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Reporting Summary

Nature Research 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 Research policies, seeAuthors & Referees and theEditorial Policy Checklist.

Statistics				
For all statistical analys	es, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.			
n/a Confirmed				
The exact sam	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement			
A statement of	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.			
A description	A description of all covariates tested			
A description	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 Give <i>P</i> values as exact values whenever suitable.				
For Bayesian a	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings			
For hierarchic	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes			
Estimates of e	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 o	code			
Policy information abo	ut availability of computer code			
Data collection	The standard Illumina NextSeq data pipeline was used to collect all sequencing data.			
Data analysis	The code used to decode the files presented in this paper is proprietary Microsoft code. However, the rest of the analysis software is in the supplemental text or is available upon request.			
	om algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.			
Data				
Accession codes, unA list of figures that	ut <u>availability of data</u> include a <u>data availability statement</u> . This statement should provide the following information, where applicable: ique identifiers, or web links for publicly available datasets have associated raw data restrictions on data availability			
The data that support the	e findings of this study are available from the corresponding author upon reasonable request.			
Field-speci	fic reporting			
Please select the one b	relow 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				

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.				
Sample size	The files were arbitrarily chosen to have an order of magnitude in size difference between each file.			
Data exclusions	No data was excluded from this study unless the sequencing coverage was too high to be comparable to the other data points, in which case the data was randomly subsampled down to 20x coverage, as is detailed in the text.			
Replication	Replication was effectively done by using three files throughout this experiment. While doing qPCR, replicates were used to determine the final mean value.			
Randomization	This is not applicable because we treat all data the same way.			
Blinding	All decoding was done blind with no reference to the DNA sequences present.			

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	
n/a	Involved in the study	n/a Involved in the study	
X	Antibodies	ChIP-seq	
x	Eukaryotic cell lines	Flow cytometry	
×	Palaeontology	MRI-based neuroimaging	
x	Animals and other organisms	·	
×	Human research participants		
×	Clinical data		