nature portfolio

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# 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.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

## 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<br>*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<br>*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 | No custom code was used for data collection. Imaging data were acquired using a Nikon Ti2-E confocal microscope and a Bio-Rad ChemiDoc chemiluminescence imaging system. |
| Data analysis | No custom code was generated for this study. Statistical analyses were performed using GraphPad Prism (version 9.0.0). Image quantification was performed using ImageJ (version 1.52e). RNA-seq data were processed using Fastp, HISAT2 and StringTie, and downstream transcriptomic analyses were conducted using the Dr. Tom multiomics platform. |

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 raw data supporting the findings of this study are available from the corresponding author upon reasonable request. Source data underlying the main figures, supplementary tables, and uncropped western blot images are provided with the submission / available

## 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 | Sex was recorded as a biological variable for the human participants. The study included 25 HIV-positive individuals (20 male and 5 female). Gender identity was not analyzed in this study. |
| Reporting on race, ethnicity, or other socially relevant groupings | Race and ethnicity were not collected and were not analyzed in this study. |
| Population characteristics | Human peripheral blood samples were collected from 25 HIV-infected individuals, including 18 individuals without stroke and 7 individuals with cerebral ischemia/ischemic stroke. Clinical characteristics are provided in Supplementary Tables 3. |
| Recruitment | Participants were recruited at Shenzhen Third People's Hospital, China. Peripheral blood samples were collected from HIV-infected individuals with or without cerebral ischemia for PBMC isolation and downstream RNA analyses. |
| Ethics oversight | The human study was approved by the Institutional Review Board of Shenzhen University (Approval No. PN-202500096) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. All ethical regulations relevant to human research participants were followed. |

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 | A total of 122 male C57BL/6 mice were used, of which 6 were excluded because of death following surgery. Sample sizes for each experiment are provided in the figure legends. The human component included 25 HIV-positive participants (18 without stroke and 7 with ischemic stroke). |
| Data exclusions | Six mice were excluded because of death following surgery. No additional exclusions were applied unless explicitly stated. |
| Replication | All experiments included independent biological replicates as indicated in the figure legends. In vitro phagocytosis experiments were repeated independently twice. |
| Randomization | Animals were randomly allocated to experimental groups using a random number generator. |
| Blinding | All assessments were performed in a blinded manner. |

# Behavioural & social sciences study design

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

| | |
|---|---|
| Study description | |
| Research sample | |
| Sampling strategy | |
| Data collection | |
| Timing | |
| Data exclusions | |
| Non-participation | |
| Randomization | |

# Ecological, evolutionary & environmental sciences study design

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

| | |
|---|---|
| Study description | |
| Research sample | |
| Sampling strategy | |
| Data collection | |
| Timing and spatial scale | |
| Data exclusions | |
| Reproducibility | |
| Randomization | |
| Blinding | |

Did the study involve field work? ☐ Yes ☐ No

## Field work, collection and transport

| | |
|---|---|
| Field conditions | |
| Location | |
| Access & import/export | |
| Disturbance | |

# 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 | Details of all primary and secondary antibodies used for immunofluorescence and western blot, including source, catalog number and dilution, are provided in Supplementary Tables 2 and 4. |
| Validation | Commercial antibodies were used according to the manufacturers'instructions, and antibody details are provided in Supplementary Tables 2 and 4. Where applicable, expected staining patterns / expected band detection were used to support specificity. |

## Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

| | |
|---|---|
| Cell line source(s) | BV2 microglial cells, HT22 neuronal cells and HEK293T cells were used in this study. BV2 and HT22 cells were used for the OGD and in vitro phagocytosis assays, and HEK293T cells were used for viral stock production. |
| Authentication | The cell lines were not further authenticated after receipt. |
| Mycoplasma contamination | The cell lines were not routinely tested for mycoplasma contamination. |
| Commonly misidentified lines (See ICLAC register) | The cell lines used in this study (BV2, HT22 and HEK293T) were not further authenticated after receipt. The authors are not aware of these cell lines being listed in the ICLAC register of commonly misidentified cell lines. |

