

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	Imaging data were acquired using platforms including Olympus FluoView31S (Ver.2.3.1.163) for confocal microscopy, Nikon Ti2 (Ver.3.13) for optical imaging, Caliper IVIS Lumina II for in vivo/ex vivo bioluminescence imaging, and Panoramic DESK for immunofluorescence slide scanning. Flow cytometry analysis was performed on CytoFLEX S.
Data analysis	Immunofluorescence images were analyzed with ImageJ v.1.46r. Neurite outgrowth was assessed using ImageJ v.1.53q (Fiji). Flow cytometric data were processed with CyExpert v.2.4.0 and FlowJo v.10.5.3 software. GraphPad Prism 9.5.0 was employed for statistical analysis. The Kaplan-Meier plotter (https://kmplot.com) was utilized to evaluate survival outcomes in pancreatic cancer and breast cancer patient cohorts. The association between ADRB2 expression and nerve and stroma-related genes and M2 macrophage infiltration in cancer was analyzed via TIMER2.0(https://compbio.cn/timer2).

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](#)

Public analyses were performed using the TIMER2.0 (<https://compbio.cn/timer2>) and Kaplan–Meier Plotter (<https://kmplot.com>) databases. All data supporting the findings of this study are available in the main text and Supplementary Information. Due to the very large file size and volume of data, additional raw data are available from the corresponding authors upon reasonable request. Source data are provided in this paper.

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	The human datasets used in this study include patients of both sexes (male and female) which applied reported findings to both sexes. Sex and gender were not considered in the study design.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, or other socially relevant groupings were not considered in the study design.
Population characteristics	The clinicopathological characteristics of pancreatic cancer patients included in human organotypic slice culture: Patient 1: female, 73 years old, TNM 1B pancreatic adenocarcinoma, with no underlying diseases, no special medications taken, no preoperative puncture performed, and no neoadjuvant therapy administered preoperatively. Patient 2: male, 36 years old, TNM 2B pancreatic adenocarcinoma, with a medical history of hypertension (for 2 years, intermittent administration of nifedipine) and diabetes mellitus (for 2 months, intermittent administration of metformin), and no neoadjuvant therapy administered preoperatively. Patient 3: male, 49 years old, TNM 2B pancreatic adenocarcinoma, with no underlying diseases, no regular medications taken preoperatively, and no neoadjuvant therapy administered preoperatively. Patient 4: male, 57 years old, TNM 2B pancreatic adenocarcinoma, with a medical history of valvular heart disease (postoperative for 6 months) and hypertension (for 2 years), with preoperative administration of rivaroxaban for 6 months and nifedipine for 2 years, and no neoadjuvant therapy administered preoperatively. Fresh pancreatic tumor tissue was obtained from patients with pancreatic adenocarcinoma undergoing surgical resection at the Union Hospital, Tongji Medical College of Huazhong University of Science and Technology. Pancreatic carcinoma tissues not required for pathological diagnostic procedures were obtained after surgical resection. All samples were stored at 4 °C until processed (within 24 hours).
Recruitment	Patients undergoing routine surgical tumor resection were informed of the study and consented by Union Hospital staff. Fresh organotypic samples were provided by surgeons, and the obtained samples were cut into thin slices and then randomly grouped, without potential self-selection bias.
Ethics oversight	The human organotypic slice culture experiment was approved by the Clinical Trial Ethics Committee of Huazhong University of Science and Technology (Wuhan, China) and the ethical approval number was 2025-S092.

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

Life sciences study design

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

Sample size	The sample sizes of this study were determined on the basis of similar published studies (Qin, et al. Nat Nanotechnol. 2025;20(2):311-324). In antitumor experiments, 4-8 mice each group were used to analyze tumor weight and microenvironment, and 6-8 mice were used to analyze the survival rate. For the expression of Adrb2, nerve density and collagen I analysis in tumor-bearing mice, the sample size for each group was 3. For other experiments, the sample size for each group was 3-6.
Data exclusions	No data were excluded in the analysis.
Replication	Experiments were independently repeated as indicated and experimental findings were reproducible (described in figure legends for further

details).

