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Reporting Summary

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Statistics

For	all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.	
n/a	Confirmed	
	\mathbf{x} The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement	
	X 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	
	X 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>	
	🗴 For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings	
	x For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes	
	x Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated	
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.	

Software and code

Policy information about availability of computer code				
Data collection	no software was used			
Data analysis	MatLab 7.12.0.635, Python 2.7.13 , NumPy 1.8.0, Matplotlib 1.4.3,			

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data

- A description of any restrictions on data availability

The authors declare that the data supporting the findings of this study are available within the paper and its supplementary information files.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

× Life sciences

Behavioural & 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

Sample size	As detailed in the Methods section we have used 64 different mRNA variants and employed cross-validation to prevent over-fitting.
Data exclusions	no data was excluded
Replication	The measurements of the frameshifting efficiencies were repeated at least 3 times, all measurements are listed in Table S1 and depicted in Fig. 1b
Randomization	n/a
Blinding	n/a

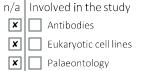
All studies must disclose on these points even when the disclosure is negative.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

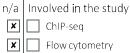
Methods



X Animals and other organisms

x Human research participants

🗶 🗌 Clinical data



Flow cytometry

MRI-based neuroimaging X