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Corresponding author(s): Lingqian Chang

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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	ACEA NovoExpress software, ALLDoc_x Software Comet Assay IV software, Geomagic Wrap Living Image Software 3, MTS TestSuite TW software Nikon NIS-Elements AR 4.3, NDP view 2.6.8, Olympus cellSens Standard 1.18, QuantSsudioTM Design & Analysis Software S-gauge (Version X64,3.7), Snap Gene 3.2.1 VEGA3 CONTROL SOFTWARE (Version 4.1), ZEN software, ZetaView 8.02.28
Data analysis	COMSOL Multiphysics (Version 5.6), DNASTAR.Lasergenen.V7.1, GraphPad Prism 8 software, Golden Software Surfer (Version 21), Geomagic Wrap Imaris software

Microsoft Office EXCEL,
ImageJ (v2.1.0)
Origin 2022
R 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 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

In this study, the data of supporting the results of research are available as source data and supplementary information files.

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	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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	The sizes of the female and male mice were not predetermined and are described in the results. The group sizes of mice access to statistical significance according to animal welfare guidelines, and were based on our experience with similar researches and the articles in the field (Liu, X. et al. Proc Natl Acad Sci U S A, 2017, doi:10.1073/pnas.0702969104; Huo Y, et al. NPJ Breast Cancer. 2021 Apr 23;7(1):45. doi: 10.1038/s41523-021-00253-5; Lu Z, et al. J Clin Invest. 2022 Jun 1;132(11):e146471. doi: 10.1172/JCI146471; Zhao X, et al. Nat Commun. 2018 Jul 17;9(1):2784. doi: 10.1038/s41467-018-04998-9.).
Data exclusions	No data was excluded.
Replication	All experiments were replicated at least three times with similar findings and the data is repeatable.
Randomization	For experiments requiring breast cancer model construction, female mice were randomly assigned to each group. For constructing acute traumatic liver injury model, equal numbers of female and male were selected and then randomly assigned to each group. For analyzing safety and efficiency of NanoFLUID-mediated in vivo transfection, female mice were randomly assighed to each group. For breast tumor experiment treating with NanoFLUID-mediated PARPi, we generated an orthotropic tumor xenograft by introducing mutant E0771 cells with gene Brca1 and p53 double knockout (E0771 Brca1/p53 KO) into the fourth mammary gland of female mice (Diaz-Cruz, et al., Breast disease 32, 85-97, doi:10.3233/bd-2010-0308 (2010); Duarte, A. A. et al. Nat Methods 15, 134-140, doi:10.1038/nmeth.4535 (2018)), and then randomly assigned to each group. For screening novel metastatic driver gene of breast cancer, PyVmT female mice were randomly assigned to each group.
Blinding	The researchers were not blinded during experiments for data collection. Data analyses were done by the same researchers. In image

Blinding

analysis, the images were randomly assigned a key by the researcher, and all images were processed using the same workflow, thereby, image analysis was blinded after collecting data.

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

The following primary monoclonal antibodies (mAbs) were purchased from Gene-Protein Link: Anti-FLAG-tag (DYKDDDDK) rabbit mAb (Cat.P01L072, 1:2000), anti-HA-tag (YPYDVPDYA) rabbit mAb (Cat.P01L073, 1:1000), anti-Myc-tag (EQKLISEEDL) mouse mAb (Cat.P01L51, 1:5000), anti-mouse secondary antibody (Cat.P03S01, 1:10000) and anti-rabbit secondary antibody (Cat.P03S02, 1:10000). Anti-GFP mouse mAb (Cat.66002-1-Ig, 1:10000) and Anti-β-actin mouse mAb (Cat.66009-1-Ig, 1:10000) were purchased from Proteintech. Anti-TNF alpha rabbit recombinant mAb (Cat.ab307164, 1:1000), anti-IL6 rabbit mAb (Cat.ab290735, 1:100), anti-IL-10 rabbit recombinant mAb (Cat.ab189392, 1:100), anti-p53 mouse mAb (Cat.ab32049, 1:2000), anti-BRCA1 rabbit pAb (Cat.ab238983, 1:1000), anti-ki67 rabbit mAb (Cat.ab16667, 1:200), anti-gamma H2A.X (phospho S139) rabbit pAb (Cat.ab11174, 1:250), anti-CD9 (Cat.ab307085, 1:1000) rabbit mAb, anti-CD63 (Cat.ab315108, 1:1000) rabbit pAb, anti-TSG101 (Cat.ab125011, 1:1000) rabbit mAb, and anti-GAPDH mouse mAb (Cat.ab8245, 1:5000) were purchased from Abcam. Anti Cleaved Caspase-3 (Asp175) rabbit pAb (Cat.9661, 1:200) was purchased from Cell Signaling Technology. Anti-puromycin mouse mAb (cat.MABE343, 1:3000) was purchased from MERCK. Anti-DUS2L rabbit pAb (Cat.PA5-49884, 1:1000) was purchased from Thermo Fisher.

