nature portfolio

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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	Image Studio v5.2 (LI-COR), IVIS Spectrum (Perkin Elmer), CytoFLEX Flow Cytometer (Beckman Coulter), BD FACSCanto-II (BD Biosciences)
Data analysis	ENCODE Transcription Factor and Histone ChIP-Seq processing pipeline (https://github.com/ENCODE-DCC/chip-seq- pipeline2), SAMtools v1.9, Bowtie2 v2.3.4.3, MACS2 v2.2.4, cutadapt v2.5, Picard Tools v2.20.7, Bedtools v2.29.0, Homer annotatePeaks v4.11, NGS plot v2.63.1, ATAC-seq pipeline (https://github.com/ENCODE-DCC/atac-seq-pipeline), Proteome Discoverer software (v2.4, Thermo Scientific), EpiProfile 2.0 software, LSF-RNAseq Pipeline from Diderote (https://github.com/diderote/LSF-RNAseq), cutadapt v2.3, DESeq2 v1.18.1 and R (version 3.4.1), gsea- 3.0.jar, Ruvseq v1.12.0. FlowJo software (FlowJo, LLC) v10.6.2

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

All raw and processed ChIP–seq, ATAC-seq, CUT&RUN and RNA-seq data have been deposited in the NCBI Gene Expression Omnibus under accession number GSE168644.Mass spectrophotometry raw files were deposited on the public repository Chorus (chorusproject.org) with the project number 1763.

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. Sample sizes were determined based on previous studies using similar techniques to enable statistical analysis.
Data exclusions	No data were excluded
Replication	Experiments were done at least in 3 biological replicates. See methods and figure captions.
Randomization	Mice were randomly divided into treatment group.
Blinding	For experiments others than animal studies investigators were not blinded to allocation during experiments and outcome assessment. However, two different individuals separately reproduced each other results for key experiments. For mouse studies, researchers were blinded to treatment group during data collection (mouse/tumor assessment and measurement, Ki67 staining)

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

Antibody	Source	Identifier	Application	WB dilution/ChIP amount	Clone	Lot
Rabbit polyclonal Anti-KDM1/LSD1 antibody ChIP grade	abcam	ab17721	western and ChIP	1:1000/10ug	N/A	GR332777379-1
Rb polyclonal anti CoREST	EMD-Millipore	07-455	WB and ChIP	1:1000/10ug	N/A	3230538
Rb polyclonal anti ER alpha	abcam	ab3575	WB and ChIP	1:1000/5ug	N/A	
Rb polyclonal Anti-FOXA1 antibody	abcam	ab23738	WB and ChIP	1:1000/5ug	N/A	
Rb polyclonal to c-JUN	abcam	ab31419	WB and ChIP	1:1000/10ug	N/A	GR03661531
Rb monoclonal Rpb1 NTD	Cell Signaling Technology	14958S	ChIP	5ug	(D8L4Y)	
Rb Anti-Histone H3 (acetyl K27) antibody - ChIP Grade	abcam	ab4729	ChIP	2ug	N/A	GR306603-1
Rabbit monoclonal SMARCC1/BAF155	Cell Signaling Technology	11956S	WB and ChIP	1:1000/10ug	D7F8S	4
Normal Rabbit IgG Polyclonal Antibody control	EMD-Millipore	12-370	IP	10ug	N/A	3281600
Rabbit polyconal Anti-Histone H3 antibody Nuclear Marker and ChIP Grade	Abcam	ab1791	WB	1:4000	N/A	GR300978-2
Rabbit polyconal Histone H3K27me3 antibody	Active Motif	39155	WB	1:1000	N/A	10918019
Rabbit polyconal Histone H3K4me2 antibody	Active Motif	39141	WB and ChIP	1:1000/2ug	N/A	01008001
Rabbit monoclonal antibody to HDAC1	Cell Signaling Technology	34589	WB	1:1000	D5C6UXP®	1
Rabbit IgG CUT&RUN Negative Control Antibody	EpiCypher	13-0042K	CUT&RUN	0.5ug	N/A	
Rabbit polyclonal H3K27ac Antibody - ChIP-seq Grade	Diagenode	C15410196	CUT&RUN	0.5ug	N/A	
Rabbit polyclonalAnti-Histone H3 (mono methyl K4) antibody - ChIP Grade	abcam	ab8895	WB and CUT&RUN	1:1000/0.5ug	N/A	
Rabbit monoclonal Anti-Vimentin antibody- Cytoskeleton Marker	abcam	ab92547	WB	1:1000	EPR3776	GR3258719-26
Mouse Monoclonal Anti-Vinculin antibody	Sigma-Aldrich	V9131	WB	1:400	hVIN1	
Mouse anti E-cadherin Monoclonal Antibody	Invitrogen	13-1700	WB	2:1000	HECD-1	
Rabbit monoclonal anti SUZ12	Cell Signaling Technology	3737	WB	1: 1000	D39F6 XP®	6
Rabbit monoclonal anti Ezh2	Cell Signaling Technology	5246	WB	1:1000	D2C9 XP®	9

