

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 Flow cytometry data was analyzed using CytExpert (V2.4).

Data analysis

Flow cytometry
All flow cytometry analysis was conducted on CytoFlex (Beckman), and the data was analyzed using Flow Jo (V10).

Pathway analysis
Pathway analysis was conducted with DAVID website

Statistical analysis
Data were analyzed using GraphPad Prism 8 software. Unpaired Student's t-test was used to analyze differences between two groups. Comparisons among multiple groups were analyzed using one-way ANOVA. The results are presented as means \pm Standard Error of Mean. All boxplots indicate median (center), 25th and 75th percentiles (bounds of box), and minimum and maximum (whiskers). $P < 0.05$ was considered statistically significant.

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 sequence data generated in this study have been deposited in the GEO database under the accession number GSE206502 and GSE249999. The remaining data are available within the Article, Supplementary Information or Source Data file. Source data 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	Male and female
Reporting on race, ethnicity, or other socially relevant groupings	No selection bias
Population characteristics	Eligible patients were 18 years or older diagnosed with hepatocellular carcinoma, Child-Pugh A class liver function, an Eastern Cooperative Oncology Group performance status of 0 to 2, no previous treatment for hepatocellular carcinoma, at least 1 measurable lesion according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and adequate organ function (white blood cell count $\geq 3.0 \times 10^9/L$, absolute neutrophil count $\geq 1.5 \times 10^9/L$, platelet count $\geq 75 \times 10^9/L$, aspartate transaminase and alanine transaminase $\leq 5 \times$ upper limit of the normal, creatinine clearance rate of $\leq 1.5 \times$ upper limit of the normal, and left ventricular ejection $\geq 45\%$).
Recruitment	Tissue samples for screening were prospectively obtained from HCC patients who received HAIC at the Sun Yat-sen University Cancer Center, Guangzhou, China, from 2020 to 2021. Samples were divided into Response and Non-Response groups after HAIC treatment evaluated by mRECIST criterion. Patients diagnosed with advanced HCC at the Sun Yat-sen University Cancer Center were enrolled for the prospective study. Tissue samples were prospectively obtained from HCC patients who received immunotherapy through needle biopsy. Written informed consent was obtained from each patient.
Ethics oversight	the Ethics Committee of Sun Yat-Sen University Cancer Center

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 used to predetermine sample size. Sample size are based on a lot of previous publications and our previous experience, which is the most optimal to generate statistically significant results. All in vitro experiments were carried out at least three times. For in vivo experiment, cohorts of 6-7 were used (stated in the figure legend) based on previous experiments
Data exclusions	No data were excluded from the analysis.
Replication	All the experiments were replicated. Three independent experiments were carried out and each experiment was performed with at least three repeats.
Randomization	All cells and the animals were randomly allocated to experimental groups. Cells were allocated into sg-PRMT3 group and sg-NC group randomly. C57BL6 mice were allocated into treatment group and control group randomly. Patients involved in this study were not divided randomly.
Blinding	For other experiments, the investigators were not blinded to group allocation, because the experimental design was complicated, the researchers were limited, and blinding feasibility was poor.

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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used

anti-PRMT3 (Abcam, Ab191562, 1:2000), anti-PRMT3 (Proteintech, 17628-1-AP, 1:1000), anti-HSP60 (Proteintech, 15282-1-AP, 1:1000), anti-ADMA (Cell Signaling Technology, 13522S, 1:1000), anti-FLAG (Cell Signaling Technology, 14793, 1:1000), anti-STAT1 (Proteintech, 10144-2-AP, 1:1000), anti-STING (Proteintech, 19851-1-AP, 1:1000), anti-p-STING (Cell Signaling Technology, # 19781S, 1:1000), anti-TBK1 (Proteintech, 28397-1-AP, 1:1000), anti-p-TBK1 (Cell Signaling Technology, 5483S, 1:1000), anti-IRF3 (Proteintech, 11312-1-AP, 1:1000), anti-p-IRF3 (Cell Signaling Technology, 29047S#, 1:1000), anti-GAPDH (Proteintech, 60004-1-Ig, 1:2000), anti-mouse IgG (Cell Signaling Technology, 7076S, 1:3000), anti-rabbit IgG (Cell Signaling Technology, 7074S, 1:3000), GZMB (Invitrogen, 17-8898-82, 2.5 ul), IFN γ (BD Horizon, 563376, 2.5 ul)

