nature portfolio

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Last updated by author(s): Jul 29, 2024

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	No public database used
Data analysis	All analysis performed using GraphPad Prism Version 10.1.1 software. No bioinformatics pipelines or R based tools used.

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 ddPCR data generated in this study are provided in the Supplementary Information and Source Data file. The raw ddPCR The ddPCR 1-dimensional (1D) and 2-dimensional (2D) plots are not publicly available, but they are available upon request from the corresponding author. The raw data (Supplementary Tables. 2-3) of individual replicates in the form of copy number is provided. Source data are provided with this paper. The data that is not available in the manuscript includes

images of the scatter plots generated by the BioRad ddPCR QX200. The actual quantitative part of the images that denote the mutant and wild-type signal generated, are the copy numbers provided in Supplementary Tables. 2-3.

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	Information provided on sex and gender, based on self-reported.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity are not among the variables tested in the current study. No bias in subject recruitment.
Population characteristics	The study population comprises patients presenting with a diagnosis of glioma, the most common central nervous system tumor. This included patients from different age categories (<40 yr, >40 yr) and varying disease severity. All healthy control subjects were screened for pertinent oncologic and neurologic medical histories.
Recruitment	All study subjects were recruited during inpatient and outpatient visits. All samples (tissue, plasma) were collected with written informed consent after the patient was advised of the potential risks and benefits, as well as the investigational nature of the study.
Ethics oversight	Our studies were conducted in accordance with principles for human experimentation as defined in the U.S. Common Rule and were approved by the Human Investigational Review Board of each study center under Partners institutional review board (IRB)-approved protocol number 2017P001581.

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	Sample size is reflective of the patients presenting to the hospital settings. No specific power calculation was performed to determine the sample size.
Data exclusions	No data excluded
Replication	Replication was performed at stages of optimization and validation. Each experimental design included at least three replicates for tissue analysis and eight replicates for plasma analysis. Biological replicates were also tested in parallel to determine the variation and biological heterogeneity, Results of this testing are also provided in Supplementary data.
Randomization	Allocation of samples in each cohort was random and determined independently by the clinical research coordinator. The only criteria was to include appropriate number of controls at each testing.
Blinding	Plasma validation testing across the three cohorts of study population was performed in blinded settings, where the experimental investigator was blinded to the sample identification, disease/control status, clinical time-point until after all testing and analysis was complete.

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

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	No clinical trial is available. The clinical data is not linked to a clinical trial.
Study protocol	Not available because the data is not obtained from a clinical trial.
Data collection	Data was collected during patient care at the institution from the first clinical diagnosis during the course of disease.
Outcomes	All outcomes were clinically determined and later correlated with our droplet digital PCR assay results.

Plants

Seed stocks	not applicable
Novel plant genotypes	not applicable
Authentication	not applicable