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.

- 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**

Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.

**Data analysis**

GraphPad Prism version 7.0 was used to generate graphs. Bio-Rad CFX Manager 3.1 for RT-PCR data analysis.

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 data that support the findings of this study are available from the corresponding author upon reasonable request.
Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

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 consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

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

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

| Sample size | In all experiments we have used at least 3-5 animals per group to perform Mann-Whitney two-tailed test analysis; no sample size calculation was necessary or performed since this study is of preclinical development stage. |
| Data exclusions | There was no data exclusions in this manuscript. |
| Replication | Where possible, all the experiments were replicated 2 times. |
| Randomization | In all experiments animals were randomly allocated between experimental groups |
| Blinding | Since this study is of pre-clinical development stage, blinding was not necessary or used in this 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 | Methods |
|---------------------------------|---------|
| n/a | Involved in the study |
| ☒ Antibodies | ☒ CHIP-seq |
| ☒ Eukaryotic cell lines | ☒ Flow cytometry |
| ☒ Paleontology and archaeology | ☒ MRI-based neuroimaging |
| ☒ Animals and other organisms | ☒ Clinical data |
| ☒ Dual use research of concern | ☒ Data exclusions |

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Eukaryotic cell lines

Policy information about *cell lines and Sex and Gender in Research*

**Cell line source(s)**
L. mexicana, L. donovani (LdWT) [MHOM/SD/62/15]

**Authentication**
L. mexicana and L. donovani (LdWT) [MHOM/SD/62/15] confirmed to be L. mexicana and L. donovani through genome sequencing

**Mycoplasma contamination**
Not tested

**Commonly misidentified lines**
No misidentified cell lines used

Animals and other research organisms

Policy information about *studies involving animals, ARRIVE guidelines* recommended for reporting animal research, and *Sex and Gender in Research*

**Laboratory animals**
Six to eight-week-old female outbred Syrian golden hamsters (Mesocricetus auratus). Female Lutzomyia longipalpis (Jacobina strain) are reared at the Laboratory of Malaria and Vector Research, NIAD/NIH.

**Wild animals**
No wild animals were used in this study

**Reporting on sex**
Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.

**Field-collected samples**
No field collected samples were used in this study

**Ethics oversight**
The animal protocol for this study has been approved by the Institutional Animal Care and Use Committee at the Center for Biologics Evaluation and Research, US FDA (ASP 1999#23). The animal protocol is in full accordance with "The guide for the care and use of animals as described in the US Public Health Service policy on Humane Care and Use of Laboratory Animals 2015." Animal experimental procedures performed at the National Institute of Allergy and Infectious Diseases (NIAID) were reviewed by the NIAID Animal Care and Use Committee under animal protocol LMK14. The NIAID DR Animal Care and Use Program complies with the Guide for the Care and Use of Laboratory Animals and with the NIH Office of Animal Care and Use and Animal Research Advisory Committee guidelines. The housing condition of animals were followed standard guidelines by NIH guidelines for the humane care and use of animals.

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