

## 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

- |                                     |                                     |  |
|-------------------------------------|-------------------------------------|--|
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>   |
| <input checked="" type="checkbox"/> | <input type="checkbox"/>            | A description of all covariates tested   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | For null hypothesis testing, the test statistic (e.g. $F$ , $t$ , $r$ ) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted<br><i>Give <math>P</math> values as exact values whenever suitable.</i>                            |
| <input checked="" type="checkbox"/> | <input type="checkbox"/>            | For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings   |
| <input checked="" type="checkbox"/> | <input type="checkbox"/>            | For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> | 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

For generating graphs or curves, GraphPad Prism 6 software was used. Fiji (ImageJ) was used for changing image colors.

Data analysis

GraphPad Prism 6 software was used for generating all data and statistics.

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

All data are available within the Article and Supplementary Files, or available from the authors upon request. Transcriptomics data is available from the SRA: PRJNA320047 or the European Nucleotide Archive: PRJEB23786.

## 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	For in vitro experiments, we took at least 8 replicated per experiment and then at least 3 to 4 independent experiments were performed. Some of the critical experiments were done by two independent investigators (double blind by Dr. Thomas Daubon et Céline Léon). We initially used R software for determining a power of 0.95. For animal experiment (survival analysis), 7 to 8 animals were used per group, as determined by R software, for getting a power of 0.95.
Data exclusions	No data were excluded from the experiments, as a sufficient number of replicates was included in each independent experiment.
Replication	Statistical test were assessed to compare the means of each experiment with the 3 or 4 independent experiments. Anova test was used to compare multi-sample experiments and student test for comparing 2 conditions.
Randomization	After mouse implantation, the animals were randomly distributed into cages for avoiding littermate variation, for the further treatments.
Blinding	Experiments from Figures 2, 3A, 3D, 4C, 4D, 4E, 5A, 6B, 6C have been done by two independent experimentators.

## 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	Involvement in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input type="checkbox"/>	<input checked="" type="checkbox"/> Clinical data

### Methods

n/a	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Antibodies

### Antibodies used

Antibody Manufacturer	Cat. No.	Working Conc/Dilution	Application	Host
AKT (11E7)	Cell Signaling 4685	1/10000	WB	Rabbit
CAIX (Carboxy Anhydrase IX)	Abcam ab15086	1/500	IF	Rabbit
CD31	BD Pharmingen 553370	1/100	IF	Rat
CD47	BD Pharmingen 556044	1/500	WB	Mouse
Cortactin	Millipore 05-180	1/500	IF	Mouse
DAPI	Fisher D1306	1/106	IF	
Endoglin (CD105)	BD Pharmingen 550546	1/50	IF	Rat
F-actin (I-19)	Santa Cruz sc-1616	1/1000	IF	Goat
Fibronectin	Abcam ab154211	1/1000	WB	Mouse
Fibronectin	Abcam ab23750	1/600	IF	Rabbit
IRE1 $\alpha$	Santa Cruz sc-20790	1/1000	WB	Rabbit
Nestin (clone 10C2)	Millipore MAB5326	1/500	IF	Mouse
pAKT (Ser473)	Cell Signaling 9271	1/1000	WB	Rabbit
pERK	Cell Signaling 9101	1/1000	WB	Rabbit
Phalloidin Rhodamine	Molecular Probes R415	1/100	IF	
Psmad1-5 (S463/465)	(41D10) Cell Signaling 9516	1/500	WB	Rabbit
Psmad2 (S465/467)/Smad3 (S423/425)	(D27F4) Cell Signaling 8828	1/100	IF	Rabbit
Psmad2 (Ser465/467)	Cell Signaling 3108	1/500	WB	Rabbit
Psmad3	Abcam ab52903	1/100	IF	Rabbit
Psmad3 (S423/425)	(C25A9) Cell Signaling 9520	1/500	WB	Rabbit
Smad1 (D59D7)	Cell Signaling 6944	1/500	WB	Rabbit
Smad2 (D43B4)	Cell Signaling 5339	1/500	WB	Rabbit
Smad3 (C67H9)	Cell Signaling 9523	1/500	WB	Rabbit
Smad4	Cell Signaling 9515	1/500	IF	Rabbit
TGFb1	Abcam ab9758	1/200	WB	Rabbit
THBS1	Santa Cruz 59886	1/200	HIC	Mouse
THBS1	Home-made from JJ.Feige	1/500	IF	Rabbit
THBS1 (A6.1)	Thermo-Scientific MA5-13398	1/500	WB	Mouse
Tubulin	Sigma T5168	1/5000	WB	Mouse

Vimentin Abcam ab16700 1/200 IF Rabbit  
 Vinculin Sigma V9131 1/500 WB Mouse

Validation

All commercial antibodies were validated by both manufacturers and independent laboratories. The home-made THBS1 antibodies coming from JJ Feige lab were validated in de Fraipont F et al, Oncogene 2004.

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)

U87MG cells were purchased from ATCC.

Authentication

All cells used for phenotypic and functional studies have been further characterized more in detail by cGH array (P3) and by cell authentication (U87) using Promega Powerplex21 Kit (Eurofins, GE).

Mycoplasma contamination

The U87 (ATCC) and P3 glioma cell lines were regularly tested for mycoplasma contamination and were all mycoplasma-free.

Commonly misidentified lines  
 (See [ICLAC](#) register)

No misidentified cell line was used in this study.

## Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

Male RAGy2C<sup>-/-</sup> mice were housed and treated in the animal facility of Bordeaux University ("Animalerie Mutualisée Bordeaux").

Wild animals

No wild animal was used in this study.

Field-collected samples

No such sample was used in this study.

Ethics oversight

All animal procedures have been done according to the institutional guidelines and approved by the local ethics committee (agreement number: 4611).

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

No clinical trial was performed in this study.

Study protocol

No clinical trial was performed in this study.

Data collection

No clinical trial was performed in this study.

Outcomes

No clinical trial was performed in this study.