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	JAX 008462	C57BL6/J	M / F	

Genetically Modified Animals

	Species	Vendor or Source	Background Strain	Other Information	Persistent ID / URL
Parent	Mouse	JAX 008462	C57BL6/J	Trp53 tm1Brn/J	
Parent	Mouse	M Tallquist	C57BL6/J	Tcf21-MerCreMer	
Parent	Mouse	JAX 007676	C57BL6/J	Rosa-mTmG	

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)	Persistent ID / URL
Acta2	Sigma-Aldrich	A5228	1:250		
BrdU	Novus Biological	NB500-169	1:200		
CHP (biotin)	3Helix		1:100		
ERG	Abcam	ab92513	1:100		
GFP	Torrey Pines Biolabs	TP401	1:100		
IsolectinB4-FITC	Sigma-Aldrich	L2895	1:50		
Ki67	Novus Biological	NB110-89717	1:100		
$p16^{Ink4a}$	Abcam	ab189034	1:100		
P53	Leica	NCL-L-p53-CM5p	1:500		
PDGFRα	R&D Systems	AF1062	1:100		
SA-555	LifeTech	S21381	1:250		
WGA-A647	Thermo-Fisher	W32466	1:100		

DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL

Cultured Cells

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL

DOI [to be added]

Data & Code Availability

Description	Source / Repository	Persistent ID / URL
Single cell RNA-seq	GSE165455	

Other

Description	Source / Repository	Persistent ID / URL

DOI [to be added]

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 (Control)	M / F	12 weeks	39	28	Yes	Tcf21-MerCreMer;p53-wt/wt
Group 2 (P53-CF Het)	M / F	12 weeks	12	11	Yes	Tcf21-MerCreMer; p53-fl/+
Group 3 (p53-CF KO)	M / F	12 weeks	34	23	Yes	Tcf21-MerCreMer; p53-fl/fl

Echocardiography N (Figure 4A-D):

Baseline:	39 (WT)	12 (HET)	34 (KO)
Day 7:	33 (WT)	12 (HET)	30 (KO)
Day 14:	31 (WT)	12 (HET)	30 (KO)
Day 21:	28 (WT)	11 (HET)	23 (KO)
Day 28:	28 (WT)	11 (HET)	23 (KO)

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

Inclusion Criteria : NA

Exclusion Criteria: Mice were only excluded from the study if a TAC stenosis pressure gradient was less than 90 mm/Hg, indicating failure of a sufficient aortic constriction. No mice were excluded due to death, removal at an earlier timepoint for histological analyses, or failure to achieve expected phenotype.

Randomization: NA

Blinding: Surgery and echo personnel are blinded to the genotype. Quantification of morphometry was performed by personnel who are blinded to genotype.

DOI [to be added]