nature research

Corresponding author(s): DBRP NCOMMS-20-48752

Last updated by author(s): Dec 17, 2020

Reporting Summary

Nature Research 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 Research 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	The DIA mass data was acquired using xCalibur3.1 from thermofisher scientific. The PRM data was acquired using Analyst2.0 from AB Sciex
Data analysis	Proteome Discoverer software suite 2.1; Skyline 3.6; SIMCA 14.0; MetaboAnalyst web tool; GraphPad Prism 7; R statistical environment

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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during and/or analysed during the current study are available in the ProteomeXchange Consortium (http://proteomecentral.proteomexchange.org) via the iProX partner repository under the accession number PXD022937. The data can be downloaded from the link (https://www.iprox.org/page/SSV024.html;url=16082593542151eNZ) with the password (Jqov). Additional data related to this paper may be requested from the authors.

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 sample-size calculation was performed in this study. We used all of available samples that we collected. Because the sample size is enough large, they are sufficient.
Data exclusions	For urine samples from colorectal cancer patients, we excluded 26.7% of patients with post-operation; a pathological diagnosis with nontubular adenocarcinoma (mucinous adenocarcinoma, melanoma, signet ring carcinoma, neuroendocrine carcinoma); accompanied with other benign or malignant tumors; abnormal renal functions; receiving chemoradiotherapy; a failure of quality control of PRM (without signals in more than 40% of peptides) or dot blot analysis (CV>20%). The enrollment criteria for healthy control subjects were as follows: (1) the absence of benign or malignant tumors; (2) a qualified physical examination finding no dysfunction of vital organs and (3) normal renal function and without albuminuria; (4) a failure of quality control of PRM (without signals in more than 40% of peptides) or dot blot analysis (CV>20%).
Replication	We performed DIA analysis on urine sample and further validated using PRM. These results were reproducible.
Randomization	The samples were analyzed randomly
Blinding	The investigators were grouped according to clinical diagnosis: CRC, CRC-LNM, CRC-LM and healthy controls, therefore no blinded analysis was performed.

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
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	anti-CORO1C (Cat. No. H00023603-M02, Abnova), anti-ARPC5 (Cat. No. sc-1666766, Santa Cruz Biotech., Dallas, TX, USA), anti-RAD23B (Cat. No. A1034, ABclonal Technology, Woburn, MA, USA), anti-GSPT2 (Cat. No. 12989-1-AP, Proteintech Group Inc., Rosemont, IL, USA) and anti-NDN (Cat. No. sc-1001224, Santa Cruz Biotech); Primary antibodies including integrin αV, integrin β1, FAK, SRC, AKT, ARHGEF7, p70S6K, 4EBP1, c-Jun, Ki67, phospho-FAK (Tyr397), phosphor-SRC (Tyr416), phosphor-AKT (Ser473), phosphor-p70S6K (Thr389), phosphor-4EBP1 (Thr37/46), phosphor-c-Jun (Ser63) and HA-tag were purchased from Cell Signaling Technology (Boston, MA, USA). Anti-Rac1 and anti-RCC2 were purchased from Abcam (Cambridge, MA, USA). Anti-JNK and anti-phospho-JNK were purchased from Santa Cruz Biotech (Dallas, TX, USA). Anti-β-actin was purchased from Proteintech Groups Inc. (Chicago, IL, USA). Anti-CORO1C (Cat No. TA349821; OriGene Technologies, Inc, Rockville, MD, USA) was used for immunohistochemical staining.
Validation	All primary antibodies were used according to the manufacturer's instructions for Western blotting (including dot blotting) and IHC.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	The human colorectal cancer cell lines DLD1, HCT116 were obtained from the National Infrastructure of Cell Line Resource

	(Beijing, China). HCT8 were purchased from the American Type Culture Collection (Rockville, MD, USA).
Authentication	All cell lines were authenticated by short tandem repeat (STR) profiling analysis.
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None of the cell lines used are listed in the ICLAC register.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Five to six-week-old female BALB/c nude mice were purchased from Beijing Huafukang Bioscience Inc. (Beijing, China).
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All experimental procedures were approved by the Institutional Animal Care and Use Committee of Cancer Hospital, Chinese Academy of Medical Sciences (No. NCC2018A016).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Human research participants

Policy information about studies involving human research participants

Population characteristics	The detailed clinical information of urine samples is shown in Table 1. The age and sex distributions were balanced among the healthy controls and three cohorts of colorectal cancer patients. Histological differentiation grade, tumor location, CEA level and TNM staging were significantly different among the three CRC patient cohorts. Notably, there were basically no statistically significant differences in these clinical parameters among the three subgroups within each cohort.
Recruitment	For urine samples, a total of 359 CRC patients were recruited from the Cancer Hospital, Chinese Academy of Medical Sciences from January 2015 to October 2018. And 298 urine samples from healthy controls were obtained from the Health Medical Center of the Cancer Hospital and PLA General Hospital from August 2014 to October 2018.
Ethics oversight	This study was approved by the Ethics Committee of Institute of Basic Medical Sciences and Cancer Hospital, Chinese Academy of Medical Sciences (No. 047-2019, Beijing, China)

Note that full information on the approval of the study protocol must also be provided in the manuscript.