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Last updated by author(s): 2025.02.08

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 *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	No software was used
Data analysis	IBM SPSS Statistics version 22

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

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	not applicable
Reporting on race, ethnicity, or other socially relevant groupings	Chinese embryos
Population characteristics	Collecting discarded embryos from patients undergoing IVF treatment.The inclusion criteria included: age ≤35, normal chromosomes of both parties; the exclusion criteria included: age>35, ovarian hypofunction, chromosomal abnormalities, combined with hyperprolactinemia, thyroid dysfunction and other endocrine diseases, previous pelvic or ovarian surgery patients with medical history, infectious disease history, family genetic history, and systemic diseases.
Recruitment	The human embryo samples were developed from abnormal fertilized zygotes from patients undergoing in vitro fertilization-embryo transfer treatment in our center. An informed consent form was signed to agree that the embryos would be discarded for scientific research purposes.
Ethics oversight	The study protocols were approved by the ethics committees of the First Affiliated Hospital of Zhengzhou University.

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

Life sciences study design

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

Sample size	In this study, a total of 80 human embryos were collected. The number of samples is sufficient for data analysis. Studies for in vitro assays were performed with three independent experiments. Error bars = 95% confidence intervals (CIs).
Data exclusions	No data were excluded.
Replication	We did three to five biological replications for luciferase reporter assay and three biological replications for flow cytometry, RT-PCR, and WB experiments.
Randomization	yes
Blinding	No blinding was used since measurements were not vulnerable to observer bias.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	All antibodies were pretested and repeatedly used in the study with detection stability. GDF15 (Proteintech,27455-1-AP), E-CAD (Proteintech,20874-1-AP), N-CAD (Proteintech, 22018-1-AP), GPX4 (Zen-bioscience, 381958), SMAD2/3 (Cell signaling technology, 8685), SMAD1 (Cell signaling technology, 6944), SMAD5 (Cell signaling technology, 12534),p-SMAD3 (Cell signaling technology, 9520), p-SMAD1/5 (Cell signaling technology, 13820), GAPDH (Bioworld, AP0063), B-ACTIN(Bioworld, AP0060)
Validation	All antibodies used in this study are validated by the researchers, the results were included in the manuscript. The datasheets of all antibodies are available in each company's website.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HTR8/SVneo from ATCC
Authentication	The authentication documents are available.
Mycoplasma contamination	Cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines was used in this study

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	KM mice (8 weeks) were purchased from Vital Lever (Beijing, China).
Wild animals	N/A
Reporting on sex	This study use female mice to caged with male mice.
Field-collected samples	This study did not use field collected samples
Ethics oversight	The study was conducted in accordance with the Laboratory animal- Guideline for ethical review of animal welfare and Measures for Ethical Review of Biomedical Research Involving Humans of China and approved by the local ethics committee of the First Affiliated Hospital of Zhengzhou University (approval number 2021-KY-0868-002).

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	The cells were seeded in advance in a 6-well plate, and the drug was added when the cell density reaches 60%-70%. After the treatment, EDTA-free trypsin was used to digest and collect the cells. When cell apoptosis was measured, Binding Buffer (KeyGen Biotech, Nanjing, China) was used to suspend the cells, Annexin V-FITC (KeyGen Biotech) and Propidium Iodide (KeyGen Biotech) were added in sequence. After reacting for 5-15 minutes at room temperature, the BD Accuri C6 Plus flow cytometer (BD Biosciences, CA, USA) was used for flow cytometry analysis, and FlowJo 10.4 (BD Biosciences) was used to analyze the different stages of apoptosis percentage of cells. When cell cycle was measured, pre-cooled 70% ethanol was added and fix the cell overnight at 4°C. The next day, PI/RNase (KeyGen Biotech) solution was added for 30 min. Cell cycle determination was performed using a BD Accuri C6 Plus flow cytometer (BD Biosciences), and the percentage of cells in different cell cycles was analyzed using FlowJo 10.4 (BD Biosciences).
Instrument	BD Accuri C6 Plus flow cytometer (BD Biosciences, CA, USA)
Software	FlowJo 10.4 (BD Biosciences)
Cell population abundance	Only one cell population was used in this study.
Gating strategy	Live cells were determined by FSC-H and SSC-H, and singlets gated with FSC-A and FSC-H. Then, the proportion of cells was analyzed specifically based on the different fluorescence intensities.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.