

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	SRA Toolkit 3.0.0
Data analysis	BioJupies, iDEP version 0.96, MetaboAnalyst, GraphPad 10.5.0

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](#)

All data supporting the findings of the study as described in the manuscript are available in the main manuscript and supporting information files. The RNA sequencing data for all patient derived glioblastoma stem cells (GSCs) have been deposited in NCBI's Gene Expression Omnibus (GEO) and are accessible through the GEO Series Accession Number GSE274672 (<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE274672>). The RNA sequencing data for all normal astrocyte samples were obtained from GEO database, accession GSE67835.

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	Recurrent patient derived GSCs were from male patients and newly diagnosed patient derived GSCs were from female patients. For normal astrocytes, we obtained 3 male and 3 female samples.
Reporting on race, ethnicity, or other socially relevant groupings	We did not collect data for these groupings.
Population characteristics	A description of the characteristics of the patient derived GSCs are provided in the main manuscript, specifying the age, tumor type at isolation, treatments, proliferative potential, and other relevant genetic information. Age related information for normal astrocytes were also provided in the main text.
Recruitment	NA
Ethics oversight	The patient samples were collected by Dr. Ivan under University of Miami Institutional Review Board approved protocol (IRB ID: 20190521). All these specimens have already been collected, and tissue was used to establish the four-patient derived glioblastoma cell lines. These established glioblastoma lines are deidentified by the University of Miami and have also been unlinked from any protected health information.

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](https://www.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 size was determined based on experimental requirements.
Data exclusions	No data were excluded.
Replication	Data from biological replicates using technical in each biological replicates were performed for the studies.
Randomization	Animals were randomly placed in the different diet groups.
Blinding	Blinded studies were performed lipidomic, metabolomic, and microbiome analyses.

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	Mouse monoclonal anti-Nestin (Cell Signaling Technology) Cat#33475S; RRID: AB_2799037. Rabbit monoclonal anti-CD133 (Cell Signaling Technology) Cat#64326S; RRID: AB_2721172. Rabbit monoclonal anti-Vimentin (Cell Signaling Technology) Cat#5741S; RRID: AB_10695459. Rabbit monoclonal anti-SOX2 (Cell Signaling Technology) Cat#3579S; RRID: AB_2195767. Rabbit monoclonal anti-Ki67 (Cell Signaling Technology) Cat#9449; RRID: AB_2797703. Goat anti-Rabbit Alexa Fluor® 555 (Cell Signaling Technology) Cat#4413; RRID: AB_10694110. Rabbit monoclonal anti-FASN (Abcam) Cat#ab128856; RRID: AB_11143234. Mouse monoclonal anti-ACADM (Abcam) Cat#ab110296; RRID: AB_10860159. Rabbit recombinant monoclonal anti-Hexokinase II (Abcam) Cat#ab209847; RRID: AB_2904621. Rabbit polyclonal anti-GLUT1 (Abcam) Cat#ab15309; RRID: AB_301844. Rabbit recombinant monoclonal anti-Nanog (Abcam) Cat#ab109250; RRID: AB_10863442. Rabbit recombinant monoclonal anti-Caspase-9 (Abcam) Cat#ab202068; RRID: AB_2889070. Mouse monoclonal anti-b-actin (Abcam) Cat#ab8226; RRID: AB_306371. Rabbit recombinant anti-legumain (Abcam) Cat#ab183028; RRID: AB_3291610. Rabbit monoclonal anti-cyclophilin (Abcam) Cat#ab178397; RRID: AB_2924975. Goat anti-Rabbit HRP conjugated antibody (Abcam) Cat#ab205718; RRID: AB_2819160. Goat anti-Mouse HRP conjugated antibody (Abcam) Cat#ab205719; RRID: AB_275504. Goat anti-Rabbit Alexa Fluor® 488 antibody (Abcam) Cat#ab150077; RRID: AB_2630356. Goat anti-Mouse Alexa Fluor® 488 antibody (Abcam) Cat#ab150113; RRID: AB_2576208. Rabbit anti-HADHA (Sigma Aldrich) Cat#HPA015536; RRID: AB_1850473. Rabbit polyclonal anti-CLOCK (ThermoFisher Scientific) Cat#PA1-520; RRID: AB_2082586. Mouse monoclonal anti-Prom1 (ThermoFisher Scientific) Cat#MA1-219; RRID: AB_2725113.
Validation	All antibodies are commercially available and were extensively validated by the manufacturer

