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Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Cell images were collected with with a Nikon Eclipse Ti2 with NIS Elements Imaging Software (Version 5.02).
Data analysis	Images analyzed with ImageJ (Version 1.51i). IHC data was analyzed using the IHC Profiler ImageJ plugin (no version number given). Tophat2 (version 2.1.1), exomePeak R/Bioconductor package (version 3.7), Homer (version 4.9) , DAVID (version 6.8), and Cufflinks (version 2.2.1) were used to analyze the RNA-seq and m6A-seq data.

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/reviewers upon request. 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 RNA-seq and m6A-seq data generated by this study have been deposited in the GEO database under the accession number GSE93911. A summary of the m6A

peaks identified by the m6A-seq experiments in the patient samples and cell lines can be found in Supplementary Tables 3 and 4. The human data for high grade serous ovarian cancer and pancreatic adenocarcinoma, as well as some data for endometrial cancer, were derived from the TCGA Research Network: http://cancergenome.nih.gov/. Source data for Figs 1-7 and Supplementary Figs 1-7 are provided in Supplementary Table 5. Unprocessed immunoblot scans are presented in Supplementary Fig. 8. All other data supporting the findings of this study are available from the corresponding author on reasonable request.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	In general, no statistical methods were used to predetermine sample size. For the animal experiments, sample size was determined based on previous experience with intraperitoneal models of ovarian cancer and literature reports. For human samples, samples were collected until we felt the sample size was sufficient to give reliable estimates. For cell and biochemical data, we aimed to collect data from three biological replicates when possible.
Data exclusions	No data were excluded from analysis.
Replication	Results were confirmed in at least three biological replicates for each experiment unless otherwise stated.
Randomization	Samples/mice/human subjects were not randomized. Controlling for covariates was unnecessary for the human samples as all comparisons were between paired tumor/normal samples collected from the same patient. We did not control for covariates in the animal experiments because all animals were the same age and sex and were purchased from the same supplier.
Blinding	For the animal experiments, investigators were blinded to group allocation during intraperitoneal injections and when assessing outcome. For the other experiments on human samples and cell lines, blinding was not performed due to feasibility.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☐	☒ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique materials used are available from the authors by request.

Antibodies

Antibodies used	(also see Supplementary Table 1) rabbit anti-METTL3 WB 1:2000 Abcam ab195352 EPR18810 rabbit anti-METTL3 IHC 1:200 ProteinTech 15073-1-AP rabbit anti-METTL14 WB 1:2000 Sigma HPA038002 rabbit anti-PHLPP2 WB/IHC 1:1000/1:100 Abcam ab71973 rabbit anti-phospho-mTOR(S2481) WB 1:2000 Abcam ab137133 EPR427(N) rabbit anti-phospho-mTOR(S2481) IHC 1:100 Cell Signaling Technologies 49F9

rabbit anti-phospho Akt(S473) WB 1:3000 Cell Signaling Technologies Cat#4060S D9E
rabbit anti-phospho Akt(T308) WB 1:3000 Cell Signaling Technologies Cat#9275S
rabbit anti-AKT WB 1:3000 Cell Signaling Technologies Cat#9272S
goat HRP-anti-GAPDH WB 1:10000 ProteinTech HRP-60004
mouse HRP-anti-Flag WB 1:1000 Sigma A8592 M2
rabbit anti-phospho Tuberin/TSC2(Thr1462) WB 1:1000 Cell Signaling Technologies Cat#3617T 5B12
rabbit anti-phospho PRAS40(Thr246) WB 1:1000 Cell Signaling Technologies Cat#2997T C77D7
rabbit anti-phospho FoxO1(S256) WB 1:1000 Cell Signaling Technologies Cat#9461T
rabbit anti-phopho p27(T157) WB 1:1000 Abcam Ab85047
rabbit anti-Rictor WB 1:1000 Cell Signaling Technologies Cat#2140S
rabbit anti-m6A IP 1:100 Synaptic Systems Cat#202003
rabbit anti-YTHDF1 IP 1:100 ProteinTech 17479-1-AP
rabbit anti-YTHDF2 IP 1:100 Aviva ARP67917_P50
rabbit anti-PRR5 IHC 1:200 ProteinTech 17948-1-AP
rabbit anti-PRR5L IHC 1:200 LSBio LS-C144364-50
donkey anti-rabbit lgG-HRP WB 1:5000 Santa Cruz Sc-2313

Validation

Validation information is provided in Supplementary Table 1. In general, we relied on data provided by the manufacturers for validation as well as references in publications.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

The HEC-1-A cells used in this study were purchased from ATCC (HTB-112). The RL95-2 cells used in this study were purchased from ATCC (CRL-1671). The T-HESCs used in this study were purchased from ATCC (CRL-4003).

Authentication

The HEC-1-A cell line was authenticated with STR profiling (IDEXX Cell Check 9 Plus). The other cell lines were not authenticated.

Mycoplasma contamination

Cells were confirmed to be free of mycoplasma (IDEXX STAT-Myco).

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals

For all animal experiments, 5 week old female athymic nude mice (Foxn1nu) purchased from Harlan were used

Wild animals

The study did not involve wild animals.

Field-collected samples

The study did not involve filed-collected samples.

Human research participants

Policy information about studies involving human research participants

Population characteristics

Information about the patient sex, age, and tumor characteristics are given in Supplementary Table 2. All patients were female and ranged in age from 38-83 and presented with endometrioid endometrial cancer of various stages and grades (with one patient diagnosed with proliferative endometrium rather than endometrial cancer). Controlling for covariates was not necessary as the analyses compared tumor and adjacent normal tissues taken from the same patient.

Recruitment

Participants were recruited from the pool of patients at Wuhan University and the University of Chicago. There may be self selection biases based on individuals who are able to seek care at these institutions. The sample should be representative of the populations served by these institutions