Supplemental Materials

Reagents and antibodies

RNeasy Fibrous Tissue Mini Kit and RNase-Free DNase Set were from Qiagen (Valencia, CA); iScript Reverse Transcription Supermix for RT-PCR and iQ™ SYBR® Green Supermix were from Bio-Rad (Hercules, CA). Phosphatase inhibitor and protease inhibitor were from Roche (Indianapolis, IN). TRIzol was from Life Technologies (Carlsbad, CA); RIPA lysis and extraction buffer was from G-Biosciences (Louis, MO); Insulin was from Sigma Aldrich (St. Louis, MO). Green fluorescent protein (GFP) plasmid was from Lonza (Allendale, NJ); SIRPα plasmid cDNA was from Open Biosystems (Lafayette, CO); SIRPα recombinant protein was from R&D Systems (Minneapolis, MN). DMEM media and fetal bovine serum (FBS) were from Mediatech (Manassas, VA). The antibodies against GAPDH (#5174), SIRPα (#13379), p-AKT (S473, #4060), AKT (#2920), GLUT4 (#2213), PI3K (p85, #4257), pY-IGF1R (Tyr1135/1136, #2969), and IGFIR (#3027) were from Cell Signaling Technology (Danvers, MA). Fibronectin (#F3648) and αSMA (#A5228) were from Sigma Aldrich (St. Louis, MO). IGF1R (#sc81464) and SIRPα (#sc-376884) for immunoprecipitation were from Santa Cruz (Dallas, TX). Picrosirius Red Stain Kit was from Polysciences (Warrington, PA).

Chronic kidney disease model

To generate the CKD model, male adult mice were anesthetized at 8-10 weeks of age, and a subtotal nephrectomy was performed. Prior to nephrectomy the kidneys were freed from the surrounding tissue and then decapsulated to preserve the adrenal gland. Animals were subjected to nephrectomy in two staged surgery. In the first stage, ~70% of the left kidney was removed. The upper and lower poles of the kidney were partially resected, leaving one-third of the kidney. Seven days later, the right kidney was removed. The mice were fed standard rodent chow or 40% high protein diet as indicated in the figure legends. Sham-treated control mice underwent surgery without damaging the kidneys and were fed the similar diets. BUN and creatinine were measured in serum collected from the facial vein. 10-14 weeks after subtotal nephrectomy surgery, the chest of anesthetized mice was opened and infused with cold phosphate-buffered saline (PBS) which was introduced into the left ventricle prior to harvest. The hearts were weighed, and immediately freeze clamped, frozen in liquid nitrogen, and maintained at -80°C until analyzed.

Systolic blood pressure measurements

A noninvasive blood pressure analysis system (BP-2000, Visitech Systems, Apex, NC) was used to measure indirect blood pressure and heart rate for conscious non-anesthetized mice using tail cuff method.

Voluntary wheel exercise model

Seven weeks - old C57BL/6 male mice were obtained from Jackson laboratories (Jackson Labs, Bar Harbor, ME). These mice were fed *ad libitum* and kept on a 12-h light/12-h dark cycle in The University of Texas Health Science Center at Houston Institute of Molecular Medicine Animal Care Center. Two days after arrival, mice were assigned at random to individual cages with wheel runners (voluntary exercise) or infrared basal activity monitoring (sedentary) (STARR Life Sciences, Oakmont, PA). The mice were familiarized with their respective cages for 48 h and then exercise recording was started. Activity data were collected with VitalView (STARR Life Sciences, Oakmont, PA) and analyzed by ClockLabs (Actimetrics, Wilmette, IL). On day 6, 4 h after dark phase initiation, their hearts were harvested. These procedures were reviewed and approved by the Animal Welfare Committee of The University of Texas Health Science Center at Houston (AWC-14-0142).

Hyperglycemia model

Mice were fasted for 16 h with free access to water, and subsequently injected with intraperitoneal (i.p.) glucose (2 g/kg, at 40-min intervals for 3 repeats). Blood was collected at 120 min after the first dose of glucose injection, and the serum SIRPα levels in response to high-glucose stimulation *in vivo* were measured. Control mice were fasted for 16 h and treated with PBS at the same time points.

SIRPα recombinant protein treatment of mice

Eight weeks - old SIRPα$^{fl/fl}$ and skeletal muscle-specific SIRPα knockout (mSIRPα$^{-/-}$) mice were treated with SIRPα recombinant protein (rSIRPα, 1 μg/g) or the same volume of PBS control by left ventricle injection for 5 min and subsequent stimulation with 10 U/kg of insulin, which was allowed to circulate for 5 min before hearts were collected. For i.p. injection, mice were treated with 1.2 μg/g rSIRPα or PBS control for 2 h with 5 min of insulin stimulation before harvest.

Doppler ultrasound examination of mouse hearts

Mice were anesthetized with 1.5–2.0% isoflurane in 2 L/min oxygen and positioned supine on a physiological monitoring platform which simultaneously regulated body temperature. Prior to imaging, hair was removed from the chest to reduce the attenuation of the ultrasound signal. Once the apex and aortic outflow tract were visualized in the same plane on B-mode in the parasternal long-axis view, the probe was rotated 90° to obtain a short-axis view at the papillary muscles level, the M-mode beam was placed through the midline of the left ventricle, and M-mode images collected. Thereafter, transmitral flow velocities were recorded from the apical view using pulse wave Doppler by setting the sample volume in the mitral orifice. In the spectral waveforms, early (E) and late (A) diastolic transmitral velocities, and E/A ratio were recorded. In the same view, tissue Doppler imaging was used to assess tissue velocity of the mitral annulus. The sampling volume was placed at the level of the mitral annulus in the septum. The E and A diastolic velocities were recorded. For the echocardiographic parameters, an average of three measurements was used for each data point when possible.

Extracellular and intracellular treatment of SIRPα in myocytes

The C2C12 mouse myoblast cell line was purchased from American Type Culture Collection (Manassas, VA) and maintained in DMEM media containing 1% penicillin-streptomycin (ThermoFisher, Logan, UT) and 10% (v/v) FBS. Cells were seeded in 6-well plates and cultured at 37 °C under 5% CO2. Myotube differentiation was initiated by switching confluent C2C12 myoblasts to DMEM containing 2% horse serum (ThermoFisher, Logan, UT). The differentiation media were changed every two days. For extracellular treatment of SIRPα, fully differentiated myotubes were starved overnight and treated with 1 μg/mL SIRPα recombinant protein for 15, 30 min, and 1, 6, and 24 h. Subsequently, cellular protein was extracted and stored at -80°C. For intracellular treatment of SIRPα, C2C12 myoblasts (10^6) or HL-1 cardiomyocytes (cultured and maintained as described [48]) were electroporated with 1.5 μg GFP control or 1.5 μg SIRPα plasmid using Neon Transfection System (Invitrogen, Carlsbad, CA). The cultured cells were maintained in DMEM or Claycomb media containing 10% FBS, respectively, for 24 h and harvested. For pY-IGF1R evaluations, C2C12 myotubes or myoblasts were cultured in low glucose (5 mM) DMEM in these extracellular and intracellular treatment.

High glucose treatment of cells

C2C12 myoblasts were maintained in high glucose (25 mM) DMEM media containing 10% FBS. Confluent C2C12 myoblasts were differentiated in low glucose (5 mM) DMEM plus 2% horse serum. Fully differentiated myotubes were starved overnight in low glucose DMEM media and subsequently treated with high glucose DMEM for 48 h. Cell or media protein was extracted with RIPA or acetone, respectively, and stored at -80°C.

