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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	ChIP-seq were performed on Illumina NovaSeq 6000. RNA-seq were performed on Illumina NovaSeq 6000. Western blots were acquired using Bio-Rad ChemiDoc Imaging System. Olympus BX53 or Zeiss LSM 880 microscopes were used for image acquisition.
Data analysis	For RNA-seq analyses, raw counts were filtered and trimmed using fastp software (version 0.12.5) to obtain clean data with default settings.The clean data were subsequently mapped to the human reference genome (GRCh38, hg38) using STAR aligner (version 2.7.0f) (Ref 3). The transcript abundance was calculated employing RSEM (ref 4).Differential expression analyses were performed using DEseq2 (version 3.14.0) with a significance threshold of p value ≤ 0.05 in the R statistical environment (version 3.5). Gene Set Enrichment Analysis (GSEA) was performed via GSEA software (version 4.0.3) with default parameters. For ChIP-seq analyses, the clean data were generated from fastp and mapped against the human reference genome (GRCh38, hg38) using Bowtie2 (version 2.3.2) under default settings. The alignments were sorted and indexed using samtools (version 1.14). Peaks were identified using MACS2 (version 2.1) and annotated with ChIPseeker (version 1.14.2). Superenhancer regions were obtained using ROSE with H3K27ac peaks . DNA motif analysis was performed using Homer (homer.salk.edu) with default settings.(51) Bigwig files produced by deepTools were visualized in Integrative Genomics Viewer (version 2.4.19).

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

RNA-seq and ChIP-seq data have been deposited in the Genome Sequence Archive in National Genomics Data Center, China National Center for Bioinformation/ Beijing Institute of Genomics, Chinese Academy of Sciences (GSA-Human: HRA008718) that are publicly accessible at https://ngdc.cncb.ac.cn/gsa-human. Gene expression data of breast cancer cell lines (T47DP and T47DR) can be found in the GEO archive under accession numbers GSE128056. All data supporting the findings of this study are available from the corresponding author upon request.

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	Patients diagnosed with EC in this study were recruited from the Sixth Affiliated Hospital, Sun Yat-sen University (Guangzhou, China). ALL the EC patients are female. No study design involved sex- and gender-based analysis in this study.
Reporting on race, ethnicity, or other socially relevant groupings	Patients diagnosed with EC in this study were recruited from the Sixth Affiliated Hospital, Sun Yat-sen University (Guangzhou, China). No study design involved race, ethnicity and racism this study.
Population characteristics	The mean age of patients recruited in this study was 56.69 ± 10.40 years old at the time of surgery.The 2023 FIGO Stage of these EC patients ranged from stage 1 to stage 4.
Recruitment	Patients diagnosed with EC in this study were recruited from the Sixth Affiliated Hospital, Sun Yat-sen University (Guangzhou, China). All patients were chemotherapy-naïve, and tumor tissues were collected from surgical specimens. The pathological features were assessed according to the 2023 International Federation of Gynecology and Obstetrics (FIGO) staging system.
Ethics oversight	The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB, 2024ZSLYEC-150). All participated patients were fully informed, followed by documentation in a written, signed, and dated informed consent form.

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 in vivo experiments, the number of mice assigned to each treatment group was selected to provide sufficient statistical power to discern significant differences.
Data exclusions	No data were excluded from analysis.
Replication	Numbers of attempts of replication were described in the manuscript.
Randomization	When tumors reached 70mm3, randomization was performed by equally dividing tumor-bearing mice of similar tumor burden into control and other treatment groups.
Blinding	Patient samples were performed in a blinded fashion when possible. Individuals who processed the patient samples for sequencing were blinded for the patient informations. The pathological features of EC patients were evaluated according by two independent pathologists who were blinded for the patient informations.

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

Antibodies

Antibodies used

Antibodies used in western blot
15910-1-AP, ALDH1A1, Proteintech
60004-1-lg , GAPDH, Proteintech
9542S , PARP1, CST
5625S , Cleaved-PARP1, CST
14220S, Caspase 3, CST
9664S, Cleaved- Caspase 3, CST
ab32063, ERα, abcam
ab275745, RARα, abcam
ab16663 , CCND1, CST

Antibodies used in IP
ab275745 , RARα, abcam
ab32063 , ERα, abcam
ab4729 , H3K27ac, abcam
13440S , BRD4, CST
2629S , Rpb1, CST

