***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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This is not applicable to our submission as we did not base our study on comparison of samples undergoing different treatments through statistical tests.

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* You should report how often each experiment was performed
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* 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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* Criteria for exclusion/inclusion of data should be clearly stated
* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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:

Replicate information can be found in the main text and the methods. Criteria for exclusion of variants based on sequencing noise can be found in the methods. The sequencing data is available on NCBI SRA under PRJNA606894.

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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)
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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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* Include model definition files including the full list of parameters used
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All data used in analyses can be found in Supplementary file 2. Code used to calculate all fitness scores from sequencing data is available on GitHub (https://github.com/johnchen93/DMS-FastQ-processing).