HL-1 cardiomyocytes were cultured to confluency in Claycomb media (containing 22 mM glucose) supplemented with 10% FBS, 0.1 mM norepinephrine, 2 mM L-glutamine, and 1% penicillin/streptomycin, starved for 6 h and treated with high glucose (90 mM) for 1, 6, 24, or 48 h. Cell or media protein was extracted with RIPA or acetone, respectively, and stored at -80°C.

3T3-L1 cells were purchased from American Type Culture Collection (Manassas, VA) and cultured in preadipocyte media (DMEM/F12 containing 10% FBS and 1% penicillin/streptomycin) in 5% CO2 in a humidified incubator at 37°C. The cells were grown to confluency in 6 wells and then treated by induction media (1.5 µg/mL insulin, 1 µM dexamethasone, 500 µM IBMX, and 1 µM rosiglitazone in the preadipocyte media). Three days after induction, cultured cells were maintained in media (1.5 µg/mL insulin in the preadipocyte media with 5 mM low glucose) for 4 days of differentiation. Fully differentiated adipocytes were serum starved overnight in low glucose DMEM, subsequently the cells were treated with high glucose (25 mM) DMEM for 48 h. Cell or media protein was extracted with RIPA or acetone, respectively, and stored at -80°C.

Uremic toxin, p-cresol sulfate, treated HL-1 cardiomyocytes

HL-1 cardiomyocytes were cultured to confluency as previously described, starved overnight and treated with uremic toxin, p-cresol sulfate (PCS) with a concentration of 40 µg/mL (212 µM) for 1, 6, 24 h. Cell or media protein was extracted with RIPA or acetone, respectively, and stored at -80°C.

Reverse transcription-quantitative polymerase chain reaction (PCR)

Total RNA of heart was extracted using TRIzol and purified with RNeasy Fibrous Tissue Mini Kit. First-strand cDNA was synthesized from 1 µg DNase-treated total RNA using Reverse Transcription Supermix for reverse transcription-quantitative polymerase chain reaction (RT-qPCR). The mRNA levels were evaluated by qPCR using SYBR Green Supermix. Reactions of qPCR were performed in 96-well format using a CFX96™ Real-Time System (Bio-Rad, Hercules, CA). The reaction volume was 10 µL, including 5 µL SYBR Green Supermix, 2 µL 2.5 µM primer, and 1 µL cDNA. The following thermal cycling profile was used: 95°C 3 min; 40 cycles of 95°C for 15 s, 60°C for 30s; followed by 55°C to 95°C increment for dissociation curve analysis. The relative mRNA levels were calculated using the comparative $2^{-\Delta\Delta CT}$ method and normalized to Cyclophilin mRNA. Sequence information of mouse primers is as follows:

Cyclophilin	F: 5’- CCGATGACGAGCCCTTG-3′	R: 5′-TCTGCTGTCTTTGGAACTTTGTC-3′
SIRPα	F: 5′-CTCTGTGGACGCCTGTAA-3′	R: 5′-GATGCTGCTGCTGTTGTT-3′
ANP	F: 5′-GAGAGAAAGAAACCAGAGTG -3′	R: 5′-GTCTAGCAGGTTCTTGAAATC-3′
BNP	F: 5′-AATTCAAGATGCAGAAGCTG-3′,	R: 5′-GAATTTTGAGGTCTCTGCTG-3′
UCP3	F: 5′-CAAGAAATGCCATTGTCAAC-3'	R: 5′-GAAGTTGTCAGTAAACAGGTG-3′
MHCα	F: 5′-AATCCTAATGCAAACAAGGG-3′	R: 5′-CAGAAGGTAGGTCTCTATGTC-3′
MHCβ	F: 5′-GATGATCTATACCTACTCGGG-3′	R: 5′-TGATGAGGATGGACTGATTC-3′
PGC1α	F: 5’-TCCTCTTCAAGATCCTGTTAC-3’	R: 5’-CACATACAAGGGAGAATTGC-3’
PPARα	F: 5’-GAATCCACGAAGCCTACC-3’	R: 5’-GCCATACACAAGGTCTCC-3’
CPT1b	F: 5’-CTGGAGGTGGCTTTGGTCC-3’	R: 5’-GGGCGTTCGTCTCTGAACTTG-3’
ACC1	F: 5’-ATTGGGCACCCCAGAGCTA-3’	R: 5’-CCCGCTCCTTCAACTTGCT-3’
GLUT1	F: 5’- CTTGCTTGTAGAGTGACGATC-3′	R: 5′-CAGTGATCCGAGCACTGCTC-3′
GLUT4	F: 5’-GAGCCTGAATGCTAATGGAG-3′	R: 5′-GAGAGAGAGCGTCCAATGTC-3′

Western blots

We homogenized 30 mg heart tissue for 1 min in 300 µL cold RIPA buffer supplemented with protease and phosphatase inhibitor cocktails. The homogenates were incubated on ice for 10 min and then centrifuged (15,600 g) at 4°C for 15 min. The supernatants were used as whole cell lysates. Protein concentration was determined by Pierce BCA Protein Assay. An equal amount of protein (80-100 µg) was separated on sodium dodecyl sulfate- polyacrylamide gel electrophoresis in tris/glycine buffer, transferred to nitrocellulose blotting membrane, blocked for 20 min, and blotted with all primary antibodies diluted (1:1000) except GAPDH (1:2000) and Fibronectin (1:3000) in blocking buffer overnight at 4°C. After 3 times of washing in TBS containing 0.1% Tween20, the membrane was incubated in secondary antibody diluted with TBS containing 0.1% Tween20 for 1 h and washed mentioned earlier above, and the protein was detected using the ChemiDoc MP Imaging System (Bio-Rad, Hercules, CA). The protein of interest was analyzed using Image Lab 6.0 (Bio-Rad, Hercules, CA), and the protein intensities were quantified using NIH ImageJ software. GAPDH was used as an internal standard unless otherwise specified to quantify western blot bands.

Immunoprecipitation

Heart tissue (20 mg), was homogenized in 200 μL immunoprecipitation (IP) lysis buffer (containing 20 mM Tris-HCL pH 8.0, 137 mM NaCl, 0.5% NP-40, 2 mM EDTA, 0.05% Triton X-100, phosphatase and protease inhibitors) and placed on rotation shaker at 4°C for 1 h. Supernatant was obtained by centrifugation (15,600 g) for 20 min at 4°C. Immunoprecipitation was performed by adding 4 μg of anti-SIRPα (Santa Cruz) or anti-IGF 1R (Santa Cruz) to 1 mg heart lysates in IP lysis buffer. After continuous agitation overnight at 4°C, 20 μL of Protein A/G Plus beads were added. The mixture was agitated in a rotational shaker for 2 h at 4°C. Following centrifugation at 450 g for 5 min, the supernatant was removed. The beads were washed five times with IP lysis buffer and western blots or Octet RED384 assay development were performed.