Randomization All samples were randomly allocated into experimental groups.

Blinding Investigators were blinded during tumor inoculation, animal grouping and animal drug treatment. Survival data were determined by blinded staff. However, investigators were not blinded to collect data of tumor volume and weight, because the same investigator processed the animals and analyzed the data. For in vitro experiments, blinding was impossible because a single investigator processed all steps of the experiment, and there was no step that introduced personal bias.

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 <i>Passer domesticus</i> , all <i>Stenocereus thurberi</i> 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	<i>Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).</i>
Location	<i>State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).</i>
Access & import/export	<i>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).</i>
Disturbance	<i>Describe any disturbance caused by the study and how it was minimized.</i>

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used

Antibodies used included those for:

(1) Immunocytochemistry: anti- β 3-tubulin (Biolegend, cat No 801208, clone TUJ1, 1/500 dilution), anti-TH (Servicebio, cat No GB 11181, 1/500 dilution), anti-Collagen I (Servicebio, cat No GB11022-3, 1/200 dilution), anti-MUC1 (Servicebio, cat No GB154939, 1/3000 dilution), anti-Ki67 (Servicebio, cat No GB151499, 1/2000 dilution), Cy3 conjugated goat anti-Rabbit IgG(Servicebio, cat No GB21303, 1/300 dilution), Cy3 conjugated Anti-Mouse IgG (Servicebio, cat No GB21301, 1/200 dilution), anti-beta 2 Adrenergic Receptor(Abcam, cat No ab182136, 1/100) and HRP conjugated Goat Anti-Rabbit IgG(Servicebio, cat No GB23303, 1/200 dilution).

(2) Antibody for western blot: Rabbit-anti-CD86 (Proteintech, cat No 13395-1-AP, 1/1000 dilution), Rabbit-anti-MMP9 (Abclonal, cat No A2095, 1/500 dilution), Rabbit-anti-MMP14 (Abcam, cat No ab51074, 1/2500 dilution), HRP-conjugated Goat anti-Rabbit IgG (Proteintech, cat No SA00001-2, 1/5000 dilution).

(3) Flow cytometer :

APC-Cyanine7 anti-mouse CD45 (BD Biosciences, cat. No 557659, clone 30-F11, 1/20 dilution), FITC anti-mouse/human CD11b (Biolegend, cat. No 101206, clone M1/70, 1/200 dilution), PE/Cyanine7 anti-mouse CD11c (Biolegend, cat. No 117318, clone N418, 1/80 dilution), Brilliant Violet 421 anti-mouse F4/80 (Biolegend, cat. No 123137, clone BM8, 1/80 dilution), Brilliant Violet 510 anti-mouse CD80 (Biolegend, cat. No 104741, clone 16-10A1, 1/40 dilution), APC anti-mouse CD86 (Biolegend, cat. No 105012, clone GL-1, 1/80 dilution), Brilliant Violet 650 anti-mouse CD206 (Biolegend, cat. No 141723, clone C068C2, 1/30 dilution), PerCP/Cyanine5.5 anti-mouse Gr-1 (Biolegend, cat. No 108428, clone RB6-8C5, 1/80 dilution), PE anti-mouse Ly-6G (Biolegend, cat. No 127607, clone 1A8, 1/80 dilution), BB700 anti-mouse CD3e (BD Biosciences, cat. No 566494, clone 145-2C11, 1/20 dilution), Brilliant Violet 650 anti-mouse CD4 (BD Biosciences, cat. No 563232, clone GK1.5, 1/20 dilution), FITC anti-mouse CD8a (Biolegend, cat. No 100706, clone 53-6.7, 1/50 dilution), Brilliant Violet 605 anti-mouse CD69 (Biolegend, cat. No 104530, clone H1.2F3, 1/80 dilution), FITC anti-human CD45 (Biolegend, cat. No 304006, clone HI30, 1/20 dilution), PE anti-mouse/human CD11b (Biolegend, cat. No 101207, clone M1/70, 1/80 dilution), PerCP/Cyanine5.5 anti-human CD14 (Biolegend, cat. No 325622, clone HCD14, 1/20 dilution), PE/Cyanine7 anti-human CD80 (Biolegend, cat. No 305218, clone 2D10, 1/20 dilution), APC anti-human CD206 (Biolegend, cat. No 321110, clone 15-2, 1/20 dilution), Brilliant Violet 421 anti-human Ki-67 (Biolegend, cat. No 350505, clone Ki-67, 1/20 dilution),

