nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies 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	N/A
Data analysis	Statistical significance was calculated using the GraphPad Prism Software (Version 7). Image Lab sofaware was used to quantified the density of western blot.

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

All data generated or analysed during this study are included in this published article. Materials generated in this study will be freely available to any researcher. upon reasonable request.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Female. Most breast cancer patients are women.
Reporting on race, ethnicity, or other socially relevant groupings	Yellow race.
Population characteristics	The patients with ER staining positive were taken into account.
Recruitment	We selected patients with ER positive breast cancer.
Ethics oversight	All human breast tumor samples were obtained from patients with informed consent. The current study (protocol# 2019006) was approved by the Institutional Review Board for human study of Wenzhou Medical University and conducted according to the principles expressed in the Helsinki Declaration.

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

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

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

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

Sample size	Based on previous studies and pilot data, a sample size of 10 per group was chosen to ensure adequate statistical power for animal experiment. 1-2 mice in each group may not be able to develop tumors, and the maximum and minimum values should be removed at last to ensure that 5-6 mice in each group can be analysed.
Data exclusions	In animal experiment, the mice which is unable to develop tumors, and the maximum and minimum values would be removed at last.
Replication	All data were repeated at least three times with similar results.
Randomization	After the sizes of xenograft tumors reached around 100 mm3, mice were randomized into groups.
Blinding	In purely observational studies where investigators are not administering interventions, knowing group allocations might not influence the outcome measurement.

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 and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used

Immunoblotting and immunoprecipitation
rabbit polyclonal antibodies against BRD4 (Cat#ab289893, 1:1000). were purchased from Abcam (UK). Rabbit antibodies against SLC7A11 (Cat#12691, 1:1000), phospho-RIP (Ser166) (Cat#44590, 1:1000), phospho-MLKL (Ser345) (Cat#37333, 1:1000), and mouse monoclonal antibodies against α-tubulin (Cat#3873, 1:5000) and β-actin (Cat#3700, 1:5000) were from Cell Signaling Technology (USA). Rabbit antibody against HA (Cat#0039, 1:1000) was purchased from Beyotime (Jiangsu, China). Mouse antibody against PARP1 (Cat#66520, 1:1000) was purchased from Proteintec (Hubei ,China).

Immunohistochemistry
Rabbit anti-USP35 polyclonal antibodies (ab128592, Abcam, Cambridge, UK) were used at 1:500 dilution. Rabbit anti-BRD4 polyclonal antibodies (cat#28486, Proteintech, Wuhan, China) were used at 1:1000 dilution. Rabbit anti-SLC7A11 antibodies (Cat#26864, Proteintech, Wuhan, China) were used at 1:50 dilution. Rabbit anti-4-HNE polyclonal antibodies (ab46545, Abcam, Cambridge, UK) were used at 1:100 dilution.

Validation

All antibodies are widely used, well validated commercial products. Details can be referred on th manufactures' websites.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

The human breast cancer cell lines (MCF-7, ZR-75-1, and MDA-MB-231) and HEK293T-17 were obtained from the American Type Culture Collection (Maryland,USA). SUM159PT cells were obtained from Asterand Bioscience (Detroit, Michigan, USA).

Authentication

Cells were detected by STR.

Mycoplasma contamination

All cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

N/A

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals

Six-week-old Balb/c nu/nu female mice

Wild animals

N/A

Reporting on sex

Given that our research focus on breast cancer, we selected female mice for research.

Field-collected samples

Housing. The mice are kept at a temperature of 21±2°C, with relative humidity between 30-70%, and a 12/12 hour light-dark cycle controlled automatically. Mice were euthanized at the end of the experiment, and xenografted tumors were dissected, weighed, and photographed.

Ethics oversight

The animal study was approved by the Institutional Animal Care and Use Committee of Wenzhou Medical University.

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

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.

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

Sample preparation	Breast cancer cells were stained with 5 μM BODIPY C11 (Thermo Fisher, 139 Cat#D3861) for 30 min after the indicated treatments. After staining, labeled cells were washed, trypsinized, resuspended in PBS, and then subjected to flow cytometry analysis.
Instrument	BD Accuri C6
Software	CytoFlex software was used to collect cells. Flow J 10.0 software was used to analyze apoptosis and lipid ROS.
Cell population abundance	At least 5000 cells were collected for analysis.
Gating strategy	1. FSC/SSC Gate:Exclude debris and dead cells by setting a gate around the main cell population cluster. 2. Single Cell Gate:Use FSC-A vs. FSC-H plot to exclude doublets. 3. Marker-Specific Gating: Use the FL1 fluorescence channel, setting the gate based on unstained controls.

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