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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For a	all statistical ar	alyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.			
n/a	Confirmed				
	The exact	exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement			
	A stateme	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly			
	The statis Only comm	atistical test(s) used AND whether they are one- or two-sided or more complex techniques in the Methods section.			
\boxtimes	A descript	scription of all covariates tested			
\boxtimes	A descript	cription of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons			
	A full desc	description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) ariation (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.				
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings				
\boxtimes	For hierar	chical 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 <u>statistics for biologists</u> contains articles on many of the points above.			
Sof	ftware an	d code			
Polic	cy information	about <u>availability of computer code</u>			
Da	ta collection	No software was used.			
Da	ta analysis	Custom python scripts were used to analysis the data.			
		g 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 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 raw sequencing data have been submitted to the NCBI Sequence Read Archive (SRA PRJNA587328 [https://dataview.ncbi.nlm.nih.gov/object/19730669]).

Research involving human participants, their data, or biological material			
		vith <u>human participants or human data</u> . See also policy information about <u>sex, gender (identity/presentation),</u> thnicity and racism.	
Reporting on sex		n/a	
Reporting on rac other socially rel groupings		n/a	
Population chara	acteristics	n/a	
Recruitment		n/a	
Ethics oversight		n/a	
Note that full inform	ation on the appr	oval of the study protocol must also be provided in the manuscript.	
Field-spe	ecific re	porting	
Please select the o	ne below that is	the best fit for your research. If you are not sure, read the appropriate sections before making your selection.	
X 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 scier	nces stu	udy design	
All studies must di	sclose on these	points even when the disclosure is negative.	
Sample size	The sample size were chosen according to the library size.		
Data exclusions	The gRNAs with	a total valid reading of less than 100 were removed.	
Replication	All experiments	of replications were successful.	
Randomization	The gRNAs for t	est the performance were randomly selected.	
Blinding	This is not relev	This is not relevant to molecular/cell biology studies	
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.	
system of method no	ved 15 refevant to	your staay. If you are not sare in a list item applies to your research, read the appropriate section service scientifical response.	
Materials & experimental systems Methods			
n/a Involved in the study n/a Involved in the study			
Antibodies ChIP-seq Eukaryotic cell lines Flow cytometry			
Animals and other organisms			
Clinical data			
Dual use research of concern			
☐ Plants			

Eukaryotic cell lines

Policy information about $\underline{\text{cell lines}}$ and $\underline{\text{Sex}}$ and $\underline{\text{Gender in Research}}$

Cell line source(s)

HEK293T cells (ATCC) were maintained in Dulbecco's Modified Eagle Medium (DMEM).

Authentication	HEK293T cells were validated by STR profiling (ATCC).
Mycoplasma contamination	Cells tested negative for mycoplasma.

Commonly misidentified lines (See <u>ICLAC</u> register)

No commonly misidentified cell line was used in the study.