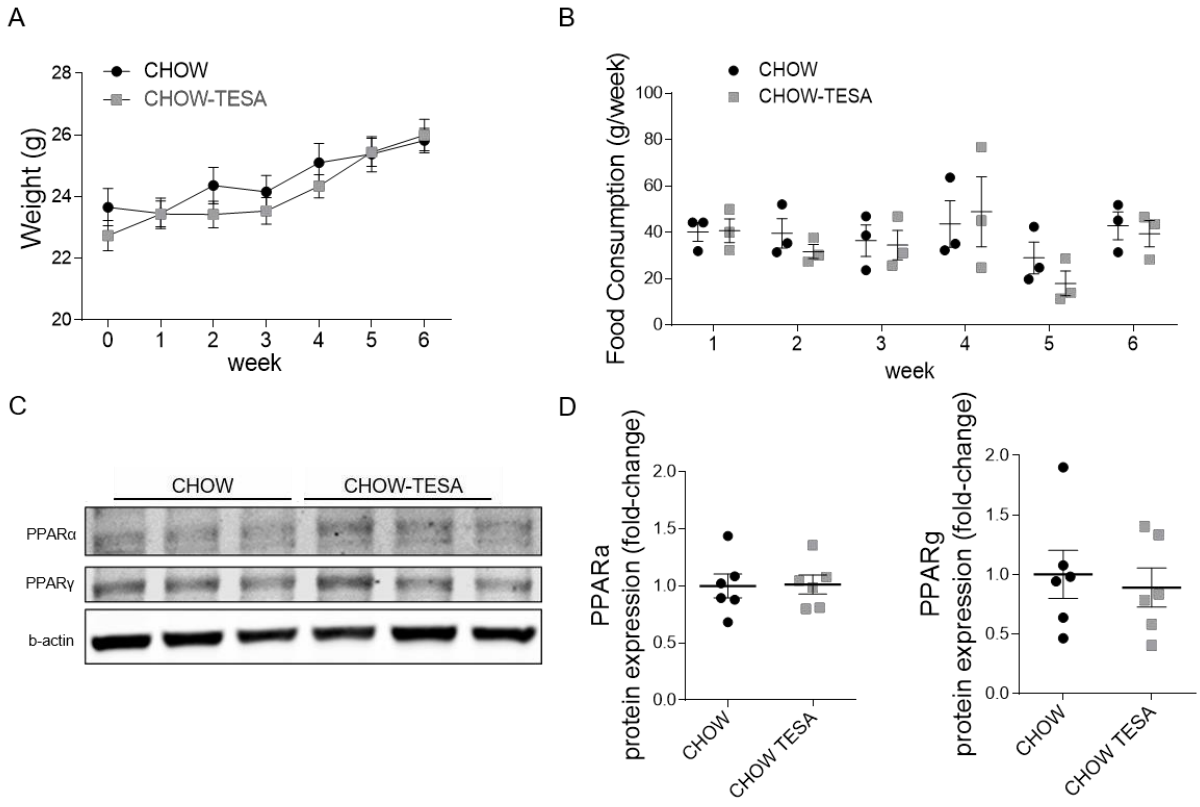

Figure S1. Body weight gain and cardiac peroxisome proliferative activated receptor alpha PPARα and PPARγ protein analysis - Weight gain rate (A), food consumption rate (B), representative immunoblot (C) and densitometric analysis (D) of cardiac PPARα, PPARγ and β-ACTIN of C57BL/6 mice fed on regular or tesaglitazar-containing chow diet (0.5μmol/kg bw) for 6 weeks. Data in graphs A and B derived from one independent experiment. Data in graphs C, D derived from two independent experiments. Statistical analysis was performed using Student's t-test, *p<0.05, (n=3-5). Error bars represent SEM.

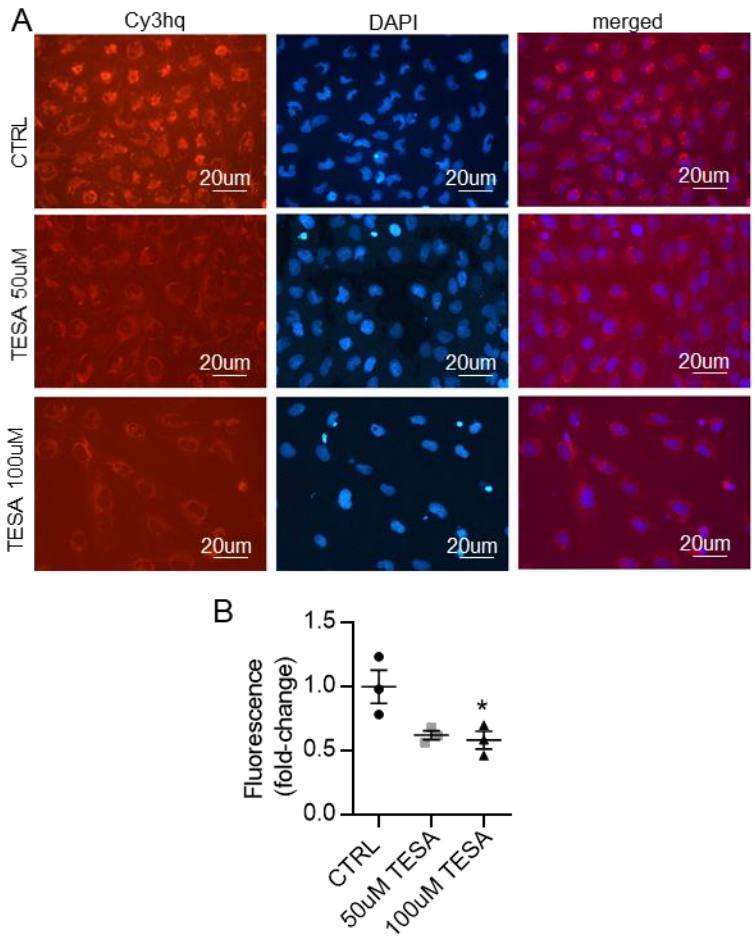

Figure S2. MitoTracker Red analysis of AC16 cells treated with tesaglitazar - Representative images obtained from fluorescence microscopy of AC16 cells stained with MitoTracker Red (A; magnification x20) and quantitation (B) of mitochondrial number/total area. AC16 cells were treated with 50μM or 100μM tesaglitazar for 24h (n=3 individual wells; number of analyzed cells per experimental group: CTRL:206, tesaglitazar 50μM: 214, tesaglitazar 100μM: 201). Statistical analysis was performed with 1-way ANOVA followed by Tukey correction. Data are derived from an independent in vitro experiment. *p<0.05. Error bars represent SEM.

