

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 (<i>Mus musculus</i>)	Charles River	C57BL/6NCrI	Female/Male	https://www.criver.com/products-services/find-model/c57bl6-mouse?region=3611

Genetically Modified Animals

Species	Vendor or Source	Background Strain	Persistent ID / URL
FLNC F93A/L98E mice	Home-made	C57BL/6NCrI	
<i>Fln</i> c floxed mice	International Knockout Mouse Consortium	C57BL/6J	MGI: 4847813
<i>Xmlc2</i> -Cre mice	International Knockout Mouse Consortium	MF1	MGI: 3712342
<i>Myh6</i> -MerCreMer mice	The Jackson Laboratory	C57BL/6J	RRID:IMSR_JAX:005657

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Persistent ID / URL
TurboGFP	Origene	MG222854	1:500 for IF 1:200 for IP	https://www.origene.com/catalog/antibodies/tag-antibodies/ta150041/mouse-monoclonal-turbogfp-antibody-clone-oti2h8
α -actinin	Abcam	ab68167	1:500 for IF	https://www.abcam.com/products/primary-antibodies/sarcomeric-alpha-actinin-antibody-ep2529y-ab68167.html
Ki67	Abcam	ab15580	1:500 for IF	https://www.abcam.com/products/primary-antibodies/ki67-antibody-ab15580.html
Cardiac troponin T	Thermo Fisher	MS-295-P1	1:500 for IF	https://efaidnbmnnnibpcajpcglclefindmkaj/https://tools.thermofisher.com/content/sfs/brochures/D11737~.pdf
Endomucin	Thermo Fisher	14-5851-82	1:100 for IF	https://www.thermofisher.com/antibody/product/Endomucin-Antibody-clone-eBioV-7C7-V-7C7-Monoclonal/14-5851-82
Collagen I	Abcam	ab34710	1:500 for IF	https://www.abcam.com/products/primary-antibodies/collagen-i-antibody-ab34710.html
Active Integrin β 1 (9EG7)	BD	553715	1:100 for IF	https://wwwbdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-rat-anti-mouse-cd29.553715
Nkx2.5	R&D Systems	AF2444	1:100 for IF	https://www.rndsystems.com/products/human-nkx25-antibody_af2444
FLAG tag	Sigma-Aldrich	F7425	1:200 for IP 1:2000 for WB	https://www.sigmaaldrich.com/US/en/product/sigma/f7425
HA tag	Santa Cruz	sc-7392	1:40 for IP 1:1000 for WB	https://www.scbt.com/p/ha-probe-antibody-f-7

DOI [to be added]

V5	Abcam	ab27671	1:2000 for WB	https://www.abcam.com/products/primary-antibodies/v5-tag-antibody-sv5-pk1-ab27671.html
FLNC	Novus Biologicals	NBP1-89300	1:1000 for WB	https://www.novusbio.com/products/flnc-antibody_nbp1-89300
GAPDH	Santa Cruz	sc-32233	1:5000 for WB	https://www.scbt.com/p/gapdh-antibody-6c5
β 1D integrin	Thermo Fisher	MA1-06906	1:2000 for WB	https://www.thermofisher.com/antibody/product/ITG B1-Antibody-clone-2B1-Monoclonal/MA1-06906
Talin1	Bio-Rad	MCA4770	1:2000 for WB	https://www.bio-rad-antibodies.com/monoclonal/human-talin-1-antibody-97h6-mca4770.html?f=purified
ILK	Cell Signaling	3862	1:2000 for WB	https://www.cellsignal.com/products/primary-antibodies/ilk1-antibody/3862
γ -SAG	Vector Laboratories	VP-G803	1:1000 for WB	N/A
Dystrophin	Abcam	ab15277	1:1000 for WB	https://www.abcam.com/products/primary-antibodies/dystrophin-antibody-ab15277.html
Xirp2	Proteintech	11896-1-AP	1:2000 for WB	https://www.ptglab.com/products/XIRP2-Antibody-11896-1-AP.htm
JUP	Sigma-Aldrich	P8087	1:2000 for WB	https://www.sigmaaldrich.com/US/en/product/sigma/p8087
Normal Rabbit IgG	Cell Signaling	2729	1:200 for IP 1:500 for IF	https://www.cellsignal.com/products/primary-antibodies/normal-rabbit-igg/2729?site-search-type=Products&N=102236+4294956287&Ntt=isotype+control&fromPage=plp
Normal Mouse IgG	Santa Cruz	sc-2025	1:80 for IP 1:500 for IF	https://www.scbt.com/p/normal-mouse-igg?requestFrom=search

DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL
pcDNA3-FLNC ABD (WT)-3 x FLAG	NM_001081185	Home-made	
pcDNA3-FLNC ABD (F93A/L98E)-3 x FLAG	NM_001081185	Home-made	
pcDNA3-ACTC1-HA	NM_009608.4	Home-made	
pCMV6-FLNC (WT)-tGFP	NM_001081185	Origene	https://www.origene.com/catalog/cdna-clones/expression-plasmids/mg222854/flnc-nm_001081185-mouse-tagged-orf-clone
pCMV6-FLNC (F93A/L98E)-tGFP	NM_001081185	Generated from pCMV6-FLNC (WT)-tGFP	
pCAX-ITGB1-FLAG	NM_010578.2	Addgene	https://www.addgene.org/30153/
pcDNA3- γ -SAG-FLAG	NM_011892.3	Home-made	

