

Major Resources Table

In order to allow validation and replication of experiments, all essential research materials listed in the Methods should be included in the Major Resources Table below. Authors are encouraged to use public repositories for protocols, data, code, and other materials and provide persistent identifiers and/or links to repositories when available. Authors may add or delete rows as needed.

Animals (in vivo studies)

Species	Vendor or Source	Background Strain	Sex	Persistent ID / URL
Mouse	Original	C57BL/6, inbred	Both	N/A

Genetically Modified Animals

	Species	Vendor or Source	Background Strain	Other Information	Persistent ID / URL
Parent - Male	Mouse	Original	C57BL/6	CRISPR/Cas9, inbred	N/A
Parent - Female	Mouse	Original	C57BL/6	CRISPR/Cas9, inbred	N/A

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)	Persistent ID / URL
ARRDC4	Abcam	ab139670	1:500-1:1000		
ARRDC4	Thermo Fisher scientific	PA5-38852	1:500-1:1000		
GLUT1	Abcam	ab115730	1:1000 or 1:400		
mCherry	Abcam	ab167453	1:1000		
HA-tag	Abcam	ab9110	1:1000-1:2000		
HA-tag	MBL	M180-7	1:2000		
FLAG-tag	Abcam	ab1162	1:2000-1:4000		
FLAG-tag	MBL	M185-7	1:2000-1:4000		
ATF4	Cell Signaling Technology	11815	1:1000		
CHOP	Cell Signaling Technology	2895	1:1000		
GAPDH	Cell Signaling Technology	8884	1:1000		
Concanavalin A	Thermo Fisher scientific	C11252	1:400		
P-cadherin	Abcam	ab51034	1:10000		
Clathrin	Cell Signaling Technology	4796	1:400		
AP2M1	Abcam	ab233712	1:400		
Sarcomeric Alpha Actinin	Abcam	ab68167	1:400		
Anti-Mouse IgG, Alexa Fluor 405	Abcam	ab175660	1:600		
Anti-Rabbit IgG, Alexa Fluor 488	Abcam	ab150077	1:600		
Anti-Mouse IgG, AMCA	Jackson ImmunoResearch Laboratories	715-155-151	1:600		

Anti-Rabbit IgG, AMCA	Jackson ImmunoResearch Laboratories	711-155-152	1:600		
Anti-Mouse IgG-HRP	Bio-rad	1721011	1:8000		
Anti-Rabbit IgG-HRP	Bio-rad	1721019	1:8000		
Rabbit IgG, Isotype Control	Abcam	ab172730	1:1000		

DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL
Human ARRDC1 WT	ATGGGGCGAGTGCAGCTCTTCGAGATCAGCCTGAGCCACGGCCGCTCGTCTACAGCCCCGGGAGCCGT TGGCTGGGACCGTGCAGCTGCAGCTGGGGGACCGCTGCCGTTCAGGACCATCCGGGTGACCTGCATAGG TTCTGCGGGGTCTCCAACAAGGCTAATGACACAGCGTGGGTAGTGGAGGAGGGTTACTTCAACAGTTC CTGTGCTGGCAGACAAGGGGAGCCTGCCCGTGGAGAGCACAGCTTCCCTTCCAGTTCTGCTTCTG CCACTGCACCCACGCTCTTTGAGGGTCTTTTCGGGAAGATCGTGACCCAGGTGAGGGCCGCCATCCACAC GCCACGGTTTTCAAGGATCACAAGTGCAGCCTCGTGTCTATATCTTGAGCCCTTGAACCTGAACAGC ATCCAGACATTGAGCAACCAACGTGGCCTCTGCCACCAAGAAGTTCTCTACAAGCTGGTGAAGACGG GCAGCGTGGTCTCACAGCCAGCACTGATCTCCGCGGCTATGTGGTGGGGCAGGCACTGCAGCTGCATGC CGACGTTGAGAACCAGTCAAGCAAGGACACCAGCCCTGGTGGCCAGTCTGTGCAGAAAGTGTCTAT AAGGCCAAGCGCTGGATCCACGACGTACGGACATTGCGGAGGTGGAGGGTGGGGGCGTCAAGGCCTGGC GGCGGGCGCAGTGGCAGCAGCAGATCTGGTGCCTGCTTGCCTGCCCCAGTCGGCCCTGCCGGGCTGCAGCCT CATCCACATCGACTACTACTTACAGGTCTCTCTGAAGGCGCCGGAAGCTACTGTGACCTCCCGGTCTTC ATTGGCAATATTGCTGTGAACCATGCCCAAGTGCAGCCCCGGCCAGGCTGGGGCTGCCTCTGGGGGCC CACCCCTGGTGGTGCCTTCCGACACCCAGGAGGAGGTGAGGCTGAGGCTGCGGCTGGCGGCCCCCA CTTCTTGACCCCGTCTTCTCTCCACCAAGAGCCATTGCAGCGCAGCCCTGCTGCCACCTTGAAGT TCTGTGCTGGTGCAGCCGAGCCCTGCCCTCAGGATGGCAGCCCTGCCTCACACCCGCTGCACCTCCCT TGTGCATTTCAACAGGTGCCACTGTCCCTACTTTGCAGAGGGCTCCGGGGGGCAGTGCCCACTACCAG CACCTGATTCTCCTCCAGAGTACAGTTCTGGGGTACCCCTATGAGGCCACCCGCTTATGAGCAG AGTGTGGCGCGCTGGAACCCAGCCTGACCCCTGAGAGC	NCBI Nucleotide database	NM_152285
Human ARRDC2 WT	ATGCTATTCGACAAGGTGAAAGCGTTCTCGGTGCAAGTGGACGGCGCAGCCGCGGGCGTGCAGCCCGTGT TTAGCGGCGGCCAGCCGTGGCGGGCGGGTCTGCTGAGCTGTCAAGCGCCGCGCTGTGGGTGCCCT GAGGTGCGCGCGCGGGGCCGCCCCAGTGCATGGACCGAGTGCAGCAGCGGGGCTCGAGCAGCGGCT TACACGCAGAGCTACAGTGAACCGTGGAGTCTGAGCCACCGCCACGCTCTGGCGCCAGATACCG GGGAGACCACGAGCTGCTCCTGGGCGCCATGAGTTCTGTTGAGCTCCAGCTGCCCCGACCCCTGGT GACATCCTCGAGGGCAAACCGGTAGTGTCCGCTACTGTATCAAGGCCACCCCTGCACCGGCCCTGGGTC CCAGCACCGCGGCAAGGAAGGTGTTCACTGTATCGAGCCTGTGACATCAACACGCCAGCCCTGCTGG