nature portfolio

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Last updated by author(s): 2023/06/30

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	scRNA seq data was performed using HiSeqXten (Illumina, San Diego, CA, USA) with a 150 bp paired-end run. Microarray-Based ST was sequenced using an Illumina sequencer (Illumina) with a 150 bp paired-end run. Bulk RNA seq data was collected by an Illumina HiSeq X10 platform (2 × 150 bp). The amplification signal of qPCR was acquired by qTOWER384G (Analytikjena). Tryptic peptides were analyzed using a Orbitrap Fusion LUMOS mass spectrometer (Thermo Fisher Scientific) coupled to an Easy-nLC 1200 via an Easy Spray (Thermo Fisher Scientific). Luciferin emission imaging of isoflurane-anesthetized animals was performed using the IVIS Spectrum (Tanon). Flow cytometry was performed using FACS (Becton-Dickinson, Bedford, MA, USA).
Data analysis	Statistical analyses were performed using the GraphPad Prism version 8.0. IHC/IF positive area and intensity were calculated by QuPath Version 0.1.2 (https://qupath.github.io/). Patients in the tissue microarray were divided into low and high SC area/iCAFs number groups according to the optimal cut-off value calculated using the X-Tile software. K-M curve and Cox regression analysis was performed to assess the association with overall survival using SPSS v23 (IBM Inc.).Migrated cells number was quantified in an automated fashion using the ImageJ v1.53e software. scRNA-seq and ST data analysis was performed by NovelBio Bio-Pharm Technology Co., Ltd. with the NovelBrain Cloud Analysis Platform. Flow cytometry results were analyzed using the FlowJo V10 software.

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

Bulk RNA sequencing data generated in this study are deposited in Gene Expression Omnibus under accession code GSE201601 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE201601]. scRNA-seq data generated in this study are deposited in Gene Expression Omnibus under accession code the GSE202742 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc= GSE202742]. ST data generated in this study are deposited in Gene Expression Omnibus under accession code GSE202740 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc= GSE202740]. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD042556 [https://www.ebi.ac.uk/pride/archive/projects/PXD042556]. The survival analyses and GSEA analyses in TCGA were derived from TCGA Research Network (http://cancergenome.nih.gov/). The remaining data are available within the Article, Supplementary Information or Source Data file. Source data are provided with 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	We collected the human pancreatic cancer and adjacent normal tissue from 187 PDAC patients, including 112 males and 75 females with median ages of 62 and 67 years old. The univariate analysis in Figure 1e included the gender, and the result showed no significant difference. Thus, we didn't include sex or gender analysis in the following study.
Reporting on race, ethnicity, or other socially relevant groupings	The samples are all from the same ethnicity. Asian.
Population characteristics	The average age of PDAC patients enrolled is 63.3 (36-86), with 27 AJCC stage Ib, 44 IIa, 71 IIb, 30 III and 15 IV.
Recruitment	All the patients were recruited at Ruijin Hospital of Shanghai Jiao Tong University School of Medicine. Informed consent was obtained by participants.
Ethics oversight	The sample collection and preparation protocol were approved by the Ruijin Hospital Ethics Committee (reference number: 2013-70).

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	No statistical method was used to predetermined sample size. The sample size was chosen based on previous experience (Moncada, R. et al. Nature biotechnology 2020; Banh, R. S. et al. Cell 2020; Su, R., et al. Nat Cell Biol 2022). Both sample size and the number of biological repeats is clearly reported in the respective figure legend. Three to more biologically independent results were used to perform statistical analyses.
Data exclusions	No data was excluded for any reasons.
Replication	All the samples in this study were collected as biological replicates and the data are highly reproducible. scRNA-seq, ST were conducted as 4 biologically replications. Tissue microarrays contain 187 paired replications. Bulk RNA seq for tumor cells, cell growth assays, cell migration, cell invasion, flow cytometry, IF, IHC, qPCR assays, MS were conducted as ≥3 biological independent experiments (the exact number is mentioned in the respective figure legend). Western blotting, ELISA, bulk RNA seq for CAFs, were conducted as ≥2 biological independent experiments (the exact number is mentioned in the respective figure legend).
Randomization	For in vitro or ex vivo studies, the cells or tissues were randomly allocated into control or treatment group. For animal studies, the mice were randomly allocated into experimental groups.
Blinding	Investigators were blinded throughout acquisition and analysis of tissue microarrays, scRNA-seq, ST, bulk RNA seq, MS. Investigators were also blinded during the in vivo study. For the cell-based experiments, the cell type and treatment condition were known because the information

of the materials was essential for experiments.

