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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

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.	Sample sizes for behavioral testing experiments were predetermined by power analysis. To determine sample size for virological and immunological studies, power analysis was performed using the following values: probability of type I error = 0.05, power = 80%, fivefold hypothetical difference in mean, and population variance of 25 fold (virological studies) or 12 fold (immunological studies).

2. Data exclusions

Describe any data exclusions.	Data was excluded from analysis for behavior testing in Figures 6 and 7 for animals who jumped or fell off the Barnes Maze table during testing. This exclusion criteria was established prior to running the experiments, and there was no difference in the number of animals excluded per experimental group.

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.	Animals were randomly assigned to mock or WNV infection and/or to vehicle or Anakinra treatment.

5. Blinding

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

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.	Prism 7 (Version 7.0c, March 1, 2017) was used to generate graphs and perform statistical analysis. FlowJo (Version 10.1r7) was used to analyze flow cytometry data.

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.	Anakinra [Kineret(R)] is available for purchase from SOBI.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	NeuN (Cell Signaling, Cat 12943S, Clone D3S3I) BrdU (Abcam, Cat ab1893, polyclonal) CD45 (Biolegend, Cat 103114, Clone 30-F11) Doublecortin (Cell Signaling, Cat 4604S, polyclonal) GFAP (BD, Cat 561483, Clone 1B4) IL-1b (R&D, Cat AF-401, polyclonal) Mash1 (BD, Cat 556604, Clone 24B72D11.1) Ki67 (Abcam, Cat AB15580, polyclonal) Synaptophysin (Synaptic Systems, Cat 101004, polyclonal)

10. Eukaryotic cell lines

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

BHK-21 [C-13] cells were used to titer viral stocks and tissues at various time points post infection. BHK cells were kindly obtained from Michael Diamond, whose lab routinely uses this cell line for viral tissue titers.

b. Describe the method of cell line authentication used.

We did not further authenticate this cell line.

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

Cell lines were not tested 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 commonly misidentified cell lines were used in this study.

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.

Wildtype: C57BL/6J mice, 8-10 weeks old were purchased from Jax for use in this study
IL-1R1-/-: B6.129S7-Il1r1-tm/mx/J mice, 8-10 weeks old used in this study from our breeding colony maintained in house.

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.

The study did not involve human research participants.

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

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

☒ 2. 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).

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

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

Methodological details

5. Describe the sample preparation.	Cells were isolated from brain regions indicated, and prepared as described in methods (under section titled Flow cytometry)
6. Identify the instrument used for data collection.	BD Biosciences, LSR-II
7. Describe the software used to collect and analyze the flow cytometry data.	FACS Diva software (BD) was used during sample collection and FlowJo (Version 10.1r7) was used to analyze the data.
8. Describe the abundance of the relevant cell populations within post-sort fractions.	Neuroblast (DCX+BrdU+) populations are small in the hippocampus, so multiple strategies were used to identify the correct population. 1) for each experiment, one animal without in vivo BrdU labeling was included to ensure specificity of BrdU antibody; 2) for each experiment, the cortex from a BrdU injected animal was used as a separate negative control, as there should be no neuroblasts in this brain region. 3) Finally, the SVZ served as a positive control, as this brain region has many neuroblasts.
9. Describe the gating strategy used.	Gating strategy provided in figure legend for Fig. S1 with plots exemplifying the strategy.

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