Octet RED384 assay development

The binding affinity between IGF1R IP lysates and purified recombinant SIRPα (rSIRPα) was performed using Octet RED384 System (Fremont, CA, USA). The assay temperature was maintained at 30°C on the Octet RED384 system. Purified Fc-containing ligand rSIRPα was immobilized onto Anti-Mouse lgG Fc Capture Biosensor at a concentration of 2.5 μg/mL for 10 min. IGF-1R IP protein was introduced into Fortébio's kinetic buffer in order to obtain a serial dilution of the analyte (5.6, 2.8, 1.4 μM). Fortébio's kinetic buffer was used as the reference control to determine the background signal. The binding assay was conducted in a 384-well tilted-bottom microplate (Fortébio). The Octet RED384 assay method was set as follows: the biosensors were first washed in PBS for 2 min for baseline stabilization. The biosensors were then dipped in diluted rSIRPα solution for 10 min, followed by 2.5 min washing in kinetic buffer to establish a new baseline. The biosensors were then transferred into different concentrations of IGF1R lysates for 5 min (association) followed by another 5 min washing procedure (dissociation) in kinetic buffer. Data were collected and analyzed using Octet Data analysis HT software 11.1 (Fremont, Menlo Park, CA). Binding kinetics were measured using one-to-one binding site model to determine the observed rate constant (kobs), the association rate constant (ka), and the dissociation rate constant (kdis). The Octet data analysis software uses the rate constant parameters to calculate the reported binding affinity constant, KD (kdis/ka).

Section and staining

For immune histochemical staining, tissues were fixed in 10% formalin, embedded in paraffin, and cut into 6 μm sections on slides. The slides were incubated with the 1:50 diluted anti-SIRPα antibody (Cell Signaling Technology). Photomicrographs of heart are shown by H&E staining. Myocardial fibrosis of the CKD hearts was evaluated by picrosirius red-stained sections which were scanned using a microscope equipped with a digital camera (Nikon, Melville, NY), and evaluation was performed using NIS-Elements Br 3.0 software and quantified using NIH ImageJ software. The collagen-stained area was calculated as a fold change of the total area, as previously described [49].

Supplemental Figures

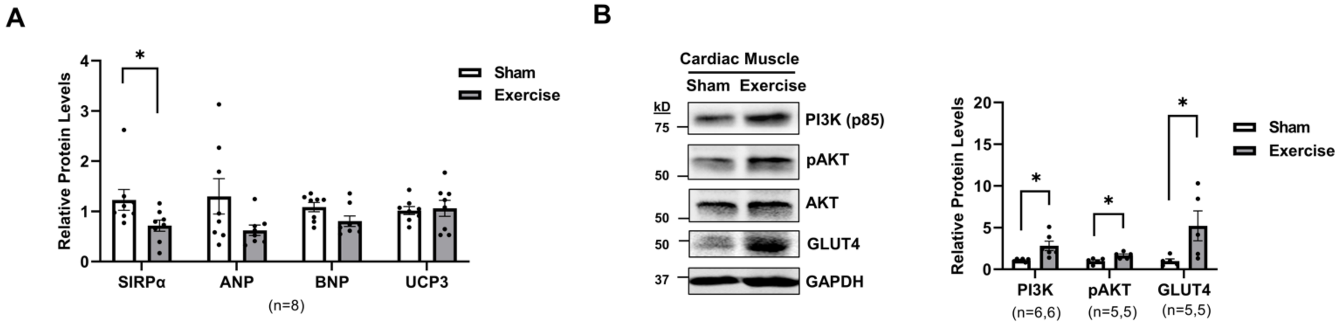

Figure S1. Acute exercise decreases SIRPα expression in cardiac muscle and improves insulin sensitivity. (A) Expression levels of SIRPα, ANP, BNP, and UCP3 were analyzed by quantitative real time-PCR and normalized relative to cyclophilin. (B) Heart lysates from Sham and Exercise treated mice were immunoblotted to detect PI3K (p85), pAKT, AKT, GLUT4, and GAPDH and representative immunoblots of averaged data are shown (left panel) with relative densities to GAPDH or pAKT to AKT are shown (right panel). Statistical significance was calculated using unpaired two-tailed Student's *t*-test (A-B). Values are expressed as means ± SEM; *p<0.05.

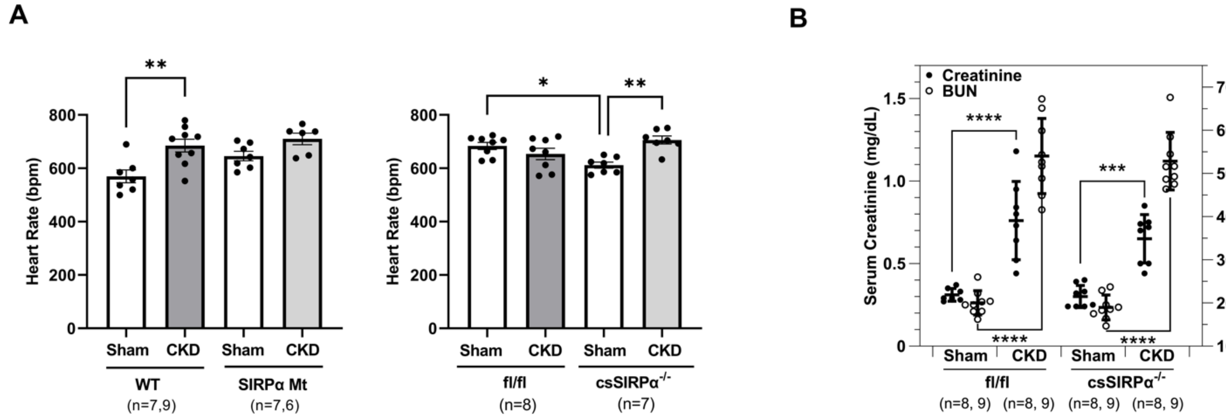

Figure S2. Heart rate and serum levels of creatinine and blood urea nitrogen (BUN) after CKD. (A) Heart rate beats per minute (bpm) from WT and SIRPα Mt with or with CKD or SIRPα$^{fl/fl}$ and csSIRPα$^{-/-}$ with or without CKD were determined. (B) Creatinine and BUN were measured at 9-10 weeks after subtotal nephrectomy in sham operated flox (SIRPα$^{fl/fl}$) mice and cardiac-specific KO (csSIRPα$^{-/-}$) mice with or without CKD. Statistical significance was calculated using one-way ANOVA with Bonferroni's multiple comparisons test (A-B). Values are means ± SEM. *p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001.

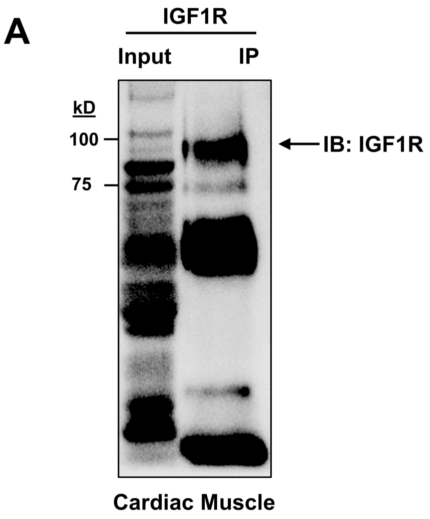

Figure S3. rSIRPα interacts with myocardial IGF1R. In heart lysates of flox CKD mice, IGF1R was immunoprecipitated and confirmed by immunoblot.

