

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 (n) 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 checked="" type="checkbox"/> | <input 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. 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> |
| <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 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	Zeiss ELYRA S1 super-resolution microscope (Zeiss), 120 kV Talos L120C TEM (Thermo Fisher Scientific), Ceta 16M CCD camera, Model 2020 advanced tomography holder (Fischione), Keyence inverted fluorescence phase contrast microscope BZX710, chemiluminescence imager (ChemiDoc™ Imaging Systems, Bio-Rad Laboratories), Cytiva AKTA pure chromatography system (Cytiva), Refeyn TwoMP mass photometer (Refeyn Ltd.), BD LSRFortessa flow cytometer
Data analysis	Zeiss Zen v2.1 software (Zeiss), GraphPad Prism8, SerialEM 82 software, Etomo in the IMOD software package, version 4.11, Etomo, Quicktime, 3D Slicer Version 5.0.2, ImageJ Fiji (NIH), Image Lab (Bio-Rad), Cytiva Unicorn 7.6 (Cytiva), DiscoverMP program (Refeyn Ltd.), Flowjo (BD Biosciences), FlowJo software

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 the raw data used for quantification and statistical analyses are available from the corresponding author upon request.

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](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	The sample size was determined based on the size of the standard deviation and the reproducibility of the data. All the sample numbers are provided. Statistical analyses were performed with data obtained from at least three independent experiments.
Data exclusions	No data points were excluded from quantifications.
Replication	All experiments were successfully reproduced at least three times. In all cases, the results reliably support conclusions stated in the manuscript.
Randomization	For quantifying immunostained samples and chromosome spreads, images were taken randomly from undefined areas. All the samples acquired were quantified to generate the data shown in the manuscript.
Blinding	Acquisition of images and quantifications were conducted in a blinded manner.

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	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Included in the study
	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Antibodies
	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eukaryotic cell lines
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Palaeontology and archaeology
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Animals and other organisms
	<input type="checkbox"/>	<input checked="" 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	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Included in the study
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	ChIP-seq
	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Flow cytometry
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	MRI-based neuroimaging

Antibodies

Antibodies used	All the antibodies used in this study are listed in the Supplementary Table 3 with Source information and catalog numbers. All antibodies are available upon request.
Validation	All the antibodies used in this study were either internally controlled, validated by siRNA, or previously published. For the VprBP, antibody, an antibody blocking was performed to confirm the validity of the antibody.

Eukaryotic cell lines

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

Cell line source(s)	U2OS and HEK293T cells were purchased from American Type Culture Collection (ATCC) and cultured as recommended by ATCC. CEM-SS and TZM-bl cells were obtained through the NIH HIV Reagent Program. human CD4+ T cells were purified and validated by flow cytometry. PBMCs from HIV-positive patients were obtained through the NIH clinical center.
Authentication	Cells have been authenticated by the vendor and used as low passage cell lines for experiments. No further authentication was performed for cell lines from ATCC.
Mycoplasma contamination	No mycoplasma contamination was found.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

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	N/A
Study protocol	N/A
Data collection	N/A
Outcomes	N/A

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	CD4+ T cells were purified using the EasySep human CD4+ T-cell isolation kit (STEMCELL Technologies)
Instrument	BD LSRFortessa

Software	FlowJo
Cell population abundance	10,000 - 20,000 cells were acquired before and after purifying PBMCs from healthy individuals. After purification, CD4+ T cells were more than 90% abundant as determined by flow cytometry.
Gating strategy	Cells were analyzed by FlowJo software with the gating strategy: FSC vs SSC>>FSC-H vs FSC-A>> SSC-H vs SSC-A>> TCR-b+CD4+.

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