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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Statistical parameters

		atistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main Methods section).
n/a	Confirmed	
	\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
		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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted Give P values as exact values whenever suitable.
\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 statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection

Mass spectrometry data were collected using MSD Chemstation Data Analysis (vE.02.0.2.1431) or Agilent Mass Hunter (vB.0802 Build 8.2.8260.0) followed by an in house developed Matlab script.

Data analysis

Mass spectrometry data were analyzed using MSD Chemstation Data Analysis (vE.02.0.2.1431) or Agilent Mass Hunter (vB.0802 Build 8.2.8260.0) followed by an in house developed Matlab script. Metastatic area and metastases number were quantified by Zen Blue software (2011). Collagen intensity was quantified with Imaris Image Analysis Software 8 (Bitplane). GNU Imagin Manipulation Program (GIMP 2.10.8) was used to manually stitch all picro-sirius images belonging to the same metastasis together. The composite images were analyzed with Image J 1.45. Microsoft excel 2013 was used for data output. Statistical data analysis was performed using GraphPad Prism 7 software.

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 <u>data availability statement</u>. 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 authors declare that all data supporting the findings of this study are available within the article, its extended data files, or from the corresponding author upon reasonable request

	est 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
	the document with all sections, see <u>nature.com/authors/policies/ReportingSummary-flat.pdf</u>
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lite scier	nces study design
II studies must di	sclose on these points even when the disclosure is negative.
Sample size	In vitro sample sizes were based on previous similar studies that have given statistical results. For in vivo experiments, sample size was determined using power calculations with B=0.8 and P<0.05, based on preliminary data and respects the limited use of animals in line with the 3 R system: Replacement, Reduction, Refinement.
Sample size Data exclusions	determined using power calculations with B=0.8 and P<0.05, based on preliminary data and respects the limited use of animals in line with
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Data exclusions	determined using power calculations with B=0.8 and P<0.05, based on preliminary data and respects the limited use of animals in line with the 3 R system: Replacement, Reduction, Refinement. Detection of outliers was performed using Grubb's test in Graphpad.

Reporting for specific materials, systems and methods

Materials & experimental systems	Methods	
n/a Involved in the study	n/a Involved in the study	
Unique biological materials	ChIP-seq	
Antibodies	Flow cytometry	
Eukaryotic cell lines	MRI-based neuroimaging	
Palaeontology		
Animals and other organisms		
Human research participants		

Antibodies

Antibodies used

Collagen staining was performed with either anti-Collagen I (Abcam, Ab34710) or anti-Collagen III (Abcam, Ab7778). Alexa Fluor 555 (Life technologies, A31272) was used as conjugated secondary antibody. Western blot analysis was performed with the following antibodies: MCT2 (LabNed 0315312), GPT2 (Santa Cruz, 398383), P5CS (Santa Cruz, 515443), GDH (Abcam, 153973), P4HA1 (Abcam, 59497), B-Actin (Sigma, A5441) and ERK1/2 (Cell signaling, 4695S).

Validation

Antibody were used as recommended in the respective data-sheets. MCT2 antibody was validated based on positive and negative control cell lines.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s) MCF10A, MCF7, HCC70 and 4T1 cell lines were purchased from ATCC. The EMT6.5 cell line was kindly provided by professor

Robin Anderson (Peter MacCallum cancer center). Fibroblasts were kindly provided by Prof. Ludo Van Den Bosch (VIB).

Myofibroblasts were kindly provided by Prof. Akira Orimo (Juntendo University).

Authentication MCF10A, MCF7 and HCC70 cell lines were validated by DNA fingerprinting.

Mycoplasma contamination All cel llines were confirmed to be mycoplasma free by Mycoalert detection kit (Lonza).

Commonly misidentified lines (See ICLAC register)

No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals Six weeks old female BALB/C mice were injected with mouse breast cancer cells through either mammary fat pad injection or

intravenously. Mice were sacrificed after 2-4 weeks.

Wild animals No wild animals were used.

Field-collected samples No field-collected samples were used.