***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
* You shouldstate the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decidedwhat sample (replicate) size (number) to use

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* You should report how often each experiment was performed
* You should includea definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
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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
* 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)
* 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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* 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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* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figureor table
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Please indicate the figures or tables for which source data files have been provided:

Fig 1, Fig 2, Fig 3, Fig 4, Fig 5, Supplementary figure 2-8 and supplementary figure 10.