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Reporting Summary

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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

- | | | |
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| <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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| <input type="checkbox"/> | <input checked="" 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
<i>Give P 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 The intensity of immunoblotting bands was quantified by the Image J Software (v 1.53).

Data analysis Statistical analyses were performed using GraphPad Prism software version 5.0 . One-way ANOVA analysis and Tukey's test or t-test was used to compare results. All software used in this study are either commercially available or open source

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 associated with this study are present in the paper or the Supplementary Materials. The protein mass spectrometry raw data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD062168. Information about all commercially available reagents is provided in Materials and Methods.

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	Research findings of this study are not restricted to a single sex and gender.
Reporting on race, ethnicity, or other socially relevant groupings	The study did not involve this item.
Population characteristics	The patients were between 26 and 69 years old and exhibited negative expression of ER, PR, and HER2.
Recruitment	The study did not involve this item.
Ethics oversight	Tissue sections of TNBC patients were obtained from the tissue bank at the Jinan University in accordance with the approval document of the Institutional Medical Ethics Committee (JNUKY-2023-0062).

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	Sample sizes were estimated based on our previously published studies (doi: 10.1002/adv.202205873. doi: 10.1038/41418-023-01128-x.doi: 10.1038/ncomms13923.).
Data exclusions	No data were excluded from the analyses.
Replication	LC-MS/MS, cell proliferation and survival experiments were independently performed for three times, following the principle of repeatability. In the animal study, data represented as the mean \pm s.d. of six mice.
Randomization	The samples for each experiment were randomized to be examined.
Blinding	During data collection and analysis, two independent investigators were blinded to the experiment assignment.

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		Methods	
n/a	Involved in the study	n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies	<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines	<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology	<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms		
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data		
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern		
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants		

Antibodies

Antibodies used	ntibodies anti-Flag (F1804, dilution: 1:1000), anti-HA (H3663, dilution: 1:1000) and anti- β -actin (A1978, dilution: 1:5000) antibodies were purchased from Sigma-Aldrich. Anti-Myc (9E10, dilution: 1:1000) antibodies were purchased from Santa Cruz Biotechnology. Anti-Phospho-AKT Substrate (23C8D2, dilution: 1:1000), anti-p-AKT (T308) (13038S, dilution: 1:1000), anti-p-AKT (Ser473) (4060S, dilution: 1:1000), anti-Rictor (D16H9) (9476, dilution: 1:1000), anti-mTOR (7C10, dilution: 1:1000), anti-AKT (pan) antibody (2920S, dilution: 1:1000) and anti-GFP (4B10, dilution: 1:1000) antibodies were purchased from CST (Cell Signaling Technology). Anti-AKT1
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(F0217, dilution: 1:1000), anti-AKT2 (F0218, dilution: 1:1000), anti-AKT3 (F0670, dilution: 1:1000), anti-PRAS40 (F0239, dilution: 1:1000) and anti-Phospho-PRAS40 (T246) (F0252, dilution: 1:1000) antibodies were purchased from Selleck. Anti-PHLPP1 (A9542, dilution: 1:500), anti-PP2A-B55 α (A24261, dilution: 1:1000) and anti-PP2A-B56 β (A14252, dilution: 1:1000) were purchased from Abclonal. Anti-UFM1 (ab109305, dilution: 1:1000) and anti-UFC1 (ab189251, dilution: 1:1000) antibodies were purchased from Abcam. Anti-UFL1 (A303-456A, dilution: 1:1000) antibodies were purchased from BETHYL. Anti-UFSP2 (16999-1-AP, dilution: 1:1000), anti-CDK5RAP3 (11007-1-AP, dilution: 1:1000) and anti-UFBP1 (21445-1-AP, dilution: 1:1000) antibodies were purchased from Proteintech. Anti-Phospho-UFL1 (T426) antibody (TP50605, dilution: 1:1000, custom antibody) was generated by immunizing rabbits with phospho-peptide, and then affinity-purified by Hangzhou HuaAn Biotechnology Co., Ltd. Light or heavy chain specific IPKine™ HRP (Abbkine Scientific Co; A25012 and A25222) were used in co-IP experiment.

