***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:

No explicit power analysis was used. Replicates numbers were decided from experience of the techniques performed and practical considerations. N numbers and statistical tests are given in figure legends and Materials and Methods section.

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* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
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* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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All the N numbers in the manuscript indicate biological replicates, which are biologically distinct samples. In the “materials and methods” section, we described the criteria used to exclude samples, if applicable.

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* Statistical analysis methods should be described and justified
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* 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)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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General information on data analysis is given at end of Methods section. Every figure legend has statistical information concerning the data representation and details of tests. Box and whisker plots (with mean and median) have been used in most cases, superimposed on mean +/- SEM. Human genetic variant analysis is provided in the corresponding parts of Materials and Methods section.

(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

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Mice and cells were assigned to different groups based solely on their genotypes. No masking was used in this study.

**Additional data files (“source data”)**

* 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
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Please indicate the figures or tables for which source data files have been provided:

All available data is uploaded. Targeted sequencing raw data of CHD patients have been deposited NCBI’s Sequence Read Archive (PRJNA579193). RNA-seq data have been deposited in NCBI’s Gene Expression Omnibus (GSE137090).