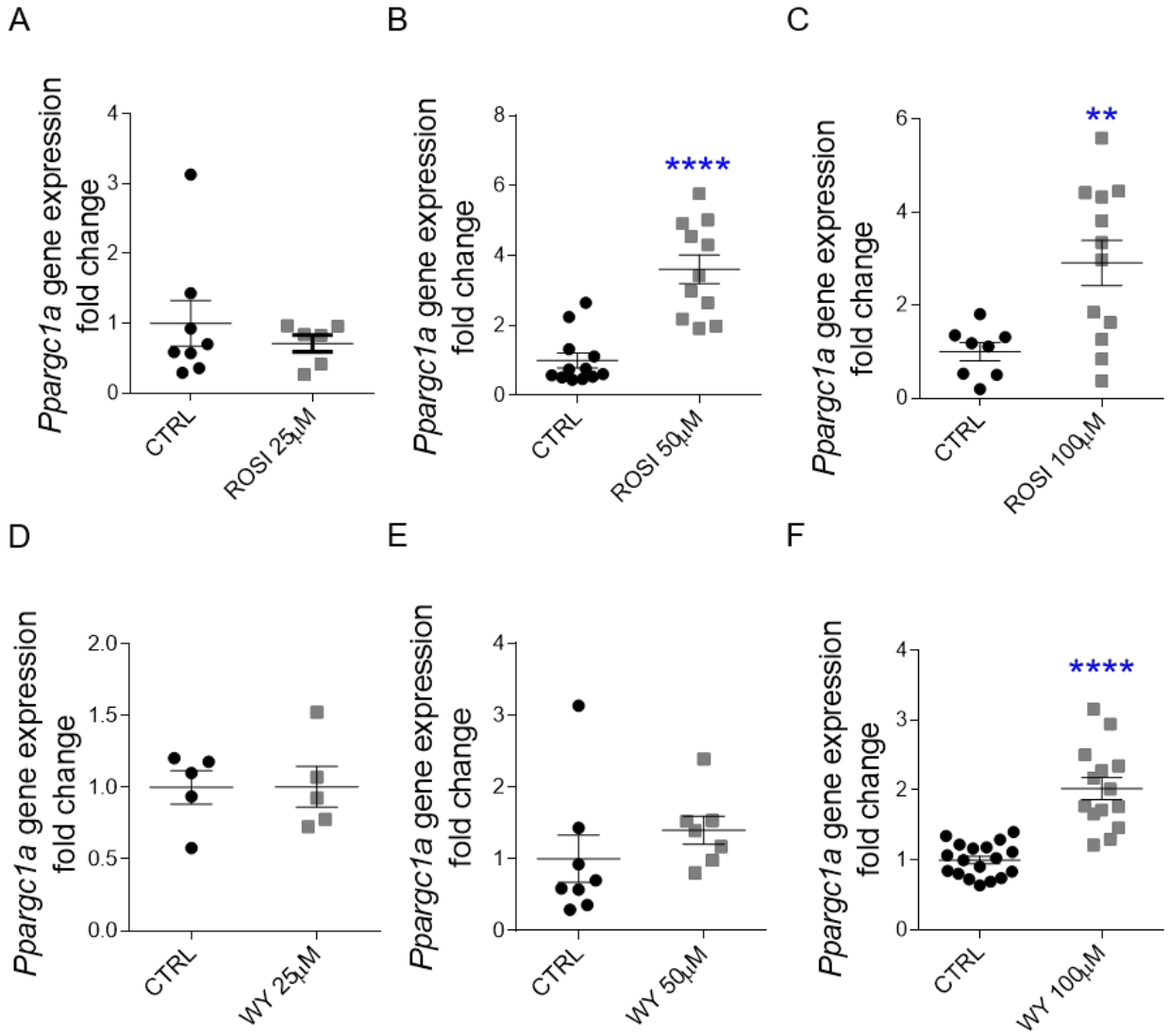

Figure S3. Rosiglitazone (PPARγ agonist) and WY14634 (PPARα agonist) dose titration for induction of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (*PPARGC1A*) gene expression in vitro - *PPARGC1A* gene expression levels in AC16 cells treated with increasing doses of rosiglitazone (25, 50 and 100μM) (A-C) and WY-14643 (25, 50 and 100μM) (D-F); n=5-18. Statistical analysis was performed with unpaired 2-tailed Student's t-test. Data in graphs A and D was collected from one experiment. Data in graphs B, C, E and F was collected from two independent experiments. **p<0.01, ****p<0.0001. Error bars represent SEM.

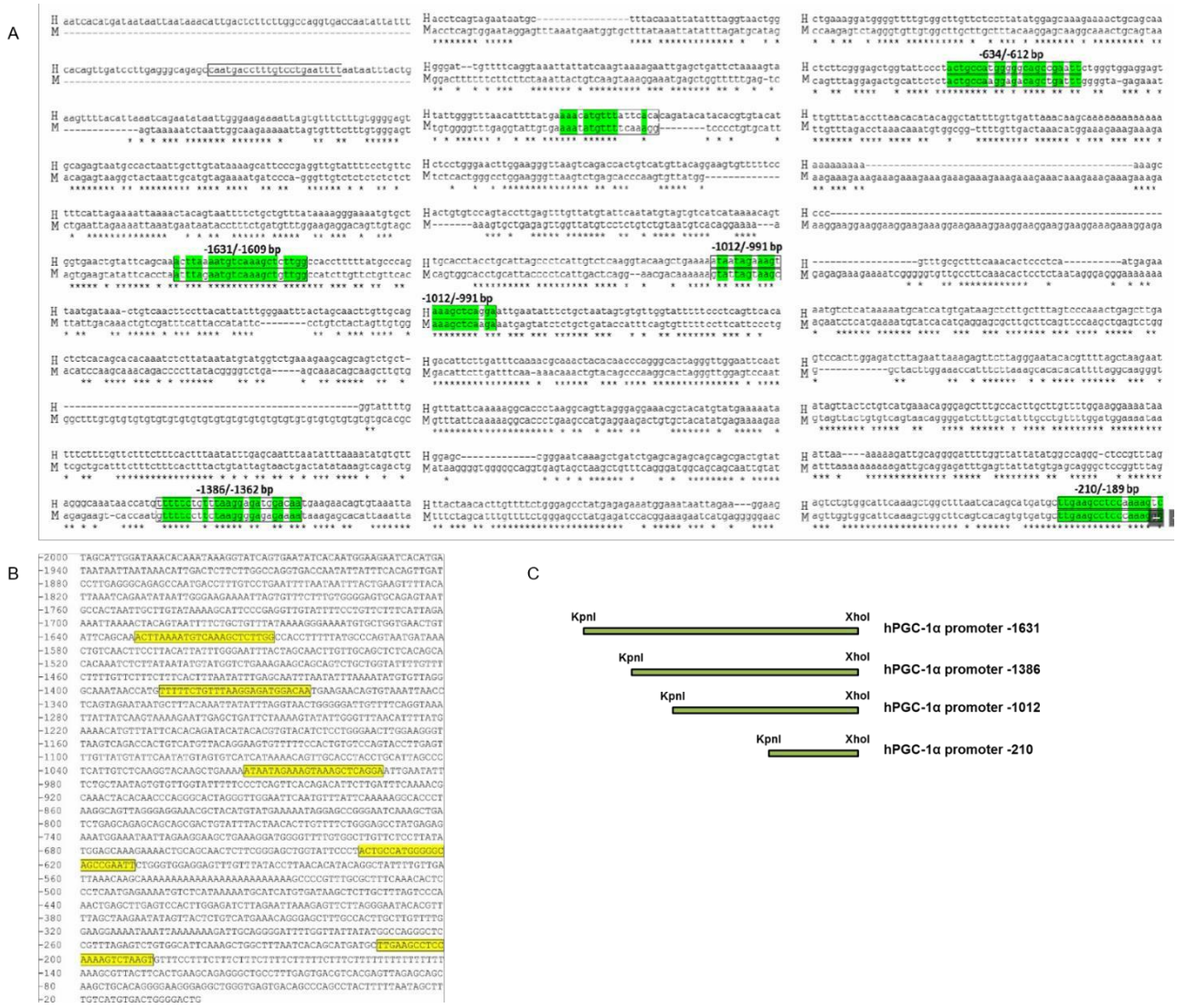

Figure S4. Human and murine peroxisome proliferator-activated receptor gamma coactivator 1-alpha (*Ppargc1a*) promoter alignment and *Ppargc1a* promoter deletion mutants - Comparison of the sequence of the human and the murine *Ppargc1aa* promoters with the CLUSTAL O (1.2.0) sequence alignment software. Conserved PPAR response elements (PPREs) that span regions - 1631/-1609 bp, -1386/-1362 bp, -1012/-991 bp, -634/-612 bp, and -210/-189 bp of the *PPARGC1A* promoter are highlighted (A). Predicted PPREs in the promoter of human *PPARGC1A* gene (B). Schematic representation of *PPARGC1A* promoter deletion mutants cloned in pGL3-BV (basic vector) luciferase reporter plasmid for luciferase promoter assays (C).

