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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	Orbitrap Exploris 120 mass spectrometer (Thermo Fisher Scientific Inc.) was used to get metabolomics data. Compound Discover version 3.2 (Thermo Fisher Scientific Inc.) software was used to analyze the data from the aforementioned plasma samples, and the metabolites were structurally identified using the mzCloud (www.mzcloud.org/), mzVault (https://mytracefinder.com/tag/mzvault/), KEGG (www.kegg.jp/), HMDB (https://hmdb.ca/), and ChemSpider (www.chemspider.com) databases.
Data analysis	Data analysis was performed using publicly software: R (version 4.3.3), R package "MetNormalizer" (version 1.3.02), R package "Mfuzz" (version 2.62.0), R package "DMwR" (version 0.4.1), R package "glmnet" (version 4.1-8), R package "pROC" (version 1.18.5), R package "ggplot2" (version 3.5.2), R package "dplyr" (version 1.1.4), R package "rstatix" (version 0.7.2), R package "reshape2" (version 1.4.4), R package "VennDiagram" (version 1.7.3), KEGG analysis was using metaboanlyst (https://www.metaboanalyst.ca/).

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

Clinical information data are included in Supplementary Data 1. Raw metabolomics data are included in Supplementary Data 3. Batch-corrected metabolomics data are included in Supplementary Data 3. Detailed predicted values from the baseline prediction model (21-PM) for all samples are available in Supplementary Data 4. Metabolite details for the key metabolite panel determined by imaging outcomes are provided in Supplementary Data 5. Metabolite details for the key metabolite panel determined by pathological outcomes are provided in Supplementary Data 6. All source data for statistical analyses are provided with this paper.

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	The study documented gender distribution through self-reported identification (78 male and 30 female participants). Complete gender-related data are available in Table 1. Gender considerations were systematically incorporated throughout our manuscript. Subsequent analyses revealed no statistically significant differences in efficacy outcomes between R and NR (p=0.643 by chi-square test).
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
Population characteristics	All 154 enrolled patients provided written informed consent and subsequently underwent neoadjuvant immunochemotherapy(NAIC). Comprehensive demographic characteristics, including age, gender, and clinical staging, are documented in Supplementary Data 1.
Recruitment	This study recruited GC patients who received neoadjuvant immunochemotherapy (NAIC) treatment at The First Affiliated Hospital, Zhejiang University School of Medicine from October 30, 2021, to June 30, 2023. All these patients had completed at least one cycle of NAIC before surgery. Inclusion criteria as following: histologically confirmed gastric adenocarcinoma by endoscopic biopsy before the treatment initiation; (2) locally advanced GC, regionally unresectable or clinical stage IV disease according to AJCC/UICC 8th staging system, which was mainly evaluated by computed tomography (CT); (3) patients receiving chemotherapy combined with immune checkpoint inhibitors with or without trastuzumab.
Ethics oversight	The study was approved by the Ethics Committee of The First Affiliated Hospital, Zhejiang University School of Medicine (IIT20230426B-R1).

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	No statistical methods were performed for sample size determination. The study cohort comprised all available serum samples (n=369) collected from 108 gastric cancer patients undergoing neoadjuvant immunochemotherapy (NAIC) at The First Affiliated Hospital, Zhejiang University School of Medicine between October 30, 2021 and June 30, 2023.
Data exclusions	No data were excluded from the analyses
Replication	Based on stringent quality control measures demonstrating good stability (see Methods and Supplementary Figure 1), each patient's plasma sample underwent single-run mass spectrometric analysis. All statistical experiments presented in Figures 1-5 were independently conducted using metabolomic data derived from 369 plasma samples collected from the 108 neoadjuvant immunochemotherapy (NAIC) patients.

Randomization	The participants in this study were recruited consecutively. Samples were randomized and blinded before analyzing by LC-MS/MS. The participants were randomly stratified sampling into a discovery set and a test set in a 8:2 ratio.
Blinding	Each sample was labeled with a numeric ID whose annotation was kept blinded during data collection and analyses. Samples were randomized and blinded before analyzing by LC-MS/MS.

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	*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.*