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.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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n/a	Со	nfirmed
	X	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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> 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

xtb 6.3.0; Molclus 1.9.9; GaussView 5; Discovery Studio 4.5; Gromacs 2018; HPLC: Empower 3; FT-MS(Bruker): ftmsControl 2.1; UPLC-MS/MS (Waters): MassLynx V4.1; UPLC-MS/MS(Shimadzu): LabSolutions 6.72; Malvern: Zetasizer Software 7.01; Confocal laser scanning microscopy: NIS 4.13; Flow Cytometer: BD CellQuest Pro

Data analysis

Bruker Compass DataAnalysis 4.4; MestReC 4.9.9.9; GraphPad prism 8.0; DAS 2.1.1; ImageJ 1.8.0; Flowjo_V10

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 supporting the findings of this study are available within the Article, Supplementary Information or Source Data file. The source data underlying Fig. 2c-e, Fig. 3c-d, Fig. 4a-f, Fig. 5a-d, f, h, Fig. 6a-c, e-g, Fig. 7a-c, e-g, i-k, supplementary Figs. 9, 12, 15, 16, 28, 32, 33, 35, 36, 37, 40, 41, 42, 43, 45, 46, 47, 49, and 50 have been deposited in the Figshare database (DOI: 10.6084/m9.figshare.20941144).

Human research participants

Policy information about <u>studies involving human research participants and Sex and Gender in Research.</u>

Reporting on sex and gender	not applicable
Population characteristics	not applicable
Recruitment	not applicable
Ethics oversight	not applicable

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 belo	w that is the best fit for your research	. If you are not sure, read the appropriate sections before making your selection.
x 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 size was selected from the general sample size in the reference. Increasing the number of parallelism could reduce the accidental error and improve the precision of the experiment. According to the statistical principle, when 'n' is increased, the corresponding precision will also be improved, and then three to four times is the most appropriate. For in vitro experiments, pharmacokinetics, and biodistribution, n=3 was selected in order to measure the distribution closer to the true distribution on the premise of cost saving. For the pharmacodynamic experiment, n=5 was selected to obtain five biological repetitions in consideration of animal individual differences and the 4R principle for the credibility of the results.

Data exclusions

No data were excluded from the analyses.

Replication

We confirmed that all repeated attempts were successful. Experiment repeat numbers are reported in Figure Legends.

Randomization

Samples were randomly allocated into experimental groups.

Blinding

The investigators were blinded to group allocation during data collection and analysis.

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 & experimer	ntal systems Methods
n/a Involved in the study	n/a Involved in the study
Antibodies	ChIP-seq
Eukaryotic cell lines	Flow cytometry
Palaeontology and ar	chaeology MRI-based neuroimaging
Animals and other or	ganisms
X Clinical data	
Dual use research of	concern
Antibodies	
Antibodies used	Ki67 Rabbit polyclonal antibody (Servicebio, GB111141) The dilution was 1:1000;
	Alexa Fluor 555 labeled anti-α-Tubulin mouse monoclonal antibody (clone name: DM1A) (baiaolaibo, YT179). The dilution was 1:100.
Validation	The species and application of primary antibody is validated by Servicebio (https://www.servicebio.cn/goodsdetail?id=2828);
	The species and application of primary antibody is validated by baiaolaibo (http://www.bjbalb.com/html/Tissue-Cell-Staining/YT179.html)
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Eukaryotic cell line	2S
,	I lines and Sex and Gender in Research
Cell line source(s)	4T1 cells (female), B16F10 cells (male) and 3T3 cells (embryo) were obtained from the Cell Bank of Type Culture Collection of
centific source(s)	Chinese Academy of Sciences (Shanghai, China). Hepa 1-6 cells (Female) were obtained from Beijing Dingguo Changsheng Biotechnology Co., Ltd.
Authentication	All cell lines validation using short tandem repeat (STR) markers were performed by GENTIC TESTING BIOTECHNOLOGY Co., Ltd. (Jiangsu, China). In detail, eighteen STR loci were amplified using multiplex PCR. One additional marker (Human TH01)
	was used to screen for the presence of human species. The cell line sample was processed using the ABI Prism 3130 XL
	Genetic Analyzer. Data were analyzed using Gene Mapper ID 3.2 software (Applied Biosystems). Appropriate positive and negative controls were run and confirmed for each sample submitted.
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination.
Commonly misidentified lin	No commonly misidentified cells lines were used in the study.

Animals and other research organisms

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

Laboratory animals	Sprague-Dawley rats (male, 6-week old) and BALB/c mice (female, 11-week old) were supplied by the Animal Center of Shenyang Pharmaceutical University (Shenyang, Liaoning, China). The living environment of animals were maintained at a temperature of ~25 °C with a 12 h light/dark cycle, with free access to standard food and water.
Wild animals	The study did not involve wild animals.
Reporting on sex	Although we have used single-sex animals in our research, we think that the research results were not only applicable to single sex. Male rats were used in the pharmacokinetic experiment, and gender had no influence on the pharmacokinetic results. Because the selected model was breast cancer, female animals were selected for pharmacodynamic experiments.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All the animal experiments were conducted according to the Guidelines for the Care and Use of Laboratory Animals approved by the Institutional Animal Ethical Care Committee (IAEC) of Shenyang Pharmaceutical University.

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

Sample preparation	Cells were obtained from the Cell Bank of Type Culture Collection of Chinese Academy of Sciences (Shanghai, China).
Instrument	BD FACSCalibur (E20200235)
Software	BD CellQuest Pro; Flowjo_V10
Cell population abundance	Only 4T1 cells was used for analysis.
Gating strategy	Rectangle or polygon gates based on FSC-H and SSC-H signals was used to exclude cell debris and clumps.

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