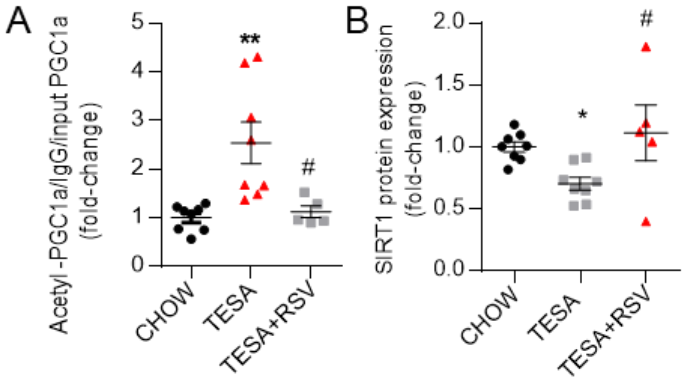

Figure S5. Resveratrol (RSV) treatment reverses the increased acetylated-peroxisome proliferator activated receptor gamma coactivator 1-alpha (ac-PGC1a) that tesaglitazar treatment exhibited. A, B: Densitometric analysis of cardiac Ac-PGC1a (A) (Figures 5A, 6E) normalized to IgG heavy chain (Figures 5A, 6E) to total PGC1a (Figures 1F, 6E), and sirtuin1 (SIRT1 (B); Figures 5B, 6F) normalized to β-ACTIN of C57BL/6 mice fed on regular chow or chow containing tesaglitazar (0.5μmol/kg bw) or combination of tesaglitazar (0.5μmol/kg bw) and RSV (100mg/kg bw/day) for 6 weeks (n=5-8; data was collected from two independent experiments). Statistical analyses were performed with 1-way ANOVA followed by Tukey post-hoc correction among groups, *p<0.05, **p<0.01 vs chow. $^{\#}$p<0.05 vs tesaglitazar. Error bars represent SEM.

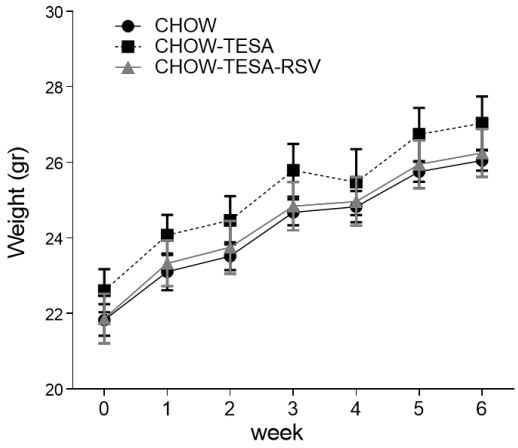

Figure S6. Body weight gain in mice treated with tesaglitazar or/and resveratrol - Weekly body weight measurements of C57BL/6 mice fed on chow diet containing tesaglitazar (0.5µmol/kg body weight) or combination of tesaglitazar (0.5µmol/kg body weight) and resveratrol (100mg/kg body weight/day) for 6 weeks (n=5). Data was collected from one experiment. Statistical analyses were performed with 1-way ANOVA followed by Tukey correction, *p<0.05. Error bars represent SEM.

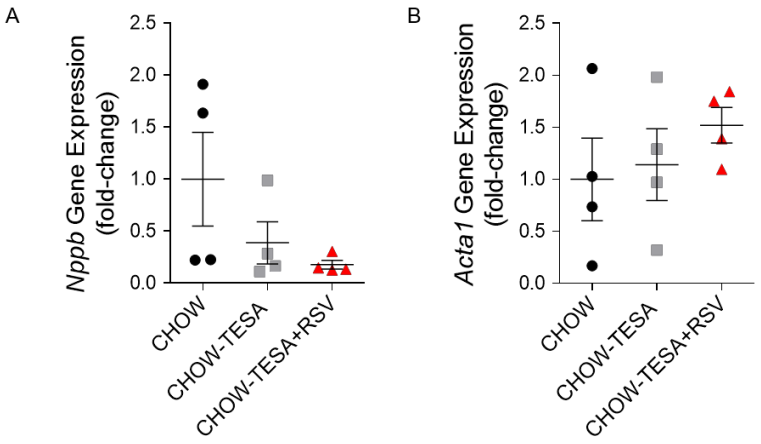

Figure S7. Heart failure related-gene expression analysis in C57BL/6 mice fed on chow with tesaglitazar or combination of tesaglitazar and resveratrol - Cardiac B-type natriuretic peptide (*NBBP*) (A) and actin alpha 1 *(ACTA1*) (B) mRNA levels of C57BL/6 mice fed on chow diet, chow diet contatining tesaglitazar (0.5µmol/kg bw) or chow diet with tesaglitazar (0.5µmol/kg bw) and resveratrol (100mg/kg body weight/day) for 6 weeks (n=4). Data was collected from one experiment. Statistical analyses were performed with 1-way ANOVA followed by Tukey correction, *p<0.05. Error bars represent SEM.

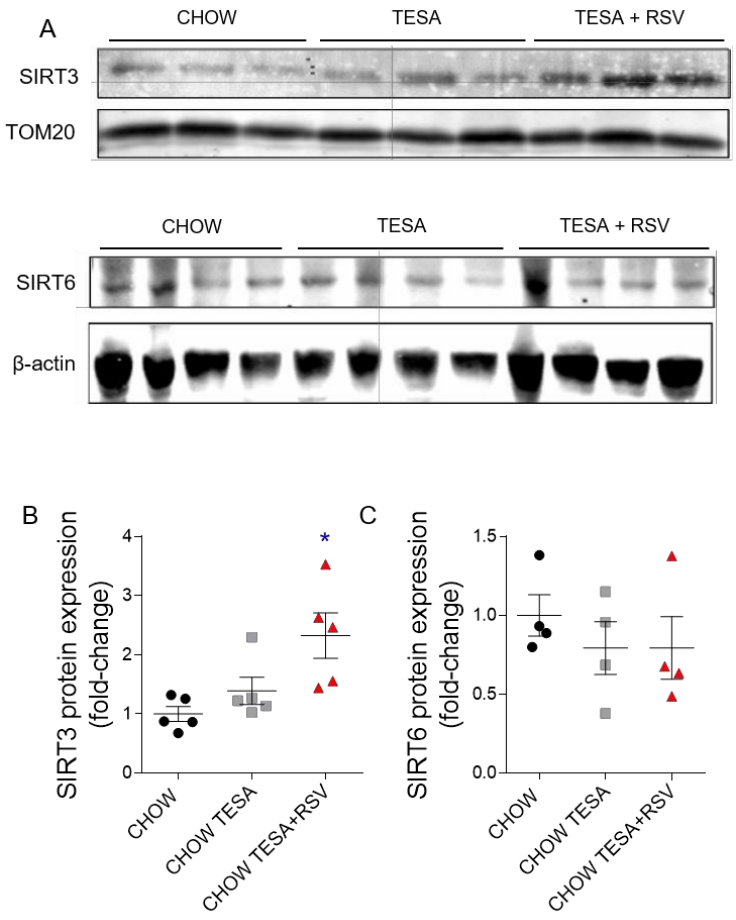

Figure S8. Effects of treatment with tesaglitazar or combination of tesaglitazar and resveratrol in sirtuin 3 (SIRT3), SIRT6 – Representative immunoblots (A) and densitometric analyses for cardiac SIRT3 (B; n=5) and SIRT6 (C; n=4) of C57BL/6 mice fed on chow diet containing tesaglitazar (0.5μmol/kg body weight) or combination of tesaglitazar (0.5μmol/kg body weight) and resveratrol (100 mg/kg/day). Data was collected from one experiment. Statistical analyses were performed with 1-way ANOVA followed by Tukey correction, *p<0.05 vs chow. Error bars represent SEM.

