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	RNA-seq expression data for TCGA-LUSC was downloaded from UCSC Xena (https://xenabrowser.net/). Mutation data and clinical information were downloaded from the Genomic Data Commons (GDC) (https://portal.gdc.cancer.gov/). External validation cohorts include GSE15701123 and CPTAC-LUSC. Dependence scores of LUSC cell lines were downloaded from DepMap (https://depmap.org/portal/download/). All data was processed by R software.
Data analysis	randomForestSRC (v3.2.3), maftools (v2.16.0), ESTIMATE (v1.0.13), clusterProfiler(v4.8.2).

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

TCGA LUSC FPKM data were downloaded from the TCGA database via the UCSC Xena (https://xena.ucsc.edu/). GSE157011 was downloaded from the GEO database

(https://www.ncbi.nlm.nih.gov/gds/). The expression data and clinic information for CPTAC-LUSC were acquired from the supplementary files in Satpathy's study24. Dependence scores of LUSC cell lines were downloaded from DepMap (https://depmap.org/portal/download/). Drug response data for human cancer cell lines (CCLs) from the GDSC website (https://www.cancerrxgene.org/, access date: September 11, 2022) and CTRP; https://portals.broadinstitute.org/ctrp). The data used in this study are available from the corresponding author 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	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	N/A
Data exclusions	N/A
Replication	N/A
Randomization	N/A
Blinding	N/A

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	N-Cadherin Rabbit mAb (Abclonal, Cat No.A19083, Lot No.4000000371); E-Cadherin (24E10) Rabbit mAb (CST, Cat No.3195S, Lot No.15); Vimentin (D21H3) XP® Rabbit mAb (CST, Cat No.5741S, Lot No.8); TGF beta Receptor I (TGFBR1) Rabbit pAb (Abclonal, Cat No.A0708, Lot No.0030410201); β-Actin Mouse mAb (Abclonal, Cat No.AC004, Lot No.3600001426).
Validation	N-Cadherin Rabbit mAb was validated by Abclonal company using N-Cadherin knockout Hela cell lines. For details, please refer to the manufacturer's description: https://abclonal.com.cn/catalog/A19083; E-Cadherin (24E10) Rabbit mAb was validated by CST company using various human cell lines. For details, please refer to the manufacturer's description: https://www.cellsignal.cn/products/primary-antibodies/e-cadherin-24e10-rabbit-mab/3195; Vimentin (D21H3) XP® Rabbit mAb was validated by CST company using Vimentin knockout Hela cell lines. For details, please refer to the manufacturer's description: https://www.cellsignal.cn/products/primary-antibodies/vimentin-d21h3-xp-rabbit-mab/5741; TGF beta Receptor I (TGFBR1) Rabbit pAb was validated by Abclonal company using 293T cell lines. For details, please refer to the manufacturer's description: https://abclonal.com.cn/catalog/A0708; β-Actin Mouse mAb was validated by Abclonal company using several cell lines such as 293T, Hela and A549 cell lines. For details, please refer to the manufacturer's description: https://abclonal.com.cn/catalog/AC004.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The NCI-H520, H226 and HCC15 cell lines were obtained from American Type Culture Collection.
Authentication	N/A
Mycoplasma contamination	N/A
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	5-week-old female NOD-SCID mice
Wild animals	N/A
Reporting on sex	female
Field-collected samples	Animal care, housing, and procedures were performed following the Guide for the Care and Use of Laboratory Animals of the Shanghai Pulmonary Hospital Ethics Committee. Animals were randomized for this study and kept under specific pathogen-free (SPF) conditions at the Laboratory Animal Center of Shanghai Pulmonary Hospital (SYXK (Shanghai) 2022-0013).
Ethics oversight	This study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (K24-311).

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