PE anti-human CD3 (Biolegend, cat. No 300307, clone HIT3a, 1/20 dilution),
 Pacific Blue anti-human CD8 (Biolegend, cat. No 344717, clone SK1, 1/20 dilution),
 APC anti-human CD69 (Biolegend, cat. No 310909, clone FN50, 1/20 dilution),
 PE/Cyanine7 anti-human/mouse Granzyme B (Biolegend, cat. No 372214, clone QA16A02, 1/20 dilution).

Validation

anti- β -tubulin, <https://www.biolegend.com/en-gb/products/alexa-fluor-594-anti-tubulin-beta-3-tubb3-antibody-13909>
 anti-TH, <https://www.servicebio.cn/goodsdetail?id=1432>
 anti-Collagen, I <https://www.servicebio.cn/goodsdetail?id=1327>
 anti-MUC1, <https://www.servicebio.cn/goodsdetail?id=14867>
 anti-Ki67, <https://www.servicebio.cn/goodsdetail?id=21813>
 Cy3 conjugated goat anti-Rabbit IgG, <https://www.servicebio.cn/goodsdetail?id=253>
 Cy3 conjugated Anti-Mouse IgG, <https://www.servicebio.cn/goodsdetail?id=251>
 anti-beta 2 Adrenergic Receptor, <https://www.abcam.cn/products/primary-antibodies/beta-2-adrenergic-receptor-antibody-epr707n-ab182136.html>
 HRP conjugated Goat Anti-Rabbit IgG, <https://www.servicebio.cn/goodsdetail?id=266>
 Rabbit-anti-CD86, <https://www.ptgcn.com/products/CD86-Antibody-13395-1-AP.htm>
 Rabbit-anti-MMP9, <https://abclonal.com.cn/catalog/A2095>
 Rabbit-anti-MMP14, <https://www.abcam.cn/products/primary-antibodies/mmp14-antibody-ep1264y-ab51074>
 HRP-conjugated Goat anti-Rabbit IgG, <https://www.ptgcn.com/products/HRP-conjugated-Affinipure-Goat-Anti-Rabbit-IgG-H-L-secondary-antibody.htm>
 APC-Cyanine7 anti-mouse CD45, https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-cy-7-rat-anti-mouse-cd45.557659?tab=product_details
 FITC anti-mouse/human CD11b, <https://www.biolegend.com/en-gb/products/fitc-anti-mouse-human-cd11b-antibody-347>
 PE/Cyanine7 anti-mouse CD11c, <https://www.biolegend.com/en-gb/products/pe-cyanine7-anti-mouse-cd11c-antibody-3086>
 Brilliant Violet 421 anti-mouse F4/80, <https://www.biolegend.com/en-gb/products/brilliant-violet-421-anti-mouse-f4-80-antibody-7199>
 Brilliant Violet 510 anti-mouse CD80, <https://www.biolegend.com/en-gb/products/brilliant-violet-510-anti-mouse-cd80-antibody-17824>
 APC anti-mouse CD86, <https://www.biolegend.com/en-gb/products/apc-anti-mouse-cd86-antibody-2896>
 Brilliant Violet 650 anti-mouse CD206, <https://www.biolegend.com/en-gb/products/brilliant-violet-650-anti-mouse-cd206-mmr-antibody-8842>
 PerCP/Cyanine5.5 anti-mouse Gr-1, <https://www.biolegend.com/en-gb/products/percp-cyanine5-5-anti-mouse-ly-6g-ly-6c-gr-1-antibody-4286>
 PE anti-mouse Ly-6G, <https://www.biolegend.com/en-gb/products/pe-anti-mouse-ly-6g-antibody-4777>
 BB700 anti-mouse CD3e, https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bb700-armenian-hamster-anti-mouse-cd3e.566494?tab=product_details
 Brilliant Violet 650 anti-mouse CD4, https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv650-rat-anti-mouse-cd4.563232?tab=product_details
 FITC anti-mouse CD8a, <https://www.biolegend.com/en-gb/products/fitc-anti-mouse-cd8a-antibody-153>
 Brilliant Violet 605 anti-mouse CD69, <https://www.biolegend.com/en-gb/products/brilliant-violet-605-anti-mouse-cd69-antibody-7864>
 FITC anti-human CD45, <https://www.biolegend.com/en-gb/products/fitc-anti-human-cd45-antibody-707>
 PE anti-mouse/human CD11b, <https://www.biolegend.com/en-gb/products/pe-anti-mouse-human-cd11b-antibody-349>
 PerCP/Cyanine5.5 anti-human CD14, <https://www.biolegend.com/en-gb/products/pe-anti-mouse-human-cd11b-antibody-349>
 PE/Cyanine7 anti-human CD80, <https://www.biolegend.com/en-gb/products/pe-cyanine7-anti-human-cd80-antibody-6174>
 APC anti-human CD206, <https://www.biolegend.com/en-gb/products/apc-anti-human-cd206-mmr-antibody-2996>
 Brilliant Violet 421 anti-human Ki-67, <https://www.biolegend.com/en-gb/products/brilliant-violet-421-anti-human-ki-67-antibody-7146>
 PE anti-human CD3, <https://www.biolegend.com/en-gb/products/pe-anti-human-cd3-antibody-753>
 Pacific Blue anti-human CD8, <https://www.biolegend.com/en-gb/products/pacific-blue-anti-human-cd8-antibody-6509>
 APC anti-human CD69, <https://www.biolegend.com/en-gb/products/apc-anti-human-cd69-antibody-1674>
 PE/Cyanine7 anti-human/mouse Granzyme B, <https://www.biolegend.com/en-gb/products/pe-cyanine7-anti-humanmouse-granzyme-b-recombinant-antibody-15582>

