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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 Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Microsoft Excel 2013, GraphPad Prism 7, SoftMaxPro, Glomax Multi, FACSDiva, Quant Studio, Live Image 4.2, and IMaris x64 8.4.1
Data analysis	Microsoft Excel 2013, GraphPad Prism 7, SoftMaxPro, Glomax Multi, FACSDiva, Quant Studio, Live Image 4.2, and IMaris x64 8.4.1

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/reviewers upon request. 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

Provide your data availability statement here.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-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 predetermine sample size.
Data exclusions	No data were excluded
Replication	All experiments were successfully reproduced.
Randomization	No randomization of samples were done - was not applicable to the research reported in this manuscript.
Blinding	For cell-based experiments, EM, histochemistry,Western blots, FACS, the the cell types were known before t experiments were performed. RNA-seq samples, Mass Spec samples, Small molecule FISH samples, samples for mitochondrial activity analysis were blinded before analysis.

Behavioural & social sciences study design

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

Study description	n/a
Research sample	n/a
Sampling strategy	n/a
Data collection	n/a
Timing	n/a
Data exclusions	n/a
Non-participation	n/a
Randomization	n/a

Ecological, evolutionary & environmental sciences study design

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

Study description	n/a
Research sample	n/a
Sampling strategy	n/a
Data collection	n/a
Timing and spatial scale	n/a
Data exclusions	n/a
Reproducibility	n/a
Randomization	n/a

Blinding: n/a

Did the study involve field work? ☐ Yes ☒ No

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials: No

Antibodies

Antibodies used: Please see Supplementary Table 1

Validation: Antibodies were validated by using multiple positive and negative control tissues and cells.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s): Human primary glioblastoma lines were established from freshly resected tumors either in our laboratory under a University of Cincinnati institutional review board (IRB) approved protocol or obtained from our collaborators. T98G, A172, U87MG and 293T cells were obtained from ATCC.

Authentication: Molecular classification of most of these lines is published (Mao P, PNAS, 110:8644-9, 2013; Carlson B, Int. J. Rad. Oncol. Biol. Phys. 75:212-19, 2009). Reference short tandem repeat (STR) have been generated for several GBM lines and PDX lines (Kim SH, Cancer Cell 29:201-13).

Mycoplasma contamination: All lines were routinely checked for mycoplasma every other week using mycoplasma-specific PCR. Contaminated cultures, if detected (very rarely) were discarded.

Commonly misidentified lines (See ICLAC register): No cell lines were used that are listed in the ICLAC register. However, U87MG was shown to be misidentified (Sci. Trans. Med, 8, 354: 354re3). This cell line was only used in one experiment.

Animals and other organisms

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

Laboratory animals: Both male and female 6-9 months old NSG mice were used for xenograft studies. Mixed background immunocompetent male and female were bread and neural stem cells were derived from E1.5 - E14.5 timed pregnant female mice..

Laboratory animals	Both male and female mice were used.
Wild animals	
Field-collected samples	

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	Human primary glioblastoma lines were established from freshly resected tumors. For glucose uptake ,virus treated cells were harvested, counted and replated in glucose free medium (15 min). Cells were then treated with 2-NBDG (100uM) for 30 minutes. After incubation cells were harvested, washed with cold PBS and resuspended in 0.5 mL PBS before FACS acquisition. For Superoxide quatification, virus transduced Cells (100000) were plated in a 12-well plate and treated with MitoSOX Red (5µM) for 10 min at 37 °C. The cells were then washed with PBS. Following labeling cells were washed and filtered through a 70 mm Sefar Nylon Lab Pak Mesh. collected as single-cell suspensions. Stained cells were acquired in FACScan flow cytometers (BD Bioscience).
Instrument	BD FACSCanto Flow Cytometer
Software	BD FACSDiva
Cell population abundance	No sorting involved in any experiment.
Gating strategy	For both experiments, initial cell population gating was placed on FSC v SSC (cell size v granularity). For MitoSOX Red stained cells, the resulting live P1 cell population was placed on PE channel for detection of Superoxide positive population. The unstained cells served as negative controls. This gated population was displayed as four quadrants for percent population analysis. Percent MitoSOX Red positive cells were in Q1 quadrant (exclusively PE positive cells). We also tried to detect differences between samples for DCFDA positive (FITC channel) simultaneously for cellular ROS. No data for DCFDA positive cells was presented or discussed in manuscript. For glucose uptake assay, P1 population was gated as described before with proper negative (unstained) controls. Cells were acquired in Alexa Fluor 488 channel. Shifted P2 population was analyzed as NBDG positive population. We performed analysis to examine percent cells with glucose uptake using FACSDiva software.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.