

Reporting Summary

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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 Data was recorded and organized in Microsoft Excel 2010 (v 14.0).

Data analysis Statistical analysis of experimental data was performed in GraphPad Prism 6. All modeling analyses were run using R software version 3.5.1. Posterior distributions of model parameters were estimated via a Markov chain Monte Carlo sampling algorithm implemented in JAGS version 4.3.0 using the rjags package. Latin Hypercube Sampling was performed with the randomLHS function of the lhs package. Model-related graphics were created using the ggplot2 and plotrix packages.

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [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 list of figures that have associated raw data
- A description of any restrictions on data availability

Numerical source data underlying the graphs shown in figures 1 and 2c are associated with each figure. Additional data that support the findings of this study are available from the corresponding author upon request.

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	Statistical methods were not used to predetermine sample size. Instead we followed the established precedence in the literature and in most of the experiments exceeded that precedence
Data exclusions	No data were excluded from the analysis.
Replication	The data were pooled from two to three independent replicates for each experiment involving mosquitoes. Although the magnitude of difference between the single- and double-feed groups varied for each experimental replicate, enhancement itself was observed in every replicate. All attempts were made to thoroughly describe the methods in this manuscript so as to provide a template for reproduction.
Randomization	Per experiment, all mosquitoes were from the same rearing cohort. The mosquitoes were randomly separated into two groups; either single feed or double feed groups. All environmental conditions were kept constant through the duration of the experiment. Litters of suckling mice were randomly assigned to cohorts of mosquitoes and individual suckling mice were randomly assigned to individual mosquitoes within the respective cohorts for the transmission studies.
Blinding	Mosquito samples were harvested by one group of researchers and processed and data analyzed by another. Similar to the mosquito samples, the right front leg of mice exposed to CHIKV infected mosquitoes were collected by one group and provided to a second group for processing and data analysis. Group 2 was unaware of the order in which samples were given to them. Only after processing and data analysis were completed for each experimental replicate were the treatments made aware to the sample order.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	All antibodies used in this study are commercially available from Fisher Scientific-Invitrogen. Flavivirus envelope antibody (clone FE1) (Catalog#171258; Lot# QJ2092901) was used at a dilution of 1:200 for the detection of ZIKV antigen in the gut of mosquitoes. The secondary antibody used was an AlexaFluor488 goat anti-mouse IgG (H+L) (Catalog# A11001; Lot# 745480) at a dilution of 1:200.
Validation	Antibodies were validated by the manufacturer (Fisher Scientific-Invitrogen).

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	All mosquito and vertebrate cell lines used in these studies were acquired from ATCC.
Authentication	These cell lines were authenticated by ATCC, but have not been authenticated by us.

Mycoplasma contamination

The cell lines are routinely monitored for mycoplasma contamination and the cell lines used in this study tested negative for mycoplasma.

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

None of the cell lines used are commonly misidentified.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

Suckling mice used in this study were CD-1 strain, of mixed sex, approximately 5 days old and obtained from Charles River Laboratories (Wilmington, MA). *Aedes aegypti* (Orlando strain, collected from Orlando, FL in 1952 and Poza Rica strain, collected from Poza Rica Mexico in 2016) and *Aedes albopictus* (Stratford strain, generation F5, collected in Stratford, CT, 2015) were used in these studies. Only female mosquitoes approximately 7 days post emergence were used for all studies.

Wild animals

N/A

Field-collected samples

N/A

Ethics oversight

All experiments involving mice were approved by and preformed under the Animal Care and Use Committee at The Connecticut Agricultural Experiment Station (P28-17).

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