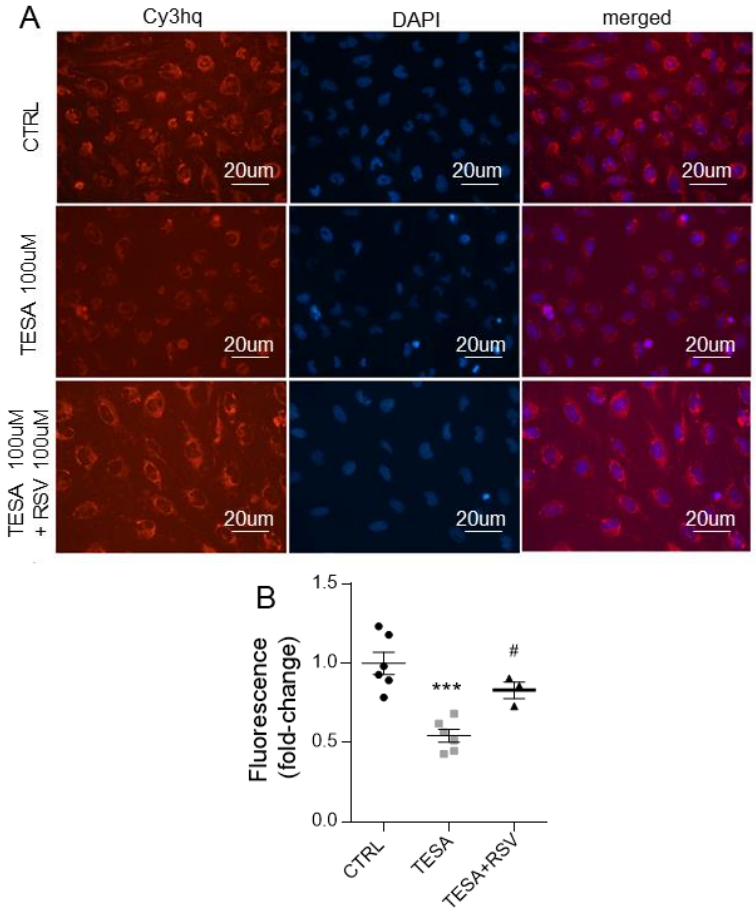

Figure S9. MitoTracker Red staining of AC16 cells treated with tesaglitazar - Representative fluorescence microscopy images of AC16 cells stained with Mitotracker Red (A; magnification x20) and quantitation of mitochondrial number/total area. AC16 cells were treated with 100μM tesaglitazar or 100μM tesaglitazar and 100μM resveratrol for 24h (number of analyzed cells: CTRL:103 (n=6 individual wells), tesaglitazar 100μM: 100 (n=6 individual wells), tesaglitazar 100μM + resveratrol 100μM: 100 (n=3 individual wells). Data was collected from one experiment. Statistical analyses were performed with 1-way ANOVA followed by Tukey correction. ***p<0.001 vs ctrl. #p<0.05 vs tesaglitazar. Error bars represent SEM.

