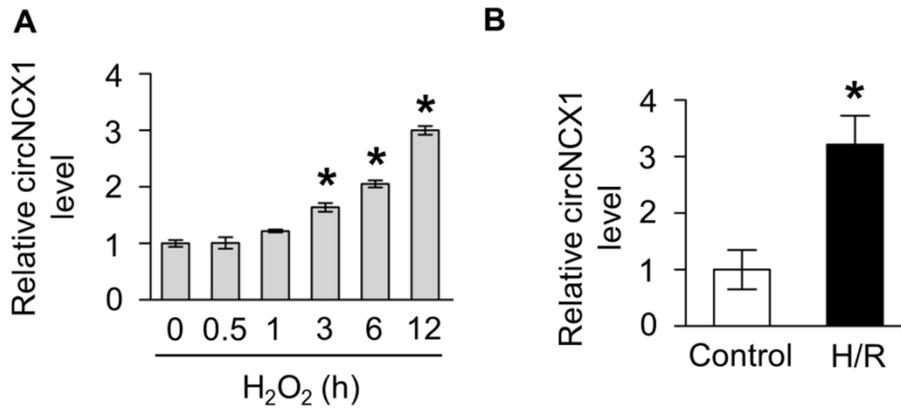


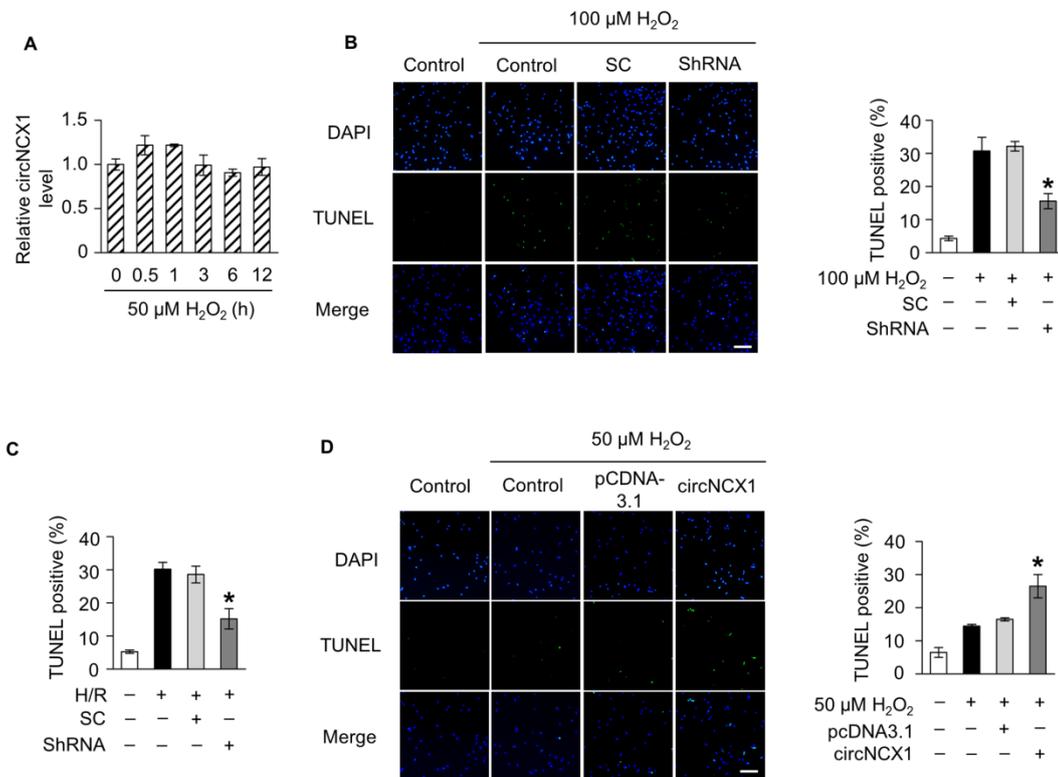
Supplementary Figure 1. (A) H9c2 cells were treated with 100 μ M H₂O₂ for 12 h. Total RNAs were isolated and reverse-transcribed. The expression level of circRNAs was analyzed by qRT-PCR. GAPDH was selected as reference. *P < 0.05 versus 0 h. n=3. (B) The detail of verification of other circRNAs in mice myocardial tissue. Their head-to-tail junction parts were amplified by divergent PCR.

Supplementary Figure-2



Supplementary Figure 2. (A) Neonatal rat cardiomyocytes were treated with 100 μ M H₂O₂. The expression level of circNCX1 was analyzed by qRT-PCR. *P < 0.05 versus 0 h. n=3. (B) Neonatal rat cardiomyocytes were treated with H/R. The expression level of circNCX1 was analyzed by qRT-PCR. *P < 0.05 versus control.