Antibodies used in IF and IHC
15910-1-AP, ALDH1A1, Proteintech

Validation

All antibodies purchased were validated by manufacturer for the relevant application. We have validated the antibodies by molecular weighs of target protein by western blot. In the case of ALDH1A1(Proteintech 15910-1-AP), ERα (abcam ab32063) , RARα (abcam ab275745) and CCND1(abcam ab16663)were also validated using siRNA knockdown and western blot.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	All commercial cell lines were purchased from Meisen Cell Technology Co., Ltd (Zhejiang, China).
Authentication	HIEC-1-A, HIEC-1-B, RL95-2, KLE, Ishikawa, MFE-296, AN3 CA, MCF7, T47D and SNG-M
Mycoplasma contamination	All cell lines were confirmed to be free of mycoplasma contamination every month.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used in this 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	female athymic BALB/c nude mice (5-8 week old), female NOD-SCID mice (5-8 week old)
Wild animals	This study did not involve wild animals.
Reporting on sex	All animal studies were conducted in female mice. ALL the EC patients are female. No study design involved sex- and gender-based

analysis in this study.

Field-collected samples: This study did not involve samples collected from the field.

Ethics oversight: All animal studies were conducted in compliance with animal protocols approved by the Animal Care and Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University and followed the National of Health Guidelines on the Care and Use of Animals (IACUC-2022112101).

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

Plants

Seed stocks: This study did not involve plants.

Novel plant genotypes: This study did not involve plants.

Authentication: This study did not involve plants.

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☒ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.

ChIP-seq data have been deposited in the Genome Sequence Archive in National Genomics Data Center, China National Center for Bioinformation/Beijing Institute of Genomics, Chinese Academy of Sciences (GSA-Human: HRA008718) that are publicly accessible at https://ngdc.cncb.ac.cn/gsa-human.

Files in database submission

EC53-H3K27ac-chip
EC55-H3K27ac-chip
EC56-H3K27ac-chip
EC57-H3K27ac-chip
EC58-H3K27ac-chip
EC65-H3K27ac-chip
EC67-H3K27ac-chip
EC68-H3K27ac-chip
EC76-H3K27ac-chip
EC77-H3K27ac-chip
EC80-H3K27ac-chip
EC81-H3K27ac-chip
EC82-H3K27ac-chip
EC83-H3K27ac-chip
EC53-Input-chip
EC55-Input-chip
EC56-Input-chip
EC57-Input-chip
EC58-Input-chip
EC65-Input-chip
EC67-Input-chip
EC68-Input-chip
EC76-Input-chip
EC77-Input-chip
EC80-Input-chip
EC81-Input-chip
EC82-Input-chip
EC83-Input-chip
HEC-1-A-H3K27ac-chip
HEC-1-A-Input-chip
HEC-1-A-H3K4me1-chip
HEC-1-AR-H3K27ac-chip
HEC-1-AR-Input-chip
HEC-1-AR-H3K4me1-chip

HEC-1-A-BRD4-chip
HEC-1-A-TF-Input-chip
HEC-1-A-ER-chip
HEC-1-A-RNAPII-chip
HEC-1-A-RAR-chip
HEC-1-AR-BRD4-chip
HEC-1-AR-TF-Input-chip
HEC-1-AR-ER-chip
HEC-1-AR-RNAPII-chip
HEC-1-AR-RAR-chip

Genome browser session
(e.g. UCSC)

https://ngdc.cncb.ac.cn/gsa-human

Methodology

Replicates

H3K27ac, H3K4me1,RARα , ERα, RNAPII and BRD4 ChIP-seq were performed in one replicates.

Sequencing depth

Sample: uniquely mapping reads
1153_H3K27AC 499402761155_H3K27AC 562712201156_H3K27AC 580413211157_H3K27AC 527126151158_H3K27AC 595247111165_H3K27AC 506132141167_H3K27AC 596392091168_H3K27AC 576094411169_H3K27AC 516750081180_H3K27AC 568561811181_H3K27AC 694814511182_H3K27AC 573757921183_H3K27AC 551618601176_H3K27AC 699880741177_H3K27AC 51320772

Antibodies

ab275745 , RARα, abcam
ab32063 , ERα, abcam
ab4729 , H3K27ac, abcam
13440S , BRD4, CST

Peak calling parameters

Peaks were called by MACS2 (version 2.1) using default settings and annotated with ChIPseeker (version 1.14.2).

Data quality

We require at least 20,000 peaks with an p value of 0.05 in histone markers in ChIP-seg.

Software

Bowtie2 (version 2.3.2), samtools version 1.14, MACS2 (version 2.1), ChIPseeker (version 1.14.2), Integrative Genomics Viewer (version 2.4.19)