nature portfolio

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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	Confocal microscopy image acquisition was performed and data collected from Zeiss LS780 and LS880. For quantitative analysis, fluorescence image data was collected using ZEN2(blue edition).Quantitative real-time PCR was performed using Applied Biosystems 7900HT cycler using SYBR-Green PCR Master Mix (Thermo Fisher Scientific). FACS data was collected from BD FACSAria Fusion Sorter. For untargeted metabolomics,The collected centroid raw MS data was converted to abf format using Reifycs Analysis Base File Converter (ver. 4.0.0). The converted files were processed in MS-DIAL software (ver. 4.60)57 for peak detection, peak alignment, and peak integration. The signature scores in single cell data were calculated using the "AddModuleScore" function in R package Seurat. The dot plots showing marker gene expression levels was visualized by "DotPlot" function in Seurat. For SMART-seq2 scRNA Sequencing PerkinElmer LabChip®GX TouchandStepOnePlus™ Real-Time PCRSystem were introduced for library quality inspection. Qualified libraries were then loaded on IlluminaHiseq platform for PE150 sequencing.For untargeted metabolomics,Raw FASTQ reads were trimmed using Trim Galore (v0.6.5) .
Data analysis	Quantitative real-time PCR data were analysed using SDS2.4 software. FACS data were analyzed with FlowJo version 10. For untargeted metabolomics, transcript quantification was performed using Salmon (v1.2.0). Salmon "quant" files were converted using Tximport (v 1.16.1).The acquired MS/MS raw data was analyzed using the Sequest HT algorithm in Proteome Discoverer (PD2.2, Thermo).

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 RNA sequencing data related to this study are available at the NCBI Gene Expression Omnibus (GEO) under accession number GSE218043 and the SMART-seq data related to this study are available at the genome sequence archive for human (GSA) under accession code PRJCA011931. Protein MS data related to this study are available at OMIX (China National Center for Bioinformation)under accession code PRJCA014088. All other supporting data of this study are available from the corresponding author on reasonable request. 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	27 male and 15 female patients.
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
Population characteristics	27 male and 15 female patients diagnosed with glioma including 11 low grade and 31 high grade. Patients ranged in age from 22 to 78 years old.
Recruitment	Glioma patients in Sichuan Province hospital preparing for surgery agreed to afford tumor samples were recruited in our study.
Ethics oversight	This study complies with all relevant ethical regulations and was approved by the Ethics Committee of Sichuan Provincial People's Hospital. Written informed consent was provided by all participants.

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 methods were used to pre-determine sample sizes but our sample sizes are similar to those reported in previous publications on GSC function and tumor cell. PMID: 36649564, PMID: 29625067,PMID: 32879489. Group sizes of 5-10 was commonly used in previous publications.
Data exclusions	No data were excluded from the analyses.
Replication	All reported in the figure legends, experiments were performed at least three times.
Randomization	For all animal studies, mice with matched sex and age randomized into different treatment groups. The experiments were not randomized.
Blinding	RNA sequencing, immunohistochemistry quantifications, IF, LC-MS/MS were performed by person blinded to the sample information. After all data were collected, the results were analyzed and decoded. Other experiments data collection and analysis were not performed blind to the conditions of the 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 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