CACCTCAAGCGGGGCTCGGAAAAGGTTGCCGATCCTGGTACTGAACCATGGCCTAGTCTCCCTTC GGCCAAGATCGACCACAAGGGCTACACCCAGGAGAGGTATCCCTGTCTTGGCAGATCGACAACGGC TCCACAGTCTGTGCTCCTCGGGCAGCGTGGTGCAGACACAGAGTTTATGGCCGAGCGCCCGAA AGCAGAAACGGGCGTGGTGGCCAGCCTCGCGGGCAGCCGGTGGGCCCGGGCAGCGGGCGCTGTGGC A GGGCCGGGCACTGCGGATCCCCCAGTGGGTCTTCCATCCTGCACTGCCGCTTACACGTGGACTAC GCACTCAAGGTCTGTGTGGATATCCAGGAACGTCCAAGCTGTGCTGGAGCTGCCACTGGTATCGGCA CCATTCCTTGCACCTTTTGGCAGCGTCTCCAGCGTGGCAGCCACGCCAGCTTCTGCTGGACTG GAGGTGGGGGCTTGCAGAGCGGCTGAGGCTCCTCCTGAGTACTCGAGGTGGTGGCCGACACTGAG GAGGCAGCCTTGGGGCAGAGCCCTTCCCGTCCGAGGACCCGATGAGCCTTGAAGGCCGTTCT TCGCCTACATCAAGAGTTCCGCTACCGCCCGCACCCCTGTACTGTGAGGAGGATCCAACCCACCTT GGGGGACATGAGGCCGCTGCATGACTTG	NCBI Nucleotide database	NM_015683
Human ARRDC3 WT	ATGGTGTGGGAAAGGTGAAGAGTTTACAATAAGCTTTGACTGTCTTAATGACAGCAATGTCCTGTGT ATTCTAGTGGGATACCGTCTCAGGAAGGTAATTTAGAAGTACTGGGAAATCAGAGTAAAATCTCT TAAAATTCATGCAAGAGGACATGCGAAAGTACGCTGGACTGAATCTAGAAAACCGCGCTCCAATACTGCC TATACAGAAATTACACTGAAGAAGTAGAGTATTTCAACATAAAGACATCTTAATTGGGCACGAAAGAG ATGATGATAATTCGAAAGGCTTCCACACTATTTCACTCAGGAAGGCATGAATATCATTACAGTTCGA GCTTCCACAGACCACTCGCTACCTCATTGAAAGCCGACATGGCAGTGTGCGCTATTGGGTGAAAGCC GAATTGCACAGGCTTGGCTACTACCAGTAAAATTAAGAAGGAATTTACAGTCTTTGAGCATATAGATA TCAACTCTTCACTACTGTACCCCCAAGCAGGCACAAAAGAAAGACACTCTGTTGCTGGTCTGTAC CTCAGGCCAATATCTTAAGTGCAAAATTAAGAAGGAAGGCTATACCCAGGTGAATCAATTCAGATA TTTGTGAGATTGAGAACTGCTCTTCCGAAATGGTGGTGCAAAAGGACCAATTTACCAAACACAGGCCT TCTATGCCAAAGGAAAATGAAGGAAGTAAAACAGCTTGTGGCTAACTTGCCTGGGGAATCCTTATCATC TGGAAAGACAGAGACGTGGAATGGCAAGTTGCTGAAAATTCACCAAGTTTCTCCCTCTATCCTGACTGT AGTATAATCCCGTGGAAATTTCACTAATGGTATATGTGGATATTCCTGGAGCTATGGATTATTTCTTA ATTTGCCACTTGTGCATCGGTACCTTCTACATCCATTTGGTAGCAGAACCTCAAGTGTAAAGCAGTCA GTGTAGCATGAATATGAACTGGCTCAGTTTACTTCTGAAAGACCTGAAGCACCACCCAGCTATGCA GAAGTGGTAAACAGAGGAACAAAGGCGGAACAATCTTGACCAAGTGTGCTGATGACTTTGAGAGAG	NCBI Nucleotide database	NM_020801