Mouse monoclonal p44/42 MAPK (Erk1/2)	Cell Signaling Technology	4696	WB	1:1000	L34F12	23
Rabbit monoclonal Phospho-p44/42 MAPK (Erk1/2) (Thr202/Tyr204)	Cell Signaling Technology	4370	WB	1:1000	D13.14.4E XP®	24
Rabbit monoclonal Anti-DPF2/REQ antibody	abcam	ab134942	WB	1:1000	EPR9206(B)	GR3275112-4
Rabbit monoclonal to ARID1A/BAF25	Cell Signaling Technology	12354	WB	1:1000	D2A8U	3
Rabbit monoclonal Anti-MBD3 antibody ChIP Grade	abcam	ab157464	WB	1:1000	EPR9913	GR117405-18
Rabbit policlonal ARID2 Antibody	Bethyl Laboratories	A302-229A	WB	1:1000	N/A	2
Rabbit policlonal anti 53BP1	Novus Biological	NB100-304	IF	1:1000		
Mouse Anti-phospho-Histone H2A.X (Ser139) Antibody	Millipore Sigma	05-636	IF	1:1000	JBW301	
RAD51	B-Bridge International	70-001	IF	1:1000		
Rabbit monoclonal anti STAT1	Cell Signaling Technology	14994	WB	1:1000	D1K9Y	4
Rabbit monoclonal Anti-LSD2 / AOF1 antibody	abcam	ab193080	WB	1:1000	EPR18508	
Rabbit monoclonal Phospho-Stat1 (Tyr701)	Cell Signaling Technology	9167	WB	1:1000	58D6	
APC anti-human CD24	BioLegend	311118	FACS	1ug	ML5	
PE anti-mouse/human CD44	BioLegend	103024	FACS	1ug	IM7]	
488 Fluor Donkey anti-Rabbit antibody	Thermo Fischer	A-21207	IF	1:1000	RRID: AB_141637	
594 Fluor Goat anti-Mouse antibody	Thermo Fischer	A-11020	IF	1:1000	RRID: AB_2534087	
Ki-67 Rabbit mAb (Mouse Preferred; IHC Formulated)	CST	12202	IF	1:400	D3B5	6

