

Life Sciences Reporting Summary

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▶ Experimental design

1. Sample size

Describe how sample size was determined.

Although pre-study sample size calculations were not made, the majority of experiments in vitro were performed using multiple batches of differentiation, and multiple technical repeats to ensure robustness. All the sample sizes in each panel/graph are provided in the Figure Legends. For in vivo experiments, we collected DRG tissues from 4 control and 4 ZIKV-infected mice. For each animals, we examined at least 5 DRGs wherein there were more than 100 DRG neurons. There were striking ZIKV infection in the spinal cord of all 4 animals. Sample size was adequate due to binary nature of the reported phenomenon (either present or absent).

2. Data exclusions

Describe any data exclusions.

None of the viable animals or cell cultures were excluded from our analyses. We also did not exclude any data points for quantification.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All attempts at replication were successful.

4. Randomization

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

Whereas randomization was not feasible for in vitro study, batch effects were minimized through simultaneous processing of cases and controls for all experiments. For the ZIKV infection in the juvenile type-I interferon receptor deficient (A129) mice, we randomly grouped the animals and performed the ZIKV injection. To induce ZIKV-infection in the embryonic brains, we randomly selected two thirds of embryos for intraventricular ZIKV injection. After the birth of pups, we collected tissues from all of the viable mice without prior knowledge of whether the individual pups were ZIKV-infected or not. The identification completely relied on immunostaining with human ZIKV antibodies.

5. Blinding

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

Blinding was not utilized in vitro study. As primarily molecular techniques were utilized, investigator bias should play a minimal role in data acquisition in this particular study. For the embryonic infection model, we performed the experiment blindly. When we collected the DRG tissues from pups, we had no prior knowledge of which animals were infected with ZIKV. The samples were identified to be ZIKV-positive or negative by researchers in Dr. Zhiheng Xu's lab. The subsequent staining with cell markers and apoptotic marker were mainly performed in Dr. Qing-Feng Wu's lab.

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.

TopHat v2.0.13 (ref, Kim, D. et al. Genome Biol. 14, R36 (2013)) and Cuffdiff v2.2.1 (ref, Trapnell, C. et al. Nat. Biotechnol. 31, 46-53 (2013)) used for data analysis are freely available at <https://ccb.jhu.edu/software/tophat/index.shtml> and <http://cole-trapnell-lab.github.io/cufflinks/cuffdiff/>. R packages ggplot2 and pheatmap used for data visualization are freely available at <http://ggplot2.org/> and the Comprehensive R Archive Network (CRAN).

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.

No unique materials were used.

9. Antibodies

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

All antibodies were validated by the manufacturer and/or by our previous publications (Tang, H. et al. Cell Stem Cell 18, 587-590 (2016); Li, C. et al. Cell Stem Cell 19, 120-126 (2016); Lee, G. et al. Nat. Biotechnol. 25, 1468-1475 (2007); Lee, G. et al. Nat. Protoc. 5, 688-701 (2010); Oh, Y. et al. Cell Stem Cell 19, 95-106 (2016)).

10. Eukaryotic cell lines

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

Undifferentiated H9 hESCs are purchased from WiCell.

b. Describe the method of cell line authentication used.

None of the cell lines used have been authenticated.

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

We have tested for mycoplasma contamination every other week and have continuously maintained a mycoplasma free laboratory for over five years.

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 commonly 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.

We provide two ZIKV-infected mouse models in the manuscript. In one of our disease model, the type-I interferon receptor deficient (A129) mice received intraperitoneal injection of ZIKV. Approximately 5×10^5 plaque-forming unit (PFU) of ZIKV SZ01 was applied to 5-week-old A129 mice which were examined 3 days post injection. For the other mouse model, the pregnant ICR mice ($n = 3$) were anesthetized at embryonic day 13.5 and injected with $1 \mu\text{L}$ of ZIKV SZ01 (6.5×10^5 PFU/mL) or culture medium as mock into the lateral ventricles of embryos using a calibrated micropipette. For each pregnant dam, two thirds of the embryos received ZIKV infection while the rest were injected with culture medium to provide littermate controls. After virus injection, the embryos were placed back into the abdominal cavity of dams and wound was closed. The dorsal root ganglion (DRG) and spinal cord (SC) tissues were harvested and analyzed at postnatal day 1. All experimental procedures were performed in accordance with protocols approved by the Institutional Animal Care and Use Committee at Beijing Institute of Microbiology and Epidemiology and conducted in a biological safety protection laboratory.

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.

This study did not involve human research participants.