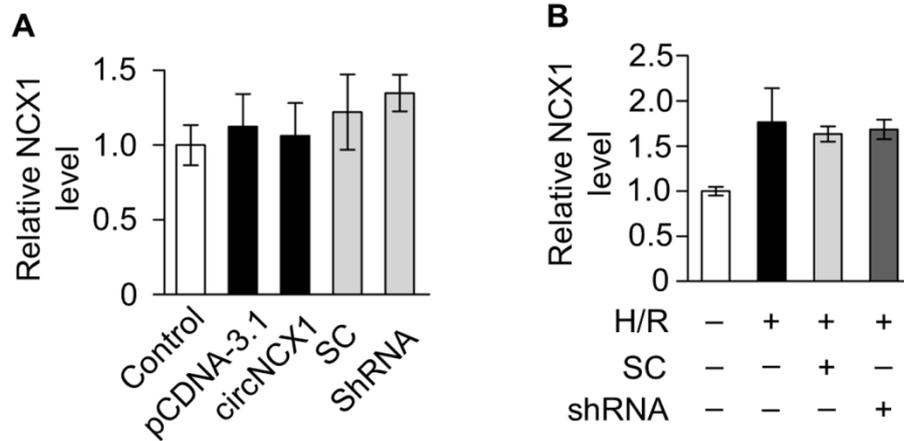
Supplementary Figure-3



Supplementary Figure 3. (A) H9c2 cells were treated with 50 μ M H₂O₂. The expression level of

circNCX1 was analyzed by qRT-PCR. n=3. **(B)** Neonatal rat cardiomyocytes were transfected with shRNA vector and treated by 100 μ M H₂O₂ for 12h. Cell apoptosis was analyzed by TUNEL assay. Scale bars, 50 μ m. *P < 0.05 versus SC. n=3. **(C)** Neonatal rat cardiomyocytes were transfected with shRNA vector and treated with H/R. Cell apoptosis was analyzed by TUNEL assay. *P < 0.05 versus SC. n=3. **(D)** Neonatal rat cardiomyocytes were transfected with circNCX1 expression vector and treated with 50 μ M H₂O₂ for 12 h. Cell apoptosis was analyzed by TUNEL assay. *P < 0.05 versus pCDNA 3.1. n=3.

Supplementary Figure-4

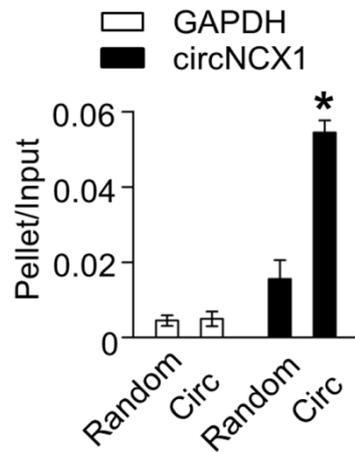


Supplementary Figure 4. (A) H9c2 cells were transfected with shRNA vector or circNCX1 expression vector. The expression levels of NCX1 mRNAs was analyzed by qRT-PCR. n=3. **(B)** H9c2 cells were transfected with shRNA vector and treated with H/R. The expression levels of NCX1 mRNAs was analyzed by qRT-PCR. n=3.