Validation

-anti KDM1-LSD1, KO validated, 197 citations https://www.citeab.com/antibodies/735963-ab17721-anti-kdm1-lsd1-antibody-nuclear-marker?des=39c7b10a7299d7ff
-anti CoREST, knockdown validated, 56 citations https://www.citeab.com/antibodies/221362-07-455-anti-corest-antibody?des=fc25c76d2aca07e4
-anti ER alpha, 23 citations https://www.citeab.com/antibodies/728748-ab3575-anti-estrogen-receptor-alpha-antibody?des=1ba4e0df1ced2e69
- anti FOXA1, KO validated, 134 citations https://www.citeab.com/antibodies/731175-ab23738-anti-foxa1-antibody?des=0660c7fee8213b22
- anti c-JUN knockdown validated in this study, 67 citations https://www.citeab.com/antibodies/715369-ab31419-anti-c-jun-antibody?des=d0533d8f7085ac32
-anti Rpb1 NTD, 31 citations https://www.citeab.com/antibodies/2455386-14958-rpb1-ntd-d8l4y-rabbit-mab?des=ebf5d646d583df7a
-anti H3K27ac ,1478 citations https://www.citeab.com/antibodies/778149-ab4729-anti-histone-h3-acetyl-k27-antibody-chip-g?des=c7a4376276c98cee
-anti SMARCC1, 27 citations https://www.citeab.com/antibodies/701347-11956-smarcc1-baf155-d7f8s-rabbit-mab?des=99fe689847d1fdac
-Normal rabbit IgG, 567 citations https://www.citeab.com/antibodies/222152-12-370-normal-rabbit-igg?des=d312535c25aff0e7
-anti H3, 3803 citations https://www.citeab.com/antibodies/763778-ab1791-anti-histone-h3-antibody-nuclear-marker-and?des=19d0e7a705c29e47
-anti H3K27me3, orthogonal validation, 250 citations, https://www.citeab.com/antibodies/82315-39155-histone-h3k27me3-antibody-pab?des=61d048528c0ebd33
- anti H3K4me2 , orthogonal validations, 52 citations, https://www.citeab.com/antibodies/82308-39141-histone-h3k4me2-antibody-pab?des=01abb281f0b852a5
-anti HDAC1, 40 citations, https://www.citeab.com/antibodies/4008726-34589-hdac1-d5c6u-xp-rabbit-mab?des=9bd5e9a685038130
-anti H3K27ac Diagenode, 90 citations, https://www.citeab.com/antibodies/3323242-c15410196-h3k27ac-antibody-chip-seq-grade?des=f58387a2db876612
-anti H3K4me1, 908 citations, https://www.citeab.com/antibodies/778274-ab8895-anti-histone-h3-mono-methyl-k4-antibody-ch?des=77b0107c2c9244cf
-anti Vimentin, KO validated, 1027 citations, https://www.citeab.com/antibodies/759376-ab92547-anti-vimentin-antibody-epr3776-cytoskelet?des=9e05cf3ba7ee3bc3
-anti vinculin, 1441 citations, https://www.citeab.com/antibodies/1038439-v9131-monoclonal-anti-vinculin-antibody-produced-in?des=0813b01714838b11
-anti E-cadherin, 274 citations, https://www.citeab.com/antibodies/12179183-13-1700-e-cadherin-monoclonal-antibody-hecd-1?des=6a098bf300445b6d
-anti SUZ12, 148 citations, https://www.citeab.com/antibodies/123399-3737-suz12-d39f6-xp-rabbit-mab?des=9a52004f8505dff4
-anti EZH2, orthogonal validation, 411 citations, https://www.citeab.com/antibodies/125154-5246-ezh2-d2c9-xp-rabbit-mab?des=3e269f5e53ce11e5
-anti ERK1/2, Orthogonal, Biological Strategies, and Knockdown validation, 504 citations, https://www.citeab.com/antibodies/124659-4696-p44-42-mapk-erk1-2-l34f12-mouse-mab?des=1eb65efe17511444
-anti pERK, Biological Strategies and Orthogonal validation, 5013 citations, https://www.citeab.com/antibodies/124275-4370-phospho-p44-42-mapk-erk1-2-thr202-tyr204-d1?des=f2be8f77e26c20d4
-anti DPF2, 6 citations, https://www.citeab.com/antibodies/778744-ab134942-anti-dpf2-req-antibody-epr9206-b?des=29a30509c7fbf6c3
-anti ARID1A, Biological Strategies and Orthogonal validation, 47 citations, https://www.citeab.com/antibodies/1201491-12354-arid1a-baf250a-d2a8u-rabbit-mab?des=d607613c61c65e44
-anti MBD3, KO validated, 17 citations, https://www.citeab.com/antibodies/737853-ab157464-anti-mbd3-antibody-epr9913-chip-grade?des=77a427d26785f43d
-anti 53BP1 validated by genetic strategy, 454 citations, https://www.citeab.com/antibodies/406753-nb100-304-53bp1-antibody?des=937cba1a663f1f71
-anti-phospho H2A.X, 2446 citations, https://www.citeab.com/antibodies/221929-05-636-anti-phospho-histone-h2a-x-ser139-antibody?des=abb2da153fb7e8ba
-anti Rad51, 5 citations, https://www.citeab.com/antibodies/1204815-70-001-anti-human-rad51-antibody-rabbit-serum?des=4d7d94f11e9854e1
-anti STAT1, validated by biological strategies, 145 citations, https://www.citeab.com/antibodies/2455404-14994-stat1-d1k9y-rabbit-mab?des=aa848af94ec03b5e
-anti LSD2, KO validated, 4 citations https://www.citeab.com/antibodies/2929671-ab193080-anti-lsd2-aof1-antibody-epr18508?des=76d7e64e6f2a9c0f