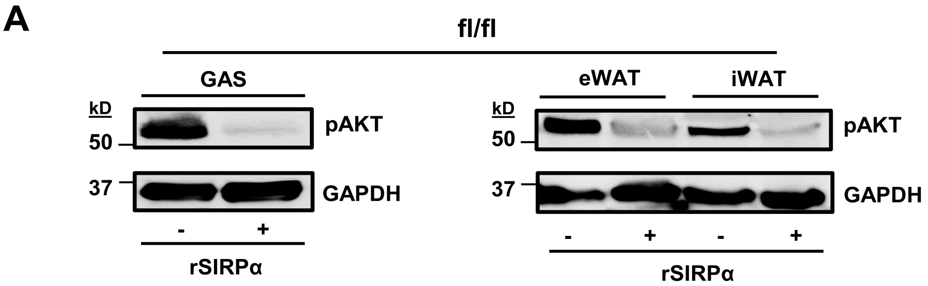

Figure S4. Exogenous SIRPα suppresses insulin signaling in the skeletal muscle and fat. Flox (SIRPα$^{fl/fl}$) mice were treated with SIRPα recombinant protein (rSIRPα; 1.2 μg/g) by intraperitoneal (i.p.) injection for 2 h. Protein lysates of gastrocnemius (GAS) and adipose tissue (epididymal white adipose tissue, eWAT; inguinal white adipose tissue, iWAT) were immunoblotted to detect pAKT and GAPDH.

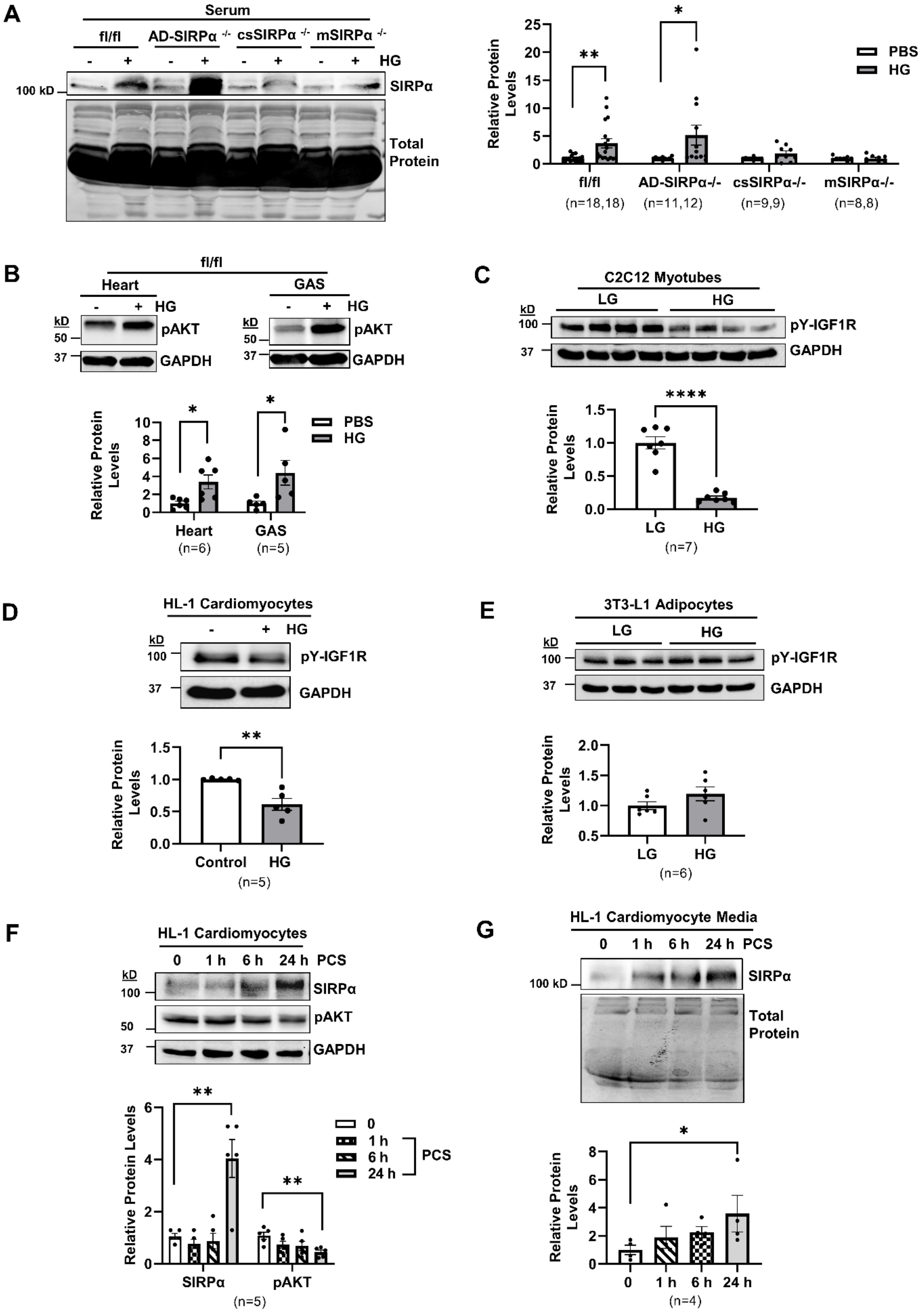
A
Serum
fl/fl
AD-SIRPα -/-
csSIRPα -/-
mSIRPα -/-
- + - + - + - + HG
100 kD
SIRPα
Total Protein
Relative Protein Levels
25
20
15
10
5
0
**
*
PBS
HG
fl/fl (n=18,18)
AD-SIRPα-/- (n=11,12)
csSIRPα-/- (n=9,9)
mSIRPα-/- (n=8,8)
B
fl/fl
Heart
GAS
- + HG
kD
50
37
pAKT
GAPDH
Relative Protein Levels
10
8
6
4
2
0
*
*
PBS
HG
Heart (n=6)
GAS (n=5)
C
C2C12 Myotubes
LG
HG
kD
100
37
pY-IGF1R
GAPDH
Relative Protein Levels
1.5
1.0
0.5
0.0
****
LG
HG
(n=7)
D
HL-1 Cardiomyocytes
- + HG
kD
100
37
pY-IGF1R
GAPDH
Relative Protein Levels
1.5
1.0
0.5
0.0
**
Control
HG
(n=5)
E
3T3-L1 Adipocytes
LG
HG
kD
100
37
pY-IGF1R
GAPDH
Relative Protein Levels
2.0
1.5
1.0
0.5
LG
HG
(n=6)
F
HL-1 Cardiomyocytes
0 1 h 6 h 24 h PCS
kD
100
50
37
SIRPα
pAKT
GAPDH
Relative Protein Levels
6
4
2
0
**
**
0
1 h
6 h
24 h
PCS
SIRPα
pAKT
(n=5)
G
HL-1 Cardiomyocyte Media
0 1 h 6 h 24 h PCS
100 kD
SIRPα
Total Protein
Relative Protein Levels
8
6
4
2
0
*
0
1 h
6 h
24 h
(n=4)