The following antibodies were used for immunofluorescence (IF) and immunohistochemistry (IHC)/ immunofluorescent (IF) staining:
R&DMAB197-100 Human CCR7 Antibody Clone 150503 (RUO) (IHC 1:200)
R&D AF2018 Human/Mouse/Rat SOX2 Antibody Polyclonal (IF 1:200)
Abcam ab36993 rabbit anti-LYVE1 Polyclonal (IHC/IF 1:200)
Abcam ab236529 rabbit anti-Podoplanin Clone EPR22182 (FC 1:300; IF:1:1000; IHC 1：4000)
Abcam ab89396 mouse anti-CCL21 Clone MMO146-2H26 (IF 1:200)
Abcam ab9498 Anti-CD31antibody Clone JC/70A (IHC/IF 1:1000)
Abcam ab150063 Donkey Anti-Rabbit IgG (Alexa Fluor 647) ® (IF 1:1000)
Abcam ab150130 Donkey Anti-Goat IgG H&L (Alexa Fluor 555) ® (IF 1:1000)
Abcam ab150105 Donkey Anti-Mouse IgG H&L (Alexa Fluor 488) ® (IF 1:1000)
Abcam ab199359 Anti-PROX1antibody Clone EPR19273 (IF 1:500)
Abcam ab19936 Anti-Podoplanin/gp36 antibody Clone RTD4E10 (IF 1:500)
R&D Systems MAB2125 LYVE-1 Antibody Clone # 223322 (IF 1:500)
The following antibodies were used for flow cytometry:
Invitrogen 17-1331-81 CD133 (Prominin-1) Monoclonal Antibody Clone 13A4 (FC 1:200)
Invitrogen 12-5381-82 PE Podoplanin Monoclonal Antibody Clone eBio8.1.1 (8.1.1) (FC 1:200)
Biolegend 353219 CD197 Monoclonal Antibody Clone G043H7 (FC 1:200)
Biolegend 372806 APC anti-human CD133 Antibody clone 7(FC 1:200)
Thermo Fisher CD197 (CCR7) Monoclonal Antibody (4B12), PerCP-Cyanine5.5 (FC 1:200)
eBioscience 25-1971-82 PE-Cvanine7 CD197 Monoclonal Antibody Clone 4B12 (FC 1:200)
Novus Biologicals NBP1-43411PECY55 PE/Cy5.5 LYVE-1 Antibody Clone ALY7 (FC 1:200)
BD Biosciences 557833 CD45 APC-Cy7 Clone 2D1 (RUO) (FC 1:200)
BD Biosciences BD Horizon™ V450 Mouse Anti-Human CD31 Clone WM59 (also known as WM-59) (RUO) (FC 1:200)
Abcam ab236529 rabbit anti-Podoplanin Clone EPR22182 (FC 1:300)
R&D Systems MAB2125 LYVE-1 Antibody Clone # 223322 (FC 1:200)
Abcam ab9498 Anti-CD31antibody Clone JC/70A (FC 1:200)
Abcam ab150063 Donkey Anti-Rabbit IgG (Alexa Fluor 647) ® (FC 1:1000)
Abcam ab150130 Donkey Anti-Goat IgG H&L (Alexa Fluor 555) ® (FC 1:1000)
Abcam ab150105 Donkey Anti-Mouse IgG H&L (Alexa Fluor 488) ® (FC 1:1000)
The following antibodies were used for western blot:
Sigma F1804-50UG Monoclonal ANTI-FLAG ® antibody produced in mouse Clone M2 (WB 1:1000)
Proteintech 60004-1-Ig GAPDH Monoclonal Antibody Clone 1E6D9 (WB 1:10000)
Proteintech 17643-1-AP HMGCS1 antibody Polyclonal (WB 1:1000)
Proteintech 60003-2-Ig MYC antibody Clone 1A5A2 (WB 1:1000)
Hui-Ou Biotechnology HOAPTMH273 HMGCS1K273AC antibody (1:500)
CST 9441S Acetylated-Lysine Antibody #9441 Clone not shown (WB 1:1000)
Antibodies targeting acetylation level of K273 in HMGCS1 were validated by adding 273K-AC-peptide, and verification of the decrease of a band of the predicted molecular weight by immunoblotting.(Fig 7c, Extended Data Fig.7a, b)

Validation

Human CCR7 Antibody: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv421-mouse-anti-human-cd197-ccr7.562555
Human/Mouse/Rat SOX2 Antibody: https://www.rndsystems.com/cn/products/human-mouse-rat-sox2-antibody_af2018
Rabbit anti-LYVE1: https://www.abcam.com/products/primary-antibodies/lyve1-antibody-ab36993.html
Rabbit anti-Podoplanin
Mouse anti-CCL21: https://www.abcam.com/products/primary-antibodies/ccl21-antibody-mm0146-2h26-ab89396.html
Anti-CD31 antibody: https://www.abcam.com/products/primary-antibodies/cd31-antibody-jc70a-ab9498.html
Anti-PROX1antibody: https://www.abcam.com/products/primary-antibodies/prox1-antibody-epr19273-ab199359.html
Anti-Podoplanin/gp36 antibody: https://www.abcam.cn/products/primary-antibodies/podoplanin--gp36-antibody-pdpn1433-ab217886.html