	CCCTTCAAGGACCACTGTTGCATATATCCAGGAGTTTCGATTCTTGCTCCACCTCTTTATTACAGAGAT TGATCCAAATCCTGATCAGTACGAGATGATAGACCATCCTGCCCTCTCGT		
Human ARRDC4 WT (1- 419)	ATGGGCGGGGAGGCTGGGTGCGCGGGCCGTGGGTGCCGAGGGCCGCGTGAAGAGCCTGGGTCTGGTG T TCGAGGACGAGCGCAAGGGCTGCTATTCCAGCGGCGAGACAGTGGCCGGGACCGTCTGAGGCGCTC CGAGCCGGTGGCCCTGCGCGCGCTGCGCTGGAGGCCAGGGGCGGCCACCGCCGCTGGGGCCGAGC ACCTGCCCGCGCCTCGGCCAGCACGCGGCCCTGGGTGCTTCTCGGAGGTGGAGTACCTGAACGTGC GCCTCAGCCTGCGGGAGCCCCGGCCGGTGAAGGCATCATTTTATTACAGCCTGGAAAACATGAATTTCC ATTTCCGTTCACTTCCATCTGAACCTTTGGTCACTCGTTTACTGGAAATATGGAAGCATTGAGTAC TGTGTGGGGCAGTGTGGAAACGACCAAGGTACCTGATCAGAGTGAAGCGGGAACCTCCAGTTGTTA GTCATGTCGATGTCAACACACCAGCATTATTAACCCCTGATTGAAAACCAAGAGAAAATGGTTGGCTG TTGGTTTTCACTTCTGGTCCAGTCTCGCTGAGTGC AAAAATTGAAAGAAAGGGATACTGTAATGGAGAA GCTATTCCAATCTATGCAGAAATAGAAAATTTTCTCTCGTCTGATTGTTCCAAAGGCTGCTATTTCC AAACGCAGACATATTTGGCTAGTGAAAAACAAGACCATTGACACATGGTGCCTGCAATGTGCGAGGAAA CCACATCGCTTCTGGGACACAGACATGGAATGGGAAAACGCTAAAAATCCACCTGTTACTCCATCC ATCCTGGATTGCTGATTATCAGAGTGGACTATTCCTTAGCTGTATACATTACATTCTCTGGTGCTAAAA AATTGATGCTCGAAGTCCATTAGTATCGGTACAATCCATATAATGGTTTTGGCAGCAGAACTCCAG CATTGCCAGCCAGTTCAGTATGGATATGAGCTGGTTGACACTGACCCTGCCAGAGCAGCTGAAGCACCA CCAAATATGCAGATGTGGTATCAGAGGAAGAATTCTAGACACATTCTCTTACCCTCAACCCCTCA ACTGTGAGGGAGAAGTGTGCTGCTGTGTTGCTGTATACAAGAATCCGGTTTCAACCCCACTCT TTATTCAGAGTTGACCCACATCTAGCGACGTAGAAGAGAGCCAGCTGTTTCTTCACTCTC	NCBI Nucleotide database	NM_183376
Human Txnip WT	ATGGTGATGTTCAAGAAGTCAAGTCTTTTGGAGTGGTCTTAAACGACCCTGAAAAGGTGTACGGCAGTG GCGAGAAGGTGGCTGGCCGGGTGATAGTGGAGTGTGTAAGTACTCGTGTCAAAGCCGTTAGGATCCT GGCTTGGGAGTGGCTAAAGTGTCTTGGATGCAGGGATCCAGCAGTGC AAAACAGACTTCGGAGTACCTG CGCTATGAAGACACGCTTCTTCTGGAAGACCAGCCAACAGGTGAGAATGAGATGGTGTATGAGACCTG GAAACAAATATGAGTACAAGTTCGGCTTGGAGTCTCAGGGGCTTGGGAACATCCTTCAAAGGAAA ATATGGGTGTGTAGACTACTGGGTGAAGGCTTTTCTGACCGCCGAGCCAGCCAACTCAAGAGACAAA AAAACTTTGAAGTAGTGGATCTGGTGGATGTCAATACCCTGATTTAATGGCAGCTGTGTCTGCTAAA AAGAAAAGAAAGTTTCTGATGTTTCTGATGGGCGGGTGTCTGTCTGCTCGAATTGACAGAAA AGGATTCTGTGAAGGTGATGAGATTTCCATCCATGCTGACTTTGAGAATACATGTTCCCGAATTGTGGT CCCAAAGTCCGATTTGGCCGCCACTTACCTTCCAAATGCCAGACCAAGGTGCTGACTCAGAAGT TGTCACTAGTCAGAGGCAATCATATTATCTCAGGGACATGCGCATATGCGCTGGCAAGACCTTCGGGT TCAGAAGATCAGGCTTCTATCTGGGCTGCAACATCCTTCGAGTTGAATTTCTTACTGATCTATGTT AGCGTTCCTGGATCCAAGAAGTGTCTTACCTGACCTGCCCTGGTAATTGGCAGCAGATCAGGTCTAAGCA GCAGAACATCCAGATGGCCAGCCGACAGCTCTGAGATGAGTTGGGTAGATCTGAACATCCCTGATAC CCCAGAAGCTCCTCCTGCTATATGGATGCTTCTGAAGATCACCATTGGAGAGCCCAACACTCCT CTGCTAGATGACATGGATGGCTCTCAAGACAGCCCTATCTTTATGTATGCCCTGAGTTCAAGTTCATGC CACCACCGACTTATACTGAGGTGGATCCCTGCATCCTCAACAACATGTGCAG	NCBI Nucleotide database	NM_006472