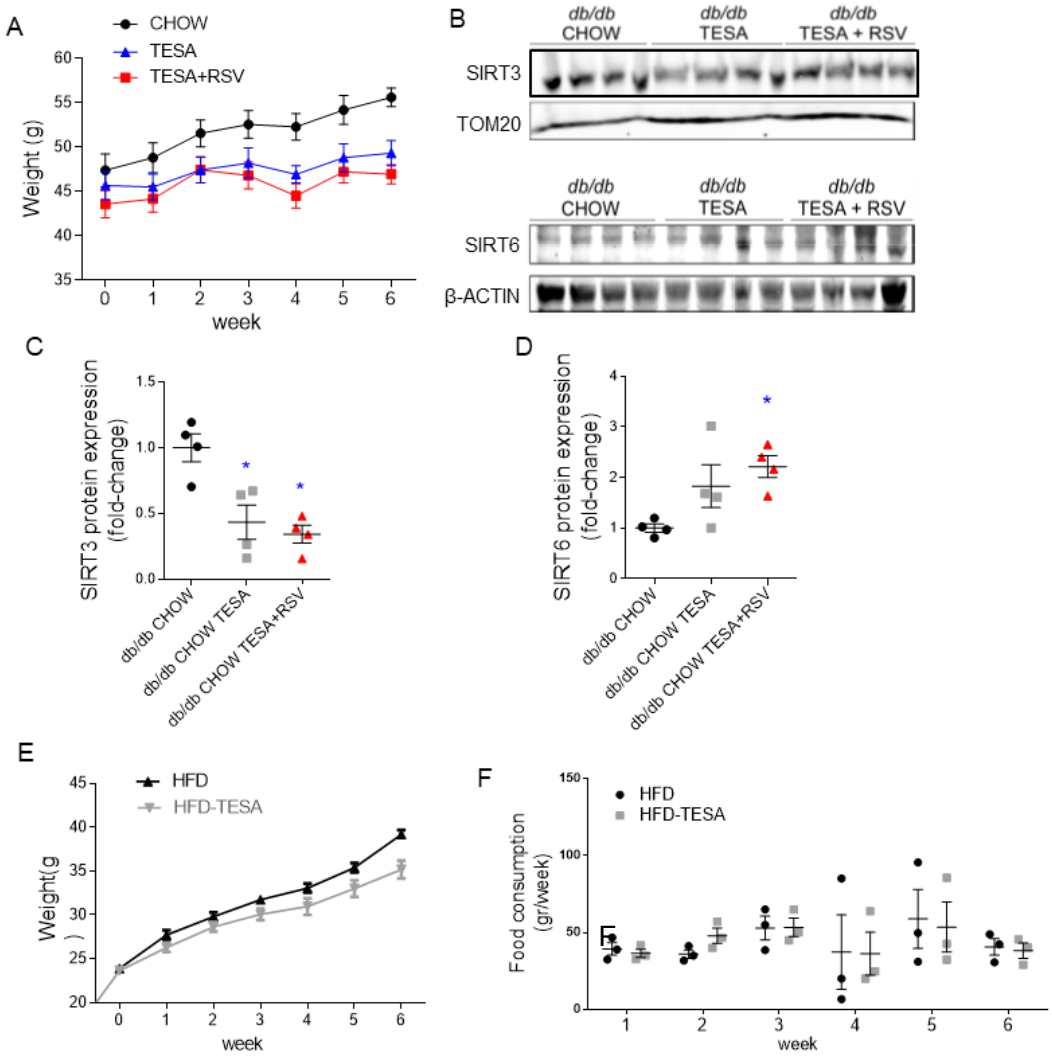

Figure S10. Body weight gain and cardiac sirtuin 3 (SIRT3), SIRT6 protein analysis in diabetic *db/db* mice treated with tesaglitazar and resveratrol – A: Weekly body weight of *db/db* mice treated with chow diet containing tesaglitazar (0.5μmol/kg body weight) or combination of tesaglitazar (0.5μmol/kg body weight) and resveratrol (100mg/kg/day) for 6 weeks. **B-D**: SIRT3, TOM20, SIRT6 and β-ACTIN representative immunoblots (B) and cardiac SIRT3 (C), SIRT6 (D) densitometric analysis (C, D) of *db/db* mice treated with chow diet containing tesaglitazar (0.5μmol/kg body weight) or combination of tesaglitazar (0.5μmol/kg body weight) and resveratrol (100mg/kg/day) (n=4). Data was collected from one experiment. **E, F:** Weight gain rate (E), food consumption rate (F) of C57Bl/6 mice fed on regular or tesaglitazar-containing (0.5umol/kg body weight) high fat diet (HFD) for 6 weeks (n=5). Data was collected from one experiment. Statistical analyses for graphs A-D were performed with 1-way ANOVA followed by Tukey correction. Statistical analysis for graphs E, F were performed with unpaired 2-tailed Student's t-tests. *p<0.05 vs chow. Error bars represent SEM.

SUPPLEMENTAL TABLES

Echocardiography parameters	CHOW	CHOW-TESA
EF (%)	80.8 ± 1.38	55.53 ± 6.32**
FS (%)	49.2 ± 1.41	28.93 ± 4.02**
HR (bpm)	470.4 ± 11.05	476.6 ± 18.11
LV Mass (mg)	103.4 ± 4.39	98.2 ± 11.09
LV Mass Cor (mg)	82.7 ± 3.51	78.5 ± 8.87
LV Vol;d (µl)	80.9 ± 11.29	59.1 ± 4.61
LV Vol;s (µl)	15.6 ± 2.31	27.1 ± 5.54
IVS;d (mm)	0.7 ± 0.06	0.8 ± 0.08
IVS;s (mm)	1.3 ± 0.09	1.1 ± 0.08
LVID;d (mm)	4.2 ± 0.26	3.9 ± 0.11
LVID;s (mm)	2.1 ± 0.14	2.79 ± 0.19*
LVPW;d (mm)	0.7 ± 0.04	0.7 ± 0.04
LVPW;s (mm)	1.4 ± 0.06	0.946 ± 0.11*

Table S1. Cardiac function analysis of C57BL/6 wild type mice treated with tesaglitazar - 2D-echocardiography parameters of C57BL/6 mice treated with chow diet or chow diet containing tesaglitazar (0.5µmol/kg body weight) for 6 weeks. Statistical analysis was performed with unpaired 2-tailed Student's t-test between groups, *p<0.05, (n=5).

Echocardiography parameters	CHOW	CHOW-TESA	CHOW-TESA+RSV
EF (%)	69.83 ± 2.85	49.56 ± 2.27***	70.08 ± 2.36###
FS (%)	39.52 ± 2.39	25.02 ± 1.40***	39.54 ± 1.87###
HR (bpm)	488.4 ± 13.06	511.4 ± 12.99	492.6 ± 21.91
LV Mass (mg)	131.43 ± 4.31	162.82 ± 14.86	172.79 ±26.85
LV Mass Cor (mg)	105.14 ± 3.45	130.25 ± 11.89	138.24 ± 21.48
LV Vol;d (ul)	82.86 ± 5.17	86.14 ± 6.50	81.81 ± 4.60
LV Vol;s (ul)	25.50 ± 3.51	43.90 ± 4.63**	24.62 ± 2.58##
IVS;d (mm)	0.92 ± 0.07	1.06 ± 0.07	1.24 ± 0.16
IVS;s (mm)	1.56 ± 0.08	1.53 ±	1.81 ± 0.18
LVID;d (mm)	4.28 ± 0.11	4.35 ± 0.14	4.26 ± 0.10
LVID;s (mm)	2.60 ± 0.15	3.26 ± 0.14**	2.58 ± 0.11##
LVPW;d (mm)	0.7 ± 0.03	0.8 ± 0.04	0.7 ± 0.03
LVPW;s (mm)	1.2 ± 0.06	0.9 ± 0.05**	1.2 ± 0.03###

Table S2. Cardiac function analysis of wild type mice treated with tesaglitazar and resveratrol. 2D-echocardiography parameters of C57BL/6 mice treated with chow diet, chow diet containing tesaglitazar (0.5µmol/kg body weight) or tesaglitazar (0.5µmol/kg body weight) and resveratrol (100 mg/kg/day) for 6 weeks. Statistical analysis was performed with were performed with 1-way ANOVA followed by Tukey correction. **p<0.01, ***p<0.001 vs chow. ##p<0.01, ###p<0.001 vs tesaglitazar. (n=7).

LIPIDS	Normalized Average			Normalized Standard Error		
	CHOW	TESA	T+R	CHOW	TESA	T+R
FC	1.00	1.03	0.93	0.04	0.03	0.03
CE	1.00	1.09	0.60	0.17	0.09	0.07
AC	1.00	2.27	0.65	0.28	0.29	0.17
MG	1.00	0.61	1.06	0.14	0.04	0.12
DG	1.00	3.09	2.61	0.21	0.44	0.74
TG	1.00	6.79****	4.75***	0.09	1.77	2.08
Cer	1.00	0.73	1.14	0.11	0.04	0.09
GM3	1.00	2.72	2.25	0.35	0.92	0.45
PA	1.00	1.30	0.74	0.04	0.09	0.07
PC	1.00	0.63	1.07	0.07	0.05	0.12
FC b	1.00	1.03	0.93	0.04	0.03	0.03
CE 18:1	1.00	1.35	0.77	0.14	0.13	0.08
CE 18:2	1.00	0.94	0.51	0.17	0.09	0.07
CE 20:2	1.00	1.32	0.71	0.12	0.08	0.07
CE 22:3	1.00	1.38	0.79	0.22	0.07	0.09
CE 22:4	1.00	1.30	0.75	0.21	0.07	0.10
CE 22:5	1.00	1.44	0.75	0.19	0.13	0.08
CE 24:4	1.00	2.49	0.97	0.28	0.45	0.14
CE 24:5	1.00	1.58	0.96	0.22	0.06	0.11
AC C16:0	1.00	2.11	0.81	0.40	0.23	0.28
AC C18:1	1.00	2.42	0.54	0.21	0.37	0.11
AC C3:0	1.00	1.15	0.63	0.31	0.11	0.06
AC C6:0	1.00	1.71	0.78	0.28	0.29	0.12
MG 16:0	1.00	0.77	1.10	0.10	0.05	0.06
MG 18:0	1.00	0.56	1.04	0.15	0.04	0.13
MG 18:2	1.00	2.52	1.86	0.13	0.20	0.69
MG 22:0	1.00	0.74	1.27	0.10	0.06	0.06
MG 22:1	1.00	0.36	0.76	0.23	0.03	0.17
DG 40:4/18:1	1.00	3.02	2.55	0.21	0.43	0.58
DG 40:6/18:1	1.00	3.10	2.62	0.22	0.45	0.77
TG 48:1/16:0	1.00	3.36*	2.35	0.11	0.70	0.88
TG 50:1/16:1	1.00	3.72**	2.92	0.18	0.84	1.06

