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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	For mass cytometry data collection, we used Fluidigm CyTOF Software version 6.7.1014. For flow cytometry data collection, we used BD FACSDiva version 8.01 and CytExpert version 2.0.0.153.
Data analysis	For analysis of mass cytometry data, we used the publically available Statistical Scaffold package with updates released accompanying this work. For both mass and flow cytometry data analysis and visualizations, we used Cytobank (cytobank.org) and CellEngine (cellengine.com). For statistical tests and data visualization, we used Prism version 6.

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

Mass cytometry data will be made publicly available at www.cytobank.org and at www.immport.org at the time of publication as we have done for our prior studies.

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	An N of 3 to 6 mice was used for each condition in each experiment, based on standard practice in the field and prior experience working with the specified mouse models. No explicit power calculation was performed.
Data exclusions	No data were excluded.
Replication	All findings were reproducible, with number of independent experiments detailed in the figure legends.
Randomization	All mice were randomly stratified into groups, with littermates evenly distributed across conditions.
Blinding	No blinding was performed or deemed necessary for these experiments.

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	Antibodies used: See extended data table 1.
Validation	Validation: All antibodies were individually tested and titrated on relevant positive and negative biological controls.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	4T1 cells were gifted from Dr. Mary-Helen Barcellos-Hoff (UCSF). AT3 cells were gifted from Dr. Ross Levine (MSKCC). SB28 cells were gifted from Dr. Hideho Okada (UCSF). LMP cells were gifted from Dr. Edgar Engleman (Stanford University). MC38 cells and B16-F10 cells gifted from Dr. Jeffrey Bluestone (UCSF).
Authentication	No additional authentication was performed.
Mycoplasma contamination	All cell lines were tested and found negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Animals and other organisms

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

Laboratory animals	Animals included wild-type female BALB/c, C57BL/6, and B6;129 F1 mice between 8-10 weeks old; female MMTV-PyMT mice on the FVB background between 6-10 weeks old; Tyr::CreER; BrafV600E/+; Ptenlox/lox mice on the C57BL/6 background between 10-13 weeks old ; and female TCR Transgenic OT-I CD45.1 mice and heterozygous CD45.2/CD45.1 mice between 8-10 weeks old.
Wild animals	No wild animals were used in these experiments.
Field-collected samples	No field-collected samples were used in these experiments.
Ethics oversight	All mice were housed in an American Association for the Accreditation of Laboratory Animal Care–accredited animal facility. Animal experiments were approved and conducted in accordance with Institutional Animal Care & Use Program protocol number AN157618.

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

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	Sample preparation is discussed at length in the methods.
Instrument	Helios CyTOF, Fluidigm; Cytoflex 5, Beckman Coulter; Foretessa X-20, BD.
Software	Fluidigm CyTOF Software version 6.7.1014; CytExpert version 2.0.0.153; BD FACSDiva version 8.01.
Cell population abundance	N/A – no populations were sorted
Gating strategy	Mass Cytometry After normalization and debarcoding of files, singlets were gated by Event Length and DNA. Live cells were identified by Cisplatin negative cells. Erythrocytes were excluded by gating on Ter119- cells. All positive and negative populations and antibody staining concentrations were determined by titration on positive and negative control cell populations. Populations were defined as follows. Neutrophils (CD45+CD11b+Ly6G+) Eosinophils (CD45+CD11b+SiglecF+) Mast Cells (CD45+CD11b+Fcer1a+CD49b+SiglecF-Ly6G-) Basophils (CD45+CD11b+Fcer1a+cKit+SiglecF-Ly6G-) pDCs (CD45+B220+PDCA1+Ly6G-SiglecF-Fcer1a-) Plasma cells (CD45+CD138+CD19-Ly6G-SiglecF-Fcer1a-) B cells (CD45+B220+CD19+CD138-Ly6G-SiglecF-Fcer1a-) CD8 T cells (CD45+CD3+CD8+TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) CD4 T cells (CD45+CD3+CD4+FoxP3-CD8-TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) Tregs (CD45+CD3+CD4+FoxP3+CD8-TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) gdTCells (CD45+CD3+TCRgd+B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) NKT Cells (CD45+CD3+NK1.1+TCRgd-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) NKT Cells, non-Black6 mice (CD45+CD3+CD49b+TCRgd-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-) NK Cells (CD45+CD3+NK1.1+CD49b+CD3-CD19-B220-CD138-Ly6G-SiglecF-Fcer1a-) NK Cells, non-Black6 mice (CD45+CD3+CD49b+CD3-CD19-B220-CD138-Ly6G-SiglecF-Fcer1a-) Macrophages (CD45+CD64+F480+Ly6G-SiglecF-CD19-B220-CD3-Fcer1a-NK1.1-CD138-) cDCs (CD45+CD11c+MHCII+CD64-F480-NK1.1-CD3-CD19-B220-CD138-Fcer1a-SiglecF-Ly6G-) cMonocytes (CD45+CD115+Ly6C+CD11c-CD64-F480-NK1.1-CD3-CD19-B220-CD138-Fcer1a-SiglecF-Ly6G-) ncMonocytes (CD45+CD115+Ly6C-CD64-F480-NK1.1-CD3-CD19-B220-CD138-Fcer1a-SiglecF-Ly6G-) ILCs (CD45+CD90+CD115-CD64-F480-NK1.1-CD3-CD19-B220-CD138-Fcer1a-SiglecF-Ly6G-) Other (CD45+CD115-CD64-F480-NK1.1-CD3-CD19-B220-CD138-Fcer1a-SiglecF-Ly6G-) Microglia (CD45+CD115high CD64high) MHC- CD11b high (Lineage Negative Other, MHC- CD11b high) MHC+ CD11b high (Lineage Negative Other, MHC+ CD11b high) Plasma Blasts (CD45+CD138+CD19+Ly6G-SiglecF-Fcer1a-)

Th1 cells (CD45+CD3+CD4+FoxP3-Tbet+CD8-TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-)
CD4-CD8- T cells (CD45+CD3+CD4-CD8-TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-)
CD4+CD8+ T cells (CD45+CD3+CD4+CD8+TCRgd-NK1.1-B220-CD19-CD138-Ly6G-SiglecF-Fcer1a-)
Naive CD8 T cells (CD45+CD3+TCRgd-NK1.1-CD8+CD44-CD62L+)
Central Memory CD8 T cells (CD45+CD3+TCRgd-NK1.1-CD8+CD44+CD62L+)
Effector Memory CD8 T cells (CD45+CD3+TCRgd-NK1.1-CD8+CD44+CD62L-)
OT1 T cells (CD45.1+CD45.2-CD3+CD8+)
Polyclonal AT3 tumor experienced CD8 T cells (CD45.1+CD45.2-CD3+CD8+)
Polyclonal healthy CD8 T cells (CD45.1+CD45.2+CD3+CD8+)

Flow Cytometry
All samples were gated for single cells by FSC-W/FSC-A and SSC-W/SSCA. Once single cells were gated, live cells were gated using the Zombie NIR fixable viability dye (BioLegend 423106).

Populations were defined as follows:
CD8 T cells [for CD38 CD101 plot] (CD45+CD3+CD8+)

OT1 Adoptively transferred cells (CD8+CD45.1+)
Healthy Donor OT1 T cells (CD8+CD45.1+CellTraceViolet+CFSE-)
AT3 Tumor Burdened OT1 T cells (CD8+CD45.1+CFSE+CellTraceViolet-)

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