

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 |
| ☐ | ☒ 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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 | AxioVision, Fluoview FV31S-SW, Zen Black, and Acquisition-velox softwares were used for acquiring microscopy-based images. |
| Data analysis | Zen Blue, Fluoview FV31S-SW, AxioVision , ImageJ, Fiji, Image Lab, BD Fortessa FACS analyzer, Proteome Discoverer 1.2, Clustal Omega, MOTIF, Conserved Domain Database, AlphaFold, and GraphPad Prism 8 were used for 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](#)

TgVMP1 IP-MS data has been deposited to PRIDE database with the identifier PXD056007 [<https://www.ebi.ac.uk/pride/archive/projects/PXD056007>]. All raw and processed data has been made available as a "Source data" file.

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	Human blood was collected from healthy volunteers. Both biological male and female subjects were used. Samples were used for red blood cell preparation and subsequently used for Plasmodium parasite culture. Study does not involve any further experimentation on the samples.
Reporting on race, ethnicity, or other socially relevant groupings	All participants in this study were staff members of the Center for Cellular and Molecular Biology (CCMB). The participant pool consisted entirely of individuals of Indian nationality with diverse backgrounds from various states across India.
Population characteristics	Individuals aged 18–50 with no history of chronic illness
Recruitment	Healthy participants were recruited from the staff of Centre for Cellular and Molecular Biology, India
Ethics oversight	Prior approval was taken from the Institutional Ethics Committee (IEC-103/2023, IEC- 38/2015, IEC-38-R1/2015, IEC-38-R2/2015 and IEC-38-R3/2015), Centre for Cellular and Molecular Biology, India for blood collection. Informed consent was obtained from donors prior to blood collection.

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	Independent experiments were performed two or more times. Sample sizes are mentioned in the corresponding methods section or the figure legend.
Data exclusions	Data were not excluded from analysis.
Replication	Experiments were performed at least 2 or more times, and reproducible results were obtained in all the biological repeats.
Randomization	N/A. Control and knockdown parasites were compared in our experiments.
Blinding	No blinding was used in this study. All the data corresponding to control and knockdown parasites within each experiment were acquired under identical settings.

