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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	Cor	nfirmed
	\boxtimes	The $\underline{\text{exact sample size}}$ (n) for each experimental group/condition, given as a discrete number and unit of measurement
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	\boxtimes	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.
\boxtimes		A description of all covariates tested
\boxtimes		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	\boxtimes	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
	\boxtimes	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes		Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
	\boxtimes	Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on <u>statistics for biologists</u> may be useful.

Software and code

Policy information about availability of computer code

Data collection

No computer code was used.

Data analysis

We used Proteome Discoverer 2.0 Mascot engine (ThermoFisher Scientific) for mass spectrometric analysis; Living Image® software (Perkin Elmer, for the Xenogen IVIS-200 imaging system) for bioluminescent image analysis; JASPAR for analysis of transcription factor (TEAD) binding sites on target genes; OLego and Quantas for RNA splicing pattern analysis; and Imaris image analysis software for live imaging analysis.

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

The data that support the findings of this study are available from the corresponding author upon request. The RNA-Seq data have been deposited at the Gene Expression Omnibus (https://www.ncbi.nlm.nih.gov/geo/) under the accession number GSE110239.

Field-spe	ecific reporting		
Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.			
\times Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences		
For a reference copy of t	the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf		
Life scier	nces study design		
	sclose on these points even when the disclosure is negative.		
Sample size	Based on the literature and our previous studies, we chose the sample size routinely used for animal experiments, reporter assays, quantitative PCR, migration and invasion assays, soft agar assays, cell proliferation assays, and ELISA.		
Data exclusions	No data were excluded.		
Replication	The experiments were repeated 2-3 times. All replication attempts were successful.		
Randomization	No method of randomization was used.		
Blinding	Investigators were not blinded to group allocation.		

Reporting for specific materials, systems and methods

Methods	
n/a Involved in the study	
ChIP-seq	
Flow cytometry	
MRI-based neuroimaging	
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Antibodies

Antibodies used

Anti-pan-TEAD, Cell Signaling Technology Cat#13295; RRID: AB_2687902 Anti-FLAG, Sigma Cat#F7425; RRID: AB_439687 Anti-HA, Santa Cruz Biotechnology Cat#sc-7392; RRID: AB_627809 Anti-cyclophilin B, ThermoFisher Scientific Cat#PA1-027A; RRID: AB_2169138 Anti-YAP, Cell Signaling Technology Cat#14074; RRID: AB_2650491 Anti-histone H3, Cell Signaling Technology Cat#9715; RRID: AB_331563 Anti-Lamin B1, Cell Signaling Technology Cat#12586; RRID: AB_2650517 Anti-tubulin, Sigma Cat#T5168; RRID: AB_477579 Anti-HSP90, BD Biosciences Cat#610419; RRID: AB_397799 Anti-GAPDH, ThermoFisher Scientific Cat#MA5-15738; RRID: AB 10977387 Anti-HA, Abcam Cat#ab9110; RRID: AB 307019

Anti-TEAD1, BD Biosciences Cat#610922; RRID: AB_398237 Anti-PyMT, Abcam Cat#ab15085; RRID: AB_301631

Validation

Pre-validated antibodies were purchased from reputable sources. All proteins are well studied and all antibodies are widely used in the literature. The catalog number and RRID are provided for each antibody. We validated the antibodies for endogenous and transfected proteins in knockdown and overexpression settings.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

MCF10A, ATCC CRL-10317; RRID: CVCL_0598 T47D, ATCC HTB-133; RRID: CVCL_0553 BT474, ATCC HTB-20; RRID: CVCL_0179 MDA-MB-157, ATCC HTB-24; RRID: CVCL_0618 BT549, ATCC HTB-122; RRID: CVCL_1092 MDA-MB-468, ATCC HTB-132; RRID: CVCL_0419 HCC1806, ATCC CRL-2335; RRID: CVCL_1258 Hs578t, ATCC HTB-126; RRID: CVCL_0332 MDA-MB-436, ATCC HTB-130; RRID: CVCL 0623

Hela, ATCC CCL-2; RRID: CVCL_0030 SUM149, Stephen P. Ethier SUM159, Stephen P. Ethier

4T1 (G418-resistant, luciferase-expressing), Mien-Chie Hung

MDA-MB-231, ATCC HTB-26; RRID: CVCL_0062 LM2 (luciferase-expressing), Xiang Zhang

HEK293FT, ThermoFisher Scientific Cat#R70007; RRID: CVCL_6911

67NR, Fred R. Miller 168FARN, Fred R. Miller 4TO7, Fred R. Miller 4T1, Fred R. Miller

Authentication

Short tandem repeat (STR) profiling was done by ATCC and MD Anderson's Characterized Cell Line Core Facility.

Mycoplasma contamination

Cell lines were tested for mycoplasma contamination with a mycoplasma detection kit and treated with Plasmocin for the prevention of mycoplasma contamination.

Commonly misidentified lines (See ICLAC register)

No cell lines used in this study are in the database of commonly misidentified cell lines.

Animals and other organisms

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

Laboratory animals

Species: mouse

Strains:

NSG mice, MD Anderson's internal supply

BALB/c mice, The Jackson Laboratory Stock#000651; RRID: IMSR_JAX:000651

MMTV-PyMT mice (C57BL/6), William Muller

MMTV-PyMT mice (FVB), The Jackson Laboratory Stock#002374; RRID: IMSR_JAX:002374 CMV-Cre mice (C57BL/6), The Jackson Laboratory Stock#006054; RRID: IMSR JAX:006054

Malat1 knockout mice (transcriptional terminator insertion at the Malat1 locus; C57BL/6), Shinichi Nakagawa

Malat1 transgenic mice (targeted transgenic expression from the ROSA26 locus; C57BL/6 and FVB), generated in this study

Age: (1) for tumor cell implantation: 6 weeks old at the time of tumor cell injection. (2) For genetically engineered mouse models: from birth to the endpoint (i.e., moribund due to tumor burdens or poor body condition).

Sex: female.

Wild animals

The study did not involve wild animals.

Field-collected samples

The study did not involve samples collected from the field.