

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 (<i>n</i>) 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. <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>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	Z-stacks of x-y confocal images were acquired using a Marianas spinning disk confocal imaging system based on Zeiss Axio Observer Z1 inverted fluorescence microscope system equipped with 63× Plan Apo PH NA1.4 objective and controlled by SlideBook software.
Data analysis	Zinba, liftOver, R package version 1.30, STAR GENCODE DESeq2, R package SlideBook (Intelligent Innovation, Denver, CO, USA)

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 RNAseq data were uploaded to GEO and assigned the accession number GSE293705.

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

Use the terms *sex* (biological attribute) and *gender* (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Reporting on race, ethnicity, or other socially relevant groupings

Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status). Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.) Please provide details about how you controlled for confounding variables in your analyses.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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

Experiments involving cell transfections, reporter assays, real-time PCR, and RNAseq were performed with a minimum of three biological replicates (n=3), as is standard practice.

Data exclusions

Data were not excluded from analysis.

Replication

Most experiments were successfully replicated; however, replication of some experiments involving CRISPR-Cas9-edited cells were challenging, as mutations that suppress C19MC expression led to rapid growth arrest and eventually cell death.

Randomization

Randomization was not applicable in the context of our study.

Blinding

Blinding was not applicable in the context of our 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 & 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

Anti-dsRNA Antibody, clone rJ2, Millipore-Sigma, Cat# MABE1134, used at 1:200 in immunofluorescence.
 anti-TLR3: R&D Systems, goat polyclonal Cat# AF1487, used at 0.2 ug/ml (1 :1000) in western blot or at 4.0 ug/ml (1:50) in immunofluorescence.
 anti-EEA1: Cell Signaling, rabbit monoclonal Cat# 3288, used at 1:50 in immunofluorescence.
 anti-LAMP1: rabbit monoclonal, Cell Signaling, Cat# 9091, used at 1:50 in immunofluorescence.
 Goat anti-mouse IgG (H+L) Alexa fluor 488 (Thermo Fisher), Cat# A-21206, used at 4 ug/ml.
 Cy5 AffiniPure Donkey Anti-Rabbit IgG (H+L), Cat# 711-175-152, used at 4 ug/ml.

Validation

The TLR3 antibody was validated by transfecting 293T cells, which express undetectable levels of TLR3 with an expression plasmid encoding TLR3 and comparing them to non-transfected cells. All the other antibodies have been used in multiple studies before.

Eukaryotic cell lines

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

Cell line source(s)

BeWo cells: Human, ATCC CCI-98
 293T cells: human, ATCC CRL-3216
 HeLa cells: Human, ATCC, CCL-2
 U-2OS cells: Human, ATCC, HTB-96
 HUVEC cells: Human, ATCC, PCS-100-010
 HTR8 cells: Human, a gift from C.H. Graham, Kingston, Ontario, Canada
 PHT cells: Primary human trophoblasts
 Human trophoblast stem cells (hTSCs), a gift of Thorold W. Theunissen, Washington University, St. Louis, MO, USA

Authentication

The cells were not authenticated.

Mycoplasma contamination

The cells were periodically tested for mycoplasma contamination.

Commonly misidentified lines
 (See [ICLAC](#) register)

No commonly misidentified cell lines were used.

Plants

Seed stocks

No plants were used in this study

Novel plant genotypes

N/A

Authentication

N/A