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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<br>*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<br>*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 | Irrelevant to experiments. |
| Data analysis | Fluorescence and afterglow images were analyzed using the Living Image 4.3 Software (PerkinElmer). NMR spectra were analyzed using Mestre Nova LITE v5.2.5-4119 software (Mestre lab Research S.L.). |

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

The authors declare that all related to this study are available in the article/and or its supplementary information files.

# 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 | We used G*power analysis to calculate and ensure the sample sizes fulfill adequate power (p>0.8). According to the experimental data and sample size (n), P value and effect size were calculated and the power was then calculated. If it is more than 80%, demonstrating the sample size is adequate. |
| Data exclusions | No data was excluded from this study. |
| Replication | Experiments were repeated at least three independent experiments with similar results. All experiments were reproduced to reliably support conclusions stated in the manuscript. |
| Randomization | Cages of mice were randomly selected and then divided into experimental groups for further treatment. |
| Blinding | Investigators were not blinded to group allocation during experiments. |

# 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 |
|---|---|
| [ ] | [x] Antibodies |
| [ ] | [x] Eukaryotic cell lines |
| [x] | [ ] Palaeontology |
| [ ] | [x] Animals and other organisms |
| [x] | [ ] Human research participants |
| [x] | [ ] Clinical data |

## Methods

| n/a | Involved in the study |
|---|---|
| [x] | [ ] ChIP-seq |
| [ ] | [x] Flow cytometry |
| [x] | [ ] MRI-based neuroimaging |

## Antibodies

| | |
|---|---|
| Antibodies used | ACSL4 antibody (1:1000; ab205199; Abcam); FPN-1 antibody (1:1000; NBP1-21502SS; Singlab Technologies Pte Ltd); GPX4 antibody (1:100; sc-166120; Axil Scientific Pte Ltd); cleaved caspase-3 antibody (1:500; 9661L; Cell Signaling Technology); ferritin antibody (1:500; MA532244; Life Technologies Holdings Pte Ltd); GAPDH antibody (1:500; sc-32233; Axil Scientific Pte Ltd). Secondary antibodies for immunoblotting which include IRDye 800 CW goat anti-mouse (1:10000; 925-32210) and IRDye 680 CW goat anti-rabbit (1:10000; 925-68071) were purchased from LI-COR Biosciences. Anti-HGF (1:500; ab83760), anti-MTA2 (1:100; ab8106), anti-VCAM-1 (1:250; ab134047) antibodies were purchased from Abcam. Secondary antibody Alexa Fluor 488 conjugated goat anti-rabbit IgG H&L (1:500; ab150077) for immunofluorescent staining was purchased from Abcam. |
| Validation | All antibodies were used in the study according to the profile of manufacturers. Antibody validation for immunofluorescence or western blotting was validated by the supplier and confirmed in Figure 3, 4, 5 and Supplementary Figures 13 and 16. |

## Eukaryotic cell lines

Policy information about cell lines

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|---|---|
| Cell line source(s) | 4T1 murine mammary carcinoma cell line, MCF-7 human breast adenocarcinoma cell line, HepG2 human hepatocellular carcinoma cell line, NIH/3T3 murine fibroblast cell line, NDF normal human dermal fibroblast cell line, MDA-MB-231 human breast adenocarcinoma cell line, PC12 rat pheochromocytoma cell line, HeLa human cervical adenocarcinoma cell line, and SKOV3 human ovarian adenocarcinoma cell line were purchased from American Type Culture Collection, ATCC |
| Authentication | These cell lines were authenticated by the supplier using STR analysis. |
| Mycoplasma contamination | No contamination was detected by the supplier using Hoechst DNA stain method, agar culture method, PCR-based assay. |
| Commonly misidentified lines (See ICLAC register) | These cell lines that we used were not listed in commonly misidentified lines in ICLAC Register. |

## Animals and other organisms

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

| | |
|---|---|
| Laboratory animals | Animal experiments in Singapore were performed in compliance with Guidelines for Care and Use of Laboratory Animals of the Nanyang Technological University-Institutional Animal Care and Use Committee (NTU-IACUC) and approved by the Institutional Animal Care and Use Committee (IACUC) for Animal Experiment, Singapore. In Singapore, female NCr nude mice (6 weeks old) were purchased from InVivos Pte Ltd (Singapore).Animal experiments in China were performed in strict accordance with the NIH guidelines for the care and use of laboratory animals (NIH Publication No. 85-23 Rev. 1985) and approved by the Institutional Animal Use and Care Committee of Shan Xi Medical University (Approval No, 2016LL141, Taiyuan, China). |
| Wild animals | Irrelevant to experiments. |
| Field-collected samples | Irrelevant to experiments. |
| Ethics oversight | No ethical issues. |

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

## Flow Cytometry

### Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☐ A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

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|---|---|
| Sample preparation | After various treatment of 4T1 cells, cells were gently washed 3 time with fresh PBS and stained with DCFH-DA reagent. Then, cells were washed 3 times in ice-cold PBS, trypsinized, and resuspended in fresh PBS for flow cytometry test. |
| Instrument | Fortessa X20 (BD Biosciences) |
| Software | FACS Diva and FlowJo v10 |
| Cell population abundance | No cell sorting was performed. |
| Gating strategy | Living single cells were selected by FSC and SSC analysis. Green fluorescence of activated DCFH-DA in cells was detected by FITC channel and histogram was provided in Supplementary Figure 11. |

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.