| | Mouse circNCX1 | Rat circNCX1 |
|--------|--|---|
| Site 1 | <p><i>Position: 492</i> target 5' G CAUAACUUCACCGC U 3' CGGC AGGGGACC GUCG UCCCCUGG miRNA 3' ACCAACU UUU 5'</p> <p>mfe: -22.1 kcal/mol</p> | <p><i>Position: 486</i> target 5' A GUG CCAUAACUUCACCGC U 3' AGU UGG AGGGGACC UCG ACU UCCCCUGG miRNA 3' G ACCA UUU 5'</p> <p>mfe: -23.3 kcal/mol</p> |
| Site 2 | <p><i>Position: 822</i> target 5' G C CAAGCA G U 3' GGC GG GAGGGGGAU A UCG CC CUUCCCCUG U miRNA 3' G A AA G UU 5'</p> <p>mfe: -26.1 kcal/mol</p> | <p><i>Position: 822</i> target 5' G CAAGCA G U 3' GGCUGG GAGGGGGAU A UCGACC CUUCCCCUG U miRNA 3' G AA G UU 5'</p> <p>mfe: -30.6 kcal/mol</p> |
| Site 3 | <p><i>Position: 855</i> target 5' A AGACA C 3' UGAAGG GACCAG ACUUCC CUGGUU miRNA 3' GUCGACCA C U 5'</p> <p>mfe: -20.0 kcal/mol</p> | <p><i>Position: 855</i> target 5' A AGACA C 3' UGAAGG GACCAG ACUUCC CUGGUU miRNA 3' GUCGACCA C U 5'</p> <p>mfe: -20.0 kcal/mol</p> |
| Site 4 | <p><i>Position: 939</i> target 5' G UC UUUGGAAGUUGA A A 3' GGC UGGU UGAG GGGACCAAG UCG ACCA ACUU CCCUGGUUU miRNA 3' G C 5'</p> <p>mfe: -29.2 kcal/mol</p> | <p><i>Position: 937</i> target 5' U GCUC UUUGGAAGUCGA A A 3' GGC UGGU UGAG GGGACCAAG UCG ACCA ACUU CCCUGGUUU miRNA 3' G C 5'</p> <p>mfe: -28.2 kcal/mol</p> |
| Site 5 | <p><i>Position: 1143</i> target 5' G CAACAUC A CACGCAGCU C 3' AGCUGG UUGAAG GG GAUCAAG UCGACC AAUUC CC CUGGUUU miRNA 3' G 5'</p> <p>mfe: -25.3 kcal/mol</p> | <p><i>Position: 1143</i> target 5' G AACAUUU A CAUGCAGCU C 3' AGCUGGU UGAAG GG GACCAAG UCGACCA ACUUC CC CUGGUUU miRNA 3' G 5'</p> <p>mfe: -29.2 kcal/mol</p> |
| Site 6 | <p><i>Position: 1311</i> target 5' U GCA CGACUUGAGC C 3' GC GAGGGGG ACCA CG CUUCCCC UGGU miRNA 3' GU ACCAA UU 5'</p> <p>mfe: -21.2 kcal/mol</p> | <p><i>Position: 1316</i> target 5' A UGACUUG C 3' GAGGGGG ACCAA CUUCCCC UGGU miRNA 3' GUCGACCAA U 5'</p> <p>mfe: -21.5 kcal/mol</p> |
| Site 7 | <p><i>Position: 1681</i> target 5' U AUCA AGG UUUGAGAACCUCU GC G 3' GGC UGG UGAAGG GGA UCGAG UCG ACC ACUUC CCU GGUUU miRNA 3' G A 5'</p> <p>mfe: -20.3 kcal/mol</p> | <p><i>Position: 1681</i> target 5' U AUCA AGG U A 3' GGC UGG UGAAGG GCUGAG UCG ACC ACUUC UGGUUU miRNA 3' G A CC 5'</p> <p>mfe: -21.1 kcal/mol</p> |
| Site 8 | <p><i>Position: 1760</i> target 5' A CCGA A 3' CAGC GG UGGAGGGGA GUCG CC ACUUCUUUU miRNA 3' A A GGUUU 5'</p> <p>mfe: -27.4 kcal/mol</p> | <p><i>Position: 1760</i> target 5' A CCGA G 3' CAGC GG UGGAGGGGA GUCG CC ACUUCUUUU miRNA 3' A A GGUUU 5'</p> <p>mfe: -27.4 kcal/mol</p> |

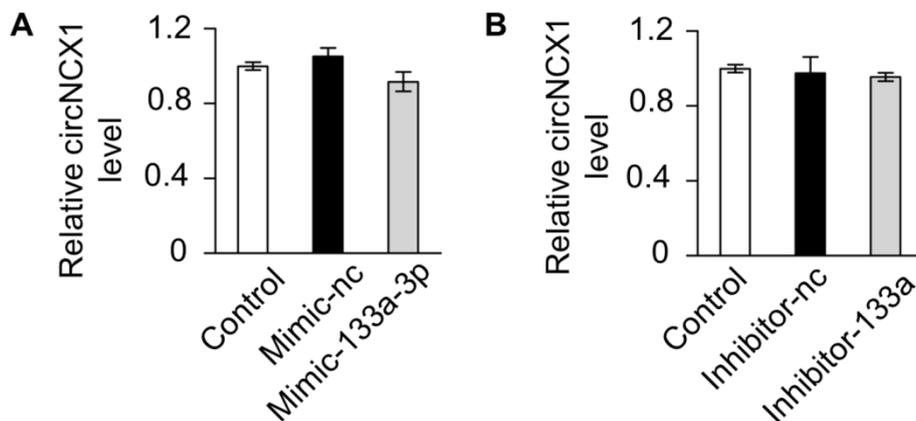
Supplementary Figure 5. Detail of the putative miR-133a-3p binding sites in mouse and rat circNCX1 sequences.

