## nature portfolio

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## **Reporting Summary**

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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n/a	nfirmed
	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
x	A description of all covariates tested
	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
x	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
×	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
×	Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
	Our web collection on statistics for biologists contains articles on many of the points above.

## Software and code

Policy information about availability of computer code

Data collection

Excluding manufacturer's software required to run the instruments described in the Methods section, no custom code was required to aquire any data in this manuscript.

Data analysis

The following software packages were used: ImageJ (version 1.46r), Fiji (version 2.14.0/1.54i), GraphPad Prism (version 10.2.3), softWoRX (version 6.5.2), AlphaFold Server (https://golgi.sandbox.google.com/)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

## Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The data reported in this article are available in the main text and its supplemental material. Source data are provided with this paper. Plasmids and yeast strains generated in this study are available from the corresponding author upon request.

Human rese	earch parti	cipants		
Policy information	about <u>studies i</u>	nvolving human research participants and Sex and Gender in Research.		
Reporting on sex a	nd gender	Not applicable. The model is S.cerevisiae		
Population charact	teristics	Not applicable		
Recruitment		Not applicable		
Ethics oversight		Not applicable		
Note that full information on the approval of the study protocol must also be provided in the manuscript.				
Field-spe	ecific re	porting		
Please select the o	ne below that i	s the best fit for your research. If you are not sure, read the appropriate sections before making your selection.		
<b>X</b> Life sciences	□ в	ehavioural & social sciences 🔲 Ecological, evolutionary & environmental sciences		
For a reference copy of	the document with	all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>		
Life sciences study design				
All studies must di	sclose on these	points even when the disclosure is negative.		
Sample size		were generated from at least 3 biological replicates except screen validation and Supplementary Figs. 5g and 6c, d which were es. Sample sizes were chosen according to or exceeding standards in the field.		
Data exclusions	No data were e	xcluded.		
Replication		were generated from at least 3 biological replicates except screen validation and Supplementary Figs. 5g and 6c, d which were es. All attempts to replicate the data were successful.		
Randomization	No randomizat	ion was performed as our study was performed with liquid yeast cultures, not individual yeast cells.		
Blinding	No blinding wa	s performed as the phenotype classifications were based on rigorous quantitative criteria.		
Reportin	g for sp	pecific materials, systems and methods		
We require informat	ion from authors	about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.		
Materials & ex	nerimental s	vstems Methods		
Antibodies				
<b>x</b> Eukaryotio	Eukaryotic cell lines			
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Animals and other organisms

Clinical data

Dual use research of concern