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

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For	all statistical analyses, 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 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.
\boxtimes	A description of all covariates tested
\boxtimes	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>
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes	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 <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about <u>availability of computer code</u>

Data collection

For direct sequencing, PCR products were purified (ExoSAP-IT Express PCR Cleanup Reagent, ThermoFisher) and sequenced directly (GENEWIZ).

For RNA-seq, RNA extraction was performed with Maxwell® RSC simplyRNA Tissue Kit (Promega) and Proteinase K. Libraries were prepared by GENEWIZ from total RNA using poly(A) enrichment of the mRNA

Data analysis

DYW domain sequences were aligned with MAFFT (v7.407)

Alignments were trimmed with TrimAl (v1.4.rev15)

FastTree (v2.1.10) was used for phylogenetic reconstitution.

EditR (http://baseeditr.com/) was used to analyze the sequencing chromatograms.

STAR (v2.9.7) was used to align fastq data

REDItools was used to determine the editing levels

Statistical analyses by the one-way ANOVA Tukey's comparison test was computed using R (v4.0.3)

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 Research guidelines for submitting code & software for further information.

Data

Validation

Validated by the manufacturer

Policy information about <u>availability of data</u>

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Uncropped and unedited images corresponding to the protein gels and blots are provided in Supplementary Figures 7 to 11. The data used to generate the graphs are available in Supplementary Data 1 and 3. Sanger sequence chromatograms used to score editing efficiencies are available as Supplementary Data 4. Transcriptome wide RNA-sequencing data are available at Sequence Read Archive under BioProject accession number PRJNA856069. Expression plasmids are available from addgene under a uniform biological material transfer agreement (accession IDs: 190955 to 190994). All other data are available from the corresponding authors on reasonable request.

Field-specific reporting				
Please select the or	ne below 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			
For a reference copy of t	the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>			
Life scier	nces study design			
All studies must dis	sclose on these points even when the disclosure is negative.			
Sample size	Three biological replicates were used for each experiment.			
Data exclusions	No data were excluded.			
Replication	All attempts were successful			
Randomization	This is not relevant to this study			
Blinding	This is not relevant to this study			
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 & exp	perimental systems Methods			
n/a Involved in th	· · · · · · · · · · · · · · · · · · ·			
☐ ☐ Antibodies ☐ ChIP-seq				
Eukaryotic cell lines				
Palaeontology and archaeology MRI-based neuroimaging				
Animals and other organisms				
Human research participants Clinical data				
Dual use research of concern				
Antibodies				
Antibodies used	Anti-His-tag mAb-HRP-DirectT, MBL D291-7			

Eukaryotic cell lines

Policy information about <u>cell lines</u>		
Cell line source(s)	HEK293T (RIKEN, RCB2202)	
Authentication	No authentication was performed	
Mycoplasma contamination	The cell line was not tested for mycoplasma contamination	
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used	