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	No software was used.
Data analysis	R studio Version 2023.12.1+402 (2023.12.1+402) was used for 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 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

Data utilized to create these models is available on Zenodo: https://doi.org/10.5281/zenodo.14538739. For the immunotherapy response analyses, data from Valero et al (DOI: 10.1038/s41588-020-00752-4) was used.

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	We utilized participant sex as a co-variate in our analyses. We analyzed data from both sexes. Sex was determined based on the sex of the patient within our institution's electronic medical record, which is usually assigned based on sex at birth. Sex-based analyses were performed by including sex as a co-variate within our mixed effects models.
Reporting on race, ethnicity, or other socially relevant groupings	We utilized race as a co-variate in our mixed effects model. The terms were provided by the participants.
Population characteristics	The median age of participants was 63 years old, with 54.4% being female. 77.8% were white, 8.4% were asian, and 6.3% were black. All patients had a diagnosis of a solid tumor that was genotyped with MSK-IMPACT. The majority of patients (71.6%) of patients received chemotherapy prior to their tumor sample analysis.
Recruitment	Patients were included if they had two or more tumor samples at MSK. Because the data for this review was taken from chart review, patients did not self select to participate in this study. However, it is possible that the patient population who seeks care at MSK (and who have 2+ tumor samples) are likely to have more aggressive tumors. Furthermore, this patient population has a high proportion of caucasian participants, which may not be representative of patient populations at hospitals internationally.
Ethics oversight	MSKCC IRB

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	Sample size was not pre-determined using any statistical analyses. Sample size was determined by how many patients fit our criteria of having at least two samples sequenced using MSK-IMPACT.
Data exclusions	Some data were excluded from our analyses, as demonstrated in supplemental figure 1. Patients with inadequate clinical information (e.g. no TMB score) were excluded as they would not have the necessary data to be included in our models. Patients with cancer types with different histologies were excluded since these tumors may have been two separate primary tumors, which would not fit with our goal of understanding tumor evolution within the same tumor. In order to ensure that tumor samples from the same tumor, we also only included tumors with at least one matching mutation, which would increase the likelihood of the samples being from the same cancer. We also excluded CNS tumors and unknown primary tumors.
Replication	We did not replicate these findings.
Randomization	No experimental groups, this was a retrospective study.
Blinding	Blinding was not relevant to our study as this was a retrospective study. Researchers also did not need to group participants as the main results of our study were objective measures from tumor sequencing (e.g. TMB, FGA, mutations).

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A