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 for data collection.
Data analysis	-All statistics were performed in R v4.2 and Python 3.9. -Kaplan-Meier survival analysis was performed using the R packages survminer v0.4.9 and survival v3.3.1. -Spearman's rank test was used to calculate correlation coefficients and raw p values between features measured on a continuous scale using the Python package scipy v.1.10.1, which were then adjusted for Bonferroni correction using the Python package statsmodels v0.13.5. -All machine learning models were built using the Python packages sklearn v1.2.1 and keras v2.8.0.

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 deidentified data required to replicate all analyses will be available online as a Supplementary Table at the time of publication.
All codes required to reproduce all the results in the paper are implemented in Python and R are available in GitHub: https://github.com/rootchang/ICBpredictor.

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	Statistics about sex are in Table 1.
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	Analysis was performed on 2881 patients from multiple cohorts. Primary and metastatic patients across a broad range of histologies and age ranges were selected based on whether they received the indicated treatments. Covariate characteristics are summarized in Table 1 including sex, age, systemic therapy history, cancer type and treatment type.
Recruitment	This study was done retrospectively and no patients were directly recruited.
Ethics oversight	The use of the patient data from the MSK1 and MSK2 cohorts was approved by the MSKCC institutional review board.

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	For cohorts other than MSK1 and MSK2, no sample size calculation were performed because they were available public data with predefined sample counts in each publication. The use of the patient data from MSK1 and MSK2 cohorts was approved by the MSKCC institutional review board. The research question (whether integrated machine learning model could predict patient outcomes with immune checkpoint blockade therapy) was specified before data collection began. Patients selected for this study were those with solid tumors diagnosed from 2014 through 2019 who received at least 1 dose of ICB at MSKCC. The sample size was based on all available patients.
Data exclusions	For the Vanguri et al. cohort, 1 sample with unknown primary tumor site was excluded. For the Kato et al. and Pradat et al. cohorts, samples were selected based on three criteria: (1) patients received immunotherapy, (2) their cancer types are included in the Chowell et al. cohort, and (3) TMB was measured. For the Ravi et al. cohort, samples without TMB measured were excluded. For the MSK1 and MSK2 cohorts, we excluded patients with a history of more than 1 cancer, those without a complete blood count within 30 days prior to the first dose of ICB, those enrolled in blinded trials, and cancer types with fewer than 25 cases. We excluded patients who received ICB in a neoadjuvant or adjuvant setting, and patients with unevaluable response.
Replication	We collected multiple datasets and used a part of data from one dataset as training set and used the other unseen data as test sets. The test sets were used to evaluate the model performance.
Randomization	No randomization was performed as this was a retrospective study.
Blinding	Blinding was not possible for the analysis as it was done retrospectively and there was no subjective analysis that was performed that could be biased by knowledge.

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