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 & 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

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

Anti-PGP9.5(Servicebio, GB11159; IHC: 1:500)
Anti-p75NRT (Abcam, ab52987; IHC and IF: 1:100)
Anti-GFAP (Proteintech, 16825; IHC and IF: 1:200)
Anti-S100B (Servicebio, GB11359; IHC: 1:150; IF: 1:500)
Anti-α-SMA (Abcam, ab5694; IHC and IF: 1:200; Western blotting: 1:1000)
Anti-IL-6 (Abcam, ab233706, ab9324; IHC and IF: 1:50)
Anti-FAP (Cell Signaling Technology [CST], 66562; IHC: 1:100; Western blotting: 1:1000)
Anti-GAPDH (Santa Cruz Biotechnology, sc-47724, Western blotting: 1:1000)
Anti-E-cadherin (CST, 3195, Western blotting: 1:1000)
Anti-N-Cadherin (CST,13116, Western blotting: 1:1000)
Anti-N-Cadherin (Proteintech, 22018-1-AP, IHC: 1:100)
Anti-Vimentin (CST, 5741, Western blotting: 1:2000)
Anti-β-catenin (CST, 8480, Western blotting: 1:1000)
Anti-Fibronectin (CST, 26836; Proteintech, Western blotting: 1:2000; 15613-1-ap, IHC: 1:200)
ANNEXINV-FITC (BD Biosciences, 556419, Flow: 5 μl)
PI (BD Biosciences, 550825, Flow: 5 μl)
Anti-Midkine (Santa Cruz Biotechnology, sc-46701, Neutralization: 10μg/mL)
Anti-IL-1α (Proteintech, 16765-1-AP; IF: 1:50, Neutralization: 10μg/mL)
Goat anti-Mouse IgG H&L antibody(HRP)(abcam, ab6789) and goat anti-Rabbit IgG H&L antibody(abcam,HRP) (ab6721) were used for Western blotting.
HRP conjugated Goat Anti-Mouse IgG (H+L)(Servicebio, GB23301) or HRP conjugated Goat Anti-Rabbit IgG (H+L) (Servicebio, GB23303) were used for IHC.
For IHC and IF, second antibodies were used as 1:200; For Western blot, second antibodies were used as 1:5000.

Validation

Antibodies used in our study have been validated by commercial providers and other researchers, and the detailed information can be found on the website from manufactures.
Anti-PGP9.5(Servicebio, GB11159), https://www.servicebio.cn/goodsdetail?id=1420
Anti-p75NRT (Abcam, ab52987), https://www.abcam.cn/products/primary-antibodies/p75-ngf-receptor-antibody-ep1039y-ab52987.html
Anti-GFAP (Proteintech, 16825), https://www.ptglab.co.jp/Products/GFAP-Antibody-16825-1-AP.htm
Anti-S100B (Servicebio, GB11359), https://www.servicebio.cn/goodsdetail?id=1185
Anti-α-SMA (Abcam, ab5694), https://www.abcam.cn/products/primary-antibodies/alpha-smooth-muscle-actin-antibody-

