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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, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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 san	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	of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons			
	cion of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)			
	thesis testing, the test statistic (e.g. $F$ , $t$ , $r$ ) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted is exact values whenever suitable.			
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 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 <u>availability of computer code</u>			
Data collection	No data collection software used.			
Data analysis	RNA alignment was performed in Geneious R9, indel analysis was performed with OutKnocker2, off-target alignment was performed with BrowserGenome, custom Python scripts were used for PAM discovery assay.			
	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				
Policy information abo	ut <u>availability of data</u>			
<ul><li>Accession codes, un</li><li>A list of figures that</li></ul>	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	ese findings are available from the corresponding author upon reasonable request.			
Field-speci	ific reporting			
Please select the one b	pelow 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			

## Life sciences study design

Materials & experimental systems

n/a Involved in the study

Commonly misidentified lines

(See ICLAC register)

Antibodies

Sample size	No sample-size calculation were performed.
Data exclusions	No data was excluded from analysis
Replication	All experiments were confirmed with independent replicates. The number of replicates for each experiment is clearly presented in the figure legends.
Randomization	Randomization was not relevant to this study.
Blinding	Blinding was not relevant to this study.
onortin	g for specific materials, systems and methods

Methods

n/a | Involved in the study ChIP-seq

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.

Eukaryotic cell lines	$\boxtimes$	Flow cytometry		
Palaeontology	$\boxtimes$	MRI-based neuroimaging		
Animals and other organism	5			
Human research participants	5			
Clinical data				
Eukaryotic cell lines				
Policy information about <u>cell lines</u>				
Cell line source(s)	HEK293T cells from the Am	American Type Culture Collection		
Authentication	Cells were not authenticated.			
Mycoplasma contamination	Cells tested negative for mycoplasma.			

Name any commonly misidentified cell lines used in the study and provide a rationale for their use.