Cultured Cells

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
HEK 293	ATCC	unknown	https://www.atcc.org/products/crl-1573

Other

Description	Source / Repository	Persistent ID / URL
Alexa Fluor® 488 AffiniPure Donkey Anti-Rabbit IgG (H+L)	Jackson ImmunoResearch	https://www.jacksonimmuno.com/catalog/products/711-545-152
Alexa Fluor® 594 AffiniPure Donkey Anti-Mouse IgG (H+L)	Jackson ImmunoResearch	https://www.jacksonimmuno.com/catalog/products/715-585-150
Alexa Fluor® 488 AffiniPure Donkey Anti-Mouse IgG (H+L)	Jackson ImmunoResearch	https://www.jacksonimmuno.com/catalog/products/715-545-150
Alexa Fluor® 594 AffiniPure Donkey Anti-Rabbit IgG (H+L)	Jackson ImmunoResearch	https://www.jacksonimmuno.com/catalog/products/711-585-152
Polyclonal Goat Anti-Rabbit Immunoglobulin/HRP	Dako	https://www.agilent.com/en/product/specific-proteins/elisa-kits-accessories/goat-anti-rabbit-immunoglobulins-hrp-affinity-isolated-2717113
Polyclonal Goat Anti-Mouse Immunoglobulin/HRP	Dako	https://www.agilent.com/en/product/specific-proteins/elisa-kits-accessories/goat-anti-mouse-immunoglobulins-hrp-affinity-isolated-2717109
Tamoxifen	Sigma-Aldrich	https://www.sigmaaldrich.com/US/en/product/sigma/t5648
4-12% SDS-PAGE gels	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/NW04125BOX
Immun-Blot PVDF Membrane	Bio-Rad	https://www.bio-rad.com/en-us/sku/1620177-immun-blot-pvdf-membrane-roll-26-cm-x-3-3-m?ID=1620177
SuperSignal™ West Femto Maximum Sensitivity Substrate	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/34096
FuGENE HD Transfection Reagent	Promega	https://www.promega.com/products/luciferase-assays/transfection-reagents/fugene-hd-transfection-reagent/
Pierce™ IP Lysis Buffer	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/87787
Halt™ Protease & Phosphatase Inhibitor Cocktail	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/78440
Dynabeads™ Protein G	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/10003D
Dulbecco's modified Eagle's medium	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/11995065
Medium 199	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/11150059
Horse serum	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/26050088
Fetal bovine serum	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/10100147
Penicillin/Streptomycin	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/15140122
Neonatal Cardiomyocyte Isolation System	Worthington	https://www.worthington-biochem.com/products/neonatal-cardiomyocyte-isolation-system
Lipofectamine™ 3000 Transfection Reagent	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/L3000001
TRIzol™ Reagent	Thermo Fisher	https://www.thermofisher.com/order/catalog/product/15596026
RNeasy mini kit	Qiagen	https://www.qiagen.com/us/products/discovery-and-translational-research/dna-rna-purification/rna-purification/total-rna/rneasy-kits?catno=74104
M-MLV Reverse Transcriptase	Promega	https://www.promega.com/products/pcr/rt-pcr/m-mlv-reverse-transcriptase/

iTaq Universal SYBR Green Supermix	Bio-Rad	https://www.bio-rad.com/en-us/product/itaq-universal-sybr-green-supermix?ID=M87FTF8UU
Sirius Red/Fast Green Collagen Staining Kit	Chondrex	https://www.chondrex.com/products/sirius-red-fast-green-collagen-staining-kit
Antigen Unmasking Solution	Vector laboratories	https://vectorlabs.com/products/histology/antigen-unmasking-solution-citric-acid-based
<i>In Situ</i> Cell Death Detection Kit	Roche	https://www.sigmaaldrich.com/US/en/product/roche/11684795910

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
Control	Male	8-10 weeks old	16	16	Yes	
<i>Fln</i> c icMut	Male	8-10 weeks old	16	3	Yes	

Sample Size: The number of animals in *Fln*c icMut group was determined by the genotypes of the mouse individuals. The number of animals in Control group was chosen to be consistent with that of *Fln*c icMut group.

Inclusion Criteria: The study included the male animals with normal body weights, as assessed by the data provided by the vendor (https://www.criver.com/sites/default/files/resources/doc_a/rm_rm_r_male_C57BL6NCr_mice_weight.pdf), prior to the echocardiographic analysis conducted before the administration of Tamoxifen.

Exclusion Criteria: Female mice were excluded to ensure the statistical robustness and mitigate the potential interference from the possible side effects of Tamoxifen on female animals (PMID: 17279326, 33850181).

Randomization: 8-10 weeks old male mice were assigned randomly to different cages during the weaning process. These assignments remained unchanged throughout the genotyping, echocardiographic analysis and administration of Tamoxifen.

Blinding: The performers of the echocardiographic analysis and the administration of Tamoxifen were blinded to the genotypes of the animals included in the study.