Figure S5. Hyperglycemia or uremia treatment stimulates SIRPα into circulation and impairs IGF1 receptor signaling. (A) Mice treated with high glucose (HG; 2 g/kg every 40 minutes × 3 doses) were compared to PBS treated mice. Serum from flox (SIRP$\alpha^{fl/fl}$) and organ specific knockout mice were immunoblotted to detect SIRPα and total protein and representative immunoblots of averaged data are shown (left panel) and relative levels are shown (right panel). (B) Protein lysates of heart and gastrocnemius (GAS) were obtained from PBS control vs. HG treated mice and immunoblotted to detect pAKT and GAPDH and representative immunoblots of averaged data are shown (top panel) with relative densities to GAPDH are shown (bottom panel). (C) C2C12 myotubes were cultured in low glucose (LG, 5 mM) media and treated with HG (25 mM) for 48 h, and cell lysate was immunoblotted to detect pY-IGF1R and GAPDH and representative immunoblots of averaged data are shown (top panel) with relative densities to GAPDH shown (bottom panel). (D) HL-1 cardiomyocytes were cultured in Claycomb media and treated with high glucose (HG, 90 mM) for 48 h. Protein lysates were immunoblotted to detect pY-IGF1R and GAPDH and representative immunoblots of averaged data are shown (top panel) and the relative densities to GAPDH are shown (bottom panel). (E) 3T3-L1 adipocyte were treated with LG media (5 mM) or HG (25 mM) for 48 h. Protein lysates were immunoblotted to detect pY-IGF1R and GAPDH and representative immunoblots of averaged data are shown (top panel) and relative levels are shown (bottom panel). (F) HL-1 cardiomyocytes were treated with PBS control or p-cresol (PCS; 212 μM) and cardiomyocytes lysates were immunoblotted with SIRPα, pAKT and GAPDH and representative immunoblots of averaged data are shown (top panel) and relative levels are shown (bottom panel). (G) SIRPα was identified in HL-1 cardiomyocyte cultured media and detected by immunoblot and representative immunoblots of averaged data are shown (top panel) with relative levels to total protein shown (bottom panel); Statistical significance was calculated using unpaired two-tailed Student's *t*-test (A-F) and Mann Whitney test (G). Values are expressed as means ± SEM; *p<0.05, ** p<0.01, **** p<0.0001.

Supplemental Tables

Table S1: CKD Patient Characteristics

Age	Gender	Race	Calcium (mg/dL)	Phosphorus (mg/dL)	PTH (ng/L)	Fasting Glucose (mg/dL)	Creatinine (mg/dL)	DM	HTN
46	M	Caucasian	8.6	9.6	572	80	12.8	no	no
65	F	Caucasian	9	3.4	319	89	8.3	yes	yes
49	F	Caucasian	9.3	8.7	171	80	10.5	no	yes
40	M	Caucasian	9.1	4.4	68	82	12.2	no	yes
53	F	Caucasian	9.3	7.9	228	88	9.2	no	yes
60	F	Caucasian	8.5	5	1060	102	7.1	no	yes
30	F	African	8.8	5.8	861	90	13.1	no	no
80	F	Caucasian	8.4	2.7	173	76	8.8	no	yes
34	M	Caucasian/ M. Eastern	9.6	3.3	39	72	15.4	no	no
59	M	Caucasian	7.5	4.5	171	75	8.7	no	yes
80	M	Caucasian	8.6	2.7	146	77	6.9	no	yes
52	F	Caucasian	7.6	5.1	412	91	11.1	no	yes
34	F	Caucasian	9.5	1.7	165	79	8.9	no	yes
23	M	Hispanic	8.8	3	299	113	19.2	no	no
75	F	Caucasian	9.5	5.9	282	99	10.2	no	yes
57	F	Caucasian	9.6	5.5	135	86	11	no	yes
77	M	Caucasian	9.1	3.2	79	77	6.8	no	yes
79	M	Caucasian	8.7	5.4	250	148	7.1	yes	yes
75	M	Caucasian	9	8.8	180	90	5.8	yes	yes
70	M	Caucasian	8.5	5.5	250	144	9.7	yes	yes

Note: PTH: parathyroid hormone; DM: diabetes; HTN: hypertension; M.: Middle

Table S2: Echocardiographic Analysis in WT and SIRPα Mt

	WT Sham	WT CKD	SIRPα Mt Sham	SIRPα Mt CKD
LVAWd (mm)	1.16±0.09	1.02±0.18	1.13±0.06	1.054±0.16
LVAWs (mm)	1.63±0.15	1.38±0.22	1.66±0.14	1.60±0.22
LVIDd (mm)	3.62± 0.41	3.73±0.32	4.08±0.20$^{\#}$	4.14±0.39
LVIDs (mm)	2.33±0.29	2.73±0.45	2.45±0.30	2.70±0.25
LVPWd (mm)	1.01±0.08	0.89±0.13	0.98±0.12	0.94±0.12
LVPWs (mm)	1.48±0.14	1.26±0.23	1.66±0.23	1.40±0.18
LV mass/height (mg/mm)	1.33±0.22	1.21±0.22	1.53±0.17	1.56±0.42
LV/BW (mg/g)	3.38±0.55	4.55±0.99*	4.28±0.63	4.91±1.33
CO (mL/min)	20.15±3.21	15.41±2.22*	25.31±2.95$^{\#}$	23.60±5.77$^{\#\#\#}$
EF (%)	65.90±5.30	53.12±11.30**	70.65±6.83	64.33±5.07$^{\#}$
FS (%)	35.66±4.06	27.26±7.64*	39.94±5.81	34.82±3.68$^{\#}$
HR (bpm)	466.16±13.55	462.41±24.59	474.26±17.14	459.27±25.19
SV (µL)	40.31±8.11	35.30±4.65	52.32±6.16$^{\#}$	50.76±12.84$^{\#\#}$
RWT (mm)	0.61±0.10	0.52±0.12	0.52±0.05	0.48±0.06
E/A	2.04±0.84	1.24±0.20*	1.47±0.35	1.52±0.22
E/e'	41. 95±8.71	46.17±7.55	42.23±13.19	47.46±11.46
MPI	1.09±0.32	0.90±0.25	0.98±0.18	0.95±0.22

Note: LVAWd : left ventricular end-diastolic anterior wall thickness; LVAWs: left ventricular end-systolic anterior wall thickness; LVIDd: left ventricular end-diastolic diameter; LVIDs: left ventricular end-systolic diameter; LVPWd: left ventricular end-diastolic posterior wall thickness; LVPWs: left ventricular end-systolic posterior wall thickness; BW: body weight; CO: cardiac output; EF: ejection fraction; FS: fractional shortening; HR: heart rate; SV: stroke volume; RWT: relative wall thickness; E/A: ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave); E/e': ratio between early mitral inflow velocity and mitral annular early diastolic velocity; MPI: myocardial performance index. Statistical significance was calculated using one-way ANOVA with Tukey's multiple comparisons test. Values are expressed as means ± SD; * p<0.05, **<0.01 Sham vs CKD; #p<0.05, ##p<0.01, ###p<0.001 WT vs SIRPα Mt.

Table S3: Echocardiographic Analysis in SIRPα$^{fl/fl}$ and csSIRPα$^{-/-}$ with CKD

	SIRPα$^{fl/fl}$ CKD	csSIRPα$^{-/-}$ CKD
LVAWd (mm)	0.77±0.08	0.80±0.09
LVAWs (mm)	0.96±0.07	1.14±0.23
LVIDd (mm)	4.27±0.35	4.62±0.37
LVIDs (mm)	3.63±0.38	3.65±0.53
LVPWd (mm)	0.75±0.19	0.65±0.13
LVPWs (mm)	0.92±0.22	0.93±0.17
LV Mass (mg)	123.09±23.75	137.20±36.91
CO (mL/min)	11.27±2.46	21.19±4.01***
EF (%)	32.63±5.27	45.12±9.52*
FS (%)	15.33±2.69	24.30±6.77*
HR (bpm)	423.17±46.77	467.66±39.32
SV (µL)	26.44±3.81	45.06±5.14****

Note: LVAWd : left ventricular end-diastolic anterior wall thickness; LVAWs: left ventricular end-systolic anterior wall thickness; LVIDd: left ventricular end-diastolic diameter; LVIDs: left ventricular end-systolic diameter; LVPWd: left ventricular end-diastolic posterior wall thickness; LVPWs: left ventricular end-systolic posterior wall thickness; CO: cardiac output; EF: ejection fraction; FS: fractional shortening; HR: heart rate; SV: stroke volume; Statistical significance was calculated using unpaired two-tailed Student's *t*-test. Values are expressed as means ± SD; *P<0.05, *** p<0.001, **** p<0.0001 SIRPα$^{fl/fl}$ CKD vs. csSIRPα$^{-/-}$ CKD.

