# nature portfolio

Corresponding author(s):	Robert N. Grass
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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	Confirmed
	$oxed{x}$ 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
x	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 <i>d</i> , Pearson's <i>r</i> ), 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

No software was used for data collection.

Data analysis

Custom scipts based on Python (v3.10) were used for data processing analysis, including filtering of sequencing data. The scripts are available at github.com/fml-ethz/cuf-cryptography. MATLAB (Version R2022b) was used to analyze overall positional base content. Plots were generated with Origin 2021b, python scripts and MS excel (Version 2402 Build 16.0.17328.20124). Ct analysis was performed on Lightcycler96 Software (Version 1.1.0.1320).

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

All raw sequencing data generated in this study have been made public on the European Nucleotide Archive under Accession Code PRJEB73810. Raw data is available on figshare: https://figshare.com/s/5ace57d8a1c360d45302 The literature data from Meiser et al.26 used in this study are available in the Figshare

database under https	s://figshare.com/	articles/dataset/SequencingData/12941786/1.		
Research inv	olving hu	man participants, their data, or biological material		
	about studies v	vith human participants or human data. See also policy information about sex, gender (identity/presentation),		
Reporting on sex ar	nd gender	Study did not involve human participants, their data or biological material		
Reporting on race, ethnicity, or other socially relevant groupings		Study did not involve human participants, their data or biological material		
Population characte	eristics	Study did not involve human participants, their data or biological material		
Recruitment		Study did not involve human participants, their data or biological material		
Ethics oversight		Study did not involve human participants, their data or biological material		
Note that full informa	ation on the appr	oval of the study protocol must also be provided in the manuscript.		
Field-spe	ocific re	norting		
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		s the best fit for your research. If you are not sure, read the appropriate sections before making your selection.		
Life sciences		ehavioural & social sciences		
Total reference copy of a	nie document with	in sections, see <u>nature, contract in reporting saminary nation</u>		
Life scier	nces stu	udy design		
		points even when the disclosure is negative.		
Sample size	Sample size (red	Sample size (referring to the 15 unique input/output/pool combinations in the study) was selected large enough to perform statistics on their		
Data exclusions	No experiments information.	experiments were excluded from the study. All experiments performed are documented in the manuscript and supplementary ormation.		
Replication	The reproducibility was tested by performing the function described in the study at least twice for each input/output pair. All these replicates were successful.			
Randomization	Experimental gr	roups do not apply to the type of study performed, therefore, no randomization had to be performed.		
Blinding	Experimental groups do not apply to the type of study performed, therefore, no blinding had to be performed.			
Reportin	g for sp	pecific materials, systems and methods		
		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 & exp	perimental s	ystems Methods		
n/a Involved in th				
X Antibodies		X ChIP-seq		
Eukaryotic cell lines    X   Flow cytometry    AAD based payraging				
	Palaeontology and archaeology  MRI-based neuroimaging  Animals and other organisms			
Clinical dat				
Dual use research of concern				
Plants				

## Plants

Seed stocks	No plants were used in this study	
Novel plant genotypes	No plants were used in this study	
Authentication	No plants were used in this study	