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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.

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	No custom code was used.
Data analysis	Statistical analysis was performed in graphpad prism v9.1.1 (225). Image analysis was performed in ImageJ v1.52. Flow-cytometry analysis was performed in FlowJo v10.8.1. IVIS acquisition and analysis were performed in Living Image v5.

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

The data supporting the findings in this study are available within the paper and its Supplementary Information. Source data for the figures are provided with this paper. All data generated in this study are available from the corresponding author on reasonable request.

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 were determined based on previous experience with murine models of cancer.
Data exclusions	No data were excluded from analysis.
Replication	The experiments were repeated as described in the figure captions.
Randomization	Mice were randomly allocated into experimental groups following tumour and CAR-T-cell injection, prior to TES injection.
Blinding	The investigators were not blinded.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	The antibodies used in the flow-cytometry analyses include: CD3-PerCP/Cy5.5 (HIT3a), CD45-PerCP/Cy5.5 (30-F11), CD4-BV510 (SK3), CD8-APC-Fire750 (SK1), PD-1 (EH12.2H7), TIM-3-BV421 (F38-2E2), Ly6G-BV711 (1A8), CD25-PE/Cy5 (M-A251), CD45RA-PE/Cy7 (HI100), CCR7-APC (G043H7), EGFR-FITC (AY13), CD3-PE/Dazzle (HIT3a), CD45-PE/Dazzle (30-F11), CD45-APC/Cy7 (30-F11), CD11b-BV421 (M1/70), Ly6G-BV510 (1A8), CD11c-PE (N418), CD3-PE/Cy7 (17A2), CD4-FITC (GK1.5), CD8-BV711 (53-6.7), F4/80-PE/Dazzle (BM8). Antibodies were obtained from Biolegend.
Validation	The antibodies used in this study have been validated by Biolegend.

Animals and other organisms

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

Laboratory animals	B6(Cg)-Tyrc-2J/J (C57BL/6 albino) and NOD.Cg-PrkdcscidIl2rgtm1Wjl/SzJ (NSG) were used in the study. The animals were either male or female and between 6 and 12 weeks old at the start of the experiment, and weighed 15–25g.
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animal procedures were approved by Harvard University's Institutional Animal Care and Use Committee, and were in compliance with guidelines from the National Institutes of Health.

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	Primary human T cells and CAR T cells were washed several times and then stained directly with viability dye and antibodies. For explanted tissue or blood samples, the samples were processed and washed using standard protocols to remove debris to form single-cell suspensions, which were stained directly with viability dye and antibodies.
Instrument	BD LSR fortessa X-20 (5 laser setup)
Software	Flow-cytometry analysis was performed in FlowJo v10.8.1.
Cell population abundance	At least 10,000 relevant events were acquired for all flow-cytometry analyses.
Gating strategy	In general, cells were first gated by FSC-A/SSC-A to remove debris, then FSC-A/FSC-H to remove doublets, followed by live/dead exclusion. Then, T cells were gated based on CD3 staining and lack of CD45 staining, followed by specific T-cell subpopulations (such as CD4 and CD8). CAR-T-cell transduction was measured using EGFR staining, whereas activated/inhibitory T-cell markers were measured using a combination of CD25, PD-1 and TIM-3. T-cell memory subpopulations were gated using CD45RA and CCR7. Central memory cells were defined CD45RA–CCR7+; effector-memory cells, CD45RA–CCR7–, and effector cells CD45RA+CCR7–. Naive and stem cell memory cells were defined CD45RA+CCR7+. Where applicable, leukocyte subsets were gated using Ly6G, CD11c and F4/80 among the CD45+ cell gate using conventional gating strategies. Neutrophils: Ly6G+CD11c–CD11b+, Macrophages: F4/80+CD11b+, Dendritic cells: CD11c+CD11b+, other myeloid cells: CD11c–F4/80–CD11b+. Positive and negatively-stained cells were determined based on fluorescence-minus-one (FMO) controls.

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