Table S4: Bio-layer Interferometry Analysis

KD (µM)	KD Error	ka (1/Ms)	ka Error	kdis (1/s)	kdis Error	Full X^2	Full R^2
147	4.58E-05	3.02E+01	9.40E+00	4.43E-03	2.09E-05	0.6691	0.9522

Note: Kinetic results for the interaction between Fc-containing ligand SIRPα and anti-mouse IGF-1R IP protein using bio-layer interferometry, Octet RED384 platform. The kinetic results of association rate constant (ka) and dissociation rate constant (kdis) and affinity (equilibrium dissociation, KD) were highly comparable.

Statistical Table

Figure	Parametric Analysis Type	p Value
1A		
BUN		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.00000004
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.00000012
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
Creatinine		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0037
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0089
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	>0.9999
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
1B	unpaired two-tailed t test	0.0016
1D	unpaired two-tailed t test	0.0074
1E	unpaired two-tailed t test	0.0001
2B		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0052
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0164
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.3587
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.7912
2C		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0135
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.4598
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.03
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.2477
2D		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0176
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0116
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.000046
2F	unpaired two-tailed t test	0.0226
2G	unpaired two-tailed t test	0.0221
2H	unpaired two-tailed t test	0.0008
3A		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.026
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0001
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0923
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0005
3B		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0022
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0028
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.2525
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.2055
3C (top panel)		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0005
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.4537
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.00000058
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
3C (bottom panel)		

fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0019
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0416
fl/fl CKD vs. csSIRPα $^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.3345
3D		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0122
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0025
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0375
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
3E		
ACC1		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0003
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.827
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.3814
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.4179
ANP		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0318
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0023
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.1028
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.5707
BNP		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0023
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.6044
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.2527
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
CPT1b		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0011
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0064
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
GLUT1		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0007
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0346
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0739
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
GLUT4		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0005
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0065
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.313
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
MHCα		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0014
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0057
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
MHCβ		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0015
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0816
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999

SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
PGC1a		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.000071
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.3809
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0222
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
PPARα		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.000019
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0186
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.4532
UCP3		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	>0.9999
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0035
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.4771
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0494
3F		
ACC1		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0158
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.1932
ANP		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0001
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	0.0012
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0781
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0093
BNP		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0009
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0186
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.9595
CPT1b		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0249
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0691
GLUT1		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.00096
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0666
GLUT4		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0033
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.2073
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
MHCα		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0119
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	0.3411
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999

fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.3315
MHCβ		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0005
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	0.2019
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.8851
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0049
PGC1α		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0022
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0021
PPARα		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0149
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.1394
UCP3		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0283
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	0.061
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0001
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
3G		
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD		
ACC1	unpaired two-tailed t test	0.4517
ANP	unpaired two-tailed t test	0.089
BNP	unpaired two-tailed t test	0.9589
CPT1b	unpaired two-tailed t test	0.2666
GLUT1	unpaired two-tailed t test	0.1405
GLUT4	unpaired two-tailed t test	0.2261
MHCα	unpaired two-tailed t test	0.1899
MHCβ	unpaired two-tailed t test	0.078
PGC1α	unpaired two-tailed t test	0.6005
PPARα	unpaired two-tailed t test	1.02
UCP3	unpaired two-tailed t test	0.9244
4A		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.000022
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.000007
4B		
αSMA		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0084
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.1455
Fibronectin		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0493
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0014
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.9935
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999

pAKT		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0054
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.1348
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.9175
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.0657
PI3K		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0117
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.0683
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
4C		
αSMA		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0027
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.1098
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
Fibronectin		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0196
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.1191
pAKT		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.8564
PI3K		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0171
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0859
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
4D		
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD		
αSMA	unpaired two-tailed t test	0.4162
fibronectin	unpaired two-tailed t test	0.0919
pAKT	unpaired two-tailed t test	0.4911
PI3K	unpaired two-tailed t test	0.6876
5A		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.0004
fl/fl Sham vs. mSIRPα$^{-/-}$Sham	one-way ANOVA with Bonferroni's	>0.9999
mSIRPα$^{-/-}$Sham vs. mSIRPα$^{-/-}$CKD	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$CKD	one-way ANOVA with Bonferroni's	0.0056
6A		
pAKT/AKT		
fl/fl PBS vs. fl/fl rSIRPα	unpaired two-tailed t test	0.00000003
mSIRPα$^{-/-}$ PBS vs. mSIRPα$^{-/-}$ rSIRPα	unpaired two-tailed t test	0.0203
pY-IGF1R/IGF1R		
fl/fl PBS vs. fl/fl rSIRPα	unpaired two-tailed t test	0.0006
mSIRPα$^{-/-}$ PBS vs. mSIRPα$^{-/-}$ rSIRPα	unpaired two-tailed t test	0.0218
6B		
pAKT 15min vs. 0	unpaired two-tailed t test	0.2634

pAKT 30 min vs. 0	unpaired two-tailed t test	0.8675
pAKT 1 h vs. 0	unpaired two-tailed t test	0.1197
pAKT 6 h vs. 0	unpaired two-tailed t test	0.0013
pAKT 24 h vs. 0	unpaired two-tailed t test	0.0371
pY-IGF1R 15 min vs. 0	unpaired two-tailed t test	0.0006
pY-IGF1R 30 min vs. 0	unpaired two-tailed t test	0.0003
pY-IGF1R 1 h vs. 0	unpaired two-tailed t test	0.0001
pY-IGF1R 6 h vs. 0	unpaired two-tailed t test	0.0067
pY-IGF1R 24 h vs. 0	unpaired two-tailed t test	0.0765
Fibronectin 15 min vs. 0	unpaired two-tailed t test	0.0752
Fibronectin 30 min vs. 0	unpaired two-tailed t test	0.0411
Fibronectin 1 h vs. 0	unpaired two-tailed t test	0.0294
Fibronectin 6 h vs. 0	unpaired two-tailed t test	0.0053
Fibronectin 24 h vs. 0	unpaired two-tailed t test	0.0014
6C		
SIRPα	unpaired two-tailed t test	0.000074
pAKT/AKT	unpaired two-tailed t test	0.0004
pY-IGF1R/IGF1R	unpaired two-tailed t test	0.0004
6D		
SIRPα	unpaired two-tailed t test	0.0275
pAKT/AKT	unpaired two-tailed t test	0.0057
pY-IGF1R/IGF1R	unpaired two-tailed t test	0.0181
7A	unpaired two-tailed t test	0.0007
7B	unpaired two-tailed t test	0.0405
7C		
0 vs. 1 h HG	unpaired two-tailed t test	0.3049
0 vs. 6 h HG	unpaired two-tailed t test	0.2716
0 vs. 24 h HG	unpaired two-tailed t test	0.0178
7D		
0 vs. 1 h HG	unpaired two-tailed t test	0.0643
0 vs. 6 h HG	unpaired two-tailed t test	0.0775
0 vs. 24 h HG	unpaired two-tailed t test	0.0019
7E	unpaired two-tailed t test	0.0012
S1A		
SIRPα	unpaired two-tailed t test	0.0476
ANP	unpaired two-tailed t test	0.0865
BNP	unpaired two-tailed t test	0.0637
UCP3	unpaired two-tailed t test	0.808
S1B		
PI3K	unpaired two-tailed t test	0.0123
pAKT	unpaired two-tailed t test	0.0184
GLUT4	unpaired two-tailed t test	0.0483
S2A (left panel)		
WT Sham vs. WT CKD	one-way ANOVA with Bonferroni's	0.0037
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Bonferroni's	0.2791
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Bonferroni's	0.1114
S2A (right panel)		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.7362
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	0.0154
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0018

fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.1223
S2B		
BUN		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	4.1E-13
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	4.4E-13
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	>0.9999
Creatinine		
fl/fl Sham vs. fl/fl CKD	one-way ANOVA with Bonferroni's	0.000004
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.0002
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	one-way ANOVA with Bonferroni's	>0.9999
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	one-way ANOVA with Bonferroni's	0.533
S5A		
fl/fl PBS vs. HG	unpaired two-tailed t test	0.0031
AD-SIRPα$^{-/-}$ PBS vs. HG	unpaired two-tailed t test	0.038
csSIRPα $^{-/-}$ PBS vs. HG	unpaired two-tailed t test	0.091
mSIRPα$^{-/-}$ PBS vs. HG	unpaired two-tailed t test	0.8011
S5B		
Heart-PBS vs. HG	unpaired two-tailed t test	0.015
Gastrocnemius-PBS vs. HG	unpaired two-tailed t test	0.0415
S5C	unpaired two-tailed t test	0.000002
S5D	unpaired two-tailed t test	0.0029
S5E	unpaired two-tailed t test	0.1706
S5F		
SIRPα 0 vs. 1 h PCS	unpaired two-tailed t test	0.1821
SIRPα 0 vs. 6 h PCS	unpaired two-tailed t test	0.5755
SIRPα 0 vs. 24 h PCS	unpaired two-tailed t test	0.0037
pAKT 0 vs. 1 h PCS	unpaired two-tailed t test	0.1061
pAKT 0 vs. 6 h PCS	unpaired two-tailed t test	0.1194
pAKT 0 vs. 24 h PCS	unpaired two-tailed t test	0.0042
S5G		
0 vs. 1 h PCS	unpaired two-tailed t test	0.3362
0 vs. 6 h PCS	unpaired two-tailed t test	0.0532
0 vs. 24 h PCS	unpaired two-tailed t test	0.1038
TABLES		
Table S2		
LVAWd (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9739
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.1803
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3752
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.3341
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.5958
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9771
LVAWs (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.1074
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0513
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0296
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.9838
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9056
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9877

LVIDd (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0863
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.9168
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.2013
KO CKD vs. WT Sham	one-way ANOVA with Tukey's	0.016
KO CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9808
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0489
LVIDs (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9977
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0809
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3598
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.1023
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.4343
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.861
LVPWd (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.782
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.1224
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3455
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.5145
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.8549
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9453
LVPWs (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.5009
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.1277
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.002
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.8132
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0512
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.2705
LV/Height (mg/mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0559
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.7958
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0993
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.3177
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9975
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.4475
LV/BW (mg/g)		
WT Sham vs. WT CKD	one-way ANOVA with Tukey's	0.0486
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.1804
WT Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0067
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9276
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.8642
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.5161
CO (mL/min)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0002
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0445
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.000011
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.2245
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.7664
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0297
EF (%)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0203

WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0068
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0003
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.9691
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3149
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.5596
FS (%)		
WT Sham vs. WT CKD	one-way ANOVA with Tukey's	0.0169
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3812
WT Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9878
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0003
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.0357
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.2336
HR (bpm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9892
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.982
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.6651
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.8938
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.4552
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.8512
SV (μL)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.005
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.6393
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0025
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0719
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9824
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.0375
RWT (mm)		
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.7946
WT CKD vs. WT Sham	one-way ANOVA with Tukey's	0.166
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	>0.9999
SIRPα Mt CKD vs. WT Sham	one-way ANOVA with Tukey's	0.0185
SIRPα Mt CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.7905
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.1684
E/A		
WT Sham vs. WT CKD	one-way ANOVA with Tukey's	0.0276
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.3252
WT Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.1948
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.8989
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.6652
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9981
E/e'		
WT Sham vs. WT CKD	one-way ANOVA with Tukey's	0.8708
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	>0.9999
WT Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.7379
WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9389
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9944
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.8647
MPI		
WT Sham vs. WT CKD	one-way ANOVA with Tukey's	0.5263
WT Sham vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9118
WT Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.7119

WT CKD vs. SIRPα Mt Sham	one-way ANOVA with Tukey's	0.9711
WT CKD vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9826
SIRPα Mt Sham vs. SIRPα Mt CKD	one-way ANOVA with Tukey's	0.9983
Table S3		
fl/fl CKD vs. csSIRPα$^{-/-}$CKD		
LVAWd (mm)	unpaired two-tailed t test	0.6071
LVAWs (mm)	unpaired two-tailed t test	0.102
LVIDd (mm)	unpaired two-tailed t test	0.1492
LVIDs (mm)	unpaired two-tailed t test	0.945
LVPWd (mm)	unpaired two-tailed t test	0.3347
LVPWs (mm)	unpaired two-tailed t test	0.9692
LV Mass (mg)	unpaired two-tailed t test	0.4617
CO (mL/min)	unpaired two-tailed t test	0.0007
EF (%)	unpaired two-tailed t test	0.022
FS (%)	unpaired two-tailed t test	0.015
HR (bpm)	unpaired two-tailed t test	0.1264
SV (μL)	unpaired two-tailed t test	0.00007

Figure	Non-parametric Analysis Type	p Value
1A		
BUN		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0003
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0045
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
Creatinine		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0038
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0244
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
1B	Mann-Whitney	0.0006
1D	Mann-Whitney	0.0003
1E	Mann-Whitney	0.00000001
2B		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0602
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.2404
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.5303
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
2C		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0984
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.8988
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1842
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.5698
2D		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1861
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0664
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0027

2F	Mann-Whitney	0.0173
2G	Mann-Whitney	0.0173
2H	Mann-Whitney	0.0043
3A		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.507
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.034
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4455
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.028
3B		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0455
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0572
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.7657
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.6605
3C (top panel)		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1019
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0004
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
3C (bottom panel)		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0153
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1388
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.9686
3D		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0645
fl/fl CKD vs. csSIRPα$^{-/-}$CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0028
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1517
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
3E		
ACC1		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0008
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.6313
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.2484
ANP		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0612
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0029
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.7117
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
BNP		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0047
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.137
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
CPT1b		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0031
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0252
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
GLUT1		

WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.00099
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0197
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1276
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.7845
GLUT4		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0015
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0095
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.9946
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
MHCα		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0068
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0367
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
MHCβ		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0071
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1726
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
PGC1a		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0005
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.2781
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1937
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
PPARα		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0003
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0489
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
UCP3		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.03
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.6269
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3247
3F		
ACC1		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0424
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.6145
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.6708
ANP		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0014
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0155
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3926
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0764
BNP		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0035
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0042
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
CPT1b		

fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0587
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1448
GLUT1		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.00094
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.8033
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.8033
GLUT4		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0006
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3183
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.5474
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
MHCα		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.013
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0932
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.8612
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.235
MHCβ		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0035
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0775
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3646
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0326
PGC1a		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0282
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0221
PPARα		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0242
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.8033
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3144
UCP3		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0489
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0031
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
3G		
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD		
ACC1	Mann-Whitney	0.4452
ANP	Mann-Whitney	0.0385
BNP	Mann-Whitney	>0.9999
CPT1b	Mann-Whitney	0.4452
GLUT1	Mann-Whitney	0.1375
GLUT4	Mann-Whitney	0.2949
MHCα	Mann-Whitney	0.3124
MHCβ	Mann-Whitney	0.0734
PGC1α	Mann-Whitney	0.6282
PPARα	Mann-Whitney	0.2949