Supplementary Figure-6



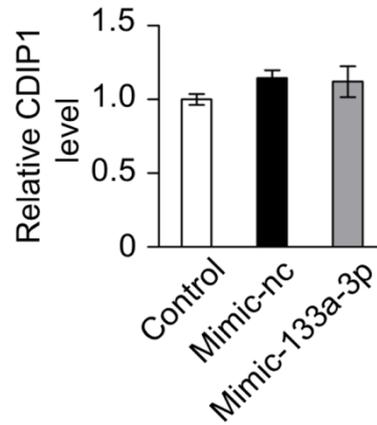
Supplementary Figure 6. Lysates of H9c2 cells were incubated with probe-coated beads. The captured RNAs were purified. The level of captured circNCX1 was analyzed by qRT-PCR. GAPDH mRNA was selected as a negative control. Pellet/Input was calculated. *P < 0.05 versus Random. n=3.

Supplementary Figure-7



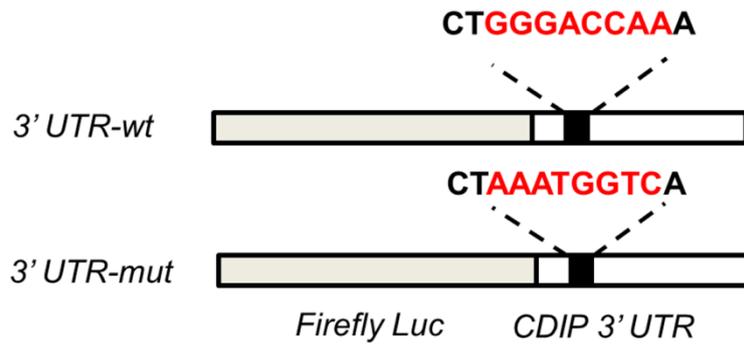
Supplementary Figure 7. H9c2 cells were transfected with miR-133a-3p mimics (A) or miR-133a-3p inhibitor (B). The expression level of circNCX1 was analyzed by qRT-PCR. n=3.

Supplementary Figure-8



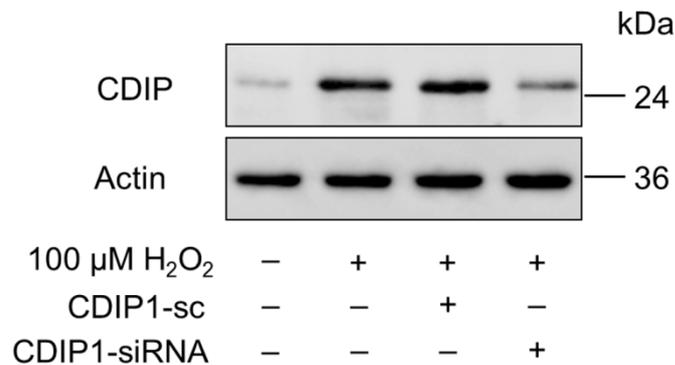
Supplementary Figure 8. H9c2 cells were transfected with miR-133a-3p mimics or control mimics. CDIP1 mRNA level was analyzed by qRT-PCR. n=3

Supplementary Figure-9



Supplementary Figure 9. Detail of the mutation of CDIP1 3' UTR.

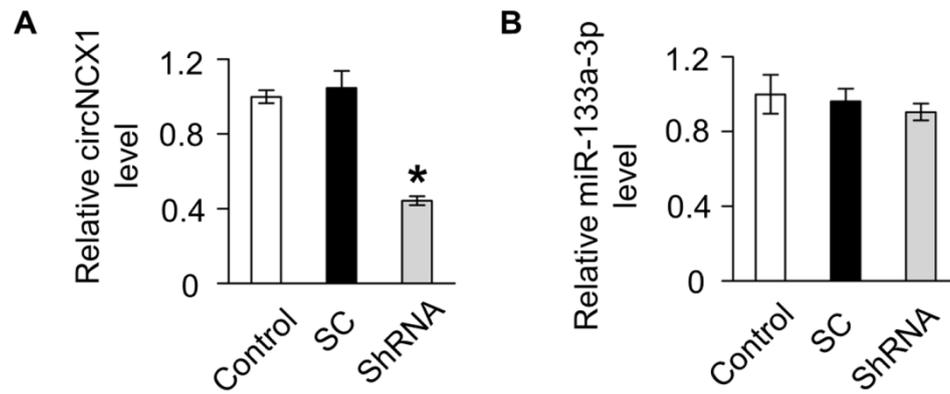
Supplementary Figure-10



Supplementary Figure 10. H9c2 cells were transfected with CDIP1 siRNA or control oligo. Cells

were treated with 100 μ M H₂O₂ for 12 h. CDIP1 level was analyzed by western-blot.

Supplementary Figure-11



Supplementary Figure 11. Mice hearts were infected by adenovirus harbored shRNA. The expression level of circNCX1 (A) or miR-133a-3p (B) in mice hearts was analyzed by qRT-PCR. n=3. *P < 0.05 versus SC.