***eLife’s* transparent reporting form**

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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
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* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Sample-size is reported in the figure legends and was estimated based on (I) the variability observed in pilot studies or in previous related experiments, (II) the expected effect size, (III) the probability to detect a minimal significance level of 0.05 and (IV) the sidedness of the test. For all animal experiments, the lowest number of animals that were expected to be required to obtain statistical significance was chosen. If possible, for aged mice more animals were included due to the expected higher (natural) mortality.

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The number of replicates is reported in the figure legends. The manuscript only contains biological replicates. All results were confirmed by multiple independent experiments and stringent statistical testing was performed to ensure reproducibility.

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* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
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Statistical tests and p-values are reported in the figure legends and described in the methods section. For bar graphs showing means, raw data is presented as point clouds.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

As stated in the methods section, animals were randomized by body weight within experimental groups. Blinding was not formally preformed. Where applicable the researcher quantifying data did not know about the nature of the different experimental groups.

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* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
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Please indicate the figures or tables for which source data files have been provided:

The data discussed in this publication have been deposited in NCBI's Gene Expression Omnibus (GEO). GEO Series accession numbers are GSE111401, GSE81096 and GSE193665.