Validation

Antibody/clone(mAb)/dilution factor/supplier name /cat.#

Rabbit anti-FLAG-tag (DYKDDDDK)/ A6R /1:2000 /Gene-Protein Link/ P01L072,
Rabbit anti-HA-tag (YPYDVPDYA) /A7H /1:1000 /Gene-Protein Link/ P01L073,
Mouse anti-Myc-tag (EQKLISEEDL) / 3E8/1:5000 /Gene-Protein Link/ P01L51,
Mouse anti-GFP/1E10H7/1:10000 /Proteintech/ 66002-1-Ig,
Rabbit anti-TNF alpha/RM1005/1:1000/abcam/ab307164
Rabbit anti-IL-6/EPR23819-103/1:100/abcam/ab290735
Rabbit anti-IL-10/JES5-2A5/1:100/abcam/ab189392
Mouse Anti-p53/Y5/1:2000/ abcam /ab32049,
Rabbit Anti-BRCA1/1:1000 /abcam/ ab238983,
Rabbit Anti-Ki67/SP6/1:200/abcam/ab16667,
Rabbit Anti-Cleaved Caspase-3 (Asp175) /1:200/Cell Signaling Technology/9661
Rabbit Anti-gamma H2A.X (phospho S139) /1:250 /abcam / ab11174,
Mouse Anti-Puromycin/12D10/1:3000/MERCK/MABE343,
Rabbit Anti-DUS2L/1:1000 /Thermo Fisher/PA5-49884
Rabbit anti-CD9 /EPR27551-92/1:1000/abcam/ ab307085
Rabbit anti-CD63 /RM1095/1:1000/abcam/ab315108
Rabbit anti-TSG101/EPR7130(B)/1:1000/abcam/ab125011
Mouse Anti-β-actin/2D4H5 /1:10000 /Proteintech /66009-1-Ig,
Mouse Anti-GAPDH/6C5/1:5000/ abcam/ ab8245,
Anti-mouse secondary antibody/ 1:10000/ Gene-Protein Link/ P03S01,
Anti-rabbit secondary antibody/ 1:10000 /Gene-Protein Link/ P03S02.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

MCF-7 and E0771 cell lines were obtained from the National Experimental Cell Resources Sharing Platform (Beijing, China). RAEC and hMSC cell lines were obtained from Tong Pai Technology.

Authentication

The E0771, MCF-7, RAEC and hMSC cell lines were identified by species identification; The E0771, MCF-7 and hMSC cell lines were tested by short tandem repeat (STR) profile. Cell lines were carefully maintained in liquid nitrogen.

Mycoplasma contamination	All cell lines were regularly detected (Mycoplasma Detection Kit, SouthernBiotech, 13100-01) for mycoplasma contamination and were negative.
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	C57 BL/6J female and male mice were purchased from SPF (Beijing) Biotechnology Co., Ltd. PyVmT female mice were purchased from Labbio Biotechnology Co., Ltd.. All mice were housed under standard condition at a 12 hours dark/light cycle and temperature of 22-24°C under specific pathogen-free conditions.
Wild animals	No wild animals were used in this study.
Reporting on sex	Breast cancer occurs mainly in female patients, therefore, in this study we constructed a mouse breast cancer model using female C57 BL/6J mice. For constructing acute traumatic liver injury model, the same number of female and male were selected and then randomly assigned. For analyzing the safety and efficacy for in vivo transfection, NanoFLUID implantation was evaluated in female mice and compared against a mastitis model that serve as the positive control. For breast tumor experiment treating with NanoFLUID-mediated PARPi, we generated an orthotropic tumor xenograft by introducing mutant E0771 cells with gene Brca1 and p53 double knockout (E0771 Brca1/p53 KO) into the fourth mammary gland of female mice and then randomly assigned. For screening novel metastatic driver gene of breast cancer, PyVmT female mice were randomly assigned.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	All experimental animal protocols were approved by the Ethics Committee of Peking University Health Science Center.

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

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	Cells were prepared for single cell suspension in 1 x PBS from the transfected cell lines or the cells dissociated from transfected organs and tissues in mice.
Instrument	NovoCyte, Agilent
Software	Cell samples were acquired on the NovoCyte (Agilent) with ACEA NovoExpress software. Flow cytometry data were analyzed using ACEA NovoExpress software.
Cell population abundance	The transfected organs/tissues were isolated, minced with scissors, and subjected to enzymatic digestion to dissociate single-

Cell population abundance	cell suspensions. Cells were counted using a hemocytometer during flow cytometry preparation, obtaining an approximate concentration of 1 × 10^6 cells/ml.
Gating strategy	Gating strategy: (1) Single cell was identified as SSC-H/FCS-H (Y-axis/X-axis) for the removal of cell debris, (2) Fluorescence signal was identified as FCS-H/GFP-H (Y-axis/X-axis).

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