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

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* 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:

A large family with twenty-three alive members was recruited in our study. The sample-size estimation does not apply to our submission.

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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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* 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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(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.)

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* 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
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* 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:

Supplementary file 1 and Supplementary file 2 were submitted as source data files for the Figure 2 and Figure 2-figure supplement 1.