

## Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

### Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- The statistical test(s) used AND whether they are one- or two-sided  
*Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
- A description of all covariates tested
- A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- For null hypothesis testing, the test statistic (e.g.  $F$ ,  $t$ ,  $r$ ) with confidence intervals, effect sizes, degrees of freedom and  $P$  value noted  
*Give  $P$  values as exact values whenever suitable.*
- For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- Estimates of effect sizes (e.g. Cohen's  $d$ , Pearson's  $r$ ), indicating how they were calculated

*Our web collection on [statistics for biologists](#) contains articles on many of the points above.*

### Software and code

Policy information about [availability of computer code](#)

Data collection

No software was used.

Data analysis

Graphpad Prism 8.0 ,ModFit LT 4.0 and Image-Pro Plus were used.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

### Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The data that support the findings of this study and unique materials are available from the corresponding authors upon reasonable request.

## Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

### Reporting on sex and gender

Use the terms *sex* (biological attribute) and *gender* (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

### Reporting on race, ethnicity, or other socially relevant groupings

Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status). Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.) Please provide details about how you controlled for confounding variables in your analyses.

### Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

### Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

### Ethics oversight

Identify the organization(s) that approved the study protocol.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

## Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences  Behavioural & social sciences  Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

### Sample size

No statistical test was used to predetermine sample size. Sample size was determined based on the experimental results that we obtained from preliminary experiments. In vivo studies, we used standard sample sizes reported in the literature previously in mouse studies. The numbers of performed experiments were indicated in each figure legend. The sample size for whole animal experiments was set to be >3 mice for each group, and for molecular biology experiments, the sample size for set to 3-6 for each group.

### Data exclusions

The data from the animals died before the completion of the whole experimental procedures were excluded from our data analysis.

### Replication

For cellular and molecular experiments, each single measurement was performed in triplicate and the results were consistently reproducible.

### Randomization

All animals and cells were randomly assigned to experimental groups.

### Blinding

The experimental designers and experimenters/data analysts were double blinded.

## Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

## Materials &amp; experimental systems

n/a	Involvement
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

## Methods

n/a	Involvement
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Antibodies

Antibodies used	ASPP1(WB,1:1000, Abclonal, A15411); ASPP1(IP,10ug/mL, Sigma, A4355); ASPP1(IF,1:200, Sigma, HPA006394); p53(WB,1:1000, Abclonal, A5761); p53(IP, 10ug/mL, Cell Signaling Technology, 2524S); p53(IF,1:200, R&D Systems, AF1355); OTUB1(WB,1:1000, Abclonal, A11656); OTUB1(IP,10ug/mL, NOUVS, NBP-149934); Collagen I(WB,1:1000, Wanleibio, WLO088); Fn(WB,1:1000, Proteintech, 15613-1-AP); a-SMA(IF,1:200, Abcam, Ab124964);b-actin(WB,1:10000, Cell Signaling Technology, 4970S); Ubiquitin (WB,1:500, Santa Cruz Biotechnology, Sc-166553)
Validation	All the primary antibody for the species and application statement on the manufacturer's websites.

## Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	ASPP1 conventional knockout mice and ASPP1 flox/flox (ASPP1-fl/fl) mice were generated by Cyagen Biosciences Inc (Guangzhou, China). PostnMerCreMer mice were purchased from The Jackson Lab (Bar Harbor, USA).
Wild animals	The study did not involve wild animals.
Reporting on sex	The incidence rate and severity of myocardial fibrosis caused by MI are affected by gender. In the adult population, the prevalence of myocardial infarction in men is higher than that in premenopausal women. However, the regulation of ASPP1 on myocardial fibrosis is not sexual dimorphic, as deletion of ASPP1 also exacerbated myocardial fibrosis development in female mice.
Field-collected samples	Our study did not involve samples collected from the field.
Ethics oversight	All mice were maintained in a temperature-controlled facility with 12 h light/dark cycle at 23±3°C and 30-70% humidity. All animal experiments were approved by the Ethic Committees of College of Pharmacy, Harbin Medical University (IRB3005821), and in accordance with the Guide for the Care and Use of Laboratory in Harbin Medical University.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

## Plants

Seed stocks	<i>Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.</i>
Novel plant genotypes	<i>Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.</i>
Authentication	<i>Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.</i>

## Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

## Methodology

Sample preparation

The transfected cardiac fibroblasts were digested with trypsin to form a single cell suspension. After centrifugation to precipitate the cells, the supernatant was discarded. The precipitated cells were resuspended by adding 1ml of pre-cooled PBS. The cells were centrifuged again and the supernatant was discarded. The cells were properly dispersed by gently flicking the bottom of the centrifuge tube. Then, 0.5 ml of propidium iodide staining solution was added, the cell precipitate was gently mixed and resuspended, and incubated at 37°C away from light for 30 min. Sieving was performed to remove oversized cell clusters. Flow-through assay was carried out with an excitation wavelength of 488 nm, and light scattering was detected at the same time.

Instrument

The samples were measured by using a Beckman Coulter flow cytometer (Beckman Coulter, USA).

Software

The results were collected by using FACScan flow cytometer with Cell Quest software and analyzed by using ModFit LT 4.0.

Cell population abundance

NA

Gating strategy

Set FSC-A and FSC-H gates under the active cell population to remove adherent cells. Establish a histogram of FSC-H and cell number. Control the CV value to 5% and set it to the G0/G1 peak; The peak position of G2/M is almost twice that of G0/G1. We are going to provide a figure in the Supplementary information showing the gating strategy.

- Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.