R&D Systems MAB2125 LYVE-1 Antibody: https://www.rndsystems.com/cn/products/mouse-lyve-1-antibody-223322_mab2125
CD133 (Prominin-1) Monoclonal Antibody (13A4) : https://www.thermofisher.cn/cn/zh/antibody/product/CD133-Prominin-1-Antibody-clone-13A4-Monoclonal/14-1331-82
PE Podoplanin Monoclonal Antibody: https://www.thermofisher.cn/cn/zh/antibody/product/Podoplanin-Antibody-clone-eBio8-1-1-8-1-1-Monoclonal/12-5381-82
CD197 Monoclonal Antibody (G043H7) : https://www.biolegend.com/en-us/products/apc-anti-human-cd197-ccr7-antibody-7536?GroupID=BLG9613
CD197 PE-Cvanine7 Monoclonal Antibody (4B12): https://www.thermofisher.cn/cn/zh/antibody/product/CD197-CCR7-Antibody-clone-4B12-Monoclonal/12-1971-82
LYVE-1 PE/Cy5.5 Antibody (ALY7): https://www.thermofisher.cn/cn/zh/antibody/product/LYVE1-Antibody-clone-ALY7-Monoclonal/50-0443-82
CD45 APC-CV7 2D1: https://www.biolegend.com/en-us/products/apc-anti-human-cd45-antibody-12397?GroupID=BLG14850
ANTI-FLAG ® antibody: https://www.sigmaaldrich.cn/CN/zh/product/sigma/f1804
GAPDH Monoclonal Antibody: https://www.ptglab.co.jp/products/GAPDH-Antibody-60004-1-Ig.htm
HMGCS1 antibody: https://www.thermofisher.cn/cn/zh/antibody/product/HMGCS1-Antibody-Polyclonal/17643-1-AP
MYC antibody: https://www.ptglab.co.jp/Products/MYC-Antibody-60003-2-Ig.htm
Acetylated-Lysine Antibody
V450 Mouse Anti-Human CD31 antibody: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/v450-mouse-anti-human-cd31.561653
APC anti-human CD133 Antibody clone 7: https://pubmed.ncbi.nlm.nih.gov/33752798/
CD197 (CCR7) Monoclonal Antibody (4B12): https://pubmed.ncbi.nlm.nih.gov/31968240/

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	GSC20, GSC2907,GSC1552,GSC23 were derived from GBM patients. LEC was brought from Lonza. HBEC-5i, 293T were brought from ATCC. HNP1 Human Neural Progenitors(ArunA Biomedical, Inc., Athens,GA) are fully differentiated and derived as adherent cells from the hESC WA09 line. Human NSC line NSC11(ALSTEM, Richmond, CA, USA) was derived from human IPS cells.
Authentication	GSC, NSC and other cell lines obtained from ATCC were routinely subjected to STR testing to confirm their identity.
Mycoplasma contamination	All cell lines were routinely tested negative for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	None

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/61 mice (The Jackson Laboratory) or NSG mice (NOD.Cg-prkdcscid Il2rgtm1Wjl/SzJ; The Jackson Laboratory), 5-6 weeks old, were randomly selected for intracranial injection. All mice were housed in specific-pathogen-free conditions at an ambient temperature of 20-26 °C and humidity of 30-70% with a 12 h:12 h light:dark cycle before use. A maximal tumour size of 15 mm in any direction was not exceeded in any experiment. Both male and female mice were used in our studies.
Wild animals	The study did not involve wild animals.
Reporting on sex	Both male and female were used in our studies.
Field-collected samples	None
Ethics oversight	All animal experiments were performed under the animal protocol approved by the Institution Animal Care and Use Committee, UCSD and Sichuan University.

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

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*