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 and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	List of antibodies used in the study for immunofluorescence assays (IFA), immunoblotting (WB), immunoprecipitation (IP), and immunoelectron microscopy (IEM) are as follows: rabbit anti-TgAMA1 antibodies (Source: BEI Resources (NR-4147); IFA (1:500)), mouse anti-TgMIC2 antibodies (Source: BEI Resources (NR-50254); IFA (1:500), WB (1:2000), IEM (1:20)), mouse anti-TgMIC3 antibodies (Source: BEI Resources (NR-50261); IFA (1:500)), mouse anti-TgROP1 antibodies (Source: BEI Resources (NR-50262); IFA (1:500), WB (1:1000), IEM (1:20)), mouse anti-TgGRA1 antibodies (Source: BEI Resources (NR-50264); IFA (1:500)), mouse anti-TgGRA2 antibodies (Source: BEI Resources (NR-50260); IFA (1:500), IEM (1:20)), mouse anti-TgSAG1 antibodies (Source: BEI Resources (NR-50255); IFA (1:500), WB (1:1000)), rabbit anti-IMC1 antibodies (Source: Dr. Abhijit S. Deshmukh's lab; IFA (1:500)), Rabbit anti-ACP polyclonal antibodies (Source: Dhanasekaran Shanmugam, IFA (1:500)), Rabbit anti-TIR1 antibody (Source: MYBIOSOURCE, WB (1:1000)), rabbit anti-GFP monoclonal antibodies (Source: Cell Signaling Technology (2956S); WB (1:1000)), rabbit anti-GFP polyclonal antibodies (Source: Invitrogen (A-11122), IFA (1:200)), Mouse anti-Myc (9B11) monoclonal antibodies (Source: Cell Signaling Technology (2276S), IFA (1:200), WB (1:1000)), mouse anti-HA(6E2) monoclonal antibodies (Source: Cell Signaling Technology (2367S); IFA (1:200), WB (1:1000)), gold-conjugated goat-anti-mouse IgG (Source: Electron Microscopy Sciences, IEM (1:20)), rabbit anti-HA monoclonal antibodies (Source: Cell Signaling Technology (C92F4); IFA (1:200), WB (1:1000), IP (5 µg/2 mg protein)), HA-Trap antibodies (ChromoTek (atma), 25 µl beads for 2 mg/ml protein), mouse anti-β-actin-HRP antibodies (Source: Invitrogen (MA5-15739); WB (1:30000)), goat anti-rabbit-HRP conjugated antibodies (Source: Jackson ImmunoResearch Laboratories Inc. (111-035-144); WB (1:20000)), goat anti-mouse-HRP conjugated antibodies (Source: Jackson ImmunoResearch Laboratories Inc. (115-035-146); WB (1:20000)), Alexa Fluor 488-conjugated F(ab') ₂ donkey anti-rabbit IgG (Source: Jackson ImmunoResearch Laboratories Inc. (711-546-152); IFA (1:1000)), Alexa Fluor 647-conjugated F(ab') ₂ donkey anti-rabbit IgG (Source: Jackson ImmunoResearch Laboratories Inc. (711-606-152); IFA (1:1000)), Alexa Fluor 488-conjugated F(ab') ₂ donkey anti-mouse IgG (Source: Jackson ImmunoResearch Laboratories Inc. (715-547-003); IFA (1:1000)), Alexa Fluor 647-conjugated F(ab') ₂ donkey anti-mouse IgG (Source: Jackson ImmunoResearch Laboratories Inc. (715-606-151); IFA (1:1000)).
Validation	Antibodies used in the study have been previously validated. Validation data are available from the manufacturers website.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	Human Foreskin Fibroblasts (HFF) (ATCC (SCRC-1041), Plasmodium falciparum D10 strain (ATCC (MRA-201)), Plasmodium falciparum 3D7 strain (BEI Resources (MRA-102)), Toxoplasma gondii RH TIR1-3FLAG (RHTIR1) (BEI Resources (NR 51145)).
Authentication	All the cell lines generated in this study are validated by PCR and expression analysis. No validation was done for cell lines procured from ATCC, BEI Resources or MR4.
Mycoplasma contamination	All cell lines were frequently tested for Mycoplasma contamination and confirmed to be negative.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified line was used in this study.

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	BALB/c mice 8-10 weeks old were used in this study.
Wild animals	No wild animals were used in this study.
Reporting on sex	Female BALB/c mice were used in this study.
Field-collected samples	No samples were collected from the field.
Ethics oversight	Animal experiments were conducted with the approval of the Institutional Animal Ethics Committee (IAEC 09/2023).

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

Plants

Seed stocks	Not used
Novel plant genotypes	Not used
Authentication	Not applicable

Flow Cytometry

Plots

Confirm that:

- ☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☐ 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).
- ☐ All plots are contour plots with outliers or pseudocolor plots.
- ☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	P. falciparum parasites grown under control (+TMP-GlcN), single knock-down (-TMP-GlcN, +TMP+GlcN) or dual knock-down (-TMP+GlcN) conditions were collected at the end of each cycle. 50 µl aliquot of each culture was fixed (2% formaldehyde in PBS), stained with YOYO-1 (10 nM YOYO-1 in PBS with 0.1% Triton X-100), and the number of infected cells was determined by counting 10,000 cells using the BD Fortessa. The related articles has been cited in the manuscript (reference # 80).
Instrument	BD Fortessa
Software	BD Fortessa FACS analyser, Flowjo software.
Cell population abundance	No sorting was performed to obtain various cell populations.
Gating strategy	Gating was performed using uninfected human red blood cells.

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