Eukaryotic cell lines

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

Cell line source(s)	Panc02 cells (cell line No BNCC338034) were purchased from BeNa Culture Collection (Beijing, China). PC12 (cell line No SCSP-517), 4T1 (cell line No TCM32), Raw264.7 (cell line No SCSP-5036), B16F10 (cell line No TCM36) and THP-1 (cell line No SCSP-567) cells were provided from Type Culture Collection of the Chinese Academy of Sciences. KPC cells were isolated from the established pancreatic tumor of a male KrasG12D/+; p53R172H/+; Pdx-1-Cre genetically engineered mouse model and kindly provided by Prof. Jun Zhao (Huazhong University of Science and Technology, Wuhan, China).
Authentication	Each cell line we used was morphologically confirmed according to the information provided by the cell-source center.
Mycoplasma contamination	Cells were tested negative for mycoplasma contamination by using the MycAway-Color one-step mycoplasma detection kit.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Palaeontology and Archaeology

Specimen provenance	<i>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). Permits should encompass collection and, where applicable, export.</i>
Specimen deposition	<i>Indicate where the specimens have been deposited to permit free access by other researchers.</i>
Dating methods	<i>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.</i>
☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight	<i>Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.</i>

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

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	C57BL/6J mice (18-20 g, 5-6 weeks old) and BALB/c mice (16-18 g, 5-6 weeks old) were purchased from Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China). Mice were housed under standard conditions (room temperature 21±1°C, relative humidity 40-70%, 12-h light-dark cycle) with free access to food and water.
Wild animals	No wild animals were used.
Reporting on sex	Male mice were used in this study for establishing Panc02, KPC and B16F10 cancer models. Female mice were used in this study for establishing orthotopic 4T1 cancer models. All cancer models were established based on our historical experience and literature reports. No sex-based analysis was performed and the sex of the animals was not expected to affect the results.
Field-collected samples	No field-collection was performed.
Ethics oversight	All animal experiments were approved by Institutional Animal Care and Use Committee at Huazhong University of Science and Technology (Wuhan, China) and the ethical approval number was IACUC-2024-4680.