Eukaryotic cell lines

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

Cell line source(s)	Patient 1 GSCs (isolated from tissue of male patient), Patient 2 GSCs (isolated from tissue of male patient), Patient 3 GSCs (isolated from tissue of female patient), Patient 4 GSCs (isolated from tissue of female patient), Luciferase tagged patient 1 GSCs (derived from Patient 1 GSCs), Luciferase tagged patient 2 GSCs (derived from Patient 2 GSCs), normal human astrocytes (ScienCell Catalog #1800; isolated from human brain cerebral cortex), hCMEC/D3 (Milipore Sigma Catalog #SCC066; derived from human temporal lobe microvessels isolated from tissue excised during surgery for control of epilepsy).
Authentication	Patient derived GSCs 1-4 were characterized at different passages for expression of multiple stemness markers; luciferase tagged patient 1 and patient 2 GSCs were characterized qualitatively through IVIS imaging and quantitatively through microplate reader luminiscence study. Human astrocytes were characterized by the manufacturer through immunofluorescence with antibody specific to GFAP. hCMEC/D3 has been extensively characterized by the company for brain endothelial phenotype.
Mycoplasma contamination	All cell lines were routinely examined and tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

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	For all our studies, male and female BALB/c athymic nude mice (Strain: 002019) and NOD.Cg-Prkdc SCID mice (Strain: 005557) at 4-5 weeks age were purchased from Jackson Laboratory.
Wild animals	N/A
Reporting on sex	We performed the experiments on both male and female animals and the specific numbers from each sex is mentioned in the figure legend, in the manuscript, and in the materials section.
Field-collected samples	N/A
Ethics oversight	All animals were handled in accordance with “The Guide for the Care and Use of Laboratory Animals” of American Association for Accreditation of Laboratory Animal Care (AAALAC), Animal Welfare Act (AWA), and other applicable federal and state guidelines. All animal work presented here was approved by Institutional Animal Care and Use Committee (IACUC) of University of Miami (UM) Miller School of Medicine. All housing, surgical procedures, and experimental protocols were approved by the IACUC Committee of UM. Animals had free access to diet and water during all experiments.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

Magnetic resonance imaging

Experimental design

Design type	Studying glioblastoma formation and proliferation
Design specifications	Mice implanted orthotopically with recurrent patient derived GSCs tagged with luciferase
Behavioral performance measures	N/A

Acquisition

Imaging type(s)	Anatomical T2-weighted RARE images
Field strength	9.4 Tesla scanner equipped with a gradient (B-GA12S HP, 660mT/m)
Sequence & imaging parameters	The animals were anesthetized using isoflurane 3% and 1-2% for anesthesia maintenance. Mice were controlled for temperature and monitored for respiration throughout the experiment.
Area of acquisition	A mouse head transceiver volume coil was used for data acquisition.
Diffusion MRI	☐ Used ☒ Not used

Preprocessing

Preprocessing software	Tumor volume (mm3) quantified by using the FMRIB software library at different timepoints from the MRI images
Normalization	For each animal which showed tumor, tumor masks were manually defined in each slice in the coronal view of the brain and the total volume was then calculated using the '-V' option of the command line tool fslstats of FSL.
Normalization template	For anatomical T2-weighted RARE images, the tumor volume is extracted from the region of interest (ROI).
Noise and artifact removal	Image were denoised and bias field corrected using DenoiseImage and N4BiasFieldVorection shell commands from Advance Normalization Tools (ANTs) software package.
Volume censoring	The dataset included only T2-weighted anatomical images of the mouse brain and not repeated images acquired in a defined time window (as for fMRI). For this reason, volume censoring wasn't applied to the dataset. Image quality at different time points was considered adequate for tumor volume quantification after image processing.

Statistical modeling & inference

Model type and settings	Additional models were not applied
Effect(s) tested	No testing was performed, volumes were directly measured and reported.
Specify type of analysis:	☐ Whole brain ☒ ROI-based ☐ Both
Anatomical location(s)	Tumor masks were manually defined in each slice in the coronal view of the brain
Statistic type for inference	N/A
(See Eklund et al. 2016)	
Correction	N/A

Models & analysis

n/a	Involvement in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis