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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but 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.	Specific sample sizes are described in figures or figure legends for all experiments. Sample size used were based on previous experience from the Berger, Adams, and Kaestner labs. No statistical test was used to pre-determine sample size.

2. Data exclusions

Describe any data exclusions.	No pre-set criterion or data exclusion was used. For RNA-seq data analyses, single-ended, 75 bp reads were mildly trimmed using Trimmomatic (version 0.32) to remove leading or trailing nucleotides whose sequencing quality was below 3. Reads whose length fell below 30 bp after trimming were also removed from downstream analysis, as a standard practice.

3. Replication

Describe whether the experimental findings were reliably reproduced.	The number of repeats for experiments is described in corresponding figure legends. Only successfully replicated/reproduced experiments are reported.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.	Genotypes of mice are known to investigators. No pre-established selection criteria for mice were used, other than genotypes and ages. When mice with desired genotypes were at appropriate ages, all mice in corresponding cages were used. No selection criteria or randomization for mice applied.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.	The investigators were blinded when assessing IHC results. Fields or sections of tissues for quantification were randomly selected and scored, as indicated in Methods.

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

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in 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 clear description of 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.	Excel and GraphPad were used to perform general statistical analyses. For RNA-seq data analyses, the following published software were used: Trimmomatic (version 0.32), STAR (version 2.3.0e), and featureCounts (version 1.5.0).

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

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.	No unique materials were used.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	A detailed description of antibodies used, including vendors and catalog numbers, was provided in Methods, under "Reagents and antibodies" section. Antibodies were validated by gene inactivation and/or biological effects, and by other published studies.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Primary BJ fibroblasts were purchased from ATCC, IMR90 from Coriell, and were described in previous studies.
b. Describe the method of cell line authentication used.	IMR90 and BJ were authenticated by previous genome-wide sequencing analyses.
c. Report whether the cell lines were tested for mycoplasma contamination.	Cells were intermittently tested for mycoplasma.
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	N/A.

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.	STING+/+ and STING-/- mice in C57BL/6 background were described previously. Mice were fed ad libitum on a regular diet, and handled following institutional regulations and guidelines. Both sexes were included in the study.

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.	N/A.