UCP3	Mann-Whitney	0.9452
4A		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.034
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0046
4B		
αSMA		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0486
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4913
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
Fibronectin		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0051
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0007
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
pAKT		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0087
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1506
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.22
PI3K		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0843
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4171
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
4C		
αSMA		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0026
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.2887
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
Fibronectin		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0242
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4158
pAKT		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
PI3K		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0242
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.1825
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
4D		
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD		
αSMA	Mann-Whitney	0.4557

fibronectin	Mann-Whitney	0.1375
pAKT	Mann-Whitney	0.366
PI3K	Mann-Whitney	0.535
5A		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.005
fl/fl Sham vs. mSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
mSIRPα$^{-/-}$ Sham vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. mSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0359
6A		
pAKT/AKT		
fl/fl PBS vs. fl/fl rSIRPα	Mann-Whitney	0.0022
mSIRPα$^{-/-}$ PBS vs. mSIRPα$^{-/-}$ rSIRPα	Mann-Whitney	0.0303
p-IGF1R/IGF1R		
fl/fl PBS vs. fl/fl rSIRPα	Mann-Whitney	0.0022
mSIRPα$^{-/-}$ PBS vs. mSIRPα$^{-/-}$ rSIRPα	Mann-Whitney	0.0317
6B		
pAKT 15min	Mann-Whitney	0.1292
pAKT 30 min	Mann-Whitney	0.3148
pAKT 1h	Mann-Whitney	0.2698
pAKT 6h	Mann-Whitney	0.0029
pAKT 24h	Mann-Whitney	0.0295
pY-IGF1R 15min	Mann-Whitney	0.0286
pY-IGF1R 30min	Mann-Whitney	0.0286
pY-IGF1R 1h	Mann-Whitney	0.0286
pY-IGF1R 6h	Mann-Whitney	0.0286
pY-IGF1R 24h	Mann-Whitney	0.0571
Fibronectin 15min	Mann-Whitney	0.1724
Fibronectin 30min	Mann-Whitney	0.0484
Fibronectin 1h	Mann-Whitney	0.0004
Fibronectin 6h	Mann-Whitney	0.0111
Fibronectin 24h	Mann-Whitney	0.0004
6C		
SIRPα	Mann-Whitney	0.0012
pAKT/AKT	Mann-Whitney	0.0012
p-IGF1R/IGF1R	Mann-Whitney	0.0022
6D		
SIRPα	Mann-Whitney	0.0079
pAKT/AKT	Mann-Whitney	0.0087
p-IGF1R/IGF1R	Mann-Whitney	0.0087
7A	Mann-Whitney	0.0022
7B	Mann-Whitney	0.0286
7C		
0 vs. 1 h HG	Mann-Whitney	0.5476
0 vs. 6 h HG	Mann-Whitney	0.3095
0 vs. 24 h HG	Mann-Whitney	0.0079
7D		
0 vs. 1 h HG	Mann-Whitney	0.2222
0 vs. 6 h HG	Mann-Whitney	0.0556
0 vs. 24 h HG	Mann-Whitney	0.0079
7E	Mann-Whitney	0.0043
S1A		

SIRPα	Mann-Whitney	0.0281
ANP	Mann-Whitney	0.1304
BNP	Mann-Whitney	0.0516
UCP3	Mann-Whitney	0.7733
S1B		
PI3K	Mann-Whitney	0.0022
pAKT	Mann-Whitney	0.0317
GLUT4	Mann-Whitney	0.0238
S2A (left panel)		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0153
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4011
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.3848
S2A (right panel)		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0475
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0096
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.4087
S2B		
BUN		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0018
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0007
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
Creatinine		
fl/fl Sham vs. fl/fl CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0017
csSIRPα$^{-/-}$ Sham vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	0.0038
fl/fl Sham vs. csSIRPα$^{-/-}$ Sham	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD	Kruskal-Wallis-Dunn's Multiple Comparisons	>0.9999
S5A		
fl/fl PBS vs. HG	Mann-Whitney	0.0004
AD-SIRPα$^{-/-}$ PBS vs. HG	Mann-Whitney	0.0026
csSIRPα $^{-/-}$ PBS vs. HG	Mann-Whitney	0.0904
mSIRPα$^{-/-}$ PBS vs. HG	Mann-Whitney	0.8609
S5B		
Heart-PBS vs. HG	Mann-Whitney	0.0152
Gastrocnemius-PBS vs. HG	Mann-Whitney	0.0159
S5C	Mann-Whitney	0.0006
S5D	Mann-Whitney	0.0079
S5E	Mann-Whitney	0.2403
S5F		
SIRPα 0 vs. 1 h PCS	Mann-Whitney	0.2222
SIRPα 0 vs. 6 h PCS	Mann-Whitney	0.5159
SIRPα 0 vs. 24 h PCS	Mann-Whitney	0.0238
pAKT 0 vs. 1 h PCS	Mann-Whitney	0.0952
pAKT 0 vs. 6 h PCS	Mann-Whitney	0.1508
pAKT 0 vs. 24 h PCS	Mann-Whitney	0.0079
S5G		
0 vs. 1 h PCS	Mann-Whitney	0.6857
0 vs. 6 h PCS	Mann-Whitney	0.1143
0 vs. 24 h PCS	Mann-Whitney	0.0286

TABLES

Table S2

LVAWd (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.3188
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.9802
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.3218
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
LVAWs (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.2915
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.1432
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0697
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
LVIDd (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.0756
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.3898
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.0349
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.2252
LVIDs (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.1143
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.7719
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.171
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
LVPWd (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.1288
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.3308
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
LVPWs (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.2932
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0102
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.2612
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
LV/Height (mg/mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.0779
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.036
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.9635
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999

WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.5362
LV/BW (mg/g)		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's	0.035
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0819
WT Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.0073
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
CO (mL/min)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.004
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.2352
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0002
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.2195
EF (%)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.3606
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.0903
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.006
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.7954
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
FS (%)		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's	0.1477
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0046
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.2764
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.8547
HR (bpm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.6144
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
SV (μL)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.0149
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0038
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.2654
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	0.0882
RWT (mm)		
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.3677
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt CKD vs. WT Sham	Kruskal-Wallis-Dunn's	0.0389
SIRPα Mt CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
E/A		

WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's	0.0854
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	0.2602
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
E/e'		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
MPI		
WT Sham vs. WT CKD	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt Sham	Kruskal-Wallis-Dunn's	>0.9999
WT CKD vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
SIRPα Mt Sham vs. SIRPα Mt CKD	Kruskal-Wallis-Dunn's	>0.9999
Table S3		
fl/fl CKD vs. csSIRPα$^{-/-}$ CKD		
LVAWd (mm)	Mann-Whitney	0.4286
LVAWs (mm)	Mann-Whitney	0.0823
LVIDd (mm)	Mann-Whitney	0.1775
LVIDs (mm)	Mann-Whitney	>0.9999
LVPWd (mm)	Mann-Whitney	0.329
LVPWs (mm)	Mann-Whitney	0.9307
LV Mass (mg)	Mann-Whitney	0.4286
CO (mL/min)	Mann-Whitney	0.0043
EF (%)	Mann-Whitney	0.0173
FS (%)	Mann-Whitney	0.0173
HR (bpm)	Mann-Whitney	0.1775
SV (µL)	Mann-Whitney	0.0043