nature research

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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work we publish. This form is published with all life science papers and is intended to promote consistency and transparency in reporting. All life sciences submissions use this form; while some list items might not apply to an individual manuscript, all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

   Describe how sample size was determined.

   Sample sizes were based on pilot and previously conducted and published experiments in which statistically significant differences were observed between groups assessed by gene expression, enumeration of myeloid subsets by flow cytometry, ventricular parameters measured by echocardiography or cardiac MRI, and survival.

2. Data exclusions

   Describe any data exclusions.

   Preestablished exclusion criteria are detailed in Materials and Methods - Statistics subsection. Importantly, for survival studies, mice dying within the first 24 hours of surgery were excluded from the study as this was attributed to technical problem rather than a reflection of the pathophysiology of myocardial infarction.

3. Replication

   Describe whether the experimental findings were reliably reproduced.

   The experimental findings were reproduced in multiple cohorts.

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups.

   No specific method of redomization was used, however echocardiographers and surgeons were blinded from genotype where possible.

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   Echocardiography, cardiac MRI, and image analysis was performed without knowledge of genotype. RNA processing and RT-PCR was performed without knowledge of genotype. Attempts were made to blind surgeons to genotype, however some strains were recognizable by subtle differences in skin and coat.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

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6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or the Methods section if additional space is needed).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒	A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly.
☐	☒	A statement indicating how many times each experiment was replicated
☐	☒	The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒	The test results (e.g. *p* values) given as exact values whenever possible and with confidence intervals noted
☐	☒	A summary of the descriptive statistics, including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒	Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	All computer code (statistical, image analysis, and bioinformatics) utilized previously reported and publicly available software packages.

For all studies, we encourage code deposition in a community repository (e.g. GitHub). Authors must make computer code available to editors and reviewers upon request. The *Nature Methods* guidance for providing algorithms and software for publication may be useful for any submission.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	All materials are commercially available with the exception of IRF3-/- and cGAS-/- mouse strains, which we received as gifts from Drs. Taniguchi and Fitzgerald respectively. This is described in the Methods section.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Antibodies with vendor and clone name are used as previously reported. All antibodies used in this study are commercially available and have been used extensively for staining the cell types and proteins we probe in our studies. Results using these antibodies have been reported in the literature by our group and by others. Antibodies, vendors, clone name, dilution are reported for each antibody.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	No eukaryotic cell lines were used.
b. Describe the method of cell line authentication used.	N/A
c. Report whether the cell lines were tested for mycoplasma contamination.	N/A
d. If any of the cell lines used in the paper are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	N/A

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Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Adult C57BL/6J (WT, stock 000664), type I interferon-inducible Cre expressing B6.Cg-Tg(Mx1-cre)1Cgn/J (Mx1-Cre, stock 003556)35, cardiomyocyte-specific Cre expressing B6.FVB-Tg(Myh6-cre)2182Mds/J (Myh6-Cre, stock 011038), Gt(ROSA)26Sortm4(ACTB-tdTomato,-EGFP)Luo/J (mTmG, stock 007576)36, MAVS deficient B6;129-Mavs,tm1Zjc>/J (MAVS-/-, stock 008634)37, TRIF functionally deficient C57BL/6J-Ticam1Lps2/J (TRIFLps2/Lps2, stock 005037)38, STING functionally deficient C57Bl/6J-Tmem173<gt>/J (STINGgt/gt, stock 017537)39, and cGAS deficient B6(C)-Mb21d1,tm1d(EUCOMM)Hmgu>/J (cGAS-/- mice were purchased from the Jackson Laboratory (stock 026554) or obtained from Fitzgerald lab after derivation from cryopreserved embryos obtained from the European Conditional Mouse Mutagenesis Program (EUCOMM)). IRF3-/- mice40 were a generous gift from Tadatsugu Taniguchi and provided by Michael Diamond. IFNAR knockout mice (IFNAR-/-) were originally from J. Sprent and were backcrossed for 12 generations at the University of Massachusetts Medical School and provided by Kate Fitzgerald. Genotyping was performed in-house using methods recommended by Jackson Laboratory, or by Transnetyx. All experiments were performed with 10 to 25-week-old animals and were carried out using age and gender matched groups without randomization. All mice were maintained in a pathogen-free environment of the Massachusetts General Hospital of University of Massachusetts animal facilities, and all animal experiments were approved by the Subcommittee on Animal Research Care at Massachusetts General Hospital or University of Massachusetts.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

No human research participants were used for this study.

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