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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

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For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

   Describe how sample size was determined.

   The sample sizes were based on previous studies of neurogenic balance during cortical development. (See Main text > Material and Methods > Experimental Design and Randomization).

2. Data exclusions

   Describe any data exclusions.

   No data was excluded.

3. Replication

   Describe whether the experimental findings were reliably reproduced.

   All data from post-optimized replications were included in the statistical analysis. (See Supplementary Information > Material and Methods > Experimental Design, and Supplementary Information > Material and Methods > Cell Counting and Statistical Analysis).

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups.

   All time-mated pregnant dams and embryos were randomly allocated to the different treatments during the surgeries. Cultured hNSCs in 6- and 24- well plates were randomly allocated to either the Mock or ZIKV infection. (See Supplementary Information > Material and Methods > Experimental Design)

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   Single blinding was performed, whereby information regarding treatment of each sample was not transferred between the animal surgeon, the microscopist and analyst, until the final data was acquired for statistical analyses.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

The statistical softwares used was GraphPad Prism software (version 6.02). The imaging software used were ImageJ (version 1.42q 276), FIJI (version 2.0.0-rc-54/1.51h), and RADIUS (Olympus, version 2.0) (See Main Text > Material and Methods > Statistical Analysis, Main Text > Material and Methods > Image acquisition and manipulation, Main Text > Material and Methods > Transmission Electron Microscopy).

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

There are neither restrictions on availability of unique materials, nor for distribution by a for-profit company.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

The manufacturers, catalog numbers, and specific concentrations of all pre-validated primary and secondary antibodies used were stated in the Main Text > Material and Methods > Immunohistochemistry, and Main Text > Material and Methods > Protein extraction and Western blot. For immunohistochemistry, the following primary antibodies were used: anti-PDI, anti-Calreticulin and anti-Calnexin (1:300, rabbit, #92516 ER-stress kit from CST (Cell Signaling Technology)); anti-Cleaved Caspase 3 (1:100, rabbit, #9661, CST), anti-Tbr1 (1:200, rabbit, ab31940, Abcam), anti-Tbr2 (1:500, rat, 14-4875-82, Ebioscience), anti-Ki67 (1:100, mouse, 550609, BD Pharmingen), anti-Sox2 (1:200, goat, sc-17320, Santa Cruz), anti-Flavivirus Group Antigen (1:1000, mouse, MAB10216, Millipore), anti-NS1 from Dengue Virus conjugated with Alexa-546 (1:500, isolated by Marie Flamand) anti-Pax6 (1:500, mouse, AB528427, DSHB), anti-GFP (1:1000, Rabbit, TP401, Torrey Pines Biolabs), anti-GFP (1:1500, Goat, ab6673, Abcam), Anti-Sox1 (1:500, Goat, AF3369 RD System), anti-Nestin (1:500, chicken, NB100-1604, Novus Biologicals), anti-Ctip2 (1:100, rat, ab28448, Abcam), anti-Satb2 (1:2000, rabbit, ab92446, Abcam), anti-Tuj1 (1:250, mouse, MMS-435P, Covance). The respective secondary antibodies used were (1:800; anti-mouse, anti-rabbit, anti-rat, anti-chicken or anti-goat) conjugated either with Alexa-488, Alexa-555, Alexa 405 or Alexa-647 (Jackson ImmunoResearch Laboratories or Life Technologies). The validation of the anti-NS1 antibody from Dengue Virus conjugated with Alexa-546 was performed in ZIKV-infected embryonic mouse brains and compared with commercially available anti-ZIKV antibody (Milipore MAB10216 clone 4G2) as shown in Supplementary Figures S3A and S3B. For immunoblotting, the following antibodies were used to detect UPR factors: rabbit anti-PERK (1/500, #3192, Cell Signalling), rabbit anti-p-PERK (Thr 980) (1/500, #3179, Cell Signalling), Rabbit anti-eIF2α (D7D3) XP® (1/500, #5324, Cell Signalling), Rabbit anti-phospho-eif2α (Ser51) (D9G8) XP® (1/500, #3398, Cell Signalling), rabbit anti-IRE1α (14C10) (1/500, #3294, Cell signalling), anti-phospho-IRE1α (S724) (1/500, Abcam, ab48187), Atf6 (1/100, #65880, Cell Signalling).

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

The only eukaryotic cell line used was human neural stem cells derived from generated from human skin fibroblast reprogrammed hIPSC from healthy donors following the procedure described in Borgs et al doi:10.1038/srep33377 (2016). (See Supplementary Information > Material and Methods > Induction of hNSCs from hIPSCs and ZIKV infection).

b. Describe the method of cell line authentication used.

The human neural stem cells were authenticated through qRT-PCR and immunohistochemistry analyses of expression of human neural stem cell markers.

c. Report whether the cell lines were tested for mycoplasma contamination.

The cell line tested negative for mycoplasma contamination.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

No common misidentified cell lines were used.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Time-mated immunocompetent NMRI (Janvier Labs, Saint Berthevin, France) were operated on either embryonic day E12.5 to E14.5. Time-mated IFN-α/βR−/− mice were operated on at embryonic day E9.5 (See Supplementary Information > Material and Methods > Animals, and Supplementary Information > Material and Methods > Intracerebroventricular (ICV) and intraperitoneal (IPL) ZIKV injection, and in utero electroporation).

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

Human fetal brain material were obtained following medical pregnancy termination and processed as described in Lambert et al doi:10.1371/journal.pone.0017753 (2011). (also see Supplementary Information > Material and Methods > Human fetal cortical samples).