

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.

n/a	Confirmed
<input type="checkbox"/>	<input checked="" type="checkbox"/> The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
<input type="checkbox"/>	<input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
<input type="checkbox"/>	<input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
<input checked="" type="checkbox"/>	<input type="checkbox"/> A description of all covariates tested
<input type="checkbox"/>	<input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
<input type="checkbox"/>	<input checked="" type="checkbox"/> 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)
<input type="checkbox"/>	<input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
<input checked="" type="checkbox"/>	<input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
<input checked="" type="checkbox"/>	<input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
<input checked="" type="checkbox"/>	<input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), 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	Commercial software from the respective instrument vendors were used to perform Quality Control on the Agilent Bioanalyzer and Perkin Elmer Labchip during RNA sequencing library preparation, but this was not directly used for data collection. Illumina sequencing and sample demultiplexing were performed by a commercial sequencing vendor.
Data analysis	<ul style="list-style-type: none">• Reference genome assembly and transcripts from Refseq database (https://www.ncbi.nlm.nih.gov/refseq/): GCF_000772875.2_Mmul_8.0.1• STAR version 2.5.3a• Salmon version 0.9.1• R scripting language version 3.5.3• Tximport R/Bioconductor package version 1.9.11• DESeq2 R/Bioconductor package version 1.22.0• Tidyverse R package version 0.7.5• Philentropy R package version 0.3.0• FactoMineR R package version 1.40• Ropls R package version 1.23.12• Limma R package version 3.38• MetaIntegrator R package version 2.1.3• Ingenuity Pathway Analysis (version year 2019)• CIBERSORT version 1.0.2• Public datasets from NCBI Gene Expression Omnibus: GSE116306, GSE103259, GSE1124, GSE33811, GSE72058, GSE116306, GSE117613, GSE46681, GSE5418, GSE119150, GSE52166, GSE34404, GSE7000, GSE156791, GSE181179, GSE50957, GSE94916, GSE15221, GSE64338,

PRJEB45911

• Public dataset from EBI ArrayExpress: E-MTAB-6413

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](#)

All data underlying the findings of this study are available as supplementary files included in this publication. The RNAseq data have been deposited in NCBI's Gene Expression Omnibus under accession code GSE265864 [<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE265864>]. Additional data supporting the findings of this study are available in Supplementary Data 7. Further information and requests for resources and reagents should be directed to and will be fulfilled by the corresponding author, Benoît Malleret (benoit_malleret@nus.edu.sg).

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

n/a

Reporting on race, ethnicity, or other socially relevant groupings

n/a

Population characteristics

n/a

Recruitment

n/a

Ethics oversight

n/a

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

The NHP sample size was determined based on prior experiments on Plasmodium coatneyi-infected Macaca mulatta (Cordy et al., 2019, JCI).

Data exclusions

No data were excluded from the analyses.

Replication

There are at least 3 biological replicates per condition. Replication is not pursued due to ethical considerations and budget constraints. Additionally, when the number of animals is sufficient, the need for replication diminishes. As for reproducibility, SEQC consortium had established that RNA-seq data are reproducible and hence technical replicates for individual samples are not needed.

Randomization

Individual animals were randomly assigned to different groups.

Blinding

Due to involvement of some investigators in animal monitoring and managing the experiments throughout the study, complete blinding was not possible. Few of these investigators were involved in analysis and completely blinded data analysis was not achieved.

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
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

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	In this study, nine splenectomized rhesus macaques (<i>Macaca mulatta</i> , Indian origin), males aged 7 to 14 years old, were randomly assigned to each of the three dosage groups (three monkeys per group). A prior study of five untreated male rhesus macaques (aged 6 to 16 years old) served as infected untreated controls, and four spleen-intact male rhesus macaques (aged 8 to 9 years old) served as uninfected controls.
Wild animals	The study did not involve wild animals.
Reporting on sex	Only male <i>Macaca mulatta</i> was used in the studies, the distribution/signalment of the animals appears to be consistent, with research experience and predominantly older males.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	Animal procedures were approved by the AFRIMSIACUC (#12-08) and conducted in strict accordance with Thai laws, including the Animals for Scientific Purposes Act, B.E. 2558 (A.O. 2015), the Animal Welfare Act, and all applicable U.S. Department of Agriculture, Office of Laboratory Animal Welfare, U.S. Department of Defense guidelines, and the Guide for the Care and Use of Laboratory Animals (National Research Council 2011). The AFRIMS facility is fully accredited by AAALAC International.

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a