Validation

Monoclonal ANTI-FLAG® M2 antibody produced in mouse Sigma-Aldrich Cat# F1804, RRID:AB_262044
<https://www.sigmaaldrich.cn/CN/zh/product/sigma/f1804>
 Human HA Monoclonal Antibody, Unconjugated, Clone HA-7 Sigma-Aldrich Cat# H3663, RRID:AB_262051
<https://www.sigmaaldrich.cn/CN/zh/product/sigma/h3663>
 β -Actin antibody, Mouse monoclonal Sigma-Aldrich Cat# A1978, RRID:AB_476692
<https://www.sigmaaldrich.cn/CN/zh/product/sigma/a1978>
 Mouse Anti-Myc tag Monoclonal Antibody, Unconjugated, Clone 9E10 Abcam Cat# ab32, RRID:AB_303599
<https://www.abcam.com/en-us/products/primary-antibodies/myc-tag-antibody-9e10-ab32>
 Phospho-AKT Substrate antibody Rabbit mAb #10001 Cell Signaling Technology Cat# 10001, RRID:AB_10950819
<https://www.cellsignal.com/products/primary-antibodies/phospho-akt-substrate-rxxxs-t-23c8d2-rabbit-mab/10001>
 Phospho-Akt (Thr308) (D25E6) XP® Rabbit mAb #13038 Cell Signaling Technology Cat# 13038, RRID:AB_2629447
<https://www.cellsignal.com/products/primary-antibodies/phospho-akt-thr308-d25e6-xp-rabbit-mab/13038>
 Phospho-Akt (Ser473) (D9E) XP® Rabbit mAb #4060 Cell Signaling Technology Cat# 4060, RRID:AB_2315049
<https://www.cellsignal.com/products/primary-antibodies/phospho-akt-ser473-d9e-xp-rabbit-mab/4060>
 Rictor (D16H9) Rabbit mAb #9476 Cell Signaling Technology Cat# 9476, RRID:AB_10612959
<https://www.cellsignal.com/products/primary-antibodies/rictor-d16h9-rabbit-mab/9476>
 mTOR (7C10) Rabbit mAb #2983 Cell Signaling Technology Cat# 2983, RRID:AB_2105622
<https://www.cellsignal.com/products/primary-antibodies/mtor-7c10-rabbit-mab/2983>
 GFP (4B10) Rabbit mAb #2955 Cell Signaling Technology Cat# 2955
<https://www.cellsignal.com/products/primary-antibodies/gfp-4b10-mouse-mab/2955>
 Akt (pan) (40D4) Mouse mAb #2920 Cell Signaling Technology Cat# 2920, RRID:AB_1147620
<https://www.cellsignal.com/products/primary-antibodies/akt-pan-40d4-mouse-mab/2920>
 Akt1 Rabbit mAb selleck Cat# F0217
<https://www.selleck.cn/antibodies/akt1-rabbit-mab.html>
 Akt2 Rabbit mAb selleck Cat# F0218
<https://www.selleck.cn/antibodies/akt2-rabbit-mab.html>
 Akt3 Rabbit mAb selleck Cat# F0670
<https://www.selleck.cn/antibodies/akt3-rabbit-mab.html>
 PRAS40 Rabbit mAb selleck Cat# F0239
<https://www.selleck.cn/antibodies/pras40-rabbit-mab.html>
 Phospho-PRAS40 (Thr246) Rabbit mAb Cat# F0252
<https://www.selleck.cn/antibodies/phospho-pras40-thr246-rabbit-mab.html>
 PHLPP1 Rabbit pAb Cat# A9542, RRID:AB_2770888
<https://www.abclonal.com/catalog-antibodies/PHLPP1RabbitpAb/A9542>
 PP2A-B55 α /PR55 α /PPP2R2A Rabbit mAb Cat# A24261
<https://www.abclonal.com/catalog-antibodies/PP2AB55PR55PPP2R2ARabbitmAb/A24261>
 PP2A-B56 β /PR61 β /PPP2R5B Rabbit pAb Cat# A14252, RRID:AB_2761113
<https://www.abclonal.com/catalog-antibodies/PP2AB56PR61PPP2R5BRabbitpAb/A14252>
 Anti-UFM1 antibody Rabbit mAb Cat# ab109305
<https://www.abcam.com/en-us/products/primary-antibodies/ufm1-antibody-epr42642-ab109305>
 UFC1 Monoclonal Antibody Rabbit Cat# ab189251
<https://www.abcam.cn/products/primary-antibodies/ufc1-antibody-epr15014-ab189251>
 UFL1 Polyclonal Antibody Rabbit Cat# A303-456A, RRID:AB_10951658
<https://www.thermofisher.com/antibody/product/UFL1-Antibody-Polyclonal/A303-456A>
 UFSP2 Polyclonal Antibody Rabbit Cat# 16999-1-AP, RRID:AB_2214070
<https://www.ptgcn.com/products/UFSP2-Antibody-16999-1-AP>
 CDK5RAP3 Polyclonal Antibody Rabbit Cat# 11007-1-AP, RRID:AB_2076869
<https://www.ptgcn.com/products/CDK5RAP3-Antibody-11007-1-AP>
 UFBP1 Polyclonal Antibody Rabbit Cat# 21445-1-AP, RRID:AB_2827383
<https://www.ptgcn.com/products/DDRGK1-Antibody-21445-1-AP>
 IPKine™ HRP, Goat Anti-Mouse IgG LCS Cat# A25012
<https://www.abbkine.cn/w/product/detail/A25012/CN/s>
 IPKine goat anti-Rabbit IgG heavy chain secondary antibody, HRP-labeled (to eliminate light chain interference) Abbkine Cat# A25222, RRID:AB_2922982
<https://www.abbkine.cn/w/product/detail/A25222/CN/s>