Validation

Anti-GAPDH (WB) (Proteintech, 60004-1-Ig, 21002053) is validated in the manuscript and validated by the manufacturer in several cell lines.
 Anti-PRMT3 (WB, IHC, IF, IP) (Abcam, Ab191562, 1001885-4) and anti-PRMT3 (Proteintech, 17628-1-AP, 1:1000) is validated in the manuscript for western blot assay, IP assay, IF assay and IHC assay, and also be validated by the manufacturer (Abcam).
 Anti-FLAG (WB, IP) (Cell Signaling TECHNOLOGY, #14793, 7) is validated in the manuscript in PLC-8024 cells and validated by the manufacturer in HEK293 cells.
 Anti-ADMA (WB) (Cell Signaling TECHNOLOGY, 13522S, 4) is validated in the manuscript for western blot assay, and also be validated by the manufacturer in MCF7 cells.
 Rabbit IgG (IP) (Proteintech, B900610, 20010170) is validated in the manuscript for IP assay in PLC-8024, Hepa1-6 and HepG2 cells, and has been extensively validated by the field.
 Anti-HSP60 (Proteintech, 15282-1-AP, 1:1000) is validated in the manuscript and validated by the manufacturer in several cell lines.
 anti-STAT1 (Proteintech, 10144-2-AP, 1:1000), anti-STING (Proteintech, 19851-1-AP, 1:1000), anti-p-STING (Cell Signaling Technology, # 19781S, 1:1000), anti-TBK1 (Proteintech, 28397-1-AP, 1:1000), anti-p-TBK1 (Cell Signaling Technology, 5483S, 1:1000), anti-IRF3 (Proteintech, 11312-1-AP, 1:1000) and anti-p-IRF3 (Cell Signaling Technology, 29047S#, 1:1000) is validated in the manuscript and validated by the manufacturer in several cell lines.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

PLC-8024 (JNO-206), HepG2 (JNO-10-14-3), HEK293T (JNO-H0488) and Hepa1-6 cells (JNO-M0144) were purchased from the Guangzhou jenniobio Biotechnology with STR (short tandem repeat) appraisal certificates.

Authentication

All the cells were authenticated using short-tandem repeat (STR) profiling.

Mycoplasma contamination

All cell lines were tested negative for mycoplasma contamination.

Commonly misidentified lines (See [ICLAC](#) register)

No commonly misidentified cell lines were used in the study.

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals

Male, four-week-old, C57BL6 and BALB/C nude mice were purchased from the GUANGDONG MEDICAL LABORATORY ANIMAL CENTER. All mice were kept under specific-pathogen free conditions in Animal Facility of Sun Yat-sen University Cancer Center. They were kept in an animal room with a 12-hour light-dark cycle at a temperature of 20-22 °C with 40-70% humidity.

Wild animals

No wild animals were used in the study.

Reporting on sex	Male
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	All animal procedures were approved by Institutional Animal Care and Use Committee (IACUC) of Sun Yat-sen University Cancer Center.

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

Flow Cytometry

Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	The tumors were digested according to the manufacturer's instructions. T cells were stained with fluorochrome-conjugated antibodies according to the manufacturer's instructions and then analyzed by fluorescence-activated cell sorting (FACS). T cells under analysis were stained with surface markers, fixed, and permeabilized with IntraPrep reagent (Beckman Coulter), and finally stained with intracellular markers, GZMB (Invitrogen, 17-8898-82), IFNgamma(BD Horizon, 563376).
Instrument	All flow cytometry analysis was performed on Flow Jo(V.10).
Software	FlowJo software and CytExpert software was used to analyze the flow cytometry data.
Cell population abundance	No cell sorting was conducted in the study.
Gating strategy	The gating strategy that was used is presented in the Supplementary Figures

- Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.