-anti phospho STAT1, biological strategies and orthogonal validation, 492 citations, https://www.citeab.com/antibodies/125838-9167-phospho-stat1-tyr701-58d6-rabbit-mab?des=8988ea0ef9685771
-anti CD24, 10 citations, https://www.citeab.com/antibodies/522306-311118-apc-anti-human-cd24-antibody?des=5fea45d648497dcb
-anti CD44, 25 citations, https://www.citeab.com/antibodies/517944-103024-pe-anti-mouse-human-cd44-antibody?des=6f9d932d4b2b8aa9
-alexa 488, 1672 citations https://www.citeab.com/antibodies/search?q=A-21207
-alexa 594, 194 citations, https://www.citeab.com/antibodies/search?q=A-11020
-kI67, 357 citations, https://www.citeab.com/antibodies/701412-12202-ki-67-d3b5-rabbit-mab-mouse-preferred-ihc-f?des=7aedd9148eadc934

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	T47D (ATTC HTB-113), MDA-MB-231(ATCC HTB-26), 293T (ATCC #CRL-3216). T47D and MCF7 tamoxifen, fulvestrant resistant and long term estrogen deprived were generated in this study.
Authentication	All cell lines generated in this study were validated by Western blotting, PCR and sequencing. T47D and MDA-MB231 were authenticated using ATCC authentication service (STR profiling).
Mycoplasma contamination	All cell lines were screened twice a month for mycoplasm contamination and are negative
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	Female, 8 weeks old NOD Scid Gamma (NSG) mice were obtained from the Jackson Laboratory (Stock No. 002374) and bred inhouse for one generation.
Wild animals	No wild animals were used in this study
Field-collected samples	No field collected samples were used in this study
Ethics oversight	All procedures involving experimental procedures with mice were approved by the Institutional Animal Care and Use Committees (IACUC) of University of Miami.

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

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.*	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE168644
Files in database submission	LTED_SMARCC1.75bp_5prime.nodup_x_LTED_input.75bp_5prime.nodup.pval.signal.bigwig LTED_RCOR1.75bp_5prime.nodup_x_LTED_input.75bp_5prime.nodup.pval.signal.bigwigq T47D_LTED9M_LSD1_KO_LSD1.nodup_x_T47D_LTED9M_LSD1_KO_input.nodup.pval.signal.bigwig T47D_LTED9M_LSD1_KO_cjun.nodup_x_T47D_LTED9M_LSD1_KO_input.nodup.pval.signal.bigwig T47D_LTED9M_LSD1_KO_H3K4me2.nodup_x_T47D_LTED9M_LSD1_KO_input.nodup.pval.signal.bigwig T47D_LTED9M_H3K4me2.nodup_x_lted_9m_input.nodup.pval.signal.bigwig k27ac_rep1_wt2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig 07_rnapol_wt2_rep1.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig T47D_WT2_LSD1.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig lted_9m_lsd1.nodup_x_lted_9m_input.nodup.pval.signal.bigwig t47d_fm_CoRest.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig T47D_WT2_ER.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig foxa1_rep1_wt2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig lted_9m_shcjun_cjun.nodup_x_lted_9m_shcjun_input.nodup.pval.signal.bigwig lted_9m_shcjun_lsd1.nodup_x_lted_9m_shcjun_input.nodup.pval.signal.bigwig lted_9m_rnapol.nodup_x_lted_9m_input.nodup.pval.signal.bigwig lted_9m_k27ac.nodup_x_lted_9m_input.nodup.pval.signal.bigwig lted_9m_cjun.nodup_x_lted_9m_input.nodup.pval.signal.bigwig 09_fm_h3k27ac_R1_merged.srt.nodup_x_01_fm_igg_R1_merged.srt.nodup.pval.signal.bigwig 10_fm_lsd1_ko_2e8_h3k27ac_R1_merged.srt.nodup_x_02_fm_lsd1_ko_2e8_igg_R1_merged.srt.nodup.pval.signal.bigwig 11_lted_h3k27ac_R1_merged.srt.nodup_x_03_lted_igg_R1_merged.srt.nodup.pval.signal.bigwig