Mouse ARRDC4 WT	ATGGGAGGCGAGGCGGGAGCCGATGGTCTCGGGCCGTGTCAAGAGCTTGGGGCTAGTGTTCGAAGATG AGAGCAAGGGCTGCTACTCAAGCGCGAGACAGTGGCCGGGACGCTGTCTGAGGCGCGAGAGCCGG TGGCCCTGCGCGGACTGCGCTGGAGGCCAGGGCCGTGCCACCTCTGCTGGGGCCGAGCGCTGGGGC CAGGGTCTGCATCGTGGGGGCTCTCCCGAGCTCCTCAGAAGTGAATACTTGAACCTGCGGTTGAGTC TGCTGGAGGCCAGCTGGTGAAGGTGTACCTTGTACAACCAGGAAAACACGAGTTTCCCTTTGCTT TCAGCTCCGCTGTAACCTTTGGCAACATCGTTTACTGGGAAGTATGGCAGTATTCAGTACTGTGTGAGG GCTGTTTTGGAACGACCCCAAGTTCAGATCAGAGCGTCAAGCAGAGCTCCAGGTTGTAGTACAGTGG ATGTCAACACACCCGCTTATTGACTCCTATGCTGAAGACGAGGAGAAAATGGTTGGCTGTTGGCTTTT CACCTCTGGTCTGTGCTACTGAGCGTCAAGATCAGAGAAAAGGGCTACTGTAACGGAGAAGCTATCCCT ATCTATGCAGAAATGAAAATGTTTCACTCCTGGTGGTTGTTCCAAAGGAGCAGCATATCCAAACCCAGA CGTACTTGGCTAGTGGAAAGACAAAGACAGTCCGGCACATGGTTGCCAATGTTGAGGAAACACATTGG TTCTGGGAGTACGGACACCTGGAATGGGAAGATGCTGAAGATCCACCTGTACCCCATCCATCCTGGAT TGCTGCATATCAGAGTGGACTACTCCTTAGCTGTATACATTATATCCCTGGTGTAAAAGATTGATGC TGGAGTGCCTTTGGTTATTGGTACAATCCATACAGTGGCTTTGGCCGAGAAAACAGCAGTGTGCGAAG CCAGTTCAGTATGGACATGTGCTGGTTGGCACTGGCCCTACCGGAGCAGCCTGAAGCACCAAAATTAT GCAGATGTGGTATCGGAAGAAAGAAATTTCCCGACACGTTCTCCGTACCCCTCAGCCCTGACTGTGACG GGGAAGCCTGCTACTCAATGTTTGCCTGCATAACAAGAAATCCGTTTCCAGCCTCCCCCTTTATTCA GGTTGATCCACATCCTGGTGTATGCCAAGAGACCCAGCCTGTATCCTTCACTCTC	NCBI Nucleotide database	NM_00104259 2
Human GLUT1 WT	ATGGAGCCAGCAGCAAGAAGCTGACGGGTGCGCTCATGCTGGCCGTGGGAGGAGCAGTCTGGCTCCC TGCAAGTTGGCTACAACACTGGAGTCAATGCCCCCAAGAGGTGATCGAGGAGTTCTACAACAGAC ATGGGTCACCGCTATGGGGAGAGCATCTGCCACACAGCCTCACCACGCTCTGTTCCCTCTCAGTGGCC ATCTTTTCTGTTGGGGGATGATTGGCTCCTTCTGTGGGCTTTTCTGTTAACCCTTTGGCCGGCGGA ATTCAATGCTGATGATGAACCTGCTGGCTTCGTGCCCGTGTCTATGGGCTTCTGAAAACCTGGGCAA GTCCTTTGAGATGCTGATCCTGGGCCCTTCACTCATCGGTGTGACTGCGGCCCTGACCACAGGCTTCGTG CCCATGTATGTGGGTGAAGTGTACCCACAGCCCTTCTGGGGCCCTGGGCACCCTGCACCACTGGGCA TCGTCGTCGGCATCCTCATCGCCAGGTGTTGGCTGGACTCCATCATGGGCAACAAGACCTGTGGCC CCTGCTGAGCATCTTCACTCCCGCCCTGCTGCAAGTGCATCGTCTGCTGCCCTTCTGCCCCGAGAGT CCCCGCTTCTGCTCATCAACCGCAACGAGGAGAACCAGGCAAGAGTGTGCTAAAGAAGCTGCGCGGGA CAGCTGAGCTGACCATGACTCTGAGGAGATGAAGGAAGAGAGTCCGCAGATGATGCGGGAGAAGAGGT CACCATCCTGGAGCTGTTCCGCTCCCCGCTACCGCCAGCCATCCTCATCGCTGTGGTGTGCTGACGCTG TCCCAGCAGTGTCTGGCATCAACGCTGCTTCTTACTCCACGAGCATCTCGAGAAGGCGGGGTGC AGCAGCCTGTGATGCAACCACTGGCTCCGGTATCGTCAACACGCGCTTCACTGTGCTGCTGTTTGT GGTGGAGCGAGCAGGCGGGGACCCCTGCACCTCATAGGCTCGTGGCATGGCGGGTTGTGCCATACTC ATGACCATCGCGCTAGCACTGCTGGAGCAGTACCCTGGATGCTATCTGAGCATCGTGGCCATCTTG		

