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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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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
	\square 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 <i>Give P values as exact values whenever suitable.</i>
	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
\boxtimes	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), 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

Bruker AV-400; FT-MS(Bruker): ftmsControl 2.1; Zetasizer (Nano ZS, Malvern Co., UK); TEM, HITACHI, HT7700, Japan; IVIS Lumina Series III; Fotric 226; Confocal laser scanning microscopy: NIS 4.13,; multimode microreader (Thermo Scientific, USA)

Data analysis

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 <u>data availability statement</u>. 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 Figure 2c-d,

		h, h, Figure 5c-d, f, i, Figure 6c-d, h, Figure 7c-d,f, h, supplementary Fig 4, 5b, 6, 7, 8, 9, 10, 12, 13b, 15, 16, 20, 23, 24, and 25 latabase (DOI: 10.6084/m9.figshare.21801139.v1)			
Human resea	arch parti	cipants			
Policy information a	about <u>studies ir</u>	nvolving human research participants and Sex and Gender in Research.			
Reporting on sex and gender not applicable		not applicable			
Population charac	cteristics	ristics not applicable			
Recruitment		not applicable			
Ethics oversight		not applicable			
Note that full informa		poval of the study protocol must also be provided in the manuscript.			
•		the best fit for your research. If you are not sure, read the appropriate sections before making your selection.			
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Life sciences		ehavioural & social sciences			
TOT a reference copy of t	ne document with	in sections, see <u>nature.com/uocuments/in-reporting-summary-nat.pur</u>			
Life scier	ices stu	udy design			
All studies must dis	close 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 parallelisms 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, n=3 was selected in order to measure the distribution closer to the true distribution on the premise of cost saving. For in vivo experiments, 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 (Nature Communications, 2022, 13(1): 1-15).				
Data exclusions	No data were ex	xcluded from the analyses.			
Replication	We confirmed t	hat 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.				
We require information	on from authors a	Decific materials, systems and methods about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material,			
system or method list	ed 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 & exp	perimental s	ystems Methods			
n/a Involved in the study n/a Involved in the study					
Antibodies					
	aryotic cell lines				
	Palaeontology and archaeology				
	Clinical data				
Dual use research of concern					
1					

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s) HUVEC were obtained from Shanghai Qingqi Biotechnology Development Co., Ltd

Authentication HUVEC lines validation using short tandem repeat (STR) markers were performed by Shanghai Qingqi Biotechnology

Development Co., Ltd. Sample DNA was extracted using Axygen's genome extraction kit and amplified using a 10-STR amplification protocol (D4S2408 as the human locus). STR loci were detected on an ABI model 3730XL 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 lines (See ICLAC register)

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 KM mice (male, 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 \sim 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.

For instance, male rats were used in the pharmacokinetic experiment, and gender had no influence on the pharmacokinetic results.

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.