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Corresponding author(s): Zhigang Tian

Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	No software was used.
Data analysis	FlowJo 7.6.2 software (Tree Star), Living Image software (PerkinElmer), Graphpad Prism 6.0 (Graphpad).

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	Sample size was estimated on the basis of similar research reported in the literature (references below). In most of the experiments, 3 to 10 mice/samples was sufficient to identify differences between groups with at least 80% power and a 5% significance level.The number of independent experiment an technical replicates was indicated in each figure legend. Reference: Yu, X. et al. The surface protein TIGIT suppresses T cell activation by promoting the generation of mature immunoregulatory dendritic cells. Nat Immunol10,48-57 (2009). Chan, C.J. et al. The receptors CD96 and CD226 oppose each other in the regulation of natural killer cell functions. Nat Immunol15,431-438 (2014). Johnston, R.J. et al. The immunoreceptor TIGIT regulates antitumor and antiviral CD8(+) T cell effector function. Cancer cell26,923-937 (2014).
Data exclusions	No data were excluded from analyses.
Replication	All experiments were reliably reproduced and every experiment shown was repeated at least three or two times as indicated in the figure legends. We have carefully reported the experimental conditions in the Online Methods and indicated precisely the nature of replicates in Figure legends.
Randomization	Mice were allocated into experimental groups randomly after the injection of tumor cells or MCA.
Blinding	The investigators were not blinded to group allocation during experiments. The experimental observations would be consistent irrespective of blinding. Conclusions were made based on independent experiments, quantitative parameters and statistical significance of the data.

Behavioural & social sciences study design

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

Study description	*Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).*
Research sample	*State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.*
Sampling strategy	*Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.*
Data collection	*Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.*
Timing	*Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Non-participation	*State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.*
Randomization	*If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.*

Ecological, evolutionary & environmental sciences study design

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

Study description	*Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.*
Research sample	*Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.*
Sampling strategy	*Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.*
Data collection	*Describe the data collection procedure, including who recorded the data and how.*
Timing and spatial scale	*Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Reproducibility	*Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.*
Randomization	*Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.*
Blinding	*Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.*

Did the study involve field work? ☐ Yes ☐ No

Field work, collection and transport

Field conditions	*Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).*
Location	*State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).*
Access and import/export	*Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).*
Disturbance	*Describe any disturbance caused by the study and how it was minimized.*

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique material used are readily available from the authors.

Antibodies

Antibodies used	Anti-mouse NK1.1 (pk136), anti-mouse CD8 (TIB210), and anti-mouse TIGIT monoclonal antibodies (13G6) were purified from cell supernatants, and the isotype control antibodies (Rat IgG) were purified from rat serum. Anti-mouse PD-L1 (Bio X cell, Catalog Number BE0101, Clone 10F.9G2). Rabbit anti-ASGM-1 (Wako Pure Chemicals, Catalog Number 986-10001). Annexin-V (BioLegend, Catalog Number 640945). 7AAD (BioLegend, Catalog Number 420404). FITC-conjugated antibodies to mouse CD3ε (Catalog Number 100306, Clone 145-2C11), CD11b (Catalog Number 101206, M1/70), CD69 (Catalog Number 104506, H1.2F3), CD107a (Catalog Number 553793, 1D4B, BD Bioscience). PE-conjugated antibodies to mice CTLA4 (Catalog Number 553720, VC10-4F10-11, BD Bioscience), FasL (Catalog Number 106606, MFL3), Granzyme B (Catalog Number 12-8822, 16G6, eBioscience), IFN-γ (Catalog Number 505808, XMG1.2), CD96 (Catalog Number 131705, 3.3), NKp46 (Catalog Number 137604, 29A1.4), PD-1 (Catalog Number 551892, J43, BD Bioscience), TNF-α (Catalog Number 506306, MP6-XT22), Tim3 (Catalog Number 119704, RMT3-23), TRAIL (Catalog Number 109306, N2B2),CD155 (Catalog Number 132206, 4.24.1), CD112 (Catalog Number FAB3869P, 829038, R & D). PerCP-Cy5.5–conjugated antibodies to mouse CD3ε (Catalog Number 100328, 145-2C11), CD8α (Catalog Number 100734, 53-6.7), IFN-γ (Catalog Number 505822, XMG1.2), NK1.1 (Catalog Number 108728, PK136). PerCP-eFluor710 conjugated antibodies to mouse TIGIT (Catalog Number 46-9501-82, GIGD7; eBioscience), PE-Cy7–conjugated antibodies to mouse NKp46 (Catalog Number 137618, 29A1.4), NK1.1 (Catalog Number 108714, PK136), IFN-γ (Catalog Number 505826, XMG1.2). Allophycocyanin (APC)-conjugated antibodies to mouse CD8α (Catalog Number 100712, 53-6.7), Gr-1 (Catalog Number 108412, RB6-8C5), perforin (Catalog Number 17-9392-80, eBioOMAK-D; eBioscience), PD-1 (Catalog Number 135210, 29F.1A12). Alexa Fluor 647-conjugated antibodies to mouse CD226 (Catalog Number 128808, 10E5), IFN-γ (Catalog Number 505814, XMG1.2), Alexa Fluor 660-conjugated antibodies to mouse TIGIT (Catalog Number 50-9501-82, GIGD7; eBioscience), APC/Cy7-conjugated antibodies to mouse CD3ε (Catalog Number 100330, 145-2C11), CD4 (Catalog Number 100414, GK1.5). FITC-conjugated antibodies to human CD8 (Catalog Number 368508, 2D1), PE-conjugated antibodies to human TIGIT (Catalog Number 372704, A15153G), PerCP-Cy5.5–conjugated antibodies to human CD3 (Catalog Number 300328, HIT3a), Alexa-647-conjugated antibodies to human CD56 (Catalog Number 557711, B159, BD Bioscience), APC/Cy7-conjugated antibodies to human CD45 (Catalog Number 557833, 2D1, BD Bioscience).Antibodies were all from BioLegend unless otherwise indicated. The primary antibodies against human CD155 (Catalog Number 81254S, clone D8A5G, Cell Signaling Technology, U.S.A.) and CD112 (Catalog Number AF2229, R & D).
Validation	Anti-TIGIT mAb (13G6) is purified from 13G6 cells (generated by ourself) and its validation data are available on Chinese Patent (ZL201210590618.9). All other antibodies are from commercial sources and their validation data are available on the manufacturer's website.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	CT26.WT, B16/F10 (B16), and 4T1 cell lines were purchased from the cell bank of the Chinese Academy of Sciences (Shanghai, China). Hybridoma cells PK136 (anti-NK1.1 in-vivo depletion) and TIB210 (anti-CD8+T, in-vivo depletion) were purchased from ATCC. 13G6 (a blocking anti-mouse TIGIT monoclonal antibody) was a novel clone generated in mouse by ourselves.
Authentication	Authentification was performed by ATCC for CT26.WT, B16/F10, 4T1, PK136 and TIB210 cell line (Method: STR profiling). Authentification was performed by us for 13G6 cell line (methods: FACS, ELISA, Western Blot et. referring to Chinese patent ZL201210590618.9)
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Palaeontology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).*
Specimen deposition	*Indicate where the specimens have been deposited to permit free access by other researchers.*