	GCTATTCCAATCTATGCAGAAATAGAAAATTGTTCC		
Human ARRDC4 truncation (191-419)	ACTTCTGGTCCAGTCTCGCTGAGTGCCAAAATTGAAAGAAAGGGATACTGTAATGGAGAA GCTATTCCAATCTATGCAGAAATAGAAAATTGTTCCCTCTCGTCTGATTGTTCCAAAGGCTGCTATTTCC AAACGCAGACATATTTGGCTAGTGGAAAAACAAGACCATTGACACATGGTCGCCAATGTGCGAGGAAA CCACATCGCTTCTGGGAGCACAGACACATGGAATGGGAAAACGCTAAAAATCCCACCTGTTACTCCATCC ATCCTGGATTGCTGCATTATCAGAGTGGACTATTCCTTAGCTGTATACATTACATTCTGGTGCTAAAA AATTGATGCTCGAACTGCCATTAGTATCGGTACAATCCATATAATGGTTTTGGCAGCAGAAACTCCAG CATTGCCAGCCAGTTCAGTATGGATATGAGCTGGTTGACACTGACCCTGCCAGAGCAGCCTGAAGCACCA CCAAATATGCAGATGGTATCAGAGGAAGAATTCTAGACACATTCTCTTACCCTCAACCCCTA ACTGTGAGGGAGAAGTGTCTGCTGTGTTTTGCCTGTATACAAGAATTCCGGTTTTCAACCCCACTCT TTATTAGAGGTTGACCCACATCCTAGCGACGTAGAAGAGAGCCAGCCTGTTTCTTCTTCTC		
Human ARRDC4 truncation (191-318)	ACTTCTGGTCCAGTCTCGCTGAGTGCCAAAATTGAAAGAAAGGGATACTGTAATGGAGAA GCTATTCCAATCTATGCAGAAATAGAAAATTGTTCCCTCTCGTCTGATTGTTCCAAAGGCTGCTATTTCC AAACGCAGACATATTTGGCTAGTGGAAAAACAAGACCATTGACACATGGTCGCCAATGTGCGAGGAAA CCACATCGCTTCTGGGAGCACAGACACATGGAATGGGAAAACGCTAAAAATCCCACCTGTTACTCCATCC ATCCTGGATTGCTGCATTATCAGAGTGGACTATTCCTTAGCTGTATACATTACATTCTGGTGCTAAAA AATTGATGCTCGAACTGCCATTAGTATCGGTACAATCCATAT		
Human ARRDC4 truncation (319-419)	AATGGTTTTGGCAGCAGAACTCCAGCATTGCCAGCCAGTTCAGTATGGATATGAGCTGGTTGACACTGACC CTGCCAGAGCAGCTGAAGCACCACCAAAATATGCAGATGGTATCAGAGGAAGAATTCTAGACACATT CCTCCTTACCCTCAACCCCTAACTGTGAGGGAGAAGTGTCTGCTGTGTTTTGCCTGTATACAAGAATTCC GGTTTTCAACCCCACTCTTATTAGAGGTTGACCCACATCCTAGCGACGTAGAAGAGAGCCAGCCTGTTTC CTTCTTCTC		
Human ARRDC4 C domain mutant of conserved motifs	ATGGGCGGGGAGGCTGGGTGCGCGCGCGCCGTGGGTGCCGAGGGCCGCGTGAAGAGCCTGGGTCTGGTG TTCGAGGACGAGCGCAAGGGCTGCTATTCAGCGGCGAGACAGTGGCCGGGCACGTGCTGCTGGAGGCGT CCGAGCCGGTGGCCCTGCGCGCGTGGCCTGGAGGCCAGGGGCGCGCCACCGCCGCTGGGGCCCGAG CACCTGCCCGCGCCTCGGCCAGCACCGCGGCCCTGGCTGTCTTCTCGGAGGTGGAGTACCTGAACGTGCG CCTCAGCCTGCGGGAGCCCCGCGCGGTGAAGGCATATTTATTACAGCCTGGAAAACATGAATTTCCATTT CGCTTTCAACTTCCATCTGAACCTTTGGTCACTCGTTTACTGGGAAATATGGAAGCATTAGTACTGTGTGC GGGAGTGTGGAAACGACCCAAGGTACCTGATCAGAGTGTAAAGCGGGAACCTCCAGGTTGTTAGTCATGTC GATGTCAACACACCAGCATTATTAACCCCTGTATTGAAAACCAAGAGAAAATGGTTGGCTGTTGGTTTTCA