

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 [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ A description of all covariates tested |
| ☐ | ☒ 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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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 effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated |

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection Next-generation sequencing data was collected and demultiplexed by Illumina NovaSeq and Huada MGI platform.

Data analysis

Cutadapt (version 1.18)
 Hisat-3n (version 2.2.1-3n-0.0.2)
 BWA MEM (version 0.7.17)
 samtools (version 1.15.1)
 Picard (version 2.27.4)
 GATK (version 3.8.1)
 R environment (version 4.2)
 Bedtools (version 2.28.0)
 Integrative Genomics Viewer, IGV (version 2.14.0)

Python3.9 <https://www.python.org/downloads/>
 Python package pysam v0.19.1 <https://pysam.readthedocs.io/en/latest/api.html>
 Python package Biopython v1.19 <https://biopython.org/>
 Detect-seq tools <https://github.com/menghaowei/Detect-seq>
 Agilent TapeStation Software <https://www.agilent.com.cn/zh-cn/product/automated-electrophoresis/tapestation-systems>
 LightCycler® Software https://lifescience.roche.com/en_cn/brands/realtime-pcr-overview.html#software

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 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](#)

All raw sequencing data generated for this paper is in full open state in NCBI GEO database and is available under accession number GEO: GSE173859

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

Population characteristics

Recruitment

Ethics oversight

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one 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 the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For all experiments with analysis, a minimum of 2 biological replicates were performed to confirm reproducibility. Experiments were performed in cell line level. And high throughput sequencing data shows a high correlation from different batch and biological experiment. So two biological replicates are sufficient to support conclusions in this paper.
Data exclusions	No data was excluded.
Replication	We tested experimental conditions with different DdCBE TALE arrays. We also performed biological replicates independently and successfully of each other.
Randomization	Because the sample size is small, randomization was not relevant for this study. Covariates were controlled for by running controls in parallel whenever applicable.
Blinding	Blinding was not performed as experimental conditions were evident.

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

n/a	Involvement in the study
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involvement in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	source: ATCC; cell lines used: HEK293T cells (ATCC CRL-3216)
Authentication	No cell lines were authenticated
Mycoplasma contamination	Cells tested negative for mycoplasma as detailed in the Methods.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.