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	Data collection is detailed in the methods. Data collection for imaging mass cytometry was performed using the Hyperion Imaging System CyTOF Software version 6.7.1014.
Data analysis	Prism 9.1.0 (GraphPad) was used for statistical analyses. Code for IMC cell segmentation was written in Matlab (version 7.10) and Python. The code is available for reviewers using the reference provided in the manuscript methods section.

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

The source data supporting findings in this study, including high-dimensional TIFF images, and associated clinical data have been deposited on Zenodo.

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	Lung cancer is the leading cause of cancer death for both males and females. Our study has equal representation of both male and female patient samples based on our 1:1 propensity score match (Table 1). Additionally, sex as a biological variable was accounted for in our analysis and subsequent correlations (Figure 1E). Our study examined fundamental biological variables without consideration of socio-cultural factors so gender was not considered.
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	Population characteristics can be found in Table 1. We obtained treatment-naive biobanked surgical resection and biopsy lung adenocarcinoma and lung squamous cell carcinoma tumor specimens. All biobanked primary lung tumor surgical specimens and biopsies of patients that had an assessment of the primary histological subtype of their tumor as well as appropriate consent were included.
Recruitment	Primary lung adenocarcinoma and lung squamous cell carcinoma patients that underwent surgical resection or biospy at the McGill University Health Centre from May 2014 to August 2023 signed a consent form for research through the McGill University Health Centre institutional biobank. This cohort was enriched for early-stage patients, therefore our findings may be biased towards these groups.
Ethics oversight	The protocol for human sample biobanking was approved (ethics, scientific and final) by the McGill University Health Centre cohort, the protocol was approved with IRB # 2014-1119 and 2019-5253.

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 sample size calculations are described in the methods section in the context of propensity score matching.
Data exclusions	All patients were included in the study following a 1:1 nearest neighbour propensity score matching with no replacement based on age, sex, stage, and smoking status.
Replication	Replication was not performed for the current study.
Randomization	Randomization was not applicable for the current study.
Blinding	Due to the retrospective nature of the clinical information presented, blinding was not applicable.

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: All antibodies used in this study were titrated for each lot. Information about all antibodies can be found in Supplementary Table 1.

Validation: Imaging mass cytometry: All imaging mass cytometry antibodies were validated. IMC antibodies were tested on multiple control tissues including tonsil, placenta, appendix, thymus, lung and tumor tissue for validation.

Plants

Seed stocks: *Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes: *Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication: *Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*