ab5694.html
Anti-IL-6 (Abcam, ab233706, ab9324), https://www.abcam.cn/products/primary-antibodies/il-6-antibody-epr21711-ab233706.html; https://www.abcam.com/products/primary-antibodies/il-6-antibody-12-2b11-2g10-ab9324.html
Anti-FAP (Cell Signaling Technology [CST], 66562), https://www.cellsignal.com/products/primary-antibodies/fap-e1v9v-rabbit-mab/66562
Anti-GAPDH (Santa Cruz Biotechnology, sc-47724), https://www.scbt.com/p/gapdh-antibody-6c5
Anti-E-Cadherin (CST, 3195), https://www.cellsignal.com/products/primary-antibodies/e-cadherin-24e10-rabbit-mab/3195
Anti-N-Cadherin (CST,13116), https://www.cellsignal.com/products/primary-antibodies/n-cadherin-d4r1h-xp-rabbit-mab/13116
Anti-N-Cadherin (Proteintech, 22018-1-AP), https://www.ptglab.co.jp/Products/N-cadherin-Antibody-22018-1-AP.htm
Anti-Vimentin (CST, 5741), https://www.cellsignal.cn/products/primary-antibodies/vimentin-d21h3-xp-rabbit-mab/5741
Anti-β-catenin (CST, 8480), https://www.cellsignal.cn/products/primary-antibodies/b-catenin-d10a8-xp-rabbit-mab/8480
Anti-Fibronectin (CST, 26836; Proteintech, 15613-1-ap), https://www.cellsignal.com/products/primary-antibodies/fibronectin-fn1-e5h6x-rabbit-mab/26836; https://www.ptglab.co.jp/Products/FN1-Antibody-15613-1-AP.htm
ANNEXINV-FITC (BD Biosciences, 556419), https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/fitc-annexin-v.556419
PI (BD Biosciences, 550825), https://www.bdbiosciences.com/zh-cn/products/reagents/cell-preparation-separation-reagents/blood-lysis/staining-and-cell-preparation/pi-rnase-staining-buffer.550825
Anti-Midkine (Santa Cruz Biotechnology, sc-46701), https://www.scbt.com/p/mk-antibody-a-9/
Anti-IL-1α (Proteintech, 16765-1-AP), https://www.ptglab.co.jp/Products/IL1A-Antibody-16765-1-AP.htm
Goat anti-Mouse IgG H&L antibody(HRP)(abcam, ab6789), https://www.abcam.cn/products/secondary-antibodies/goat-mouse-igg-hl-hrp-ab6789.html
Goat anti-Rabbit IgG H&L antibody(HRP) (abcam, ab6721), https://www.abcam.cn/products/secondary-antibodies/goat-rabbit-igg-hl-hrp-ab6721.html
HRP conjugated Goat Anti-Mouse IgG (H+L)(Servicebio, GB23301), https://www.servicebio.cn/goodsdetail?id=264
HRP conjugated Goat Anti-Rabbit IgG (H+L) (Servicebio, GB23303), https://www.servicebio.cn/goodsdetail?id=266

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Panc-1 (CRL-1469™), CFPAC-1 (CRL-1918™), RSC96 (CRL-2765™), sNF96.2(CRL-2884™) were purchased from ATCC. NF, CAF1 and CAF1 were isolated from human normal/tumor tissues. hPSC was a gift from Dr. Yuan Fang, which were purchased from ScienCell Research Laboratories, Carlsbad, CA (the HPaSteC cells, #3830).
Authentication	Primary fibroblasts were confirmed by morphology and expression of CAF markers, including α-SMA and FAP, by Western blotting and IF. All cell lines were authenticated by STR profiling.
Mycoplasma contamination	All cell lines were tested negative using PCR Mycoplasma Detection Kit (G238, ABM)
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Palaeontology and Archaeology

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). Permits should encompass collection and, where applicable, export.*
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.

Ethics oversight	*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.*

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	Nude BALB/c mice (6 weeks old) were purchased from the Chinese Academy of Sciences (Shanghai, China) and maintained in a specific pathogen-free facility. Animals were housed in an negative pressured isolator under 12h light-dark cycles with temperature at 22 C and humidity set points 50-60%

Wild animals	This study did not involve wild animals.
Reporting on sex	Female or male mice were used in this study. Sex was not considered in study design.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All experiments performed on mice were approved by the review board on the use of living animals at Ruijin Hospital.

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.*

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, mosiacism, 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 *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 the cell cycle assay, 1×106 cells were collected and fixed in 75% ethanol at 4°C overnight. DNA was stained using propidium iodide (PI)/RNase Staining Buffer (BD Biosciences, USA), according to the manufacturer's instructions. For the apoptotic assay, 1×106 cells were incubated with 5 µL of FITC-conjugated annexin V (BD Biosciences, 556419) and 5 µl of PI (BD Biosciences, 550825) for 15 min at room temperature in the dark.
Instrument	FACS (Becton-Dickinson, Bedford, MA, USA)
Software	Flow cytometry was performed using FACS (Becton-Dickinson, Bedford, MA, USA), and the results were analyzed using the FlowJo V10 software.
Cell population abundance	5,000 cells were acquired for each sample. No cell sorting was performed in this manuscript.
Gating strategy	The FACS assay used in this study is an the established protocol for cell cycle and apoptotic assay analysis.

☒ 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.*