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

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
☐	☐ Public health
☐	☐ National security
☐	☐ Crops and/or livestock
☐	☐ Ecosystems
☐	☐ Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
☐	☐ Demonstrate how to render a vaccine ineffective
☐	☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☐	☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☐	☐ Increase transmissibility of a pathogen
☐	☐ Alter the host range of a pathogen
☐	☐ Enable evasion of diagnostic/detection modalities
☐	☐ Enable the weaponization of a biological agent or toxin
☐	☐ Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.

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 <i>May remain private before publication.</i>	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

(1) Cultured cells were collected, washed with PBS for three time, then cells were collected for cytometric analysis.
 (2) Mouse tumors: For the analysis of tumor immune microenvironment, tumor tissues were collected, rinsed with PBS, and minced into small pieces. These pieces were placed in 6-well plates containing 4 mL of digestion solution composed of 0.8 mg mL⁻¹ collagenase type I and 5 µg mL⁻¹ DNase I, and incubated at 37°C for 40 min. Digestion was terminated by adding 2 mL of RPMI 1640 complete medium. Single-cell suspensions were obtained through mechanical dissociation using a mesh cell strainer, followed by filtration through a 40 µm nylon mesh and erythrocyte lysis treatment.
 (3) Human tumors: tumor slices were digested with 0.8 mg mL⁻¹ collagenase type I and 5 µg mL⁻¹ DNase I, mechanically dissociated using a mesh cell strainer, and filtered to obtain single-cell suspensions.

Instrument

CytoFLEX S

Software

The software used for collecting and analyzing was Beckman Coulter cytExpert 2.4.0.28.

Cell population abundance

No cell sorting was performed.

Gating strategy

Cells were gated by FSC/SSC gates and then FSC/FSC-A to select single cells. After that the detail gating strategy was showed as follows:

(1) Mouse:

DCs (CD45+CD11c+F4/80-),
 MDSCs (CD45+CD11b+Gr-1+),
 Neutrophils (CD45+CD11b+Ly6G+),
 Macrophages (CD45+CD11b+F4/80+),
 T cells (CD45+CD3+),
 CD80+CD86+DCs (CD45+CD11c+F4/80-CD80+CD86+),
 M1-like TAMs (CD45+CD11b+F4/80+CD11c+, CD45+CD11b+F4/80+CD80+, CD45+CD11b+F4/80+CD86+),
 M2-like TAMs (CD45+CD11b+F4/80+CD206+),
 CD69+CD8+T cells (CD45+CD3+CD8+CD69+),
 GzmB+CD8+T cells (CD45+CD3+CD8+GzmB+).

(2) Human:

Ki67+ tumor cells (CD45-Ki67+),
 M1-like TAM (CD45+CD11b+CD14+CD80+),
 M2-like TAMs (CD45+CD11b+CD14+CD206+),
 CD8+T cells (CD45+CD3+CD8+),
 CD69+CD8+T cells (CD45+CD3+CD8+CD69+),
 GzmB+CD8+T cells (CD45+CD3+CD8+GzmB+).

- ☒ 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)	<i>Specify: functional, structural, diffusion, perfusion.</i>
Field strength	<i>Specify in Tesla</i>
Sequence & imaging parameters	<i>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.</i>
Area of acquisition	<i>State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.</i>
Diffusion MRI	☐ Used ☐ Not used

Preprocessing

Preprocessing software	<i>Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).</i>
Normalization	<i>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.</i>
Normalization template	<i>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.</i>
Noise and artifact removal	<i>Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).</i>
Volume censoring	<i>Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.</i>

Statistical modeling & inference

Model type and settings	<i>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).</i>
Effect(s) tested	<i>Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.</i>
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	<i>Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.</i>
(See Eklund et al. 2016)	
Correction	<i>Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).</i>

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	<i>Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).</i>
Graph analysis	<i>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.).</i>
Multivariate modeling and predictive analysis	<i>Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.</i>