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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.

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 *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 *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	Flow cytometry data were collected on BD LSRFortessa using BD FACSDIVA software. Blot images were acquired with ChemiDoc MP system (BioRad).
Data analysis	Flow cytometry data was analyzed using Flowjo v9.3.2. GraphPad Prism 7 is a graphing software that was used for figure generation and statistical analyses.

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. 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 RNA-Sequencing data in this study will be publicly available upon acceptance of 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	Sample sizes for experiments were estimated based on previous experience. All in vitro experiments were repeated at least three separate times (three different T cell donors or T cells from three different mice). For in vivo experiments using NSG mice, all experiments were repeated using two different T cell donors with at 3-4 mice in each group (7-8 mice/group in total). For in vivo syngeneic mouse models, B16-OVA experiments with 1M and 2M T cells were repeated 2 times (2 preparations of OT-1/WT T cells from 2 OT1/WT splenocytes) with 7-8 mice/group. The syngeneic pancreatic model were performed 2 time with 8 mice/group.
Data exclusions	No data was excluded.
Replication	All experiments included showed similar/similar trend in repeated attempts.
Randomization	Samples and organisms were randomly allocated to groups for in vitro experiments except for the BXPC3 in vivo experiment where mice were allocated to groups based on initial tumor signal to ensure average tumor burden is comparable.
Blinding	Investigators were not blinded to study.

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
☐	☒ Animals and other organisms
☐	☐ Human research participants
☐	☐ Clinical data

Methods

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

Antibodies

Antibodies used

The following antibodies used for the flow cytometry analysis were obtained from BD Biosciences:
APC-conjugated anti-CD4 (Clone RPA-T4), FITC-conjugated anti-CD8 (Clone RPA-T8), Alexa Fluor 700-conjugated anti-CD8 (Clone RPA-T8), PE-conjugated anti-IL17A (Clone SCPL1362), Alexa Fluor 647-conjugated anti-IFN (Clone B27), Alexa Fluor 647-conjugated anti-CD271 (NGFR, Clone C40-1457), APC-conjugated anti-CD45RO (Clone UCHL1), PE-conjugated anti-CD45RA (Clone H100), PE-Cy7-conjugated anti-CD28 (Clone CD28.2), BV421-conjugated anti-CD27 (Clone M-T271), PE-Cy7-conjugated anti-CD279 (PD1, Clone EH12.1), BV711-conjugated anti-Tim3 (Clone 7D3), PE-conjugated anti-CD223 (LAG3, Clone T47-530), Alexa Fluor 647-conjugated anti-Ki67 (Clone B56), PE-conjugated Annexin V, 7AAD, PE-conjugated rat-anti-mouse IgG1 (Clone X56), APC-Cy7-conjugated anti-CD3 (Clone SK7), PE-conjugated anti-granzyme B (Clone GB11), PE-conjugated anti-CD101 (Clone V7.1), PE-conjugated anti-TNF- (Clone MAB11), PE-conjugated anti-CD45 (Clone HI30). FITC-conjugated rat anti-mouse CD19 (Clone 1D3), APC-Cy7-conjugated hamster anti-mouse CD3e (Clone 145-2C11), PE-conjugated rat anti-mouse Ly6G (Clone 1A8), BV421-conjugated rat anti-mouse Ly6C (Clone AL21), APC-Cy7 rat anti-mouse CD11b (Clone M1/70), PerCP-Cy5.5-conjugated hamster anti-mouse CD11c (Clone HL3), PerCP-Cy5.5-conjugated rat anti-mouse CD4 (RM4-5), PE-conjugated rat anti-mouse V 2 TCR (Clone B20.1), FITC-conjugated rat anti-mouse Vb5.1 5.2 TCR (Clone MR9-4).
The following antibodies were obtained from Thermo: Alexa Fluor 647-conjugated anti-CD19 (Clone SJ25-C1), Alexa Fluor 594-conjugated anti-GFP (Polyclonal).
The following antibodies were obtained from Biolegend: BV711-conjugated rat anti-mouse CD45 (Clone 30-F11), APC-conjugated rat anti-mouse CD8 (Clone 53-6.7), APC-conjugated rat anti-mouse CD64 (Clone X54-5/7.1), PE-Cy7-conjugated rat anti-mouse F4/80 (Clone BM8).
For western blot antibodies, the following primary and secondary antibodies were used: anti-IL23R (Novus Biological 1:1000 Dilution), anti-GAPDH (clone 6C5, Santa Cruz, 1:1000 Dilution), anti-phospho-STAT3(Tyr705) (clone D3A7, Cell Signaling

	Technology, 1:1000 dilution), anti-phospho-STAT3(Ser727) (clone 6E4, Cell Signaling Technology, 1:1000 Dilution), anti-STAT3 (clone D3Z2G, Cell Signaling Technology, 1:1000 Dilution) and anti-CD3z(clone 6B10.2, Santa Cruz, 1:1000 Dilution).
Validation	All flow cytomety antibodies were validated with negative and positive cell line. For Western blots, antibodies were validated by a recombinant protein.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	The CHLA-255 neuroblastoma cell line was provided by L.S. Metelitsa of Baylor College of Medicine. The LAN-1 cell line was obtained from M. Brenner at Baylor College of Medicine. Human PDAC cell line BXPC-3 and T2 were purchased from American Type Culture Collection (ATCC). Mouse melanoma B16-OVA was provided by Dr. Benjamin Vincent at University of North Carolina at Chapel Hill. Mouse PDAC KPC-4662 cell line was provided by Yuliya Pylayeva-Gupta at University of North Carolina at Chapel Hill.
Authentication	All cell lines were routinely tested for cell surface markers.
Mycoplasma contamination	All cell lines were routinely tested for mycoplasma.
Commonly misidentified lines (See ICLAC register)	None of cell line used are commonly misidentified lines based on ICLAC register V9.

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	6-8 week old NSG mice (UNCCH in-house breeding), 6-8 week old C56BL/6 mice (Jackson or UNCCH in-house breeding) and 6-8 week old OT1 (C57BL/6-Tg(TcraTcrb)1100Mjb/J) mice (Jackson) were used.
Wild animals	N/A
Field-collected samples	N/A
Ethics oversight	All mouse experiments were performed in accordance with UNC Animal Husbandry and Institutional Animal Care and Use Committee (IACUC) guidelines and were approved by UNC IACUC.

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

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.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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	*Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.*
Study protocol	*Note where the full trial protocol can be accessed OR if not available, explain why.*
Data collection	*Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.*
Outcomes	*Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.*

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	For surface staining, cells were incubated with antibodies at room temperature for 15mins or at 4OC for 30min. For intracellular staining, cells were fixed and permeabilized using Cytofix/CytoPerm (BD Biosciences) for 15mins at room temperature and washed with 1X PermWash (BD Biosciences). Subsequent staining was performed using 1X PermWash as staining and wash buffer. For CellTrace Violet (CTV) staining, cells were labeled with 5uM CTV (Thermo) before culture. In most assays, cells were stained with Zombie Aqua Live/Dead Discrimination dye (Biolegend) to gate out dead cells for analysis.
Instrument	Flow cytometry data were collected on BD LSRFortessa (BD Biosciences)

Software	BD FACSDIVA
Cell population abundance	N/A
Gating strategy	Gating is shown.

☒ 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