CTTCTGGTCCAGTCTCGCTGAGTGCCAAAATTGAAAGAAAGGGATACGCTAATGGAGAAGCTATTCCAATCT ATGCAGAAATAGAAAATTGTTCTCTCGTCTGATTGTTCCAAAGGCTGCTATTTTCCAAACGAGACAGCTGC GGCTAGTGGAAAAGCAAAGACATTCGACACATGGTCGCCAATGCGCAGGAGCCGCGCCGCTTCTGGGA GCACAGACATGGAATGGGAAAGCGCTAAAAATCCCACCTGTTACTCCATCCATCCTGGATTGCTGCATTAT CAGAGTGGACTATTCCTTAGCTGTATACATTACATTCTGGTGTGACGATTGATGCTCGAACTGCCATTA GTGATCGGTACAATCCATATAATGGTTTTGGCAGCAGAACTCCAGCATTGCCAGCCAGTTCAGTATGGAT ATGAGCTGGTTGACACTGACCCTGCCAGAGCAGCTGAAGCACCACCAAAATATGCAGATGGTATCAGAG GAAGAATTCTAGACACATTCTCCTTACCCTCAACCCCTAACTGTGAGGGAGAAGTGTGCTGCTGTGT TTGCTGTATACAAGAATTCGGTTTTCAACCCCACTCTTATTAGAGGTTGACCCACATCCTAGCGACGTA GAAGAGAGCCAGCCTGTTTCTTCTTCTC		
Interaction-defect Human ARRDC4	ATGGGCGGGGAGGCTGGGTGCGCGCGCGCCGTGGGTGCCGAGGGCCGCGTGAAGAGCCTGGGTCTGGTG TTCGAGGACGAGCGCAAGGGCTGCTATTCAGCGGCGAGACAGTGGCCGGGCACGTGCTGCTGGAGGCGT CCGAGCCGGTGGCCCTGCGCGCGTGGCCTGGAGGCCAGGGGCGCGCCACCGCCGCTGGGGCCCGAG CACCTGCCCGCGCCTCGGCCAGCACCGCGGCCCTGGCTGTCTTCTCGGAGGTGGAGTACCTGAACGTGCG CCTCAGCCTGCGGGAGCCCCGCGCGGTGAAGGCATATTTATTACAGCCTGGAAAACATGAATTTCCATTT CGCTTTCAACTTCCATCTGAACCTTTGGTCACTCGTTTACTGGGAAATATGGAAGCATTAGTACTGTGTGC GGGAGTGTGGAAACGACCCAAGGTACCTGATCAGAGTGTAAAGCGGGAACCTCCAGGTTGTTAGTCATGTC GATGTCAACACACCAGCATTATTAACCCCTGTATTGAAAACCAAGAGAAAATGGTTGGCTGTTGGTTTTCA CTTCTGGTCCAGTCTCGCTGAGTGCCAAAATTGAAAGAAAGGGATACTGTAATGGAGAAGCTATTCCAATCT ATGCAGAAATAGAAAATTGTTCTCTCGTCTGATTGTTCCAAAGGCTGCTATTTTCCAAACGAGACATATTT GGCTAGTGGAGCAGCAAAGACCATTGACACATGGTCGCCAATGTGCGAGGAAACCATCGCTTCTGGGA GCACAGACATGGAATGGGAAAACGCTAAAAATCCCACCTGTTACTCCATCCATCCTGGATTGCTGCATTAT CAGAGTGGCTATTCTTAGCTGTATACATTACATTCTGGTGTGCTGCTGCAACTGCCATTA GTGATCGGTACAATCCATATAATGGTTTTGGCAGCAGAACTCCAGCATTGCCAGCCAGTTCAGTATGGAT ATGAGCTGGTTGACACTGACCCTGCCAGAGCAGCTGAAGCACCACCAAAATATGCAGATGGTATCAGAG GAAGAATTCTAGACACATTCTCCTTACCCTCAACCCCTAACTGTGAGGGAGAAGTGTGCTGCTGTGT TTGCTGTATACAAGAATTCGGTTTTCAACCCCACTCTTATTAGAGGTTGACCCACATCCTAGCGACGTA GAAGAGAGCCAGCCTGTTTCTTCTTCTC		
PCR primers for the ARRDC4 KO allele	F (forward) 5'-AAGTATGCGTTTGAAGGAGTTAGGG-3' R1 (reverse) 5'- CAAGTGGAGACCTCCAGAGAATGTAG-3' R2 (reverse) 5'- TTGACTAGAACATGAACCTGTGGCTGC-3'		