LIPIDS	CHOW Average	TESA Average	T+R Average	CHOW SE	TESA SE	T+R SE
TG 50:2/16:1	1.00	10.00****	7.13****##	0.10	2.75	3.32
TG 50:3/16:1	1.00	16.05****	10.68****####	0.15	4.91	5.45
TG 52:5/20:4	1.00	18.18****	13.81****####	0.06	5.13	7.10
TG 54:5/20:4	1.00	8.52****	6.67****	0.05	2.47	2.51
TG 56:5/18:1	1.00	7.86****	6.22****	0.06	2.52	1.88
TG 56:5/20:4	1.00	4.29***	4.01**	0.12	1.13	0.95
TG 58:8/22:6	1.00	7.17****	6.03****	0.08	1.96	2.11
TG 60:7/22:6	1.00	2.34	2.10	0.24	0.13	0.61
TG 60:8/22:6	1.00	2.85	2.85	0.23	0.38	0.56
TG 60:9/22:6	1.00	2.98	2.48	0.16	0.48	0.44
Cer d18:1/16:1	1.00	0.73	1.14	0.11	0.04	0.09
MhCer d18:0/16:1	1.00	0.98	0.98	0.06	0.07	0.03
MhCer d18:0/18:1	1.00	0.85	1.14	0.04	0.06	0.05
MhCer d18:0/26:1	1.00	0.77	1.00	0.08	0.04	0.03
MhCer d18:1/18:1	1.00	0.73	1.03	0.08	0.03	0.04
LacCer d18:0/20:0	1.00	0.73	0.98	0.07	0.04	0.04
SM d18:1/16:1	1.00	0.73	0.99	0.07	0.02	0.04
SM d18:1/18:1	1.00	0.72	1.05	0.06	0.05	0.05
SM d18:1/20:0	1.00	0.69	1.02	0.07	0.05	0.02
SM d18:1/20:1	1.00	1.70	1.18	0.08	0.13	0.12
SM d18:1/22:0	1.00	1.70	1.22	0.06	0.13	0.13
SM d18:1/22:1	1.00	1.82	1.94	0.12	0.31	0.31
SM d18:1/24:0	1.00	1.35	2.27	0.15	0.38	0.40
SM d18:1/24:1	1.00	0.99	0.58	0.06	0.33	0.14
dhSM d18:0/24:0	1.00	0.71	1.19	0.08	0.04	0.10
dhSM d18:0/24:1	1.00	0.69	0.55	0.10	0.06	0.02
Sulf d18:1/16:0	1.00	0.72	0.52	0.14	0.07	0.05
Sulf d18:1/16:1	1.00	0.33	0.67	0.23	0.07	0.21
Sulf d18:1/20:1	1.00	0.84	1.19	0.13	0.05	0.09
GM3 d18:0/16:0	1.00	3.26*	2.63	0.25	1.09	0.78

LIPIDS	CHOW Average	TESA Average	T+R Average	CHOW SE	TESA SE	T+R SE
GM3 d18:0/20:0	1.00	2.98	2.03	0.29	1.11	0.40
GM3 d18:0/22:0	1.00	3.03	2.79	0.29	1.04	0.68
GM3 d18:0/26:0	1.00	2.71	2.02	0.18	0.80	0.48
GM3 d18:1/16:0	1.00	2.78	2.06	0.39	1.01	0.42
GM3 d18:1/18:1	1.00	3.28*	2.11	0.38	1.30	0.37
GM3 d18:1/22:0	1.00	2.59	2.25	0.36	0.84	0.44
GM3 d18:1/24:1	1.00	2.75	2.36	0.39	0.96	0.55
GB3 d18:1/16:0	1.00	1.86	0.98	0.06	0.21	0.21
PA 32:0	1.00	1.44	0.83	0.05	0.08	0.08
PA 34:0	1.00	1.04	0.69	0.07	0.03	0.03
PA 34:1	1.00	1.31	0.76	0.03	0.10	0.05
PA 34:2	1.00	1.55	0.73	0.15	0.15	0.12
PA 36:1	1.00	1.14	0.72	0.08	0.09	0.05
PA 36:2	1.00	1.38	0.76	0.05	0.12	0.07
PA 36:3	1.00	1.40	0.79	0.03	0.10	0.05
PA 36:4	1.00	1.46	0.85	0.12	0.17	0.14
PA 38:0	1.00	1.19	0.86	0.04	0.08	0.08
PA 38:4	1.00	1.10	0.71	0.07	0.08	0.05
PA 38:5	1.00	1.38	0.74	0.09	0.17	0.11
PA 38:6	1.00	1.32	0.70	0.12	0.12	0.11
PC 32:0	1.00	0.78	1.00	0.04	0.04	0.11
PC 32:1	1.00	0.82	1.02	0.07	0.05	0.05
PC 34:0	1.00	0.67	1.18	0.07	0.02	0.07
PC 34:1	1.00	0.60	1.12	0.06	0.04	0.08
PC 34:2	1.00	0.60	1.00	0.11	0.07	0.11
PC 36:0	1.00	0.59	1.12	0.07	0.04	0.12
PC 36:1	1.00	0.64	1.14	0.07	0.03	0.12
PC 36:2	1.00	0.62	1.10	0.08	0.05	0.15
PC 36:3	1.00	0.61	1.09	0.09	0.06	0.11
PC 36:4	1.00	0.62	1.04	0.06	0.03	0.12

LIPIDS	CHOW Average	TESA Average	T+R Average	CHOW SE	TESA SE	T+R SE
PC 38:0	1.00	0.72	1.10	0.08	0.03	0.03
PC 38:1	1.00	0.72	0.99	0.07	0.01	0.01
PC 38:2	1.00	0.53	0.97	0.14	0.04	0.15
PC 38:3	1.00	0.53	1.09	0.09	0.09	0.19
PC 38:4	1.00	0.53	1.16	0.11	0.08	0.20
PC 38:5	1.00	0.52	1.18	0.09	0.06	0.17
PC 38:6	1.00	0.46	1.10	0.11	0.08	0.19
PC 40:4	1.00	0.48	1.28	0.13	0.07	0.32
PC 40:5	1.00	0.52	1.18	0.11	0.07	0.19
PC 40:6	1.00	0.50	1.04	0.10	0.08	0.19
PC 40:7	1.00	0.65	1.08	0.09	0.04	0.10
PC 42:5	1.00	1.69	1.09	0.15	0.20	0.18
PC 42:6	1.00	0.67	0.97	0.08	0.07	0.16
PC 42:7	1.00	0.81	1.03	0.06	0.06	0.04
PCe 32:1	1.00	0.80	1.20	0.06	0.05	0.00
PCe 34:0	1.00	0.69	0.99	0.04	0.03	0.07
PCe 34:1	1.00	0.65	1.01	0.07	0.04	0.10
PCe 34:2	1.00	0.57	0.91	0.09	0.04	0.09
PCe 36:0	1.00	0.56	1.00	0.12	0.04	0.17
PCe 36:1	1.00	0.54	0.97	0.09	0.04	0.14
PCe 36:2	1.00	0.52	0.87	0.10	0.06	0.18
PCe 36:3	1.00	0.51	0.91	0.10	0.06	0.12
PCe 36:4	1.00	0.60	1.14	0.08	0.05	0.13
PCe 38:0	1.00	0.63	1.14	0.06	0.06	0.07
PCe 38:1	1.00	0.53	1.04	0.11	0.04	0.17
PCe 38:2	1.00	0.50	1.02	0.14	0.08	0.25
PCe 38:3	1.00	0.32	0.90	0.19	0.05	0.28
PCe 38:4	1.00	0.45	1.06	0.15	0.07	0.22
PCe 38:5	1.00	0.48	1.15	0.13	0.08	0.13
PCe 38:6	1.00	0.44	1.15	0.10	0.08	0.17
PCe 40:4	1.00	0.47	1.03	0.13	0.06	0.23
PCe 40:5	1.00	0.62	0.99	0.08	0.04	0.14
PCe 40:6	1.00	0.69	1.06	0.11	0.03	0.10
PCe 40:7	1.00	0.72	1.09	0.08	0.03	0.03