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18_fm_lsd1_ko_2e8_h3k4me1_R1_merged.srt.nodup_x_02_fm_lsd1_ko_2e8_igg_R1_merged.srt.nodup.pval.signal.bigwig
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22_t47d_lted_shlsd1_2e4_h3k4me1_R1_merged.srt.nodup_x_06_t47d_lted_shlsd1_2e4_igg_R1_merged.srt.nodup.pval.signal.bigwig
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08_rnapol_wt2_rep2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig
foxa1_rep2_wt2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig
k27ac_rep2_wt2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig
er_rep2_wt2.nodup_x_T47D_WT2_input.nodup.pval.signal.bigwig
T47D_FM_cjun_rep1.nodup.30M_x_T47D_FM_2x_rep1_input_fastq.gz.nodup.30M.pval.signal.bigwig
T47D_FM_cjun_rep2.nodup.30M_x_T47D_FM_2x_rep2_input.nodup.30M.pval.signal.bigwig
T47D_FM_CoREST_rep2.nodup.30M_x_T47D_FM_1x_rep2_input.nodup.30M.pval.signal.bigwig
T47D_FM_LSD1_5ug.nodup_x_T47D_FM_Input.nodup.pval.signal.bigwig
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T47D_LTED9m17d_SMARCC1_rep2.nodup.30M_x_T47D_LTED9m17d_2x_rep2_input.nodup.30M.pval.signal.bigwig
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T47D_LTED21M_DMSO_cjun_rep2.nodup.30M_x_T47D_LTED21M_DMSO_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED21M_Corin_cjun_rep1.nodup.30M_x_T47D_LTED21M_Corin_rep1_input.nodup.30M.pval.signal.bigwig
T47D_LTED21M_Corin_cjun_rep2.nodup.30M_x_T47D_LTED21M_Corin_rep2_input.nodup.30M.pval.signal.bigwig
5-LTED-9MO-CTL-ANTI-FOXA1-REP1.srt.nodup_x_1-LTED-9MO-CTL-INPUT-REP1.srt.nodup.pval.signal.bigwig
6-LTED-9MO-CTL-ANTI-FOXA1-REP2.srt.nodup_x_2-LTED-9MO-CTL-INPUT-REP2.srt.nodup.pval.signal.bigwig
7-LTED-9MO-LSD1-KO-ANTI-FOXA1-REP1.srt.nodup_x_1-LTED-9MO-CTL-INPUT-REP1.srt.nodup.pval.signal.bigwig
8-LTED-9MO-LSD1-KO-ANTI-FOXA1-REP2.srt.nodup_x_2-LTED-9MO-CTL-INPUT-REP2.srt.nodup.pval.signal.bigwig
T47D_LTED21M_DMSO_H3K4me2_rep1.nodup.30M_x_T47D_LTED21M_DMSO_rep1_input.nodup.30M.pval.signal.bigwig
T47D_LTED21M_DMSO_H3K4me2_rep2.nodup.30M_x_T47D_LTED21M_DMSO_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED21M_Corin_H3K4me2_rep1.nodup.30M_x_T47D_LTED21M_Corin_rep1_input.nodup.30M.pval.signal.bigwig
T47D_LTED21M_Corin_H3K4me2_rep2.nodup.30M_x_T47D_LTED21M_Corin_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED_LSD1_KO_SMARCC1_rep1.nodup.30M_x_T47D_LTED_LSD1_KO_2x_rep1_input.nodup.30M.pval.signal.bigwig
T47D_LTED_LSD1_KO_SMARCC1_rep2.nodup.30M_x_T47D_LTED_LSD1_KO_2x_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED_LSD1_KO_H3K4me2_rep2.nodup.30M_x_T47D_LTED_LSD1_KO_1x_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED_LSD1_KO_cjun_rep2.nodup.30M_x_T47D_LTED_LSD1_KO_1x_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED_shcontrol_cjun_rep2.nodup.30M_x_T47D_LTED_shcontrol_rep2_input.nodup.30M.pval.signal.bigwig
T47D_LTED_shcjun_cjun_rep2.nodup.30M_x_T47D_LTED_shcjun_rep2_input.nodup.30M.pval.signal.bigwig
09_rnapol_537_rep1.nodup_x_T47D_537_input.nodup.pval.signal.bigwig
10_rnapol_537_rep2.nodup_x_T47D_537_input.nodup.pval.signal.bigwig
er_rep1_537.merged.nodup_x_ctl_for_rep1.pval.signal.bigwig
er_rep2_537.merged.nodup_x_ctl_for_rep2.pval.signal.bigwig
foxa1_rep1_537.nodup_x_T47D_537_input.nodup.pval.signal.bigwig
foxa1_rep2_537.nodup_x_T47D_537_input.nodup.pval.signal.bigwig
T47D_537_LSD1_33_1.nodup_x_T47D_537_input_rep2.nodup.pval.signal.bigwig
T47D_537_LSD1_79_1.nodup_x_T47D_537_input_rep2.nodup.pval.signal.bigwig
T47D_537_LSD1.nodup_x_T47D_537_input.nodup.pval.signal.bigwig

Genome browser session
(e.g. UCSC)

All bigwig files were uploaded to GEO https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE168644

Methodology

Replicates

All chip-seq were done in biological duplicates. Moreover, LSD1 and cJUN chip-seq were validated by ChIP-qPCR and genetic depletion in this study.