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	Cell lines HEK293T, MCF 10A, MDA-MB-231, HCC1806, MCF-7, T47D, BT-474 and SK-BR-3 cells were purchased from ATCC (American Type Culture Collection). HEK293T, MDA-MB-231, MCF-7 and BT-474 cells were cultured in Dulbecco's Modified Eagle's medium (DMEMGibco) supplemented with 10% FBS (Gibco). HCC1806 and T47D cells were cultured in RPMI-1640 medium (Gibco) supplemented with 10% FBS. SK-BR-3 cells were cultured in McCoy's 5A medium (Gibco) supplemented with 10% FBS. MCF 10A cell were cultured in specific epithelial culture medium (Procell Life Science & Technology Co., Ltd. Wuhan, China). All cells were maintained in a humidified cell incubator with 5% CO ₂ at 37°C.
Authentication	The cell lines were authenticated by the providers through morphology, karyotyping and PCR-based approaches. After receipt of the cell lines, visual inspection of their cellular morphology in culture was routinely performed and no further authentication was conducted in our lab.
Mycoplasma contamination	All cell lines used in this study were negative for the tests of mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study.

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	4-6-weeks-old BALB/c female nude mice were obtained from Jicui Yaokang Biotechnology Co., Ltd. of China, and were randomly allocated to experimental groups. All animals were housed at a suitable temperature (22-24°C) and humidity (40-70%) under a 12/12-h light/dark cycle with unrestricted access to food and water for the duration of the experiment.
Wild animals	The study did not involve wild animals.
Reporting on sex	Female BALB/c nude mice (4-6 weeks old) .
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animal experiments were performed in accordance with a protocol approved by the Institutional Animal Care and Use Committee of the JINAN University (20241227-03) .

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

Plants

Seed stocks	The study did not involve this item.
Novel plant genotypes	The study did not involve this item.
Authentication	The study did not involve this item.