LIPIDS	CHOW Average	TESA Average	T+R Average	CHOW SE	TESA SE	T+R SE
PCe 42:5	1.00	0.57	0.93	0.09	0.05	0.17
PCe 42:6	1.00	0.72	1.05	0.06	0.06	0.17
PCe 42:7	1.00	0.78	0.96	0.07	0.02	0.06
PE 34:2	1.00	1.27	0.84	0.12	0.14	0.06
PE 36:0	1.00	0.50	0.85	0.27	0.03	0.06
PE 36:1	1.00	1.18	1.29	0.07	0.11	0.07
PE 38:0	1.00	0.40	0.75	0.29	0.05	0.09
PE 38:1	1.00	0.36	0.85	0.30	0.01	0.06
PE 38:2	1.00	0.69	0.99	0.08	0.05	0.15
PE 38:4	1.00	0.70	1.03	0.15	0.06	0.09
PE 38:5	1.00	0.61	0.89	0.09	0.05	0.07
PE 40:4	1.00	0.36	0.67	0.20	0.09	0.24
PE 40:6	1.00	0.41	0.67	0.33	0.02	0.08
PE 42:6	1.00	0.37	0.66	0.17	0.05	0.17
PE 42:7	1.00	0.56	0.99	0.11	0.06	0.12
PEp 36:4	1.00	0.86	1.28	0.12	0.08	0.09
PEp 38:4	1.00	0.68	1.04	0.16	0.04	0.07
PEp 38:5	1.00	0.61	0.94	0.27	0.07	0.04
PEp 38:6	1.00	0.50	0.85	0.27	0.03	0.06
PEp 40:5	1.00	0.40	0.80	0.29	0.03	0.12
PEp 40:6	1.00	0.36	0.72	0.30	0.04	0.10
PEp 40:7	1.00	0.36	0.85	0.30	0.01	0.06
PEp 42:5	1.00	0.38	0.69	0.15	0.08	0.21
PEp 42:6	1.00	0.41	0.72	0.12	0.03	0.12
PS 38:0	1.00	0.68	0.88	0.13	0.04	0.06
PS 42:7	1.00	0.81	1.01	0.06	0.02	0.12
PI 38:3	1.00	1.99	1.94	0.22	0.82	0.30
PI 42:7	1.00	1.56	2.24	0.18	0.71	0.32
PG 30:0	1.00	1.15	0.73	0.11	0.08	0.07
PG 34:0	1.00	1.22	1.01	0.15	0.06	0.03
PG 36:4	1.00	4.56***	2.33#	0.40	0.86	0.54
PG 38:1	1.00	1.82	0.93	0.31	0.22	0.15
PG 38:2	1.00	1.74	0.91	0.32	0.22	0.16
BMP 30:0	1.00	0.41	0.88	0.13	0.15	0.22
BMP 32:0	1.00	0.41	0.79	0.15	0.05	0.21

LIPIDS	CHOW Average	TESA Average	T+R Average	CHOW SE	TESA SE	T+R SE
BMP 38:5	1.00	1.02	0.81	0.14	0.04	0.06
AcylPG 16:0-34:1	1.00	1.11	0.84	0.08	0.08	0.04
AcylPG 16:0-38:4	1.00	0.68	0.88	0.10	0.02	0.08
LPCe 16:1	1.00	0.81	0.88	0.04	0.16	0.10
LPCe 20:1	1.00	0.72	0.83	0.09	0.05	0.11
LPCe 20:2	1.00	0.33	0.58	0.19	0.08	0.22
LPCe 20:3	1.00	0.81	0.63	0.10	0.06	0.06
LPE 20:1	1.00	0.67	0.51	0.13	0.04	0.11
LPE 20:2	1.00	0.88	0.63	0.09	0.13	0.05
NAPE 16:0/18:0/20:4	1.00	0.43	0.60	0.17	0.08	0.09
NAPE p18:0/18:1/20:4	1.00	1.08	0.83	0.09	0.05	0.02
NAPE p18:0/22:4/20:4	1.00	0.43	0.94	0.26	0.07	0.06
NAPE p18:0/22:6/20:4	1.00	0.52	0.81	0.15	0.03	0.07
NAPE p18:1/20:4/20:4	1.00	0.71	1.00	0.12	0.08	0.03
NAPS 16:0-36:1	1.00	3.79**	1.69	0.48	0.67	0.54
NAPS 16:0-38:3	1.00	1.36	0.16	0.53	0.17	0.05
NSer 16:1	1.00	1.11	0.59	0.21	0.16	0.06
NSer 18:1	1.00	1.27	0.71	0.21	0.11	0.07

Table S3. Cardiac lipid species in mice treated with chow diet containing tesaglitazar or combination of tesaglitazar and resveratrol, compared to mice fed on control chow diet. Statistical analysis was performed with 1-way ANOVA followed by Tukey correction (n=4). Data was collected from one experiment. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 vs chow. $^{\#}$p<0.05, $^{\#\#}$p<0.01, $^{\#\#\#\#}$p<0.0001 vs tesaglitazar.

Echocardiography parameters	Groups		
	CHOW	CHOW-TESA	CHOW-TESA+RSV
EF (%)	68.9 ± 2.56	52.8 ± 3.58*	67.1 ± 3.16$^{\#}$
FS (%)	38.4 ± 2.19	27.1 ± 2.32*	37.1 ± 2.39$^{\#}$
HR (bpm)	474.2 ± 5.71	476.6 ± 11.50	487.4 ± 13.50
LV Mass (mg)	137.2 ± 4.76	130.7 ± 6.61	124.3 ±3.21
LV Mass Cor (mg)	109.7 ± 3.81	104.6 ± 5.29	99.4 ± 2.56
LV Vol;d (ul)	79.8 ± 7.70	91.0 ± 3.61	83.1 ± 2.86
LV Vol;s (ul)	24.4 ± 1.86	42.84 ± 3.37*	27.32 ± 2.74$^{\#}$
IVS;d (mm)	0.9 ± 0.05	0.8 ± 0.06	0.7 ± 0.03
IVS;s (mm)	1.4 ± 0.04	1.1123 ± 0.04 **	1.2 ± 0.07
LVID;d (mm)	4.2 ± 0.17	4.5 ± 0.08	4.3 ± 0.06
LVID;s (mm)	2.6 ± 0.08	3.25 ± 0.11**	2.70 ± 0.11$^{\#}$
LVPW;d (mm)	0.8 ± 0.06	0.7 ± 0.04	0.8 ± 0.03
LVPW;s (mm)	1.3 ± 0.06	0.94 ± 0.02**	1.18 ± 0.07$^{\#}$

Table S4. Cardiac function analysis of diabetic *db/db* mice treated with tesaglitazar and resveratrol. 2D-echocardiography parameters of *db/db* mice treated with chow containing tesaglitazar (0.5µmol/kg body weight) or combination of tesaglitazar (0.5µmol/kg body weight) and resveratrol (100mg/kg body weight/day) for 6 weeks. Statistical analysis was performed with 1-way ANOVA followed by Tukey correction. *p<0.05, **p<0.01 vs chow. $^{\#}$p<0.05, $^{\#\#}$p<0.01 vs tesaglitazar. (n=4).