Dating methods	*If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

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

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	C57BL/6 J, BALB/c, and NOD-SCID mice were purchased from the Shanghai Experimental Animal Center (Shanghai, China). SCID mice were purchased from Beijing Vital River Company (Beijing, China). C57BL/6 J Tigit–/– mice were obtained from the Bristol-Myers Squibb Company (New York, NY, U.S.A.). C57BL/6 J Nfil3+/– mice were provided by Dr. Tak W. Mak (University of Toronto, Toronto, Ontario, Canada), and Nfil3–/–mice were bred in-house. C57BL/6 J GKO (IFN-γ–deficient) mice were provided by Dr. Shaobo Su (Shantou University, Shantou, China). C57BL/6 J Cd4–/– mice were kind gifts from Dr. Li Bai and Dr. Zhexiong Lian (University of Science and Technology of China, Hefei, China). C57BL/6 J Ncr1iCre/+ mice mice were obtained from Dr. Eric Vivier (INSERM, France). C57BL/6 J Tigitfl/fl mice were obtained from Dr. Zusen Fan (Institute of Biophysics, Chinese Academy of Sciences, China). Tigitfl/fl- Ncr1iCre/+ mice were obtained by crossing Ncr1iCre/+mice with Tigitfl/fl mice. Rag2-/-mice were kindly provided by Dr. Xin Wang (Inner Mongolia University, Hohhot, China). All mice were maintained in a specific pathogen-free facility for use according to the guidelines for experimental animals at the University of Science and Technology of China. Male mice were used between 6-8 weeks of age.
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.

Human research participants

Policy information about studies involving human research participants

Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, 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.*

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.*	*For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.*
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

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	Tumor was cut into small pieces, followed by treatment with collagenase I (0.1% w/v, Sigma) and DNAse (0.005% w/v, Sigma) in DMEM (1 h at RT, 220 rpm). Lung was cut into small pieces, followed by treatment with collagenase I (0.1% w/v, Sigma) in DMEM (1h at RT, 220 rpm). Liver was homogenized through a 70 micron filter in PBS. Single cell suspensions of tumor, lung and lung were purified on a 40%/70% Percoll gradient (800 g at 23°C for 30 min). Spleen was homogenized through a 70 micron filter in PBS, and single cell suspensions of splenocytes were treated with ACK Lysis buffer to lyse RBC.
Instrument	LSR-II or FACS-Calibur (BD Biosciences).
Software	BD FACS DIVA was used for collection and analysis was done in FlowJo7.6.2.
Cell population abundance	e Not applicable.
Gating strategy	Starting cells were gated by FSC/SSC gates. These cells were further gated by CD45 for leukocytes. Next, CD3-NK1.1+, CD3-NKp46 +, CD3+CD8+, or CD3+CD4+ cells were analyzed in CD45+ gate.

☒ 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	*Indicate task or resting state; event-related or block design.*
Design specifications	*Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.*
Behavioral performance measures	*State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).*

Acquisition

Imaging type(s)	*Specify: functional, structural, diffusion, perfusion.*
Field strength	*Specify in Tesla*
Sequence & imaging parameters	*Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.*
Area of acquisition	*State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software	*Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).*
Normalization	*If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.*
Normalization template	*Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.*
Noise and artifact removal	*Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).*

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

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

Statistic type for inference
(See Eklund et al. 2016)

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

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

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.