Sequencing depth

All ChIP-seq experiments were performed in a Nova-seq 75bp single-end and 30-40M were sequenced with >90% of mappable reads. ATAC-seq experiments were performed in a Nova-seq 75bp paired-end and 40M were sequenced with >90% of mappable reads. CUT&RUN experiments were performed in a Nova-seq 75bp paired-end and 8M were sequenced with >90% of mappable reads. RNA-

seq experiments were performed in a Nova-seq 100bp single-end and 20-30M were sequenced with >90% of mappable reads.

Antibodies

Antibodies Supplier Catalog
Rabbit polyclonal Anti-KDM1/LSD1 antibody ChIP grade abcam ab17721 Lot:GR332777379-1
Rb polyclonal anti CoREST EMD-Millipore 07-455 Lot:3230538
Rb polyclonal anti ER alpha abcam ab3575
Rb polyclonal Anti-FOXA1 antibody abcam ab23738
Rb polyclonal to c-JUN abcam ab31419 GR03661531
Rb monoclonal Rpb1 NTD Cell Signaling Technology 14958S (D8L4Y)
Rb Anti-Histone H3 (acetyl K27) antibody - ChIP Grade abcam ab4729 Lot:GR306603-1
Rabbit monoclonal SMARCC1/BAF155 Cell Signaling Technology 11956S D7F8S Lot:4
Rabbit polyconal Histone H3K4me2 antibody Active Motif 39141 Lot: 01008001
Rabbit IgG CUT&RUN Negative Control Antibody EpiCypher 13-0042K
Rabbit polyclonal H3K27ac Antibody - ChIP-seq Grade Diagenode C15410196
Rabbit polyclonalAnti-Histone H3 (mono methyl K4) antibody - ChIP Grade abcam ab8895

Peak calling parameters

Peaks were called/signal tracks were generated using MACS2 v2.2.4, and peaks with fold change > 3.5 compared to input and FDR < 0.05 were used for subsequent analysis. Only default parameters were used. Bigwig file output from MACS was visualized in the UCSC genome browser. Homer annotatePeaks v4.11 was used for peak annotation and Bedtools v2.29.0 intersect was used to determine peak overlaps and assign target genes.

Data quality

Chipseq data was validated by looking at the replicates as well as ChIP-qPCR and chipseq experiments in knockout and knockdown cells.

Software

Single-end ChIP-seq fastq files were processed using the ENCODE Transcription Factor and Histone ChIP-Seq processing pipeline (https://github.com/ENCODE-DCC/chip-seq-pipeline2). Reads were trimmed using cutadapt v2.5. Reads were aligned to the hg19 genome using Bowtie2 v2.3.4.3, and the SAMtools v1.9 was used to convert the output file to the BAM format. Duplicates were removed using Picard Tools v2.20.7. Peaks were called/signal tracks were generated using MACS2 v2.2.4, and peaks with fold change > 3.5 compared to input and FDR < 0.05 were used for subsequent analysis. Only default parameters were used. Bigwig file output from MACS was visualized in the UCSC genome browser. Homer annotatePeaks v4.11 was used for peak annotation and Bedtools v2.29.0 intersect was used to determine peak overlaps and assign target genes. NGS plot v2.63.1 from the Shen Lab (https://github.com/shenlab-sinai/ngsplot) was used to generate heatmaps and density plot.

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

For staining of the luminal and basal cell surface markers CD24 and CD44, respectively, 1 million freshly harvested cells were washed with cold PBS and pelleted. Cell pellets were dissolved in 100 uL of 1xPBS/BSA 0.5% and incubated in the presence of 1 ug of APC anti-human CD24 [ML5] (BioLegend-311118) and 1 µg of PE anti-mouse/human CD44 [IM7]. Cells were incubated with the antibodies in the dark for 30min at 4C and washed twice with cold 1xPBS.

Instrument

FACS Aria IIu sorter,CytoFLEX Flow Cytometer (Beckman Coulter)

Software

FlowJo,LLC

Cell population abundance

CD24 positive cells abundance went from 99.8% (parental) to 0.69% (reprogrammed) during resistance evolution while CD44 positive cells went from 0.042% (parental) to 96.5% (reprogrammed)

Gating strategy

T47D parental cells staining was used to define CD24 positive cells and CD44 negative.

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