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	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	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 statis Only comm	tical test(s) used AND whether they are one- or two-sided non tests should be described solely by name; describe more complex techniques in the Methods section.				
\boxtimes	A descript	tion of all covariates tested				
\boxtimes	A descript	tion of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons				
	A full deso	cription of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) ation (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>					
\boxtimes	For Bayes	ian 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				
	ı	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.				
So	ftware an	d code				
Poli	cy information	about <u>availability of computer code</u>				
Da	ata collection	Commercial PacBio software (proprietary, version # not available) was used to collect basecalls for analysis.				
Da	ata analysis	All scripts & version numbers used are available on GitHub at: https://github.com/RamaniLab/SAMOSA-ChAAT				
		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

Il processed data is available at Zenodo (https://doi.org/10.5281/zenodo.5770727); raw data and processed data is at GEO accession GSE197979.

	olving nu	man participants, their data, or biological material	
		with human participants or human data. See also policy information about sex, gender (identity/presentation), athnicity and racism.	
Reporting on sex and gender Reporting on race, ethnicity, or other socially relevant groupings Population characteristics		N/A	
		N/A	
		N/A	
Recruitment		N/A	
Ethics oversight		N/A	
Note that full informa	tion on the appr	roval of the study protocol must also be provided in the manuscript.	
Field-spe	cific re	porting	
<u>.</u>		s the best fit for your research. If you are not sure, read the appropriate sections before making your selection.	
Life sciences	В	Behavioural & social sciences Ecological, evolutionary & environmental sciences	
For a reference copy of t	he document with	all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>	
Life scier	nces stu	udy design	
All studies must dis	close on these	points even when the disclosure is negative.	
Sample size	Sample sizes were determined according to convention for in vivo experiments (i.e. two separate biological experiments per condition). Sample sizes for single-molecule experiments were not predetermined, but determined by the number of molecules sequenced on the sequencer		
Data exclusions	exclusions Data were not excluded from analyses.		
Replication	Replication was	s successful and experiments were performed at least in duplicate.	
Randomization	Randomization was not used or relevant to this molecular biological / genomic study replicate samples were treated completely separately and used to ascertain reproducibility		
Blinding	Blinding was not relevant to this study, as the data analyses performed here are all genomic analyses.		
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		ystems Methods	
n/a Involved in th	e study	n/a Involved in the study	
X Antibodies	ChIP-seq		
	H 10		
Eukaryotic	cell lines ogy and archaeol	Flow cytometry MRI-based neuroimaging	

Clinical data

Dual use research of concern

Eukaryotic cell lines

Policy information about <u>cell lines and Sex and Gender in Research</u>

E14 cells were a gift from the Elphege Nora lab; SNF2h KO and WTAB cells were provided under MTA by the Dirk Schubeler Cell line source(s) group at FMI.

Authentication SNF2h KO and WTAB cell lines were validated by matching molecular signal to signal presented by the Schubeler group in a prior publication. E14 cells were not authenticated.

All cell lines tested negative for mycoplasma. Mycoplasma contamination

Commonly misidentified lines No cell lines used in this study are on the ICLAC register. (See <u>ICLAC</u> register)