nature research

Corresponding author(s): Jian Feng

Last updated by author(s): Apr 8, 2021

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 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 *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	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 *Give P values as 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 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	All software are listed in the Materials section (page 17 of the manuscript).
Data analysis	SPSS 13.0 was used for statistical analysis in primary research paper, https://advances.sciencemag.org/content/6/20/eaaz0298

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

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 list of figures that have associated raw data
- A description of any restrictions on data availability

The data generated by the protocol can be found in https://advances.sciencemag.org/content/6/20/eaaz0298

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

Life sciences study design

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

Sample size	One cell line was used in the protocol to illustrate the process of converting primed hPSCs to the naive state.
Data exclusions	No data was excluded.
Replication	The protocol has been applied to several other cell lines in https://advances.sciencemag.org/content/6/20/eaaz0298
Randomization	Cells were evenly plated on multiwell plates. There was no randomization as the cells show no obvious variation between wells.
Blinding	Blinding was not relevant for the purpose of the protocol.

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	Involved in the study
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Information on antibody is provided in Supplementary Table S7 in https://advances.sciencemag.org/content/6/20/eaaz0298
Validation	The antibodies have been validated by vendors and by our own experiments.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	hESC lines H1 and H9 were from WiCell. RUES2 were from Rockefeller University. Human iPSCs C005 and N004 were made by us and are published before.
Authentication	All hESCs were directly purchased from reputable vendors. Our own iPSCs have been authenticated in previous publications cited.
Mycoplasma contamination	All cells were tested regularly for mycoplasma contamination by PCR. No mycoplasma was detected.
Commonly misidentified lines (See ICLAC register)	Not applicable.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	E13.5 embryos from timed pregnant Hsd:NSA (CF-1) mice (Envigo, order code 033) were used to make MEF cells. Blastocysts were from C57BL/6J mice (Jackson Laboratory, stock number 000664). Injected blastocysts were transferred to foster mice (Hsd:ICR (CD-1) (Envigo, order code 030).
Wild animals	Not applicable.
Field-collected samples	Not applicable.
Ethics oversight	Our animal experiments are approved by the Institutional Animal Care and Use Committees of Roswell Park Comprehensive Cancer Center and University at Buffalo. The University at Buffalo/Roswell Park Comprehensive Cancer Center Stem Cell Research Oversight (SCRO) Committee has approved all experiments on hPSCs in the study. The University at Buffalo Institutional Review Board has determined that the use of human cells in the study is not human subject research.

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