## Palaeontology and Archaeology

| | |
|---|---|
| Specimen provenance | |
| Specimen deposition | |
| Dating methods | |

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

| | |
|---|---|
| Ethics oversight | |

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

## 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 | Male C57BL/6 mice (7 weeks old) were purchased from GemPharmatech and housed under a 12 h light/12 h dark cycle with ad libitum access to food and water. |
| Wild animals | No wild animals were used. |
| Reporting on sex | Only male mice were used in this study. |
| Field-collected samples | No field-collected samples were used. |
| Ethics oversight | All animal experiments were approved by the Experimental Animal Ethics Committee of Shenzhen University (Approval No. A202501325) and performed in accordance with the approved institutional protocol and relevant guidelines for animal care and use. We have complied with all relevant ethical regulations for animal use. The animal experiments are reported in accordance with the ARRIVE guidelines. |

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

## Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

| | |
|---|---|
| Clinical trial registration | This study is not a clinical trial. |
| Study protocol | This was an observational human-sample component embedded within a translational life-science study. PBMC samples were collected from HIV-infected individuals with or without cerebral ischemia. |
| Data collection | Clinical characteristics and PBMC samples were collected from 25 HIV-positive participants at Shenzhen Third People's Hospital. PBMCs were isolated for RNA extraction and transcriptomic analysis. |
| Outcomes | The human outcome measures included transcriptomic assessment of PBMCs, including C1ql2 expression and related markers, in HIV-infected individuals with or without cerebral ischemia. |

## Dual use research of concern

Policy information about dual use research of concern

### Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

| No | Yes | |
|---|---|---|
| ☑ | ☐ | Public health |
| ☑ | ☐ | National security |
| ☑ | ☐ | Crops and/or livestock |
| ☑ | ☐ | Ecosystems |
| ☑ | ☐ | Any other significant area |

### Experiments of concern

Does the work involve any of these experiments of concern:

| No | Yes | |
|---|---|---|
| ☑ | ☐ | Demonstrate how to render a vaccine ineffective |
| ☑ | ☐ | Confer resistance to therapeutically useful antibiotics or antiviral agents |
| ☑ | ☐ | Enhance the virulence of a pathogen or render a nonpathogen virulent |
| ☑ | ☐ | Increase transmissibility of a pathogen |
| ☑ | ☐ | Alter the host range of a pathogen |
| ☑ | ☐ | Enable evasion of diagnostic/detection modalities |
| ☑ | ☐ | Enable the weaponization of a biological agent or toxin |
| ☑ | ☐ | Any other potentially harmful combination of experiments and agents |

## Plants

Seed stocks

Novel plant genotypes

Authentication

## ChIP-seq

### Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
*May remain private before publication.*

Files in database submission

Genome browser session
(e.g. UCSC)

### Methodology

Replicates

Sequencing depth

Antibodies

Peak calling parameters

Data quality

Software

## 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

Instrument

Software

Cell population abundance

Gating strategy

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

## Magnetic resonance imaging

### Experimental design

Design type

Design specifications

Behavioral performance measures

Imaging type(s)

Field strength

Sequence & imaging parameters

Area of acquisition

Diffusion MRI ☐ Used ☐ Not used

### Preprocessing

Preprocessing software

Normalization

Normalization template

Noise and artifact removal

Volume censoring

### Statistical modeling & inference

Model type and settings

Effect(s) tested

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference

(See Eklund et al. 2016)

Correction

## Models & analysis

| n/a | Involved in the study |
|---|---|
| ☐ | ☐ Functional and/or effective connectivity |
| ☐ | ☐ Graph analysis |
| ☐ | ☐ Multivariate modeling or predictive analysis |

Functional and/or effective connectivity

Graph analysis

Multivariate modeling and predictive analysis