Echocardiography parameters	HFD	HFD-TESA
EF (%)	71.7 ± 0.8	55.53 ± 6.32**
FS (%)	40.4 ± 0.7	28.93 ± 4.02**
HR (bpm)	535 ± 9.7	476.6 ± 18.11
LV Mass (mg)	103.6 ± 7.3	98.2 ± 11.09
LV Mass Cor (mg)	82.9 ± 5.9	78.5 ± 8.87
LV Vol;d (ul)	65.4 ± 3	59.1 ± 4.61
LV Vol;s (ul)	18.5 ± 1.3	27.1 ± 5.54
IVS;d (mm)	0.7 ± 0.04	0.8 ± 0.08
IVS;s (mm)	0.9 ± 0.1	1.1 ± 0.08
LVID;d (mm)	3.9 ± 0.07	3.9 ± 0.11
LVID;s (mm)	2.3 ± 0.06	2.79 ± 0.19*
LVPW;d (mm)	0.8 ± 0.08	0.7 ± 0.04
LVPW;s (mm)	1.2 ± 0.06	0.946 ± 0.11*

Table S5. Cardiac function analysis of C57BL/6 wild type mice treated with high fat diet (HFD) or HFD plus tesaglitazar - 2D-echocardiography parameters of C57BL/6 mice fed on HFD or tesaglitazar-containing HFD (0.5µmol/kg body weight) for 6 weeks. Statistical analysis was performed with unpaired 2-tailed Student's t-test between groups, *p<0.05, **p<0.01. (n=5).

Antibodies	Company source	Catalogue number	Dilutions used in this study
Anti-PGC1α	Abcam	ab54481	1:1000
Anti-SIRT1	Abcam	ab12193	1:1000
Anti-β-ACTIN	Santa Cruz	SC-47778	1:1000
Anti-PPARα	Santa Cruz	SC-9000	1:1000
Anti-PPARγ	Santa Cruz	SC-7273	1:1000
Anti-SIRT3	Santa Cruz	SC-365175	1:500
Anti-SIRT6	Cell Signaling	D8D12	1:1000
Anti-Ac-Lysine	Santa Cruz	SC-81623	2µg
Anti-TOM-20	Santa Cruz	SC-136211	1:1000

Table S6. Antibodies that were used in the Western Blot and immunoprecipitation analyses of this study.

Gene	Forward primer (5´->3´)	Reverse primer (5´->3´)
m18S	CCATCCAATCGGTAGTAGCG	GTAACCCGTTGAACCCCATT
m36B4	GCGACCTGGAAGTCCAACTAC	ATCTGCTGCATCTGCTTGG
mPpargc1a	CACGCAGCCCTATTCA	GTCGTACCTGGGCCTA
mPpargc1b	AACCCAACCAGTCTCACAGG	CTCCTAGGGGCCTTTGTTTC
mAcadVl	CCGGTTCTTTGAGGAAGTGAA	AGTGTCGTCCTCCACCTTCTC
mPpara	TGCAAACTTGGACTTGAACG	GATCAGCATCCCGTCTTTGT
mCd36	TGTGTTTGGAGGCATTCTCA	TGGGTTTTGCACATCAAAGA
mCpt1b	CCCATGTGCTCCTACCAGAT	CCTTGAAGAAGCGACCTTTG
mLpl	GCTGGTGGGAAATGATGTG	TGGACGTTGTCTAGGGGGTA
mPparg	GAGTGTGACGACAAGATTTG	GGTGGGCCAGAATGGCATCT
mAcadm	GATGCATCACCCTCGTGTAAC	AAGCCCTTTTCCCCTGAA
mAcox1	GGATGGTAGTCCGGAGAACA	AGTCTGGATCGTTCAGAATCAAG
mEsrra	CCTTCCCTGCTGGACCTC	CGACACCAGAGCGTTCACT
mAngptl4	GGAAAAGATGCACCCTTCAA	TGCTGGATCTTGCTGTTTTG
mTfam	CCGAAGTGTTTTTCCAGCAT	GGCTGCAATTTTCCTAACCA
mAvadL	TTTCCGGGAGAGTGTAAGGA	ACTTCTCCAGCTTTCTCCCA
mUcp 3	TGCTGAGATGGTGACCTACGA	CCAAAGGCAGAGACAAAGTGA
mUcp 2	TCATCAAAGATACTCTCCTGAAAGC	TGACGGTGGTGCAGAAGC
mSirt1	ATCGGCTACCGAGGTCCATA	ACAATCTGCCACAGCGTCAT
mCol1a1	GCTTCACCTACAGCAACCCTT	TTCGATGACTGTCTTGCCCC
mActa1	CGCTCTTGTGTGTGACAACG	CCACGATGGATGGGAACACA
mNppb	CAGCTCTTGAAGGACCAAGG	TCCGATCCGGTCTATCTTGT
mNppa	CTGGGACCCCTCCGATAGAT	CACTCTGGGCTCCAATCCTG
mPpard	TGGAGCTCGATGACAGTGAC	GTACTGGCTGTCAGGGTGGT
mCoxII	GCCGACTAAATCAAGCAACA	CAATGGGCATAAAGCTATGG
mB-globin	GAAGCGATTCTAGGGAGCAG	GGAGCAGCGATTCTGAGTAGA
hRPS13	CCTTCACAGATCGGTGTAATCC	TCAGGAAGCAAGTCCCTTAGA
hPPARA	GGAGGTCCGCATCTTTCACT	CAGGTCCAAGTTTGCGAAGC
hPPARG	GCTGTGCAGGAGGAGATCACAGA	GGGCTCCATAAAGTCACCAA
hPPARGC1A	CCTTGCAGCACAAGAAACA	CTGCTTCGTCGTCAAAAACA
h18S	GCAATTATTCCCCATGAACG	GGCCTCACTAAACCATCCAA
PPARGC1A-1631 /-1609bp promoter (ChIP)	TTGACTGTGTGGAAAGTAGAGCCC	CTCCCACAAAGAAACACTAATTTTT
PPARGC1A +120 R-Luc	AAAAAACTCGAGAAAAGCAAGGAGAAAGGGAA	
PPARGC1A -1631 F-Luc	AAAAAAGGTACCTACCCCCGAGGTTGTATTTTCCTG	
PPARGC1A -1386 F-Luc	AAAAAAGGTACCTTTTTCTGTTTAAGGAGATGGACAA	
PPARGC1A -1012 F-Luc	AAAAAAGGTACCAGTGTCATCATAAAACAGTTGCAC	
PPARGC1A -210 F-Luc	GGGGGGTACCAAAGATTGCAGGGGATTTTG	

Table S7. Set of primers used for this study. Sequences of primers that were used for qRT-PCR, chromatic immunoprecipitation or for amplification of *PPARGC1A* promoter that was used for luciferase promoter analyses.

A)

Ingredient	g (%)
Casein	22.8
Maltodextrin	22.0
Sucrose	14.02
Lard	35.85
Mineral Mix	4.0
Vitamin Mix	1.0
Choline Chloride	0.13
DL-Methionine	0.2
Total	100

B)

	kcal/g	kcal (%)
Carbohydrate	1.43	26
Protein	0.82	15
Fat	3.24	59
Total	5.49	100

Tables S8. Ingredients (A) and representation of carbohydrates, proteins and fat (B) in the energetic input of high-fat diet (HFD)-fed mice.

SUPPLEMENTAL REFERENCES

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