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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.

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 software was used to collect the data
Data analysis	Matlab (R2018b, The Mathworks, Inc., Natick, MA, USA) was employed for all statistical analyses conducted.

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. 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

Source data for figures 1, 2 and 4 are available for this paper. All other data that support the plots within this paper and other 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

Life sciences study design

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

Sample size	Several patient datasets were included in our study: Breast cancer (n=129), Head and Neck cancer (n=92), Rectal cancer (n=23), High-grade gliomas (n=44), Brain metastasis (n=5), Lung (n=186), Low-grade gliomas (n=82) and Hamartomas (n=5).
Data exclusions	Patients not fulfilling the inclusion criteria were excluded. The inclusion criteria were: In Breast Cancer with FDG studies, newly diagnosed locally advanced breast cancer with clinical indication of neoadjuvant chemotherapy, lesion uptake higher than background, absence of distant metastases confirmed by other methods previous to the request of the PET/CT for staging and breast lesion size of at least 2 cm and ; in Head & Neck cancer, availability of pretreatment PETstudies, presence of a well-defined primary tumour; in Rectal cancer, histological confirmation of advanced rectal cancer diagnosis and availability of pretreatment PET/CT; in High-grade gliomas, pathologically confirmed brain glioma and unifocal lesions; Breast cancer with FLT studies, primary breast cancer measuring 2.0 cm or more, being a candidate for neo-adjuvant chemotherapy and surgical resection of residual primary tumour after chemotherapy, and no evidence of stage IV disease; in Lung cancer with FDG studies, patients that received surgery were included; in Lung cancer with CT scans and temporal follow-up, enrollment was limited to those aged 50 years or older, with a smoking history of at least 10 pack-years, no previous cancer and general good health. Participants harboring parenchymal solid or part-solid non calcified nodule with at least three or more follow-up CTs were identified according to specified criteria in the protocol; in Low-grade gliomas receiving either no treatment or only surgery for which at least five post-surgery consecutive images showing tumour growth were available; in Hamartomas, longitudinal follow-up was mandatory.
Replication	Not applicable.
Randomization	Not applicable.
Blinding	Not applicable.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☐	☒ Clinical data

Methods

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

Animals and other organisms

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

Laboratory animals	Two animal models were used: 1) 17 female (2-3 months old) Foxn1nu mice for glioma xenographs and 2) 37 Athymic nu/nu (Harlan) mice of 4-8 weeks of age for brain metastasis
Wild animals	Not applicable.
Field-collected samples	Not applicable
Ethics oversight	Animal care and experimental procedures were performed in accordance to the European Union and National guidelines for the use of animals in research and were reviewed and approved by the Research Ethics and Animal Welfare Committee: for animal model 1) at our institution (Instituto de Salud Carlos III, Madrid) (PROEX 244/14); for animal model 2) approved at CNIO (PROEX 211/17)

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

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	The study used data from several retrospective observational studies (not registered in any international database)
Study protocol	SCALAWS, FuMeGa, ACRIN6688 (TCIA), METMATH and SCALAMATH
Data collection	Data for SCALAWS, FuMeGa, ACRIN, METMATH and SCALAMATH studies were collected between 2007 and 2019.
Outcomes	Not applicable.

Magnetic resonance imaging

Experimental design

Design type	Retrospective.
Design specifications	Not applicable.
Behavioral performance measures	Not applicable.

Acquisition

Imaging type(s)	T1+Gd sequences.
Field strength	1, 1.5 and 3 T.
Sequence & imaging parameters	Postcontrast T1-weighted sequence was gradient echo using 3D spoiled-gradient recalled echo or 3D fast-field echo after intravenous administration of a single-dose of gadobenate dimeglumine (0.10 mmol/kg) with a (6-8)-min delay. All MRI studies were performed in the axial plane with either a 1.5 T Siemens scanner, a 3 T Philips scanner and a 1 T Philips scanner. Imaging parameters were no gap, slice thickness of 1 - 1.6 mm, 0.438-0.575 mm xy resolutions, and 0.8 - 1.3 mm spacing between slices.
Area of acquisition	Whole brain scan.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	Not applicable.
Normalization	Not applicable.
Normalization template	Not applicable.
Noise and artifact removal	Not applicable.
Volume censoring	Not applicable.

Statistical modeling & inference

Model type and settings	Not applicable.
Effect(s) tested	Not applicable.

Specify type of analysis: ☐ Whole brain ☒ ROI-based ☐ Both

Anatomical location(s): Brain.

Statistic type for inference (See Eklund et al. 2016)	Not applicable.
Correction	Not applicable.

Models & analysis

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

Multivariate modeling and predictive analysis: Nonlinear regression analysis using Mean Square Errors (MSE) to fit model equations.