nature portfolio

Corresponding author(s): Ho Yin Edwin Chan
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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 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 DNA gels and western blots were visualized using Bio-rad ChemiDoc Touch Imaging System. Thermal cycling was performed on Bio-Rad CFX96 Real-time PCR detection system. Confocal images were acquired on an Olympus IX-81 FV1000 confocal microscope.
Data analysis	The intensity of the protein or DNA bands were quantified using the ImageJ software version 1.52k. Confocal images were analyzed using Olympus Fluoview software Version 4.2a. GraphPad Prism version 9.2.0 was used for statistical analysis.

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 human, rat and mouse PAPD5 promoter sequences were withdrawn from GenBank under the accession numbers NC_000016.10, NC_051354.1 and NC_000074.7, respectively. Transcription factor binding sites were predicted using Transcription factor affinity prediction (http://trap.molgen.mpg.de/cgi-bin/trap_form.cgi), PROMO (http://alggen.lsi.upc.es/cgi-bin/promo_v3/promo/promoinit.cgi?dirDB=TF_8.3.) and JASPAR (http://jaspar.genereg.net/) databases.

Target prediction of miRNAs was performed using miRDB (5.0) and TargetScan (7.2). The intersection of target genes predicted by both databases were used for functional analysis using KOBAS.

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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	The sample sizes are provided for each experiment in the respective figure legends. Sample sizes were chosen based on statistical requirements.
Data exclusions	No data exclusions was done.
Replication	Experimental data were collected from at least three independent trials. Number of biological replicates of cell cultures or animals were described in the legend section of the manuscript.
Randomization	Cell wells and animals were randomly assigned to groups for performing the studies.
Blinding	Each experiment reported in this study was performed blind. The individuals conducting the experiments were blinded to group allocation as well as the allocation sequence.

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

Primary antibodies used for immunoblotting were anti-PAPD5 (PA5-46747, 1:1,000) from Invitrogen; anti-p-TAK1 (4536, 1:1,000), anti-t-TAK1 (4505, 1:2,000), anti-p-MKK4 (9156, 1:1,000), anti-t-MKK4 (9152, 1:2,000), anti-p-MKK7 (4171, 1:1,000), anti-t-MKK7 (4172, 1:2,000), anti-p-JNK (9251, 1:2,000), anti-t-JNK (9252, 1:2,000), anti-TAB1 (3226, 1:2,000), anti-TAB2 (3745, 1:2,000), anti-cleaved caspase 3 (9664, 1:500) and anti-myc (2276, 1:2,000) from Cell Signaling Technology; anti-Huntingtin (MAB5374, 1:1,000) from Merck Millipore; anti-HA (H3663, 1:2,000) from Sigma-Aldrich; anti-YY1 (ab109237, 1:2000) and anti-β-tubulin/dβ-tubulin (ab6046, 1:2,000) from Abcam; anti-GFP (632381, 1:4,000) from Clontech, and anti-dYY1 (orb806899, 1:1,000) from Biorbyt. Secondary antibodies used for immunoblotting were goat anti-rabbit (11-035-045, 1:5,000) and goat anti-mouse (115-035-062, 1:5,000) from Jackson ImmunoResearch.

The primary antibodies used for immunocytochemistry were anti-TUJ1 (1: 1,000, 801202, BioLegend), anti-TBR1 (1:300, ab31940, Abcam) and anti-YY1 (1:200; ab109237, Abcam). Secondary antibodies used for immunocytochemistry were Alexa Fluor 594 Donkey anti-Mouse IgG (H+L) (1:500, A-21203, Thermo Fisher Scientific) and Alexa Fluor 647 Donkey anti-Rabbit IgG (H+L) (1:500, A-31573, Thermo Fisher Scientific).

Validation

All the antibodies were obtained from commercial sources and the lots were validated on the manufacturer websites. Detailed validation and applications in published literature can be found on respective company websites.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

SK-N-MC cells, ATCC®, HTB-10TM;
iPSC line Control_1, European Bank for induced pluripotent Stem Cells (EBiSC), STBCi064-A;
iPSC line Control_2, European Bank for induced pluripotent Stem Cells (EBiSC), STBCi026-A;
iPSC line HD, Coriell Institute for Medical Research (Coriell), GM23225.

Authentication

According to the manufacturer, the SK-N-MC cell line is a permanent line derived from human neuroepithelioma brain which is a suitable transfection host. The SK-N-MC cell line is available and authenticated at ATCC.
The Control_1 and Control_2 iPSC lines obtained from EBiSC were authenticated at European Collection of Authenticated Cell Cultures (ECACC).
The HD iPSC line obtained from Coriell was authenticated at NIGMS Human Genetic Cell Repository.

Mycoplasma contamination

Cells are negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly mis-identified cell lines were used, according to the ICLAC Register.

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

Fly lines GMR-GAL4, UAS-DsRedCAG0/100, UAS-Httexon1Q93, UAS-flMJDQ27/84, UAS-CTG60/480 and UAS-CGG90-EGFP were described previously. The UAS-PAPD5 dsRNA line (GD19799) and UAS-dYY1 dsRNA line (GD39529) were obtained from Vienna Drosophila RNAi Center. The UAS-dYY1 line (F000151) was obtained from FlyORF. All flies were maintained in cornmeal culture medium and genetic crosses were set up in a 21.5°C incubator

Wild animals

No wild animals were involved in this study.

Reporting on sex

Both male and female flies were used in this study.

Field-collected samples

No field-collected samples were involved in this study.

Ethics oversight

All animal procedures were approved by the CUHK Animal Experimentation Ethics Committee (and their care was in accord with the institutional and Hong Kong guidelines).

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