Cultured Cells

DOI [to be added]

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
HEK 293 cell	ATCC		
HEK 293T cell	ATCC		
HT 1080 cell	ATCC		

Data & Code Availability

Description	Source / Repository	Persistent ID / URL
ARRDC4 knock out Mouse Heart Analysis	Gene Expression Omnibus	Accession number: GSE186336

Other

Description	Source / Repository	Persistent ID / URL
ATF4 (primer, FAM, human)	Thermo Fisher scientific	Hs00909569_g1
ATF4 (primer, FAM, mouse)	Thermo Fisher scientific	Mm00515324_m1
ATF6 (primer, FAM, human)	Thermo Fisher scientific	Hs00232586_m1
ATF6 (primer, FAM, mouse)	Thermo Fisher scientific	Mm01295317_m1
XBP1 (primer, FAM, human)	Thermo Fisher scientific	Hs00231936_m1
XBP1 (primer, FAM, mouse)	Thermo Fisher scientific	Mm00457357_m1
CHOP (primer, FAM, human)	Thermo Fisher scientific	Hs00358796_g1
CHOP (primer, FAM, mouse)	Thermo Fisher scientific	Mm00492097_m1
GAPDH (primer, FAM, human)	Thermo Fisher scientific	Hs02786624_g1
GAPDH (primer, FAM, mouse)	Thermo Fisher scientific	Mm99999915_g1
ARRDC4 (primer, FAM, human)	Thermo Fisher scientific	Hs00411771_m1
ARRDC4 (primer, FAM, mouse)	Thermo Fisher scientific	Mm00508442_m1
BNP (primer, FAM, mouse)	Thermo Fisher scientific	Mm01255770_g1
COL1A1 (primer, FAM, mouse)	Thermo Fisher scientific	Mm00801666_g1
COL3A3 (primer, FAM, mouse)	Thermo Fisher scientific	Mm00802331_m1
ARRDC4 siRNA	Thermo Fisher scientific	4392422 (S40820)
Negative control siRNA	Thermo Fisher scientific	4390843
Dynamin inhibitor (Dyngo® 4a)	Abcam	ab120689
GlcNac (N-Acetyl-D-glucosamine)	Sigma-Aldrich	A8625
UDP-GlcNac (Uridine 5'-diphospho-N-acetylglucosamine sodium salt)	Sigma-Aldrich	U4375
L-(+)-Lactic acid solution	Sigma-Aldrich	199257
pCDH-CMV-MCS-EF1-GFP-T2A-Puro	System Biosciences	
pEGFP-C3	Clontech	
ERAI ER Stress Detector HD	Cosmo Bio	STDTC-1
OKD Oxidative Stress Detector	Cosmo Bio	STDTC-3
PureFection™ Transfection Reagent	System Biosciences	LV750A
MagStrep "type3" Strep-Tactin® beads	IBA Lifesciences	2-1613-002
CellBrite® Blue	Biotium	30024
Pitstop®2, clathrin inhibitor	Abcam	ab120687
Pitstop®2, clathrin inhibitor-negative control	Abcam	ab120688

ARRIVE GUIDELINES

The ARRIVE guidelines (<https://arriveguidelines.org/>) are a checklist of recommendations to improve the reporting of research involving animals. Key elements of the study design should be included below to better enable readers to scrutinize the research adequately, evaluate its methodological rigor, and reproduce the methods or findings.

Study Design

Groups	Sex	Age	Number (prior to experiment)	Number (after termination)	Littermates (Yes/No)	Other description
Group 1	M/F	12-week	16/14	30	Yes	Sham surgery (WT)
Group 2	M/F	12-week	15/15	30	Yes	Sham surgery (ARRDC4 KO)
Group 3	M/F	12-week	28/30	58	Yes	MI surgery (WT)
Group 4	M/F	12-week	28/29	57	Yes	MI surgery (ARRDC4 KO)

Sample Size: Please explain how the sample size was decided Please provide details of any *prior* sample size calculation, if done.

Sample size for MI surgery was calculated as n=20/per group using G*Power 3.1.9.2 with two-tail, α -error = 0.05, Power = 0.8, Effect size d = 1.0, and allocation ratio between two groups = 1.0. Taking into account for technical dropouts, the number of experiment was set with a minimum of n=20 per group.

5% difference of infarct size between the two groups and the standard deviation = 5% based on our previous report (J Mol Cell Cardiol. 2021 Jun;155:36-49. doi: 10.1016/j.yjmcc.2021.02.013.PMID: 33652022) were used for Effect size d estimation.

Inclusion Criteria

Animals were genotypes between 2 wks and 3 wks of age, and only homozygous or wild-type mice were included. Both genders aged 12 wks old were included for the study of the MI or sham procedures.

Exclusion Criteria

All heterozygous mice were excluded and used as breeding pairs.

Any animal showing signs of distress (extreme lethargy, wounds or ulcers) were planned to be immediately sacrificed. During and after the procedure, we monitored the level of pain/distress for mice. If any clinical signs were detected, we would have stopped the procedure. If the condition was severe, the animals would have been euthanized. However, we did not experience any of the above.

Randomization

The study was randomly performed.

Blinding

Some studies were unbiased in nature (RNAseq, qPCR, biochemical assays etc). In those cases, we performed under non-blinded manner.