Reporting Summary

Nature Research 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 Research 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.

- [ ] 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: qRT-PCR: StepOne Plus; MATLAB R2016a; ImageJ 1.52a

Data analysis: GraphPad Prism 8.0.1; Microsoft Excel 2016.13; Photoshop 2015.1.2; ImageJ 1.52a; MATLAB R2016a

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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The Raw and processed RNA-Sequencing data from this study have been submitted to the NCBI Gene Expression Omnibus (GEO; http://www.ncbi.nlm.nih.gov/geo/) under accession number GSE64032. Microarray data for this study has also been deposited onto the GEO database, GSE95164. The other data that support the findings of this study are available from the corresponding author upon reasonable request.
Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

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

Sample size: Sample size for each experiment is indicated in the legend or methods. No statistical tests were used to pre-determine sample size. Sample size was chosen based on previous experiments and comparable studies in literature, which is most optimal to generate statistically significant results.

Data exclusions: No data was excluded for analysis.

Replication: Each animal experiment presented in the paper was repeated in multiple animals (≥ 6 per experiment), and all results in the paper are drawn from the analysis of multiple animals. For other experiments, all attempts at replication were successful. The number of replications was stated in the figure legends of Methods.

Randomization: For animal experiments, animals were assigned randomly to experimental and control groups. Cells were all plated at the same time and wells were randomly selected for different treatment with stimuli or inhibitors.

Blinding: Blinding was not applicable as it was not a randomized clinical trial.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems:

| n/a | Involved in the study |
|-----|----------------------|
| ☒ | Antibodies |
| ☒ | Eukaryotic cell lines |
| ☒ | Palaeontology and archaeology |
| ☒ | Animals and other organisms |
| ☒ | Human research participants |
| ☒ | Clinical data |
| ☒ | Dual use research of concern |

Methods:

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

Antibodies:

- Antine-MARS (Sigma HPAO04125), rabbit anti-AVIL (Abcam ab72210), rabbit anti-PARP (Cell Signaling 9542), rabbit anti-Cleaved Caspase-3 (Cell Signaling 9664), and mouse anti-GAPDH (Ambion Am4300), rabbit anti-Ki67 (Abcam, ab16667)

Validation: Antibody validation was deferred to the manufacturers and was supported by multiple publications.

Eukaryotic cell lines:

- Policy information about cell lines
- Cell line source(s): U87, A712, T98G (ATCC); NSC (Millipore); GSC/GIC cells (gifts from Dr. Krishna Bhat, MD Anderson); Immortalized human astrocytes (gift from Dr. Russ Pieper, University of California San Francisco).
- Authentication: None of the cell lines have been authenticated.
- Mycoplasma contamination: Cell lines were not tested for mycoplasma contamination but no indication of contamination was observed.
- Commonly misidentified lines (See ICLAC register): No commonly misidentified cell lines were used.
## Animals and other organisms

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

| Laboratory animals | Immunocompromised SCID/NCr BALB/c adult male mice (6-8 weeks old) were used. |
|--------------------|---------------------------------------------------------------------------|
| Wild animals       | No wild animals were used in this study.                                  |
| Field-collected samples | No field-collected samples were used in this study.                      |
| Ethics oversight   | The mouse work was performed under the study protocol 4234 as approved by the University of Virginia Institutional Animal Care and Use Committee. |

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

## Magnetic resonance imaging

### Experimental design

| Design type | Measurement of tumor growth in GBM-tumor bearing mice. |
|-------------|--------------------------------------------------------|
| Design specifications | In each session of MRI imaging, coronal images of the brain tumor were acquired in each mouse. It took 30 mins per mouse. |
| Behavioral performance measures | Mice were sedated for the MRI imaging of the GBM tumor. The heart rate was monitored during the imaging to ensure the heart rate remained constant. |

### Acquisition

| Imaging type(s) | Structural |
|-----------------|------------|
| Field strength  | 7Tesla     |
| Sequence & imaging parameters | T1-weighted serial coronal images of each brain were acquired at 1 mm intervals with a 5 x 5 mm field, and a 256 x 256 pixel resolution. |
| Area of acquisition | Whole brain was scanned. |
| Diffusion MRI | Not used |

### Preprocessing

| Preprocessing software | ImageJ version 1.52a was used for measuring tumor volumes. All brain sections for each mouse was imported as an image sequence. |
|------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Normalization | All images from all mice were adjusted for equal brightness and contrast. |
| Normalization template | No specific template was used. |
| Noise and artifact removal | A luminosity histogram was first generated for a selected area of the left cerebrum that was grossly tumor-free. This served as an internal control for background. |
| Volume censoring | No volume censoring was done. |

### Statistical modeling & inference

| Model type and settings | No statistical modeling was done with these images. |
|-------------------------|----------------------------------------------------|
| 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 | 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 |