Data S1. Supplementary Materials and methods

Confirmation of transgenic mouse model. DNA was extracted from ear tissue (~10 mg for each mouse). The ear tissue was cut and shredded, and then 100 μl EDTA-NaOH solution was added. After boiling in a 95˚C water bath for 1 h, 100 μl of Tris HCl solution was added. After swirling, the required DNA was obtained by centrifugation (17,000 g for 10 min at 4˚C). Using DNA polymerase and the PCR Kit (Beyotime, D7237), the plate DNA from each mouse was amplificated using primer (forward, 5'-GTTTTGAATCTTGCCTTGTTTC-3' and reverse, 5'-TATGTCATCAACTTTTCAGGTTAC-3') to obtain a 335-bp DNA fragment. Thermal cycle conditions: STEP1 (initial denaturation): 94˚C for 3 min, STEP2 (denaturation): 94˚C for 30 s, STEP3 (annealing): 55˚C for 30 s, STEP4 (extension): 72˚C for 2 min, STEP5 (Cycle): Go to STEP2 for 30 cycles, STEP6 (final extension): 72˚C for 10 min. Following amplification, DNA electrophoresis was performed on 1.5% agarose gel, and bands were visualized with ethidium bromide (Beyotime, D0139).

Phosphoproteome analysis. The proteomic data were analyzed by MaxQuant (Version 1.6.6.0). Proteins were identified by searching MS and MS/MS data of peptides against a decoy version of Mus musculus-reviewed Uniprot (June 2018, uniprot.org/help/downloads) with the criteria of false discovery rate <0.01. At least two unique and razor peptides were required for the quantification. Digestion mode was trypsin/P; fixed modifications were phosphorylation (STY), oxidation (M), and Carbamidomethyl (C). First, search peptide tolerance was 20 ppm and the main search peptide tolerance was 4.5 ppm. MSstatsTMT package in the RStudio software, was used for quality inspection and statistical analysis of the phosphorylated proteome.

Figure S1. Sequence in the F2 generation mice. (A) F2 generation mouse DNA samples were amplified using primers [forward, 5'-GTTTGAATCTTGCCTTGTGTTTC-3' and reverse, 5'-TATGTCATCAACTTTCAGGTTAC-3') to obtain a 335 bp DNA fragment. (B) DNA sequencing using 5'-TATGTCATCAACTTTCAGGTTAC-3' primers. (C) Sequence map. Upper panel is the heterozygote, the black arrows show the corresponding sites T/G, T/A heterozygous; lower panel is the homozygote, the red arrows show corresponding sites are all the substitutions of the bases G/G, A/A. WT, wild-type; M, marker.

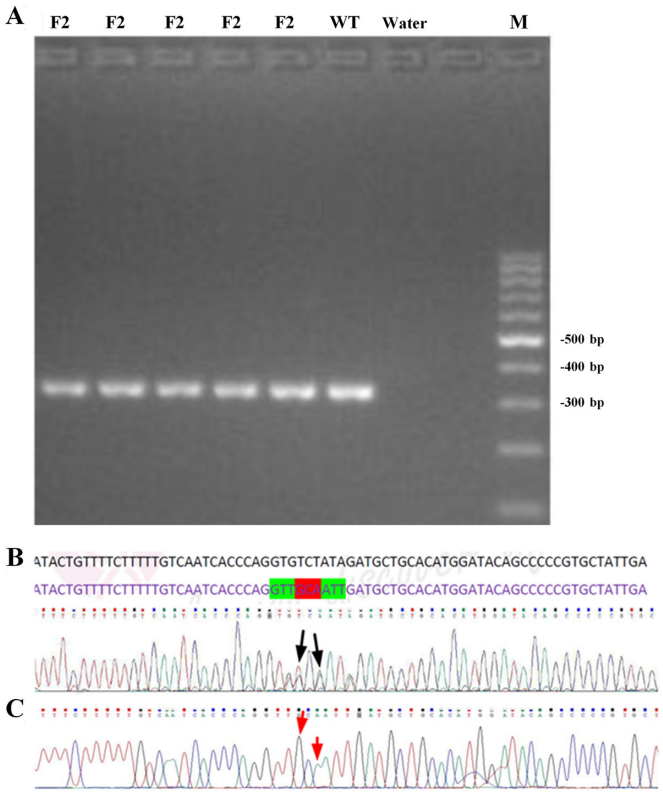

Figure S2. Original western blots. SO, sham operation; MI, myocardial ischemia; S, stable; SCD, sudden cardiac death; MT, MitoTEMPO; TG, transgenic; ox-CaMKII, oxidized-Ca^{2+}/calmodulin-dependent protein kinase.

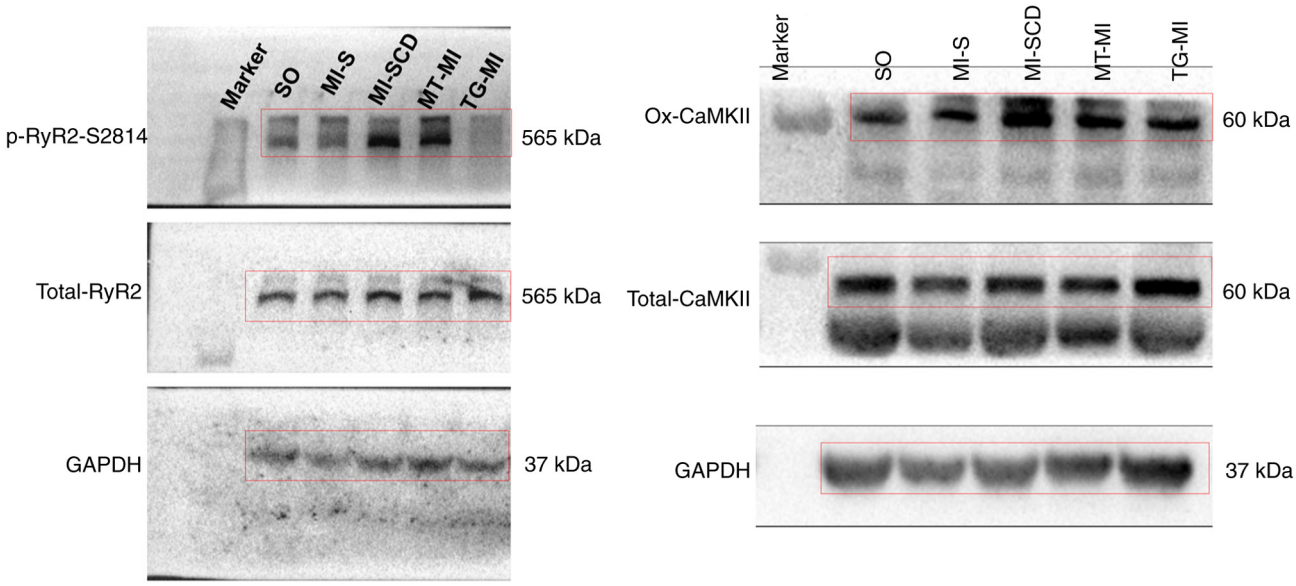

Table SI. Time to MI following coronary ligation in experimental mice.

A, MI-S	
Mouse no.	Time, min
MI-S1	70
MI-S2	70
MI-S3	70
MI-S4	70
MI-S5	70
MI-S6	70
MI-S7	70
MI-S8	70
MI-S8	70
MI-S9	70
MI-S10	70
MI-S11	70
MI-S12	70
MI-S13	70
MI-S14	70
MI-S15	70
MI-S16	70
MI-S17	70
MI-S18	70
MI-S19	70
MI-S20	70
MI-S21	70
MI-S22	70
MI-S23	70
MI-S24	70
MI-S25	70

MI-S26	70
MI-S27	70
MI-S28	70
MI-S29	70
MI-S30	70
MI-S31	70
MI-S32	70
MI-S33	70
MI-S34	70
MI-S35	70
B, MI-SCD	
Mouse no.	Time, min
MI-SCD1	7
MI-SCD2	9
MI-SCD3	10
MI-SCD4	13
MI-SCD5	14
MI-SCD6	16
MI-SCD7	16
MI-SCD8	19
MI-SCD9	19
MI-SCD10	20
MI-SCD11	20
MI-SCD12	20
MI-SCD13	22
MI-SCD14	23
MI-SCD15	23
MI-SCD16	24
MI-SCD17	25

MI-SCD18	26
MI-SCD19	28
MI-SCD21	33
MI-SCD22	36
MI-SCD23	40
MI-SCD24	41
MI-SCD25	44
MI-SCD26	45
MI-SCD27	48
C, MT-MI	
Mouse no.	Time, min
MT-MI1	18
MT-MI2	25
MT-MI3	25
MT-MI4	27
MT-MI5	37
MT-MI6	37
MT-MI7	70
MT-MI8	70
MT-MI9	70
MT-MI10	70
MT-MI11	70
MT-MI12	70
MT-MI13	70
MT-MI14	70
MT-MI15	70
MT-MI16	70
MT-MI17	70
MT-MI18	70

MT-MI19	70
MT-MI20	70
MT-MI21	70
MT-MI22	70
MT-MI23	70
MT-MI24	70
MT-MI25	70
MT-MI26	70
D, TG-MI	
Mouse no.	Time, min
TG-MI1	17
TG-MI2	17
TG-MI3	21
TG-MI4	22
TG-MI5	25
TG-MI6	30
TG-MI7	53
TG-MI8	70
TG-MI9	70
TG-MI10	70
TG-MI11	70
TG-MI12	70
TG-MI13	70
TG-MI14	70
TG-MI15	70
TG-MI16	70
TG-MI17	70
TG-MI18	70
TG-MI19	70

TG-MI20	70
TG-MI21	70
TG-MI22	70
TG-MI23	70
TG-MI24	70
TG-MI25	70
TG-MI26	70
TG-MI27	70
TG-MI28	70
TG-MI29	70
TG-MI30	70
TG-MI31	70
TG-MI32	70

MI, myocardial ischemia; S, stable; SCD, sudden cardiac death; MT, MitoTEMPO; TG, Transgenic..

Table SII. Ratio of oxidized to total Ca^{2+}/calmodulin-dependent protein kinases (CaMKII, normalized to sham operation group, SO).

MI-S	MI-SCD	MT-MI	TG-MI
1.447	3.252	1.545	0.917
1.433	1.476	1.714	1.197
1.081	1.657	0.761	0.738
0.625	3.299	0.473	1.244
1.246	2.256	1.226	1.024

MI, myocardial ischemia; S, stable; SCD, sudden cardiac death; MT, MitoTEMPO; TG, transgenic. Each row represents one sample.

Table SIII. Ratio of phosphorylated to total ryanodine receptor 2 -S2814 (normalized to sham operation group, SO).

MI-S	**MI-SCD**	**MT-MI**	**TG-MI**
1.637	1.898	2.005	0.433
1.745	2.189	0.543	0.407
0.819	2.240	0.533	0.334
0.654	2.222	1.368	0.304
1.402	1.245	1.514	0.365

MI, myocardial ischemia; S, stable; SCD, sudden cardiac death; MT, MitoTEMPO; TG, transgenic. Each row represents data from one sample.