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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 data was collected by Illumina NovaSeq 6000 (Novogene Inc.). RNA-seq data was collected by Illumina NovaSeq 6000 (Novogene Inc.) and Illumina HiSeq 2500. an EASY-nLC 1200 UHPLC system (ThermoFisher Scientific) coupled to a Q Exactive HF-X mass spectrometer (ThermoFisher Scientific) was used collect proteomic data.
Data analysis	ChIP-seq were mapped to the Homo sapiens reference genome (hg19) by Bowtie2. Normalized genome-wide signal-coverage tracks from raw-read alignment files were built by Samtools, deeptools, and MACS2. Visualization of the ChIP-seq signal at enriched genomic regions (Profile and Heatmap) was achieved by using deepTools. Peak-associated genes and motif were identified by using the annotate Peaks function of HOMER. The 50 hallmark gene sets in the MSigDB databases (https:// www.gsea-msigdb.org/gsea/msigdb) were used for the Gene Set Enrichment Analysis (GSEA) or Gene Set Variation Analysis (GSVA) in RNA-seq. GraphPad Prism 8.0 software was used for statistical analyses. Mascot 2.3 was used for proteomic analysis.

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 RNA-seq and ChIP-seq data generated in this study have been deposited in Sequence Read Archive (SRA) repository under SRA accession number PRJNA934109(https://dataview.ncbi.nlm.nih.gov/object/PRJNA934109?reviewer=fqfhjlf9g569so060sgh73fghi) and PRJNA934165(https://dataview.ncbi.nlm.nih.gov/object/PRJNA934165?reviewer=lso5hn8gfi4f0uh2ahcnbsq7o3), respectively. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD040150(Reviewer account details: Username: reviewer_pxd040150@ebi.ac.uk; Password: ahGtvEao).

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Considering breast cancer is mainly a female disease, we only included the female patients in this study.
Population characteristics	Chinese female breast cancer patients (over age 20) who had breast cancer treatment.
Recruitment	The samples of patients diagnosed with breast cancer by immunohistochemical analysis were selected. The breast tumor samples, normal adjacent tissue samples and breast cancer lymph node metastasis samples were obtained from the same patients. The breast cancer tissues used in this study was obtained from the Second Affiliated Hospital of Chinese University of Hong Kong with written consent from patients. There were no bias on the selection of patients.
Ethics oversight	Ethics approval was obtained from the institutional ethics committee of the Second Affiliated Hospital of Chinese University of Hong Kong.

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	Sample sizes (n=/>3). Sample size as estimated according to previous successful experience and to be large enough to obtain reproducible results.
Data exclusions	No data were excluded from the analyses.
Replication	Experiments in the article were reliably reproduced based on successful attempts to replicate experiments.
Randomization	In metastasis assay, the mice were randomly assigned into different experimental groups.
Blinding	Investigators were not blinded to group allocation during data collection and/or analysis. We used appropriate statistical tests to confirm significant differences; therefore, blinding was not applicable.

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

Methods

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

Antibodies

Antibodies used

Mouse monoclonal anti-GAPDH (#AC002, ABclonal Technology, China) was used for Western blot;
Rabbit polyclonal anti-β-ACTIN (#20536-1-AP, Proteintech, China) was used for Western blot;
Rabbit monoclonal anti-E-cad (#3195S, Cell Signaling Technology, USA) was used for Western blot;
Rabbit monoclonal anti-SNAIL (#3879S, Cell Signaling Technology, USA) was used for Western blot;
Mouse monoclonal anti-STAT3 (#60199-1-Ig Proteintech, USA) was used for Western blot and Immunoprecipitation;
Rabbit monoclonal anti-p-STAT3Y705 (#9145S, Cell Signaling Technology, USA) was used for Western blot, Immunoprecipitation and Chromatin Immunoprecipitation;
Rabbit monoclonal anti-HA (#3724S, Cell Signaling Technology, USA) was used for Western blot and Immunoprecipitation;
Mouse monoclonal anti-FLAG (#8146S, Cell Signaling Technology, USA) was used for Western blot;
Rabbit monoclonal anti-FLAG (#14793S, Cell Signaling Technology, USA) was used for Western blot and Immunofluorescence;
Rabbit monoclonal anti-GST (#AF2299, Beyotime, China) was used for Western blot and Pulldown;
Rabbit polyclonal anti-L3MBTL3 (#ab99928, Abcam, UK) was used for Western blot, Immunoprecipitation and Immunohistochemistry;
Rabbit polyclonal anti-L3MBTL3 (#A7289, ABclonal Technology, China) was used for Western blot;
Rabbit polyclonal anti-L3MBTL3(#a302-854a, Bethyl, USA) was used for Chromatin Immunoprecipitation;
Rabbit polyclonal anti-SNAIL (#A5544, ABclonal Technology, China) was used for Immunohistochemistry;
Mouse monoclonal anti-E-cad (#610181, BD Biosciences, USA) was used for Immunofluorescence.

Validation

All antibodies have been validated on the product webpages or literature, including:
Mouse monoclonal anti-GAPDH (#AC002, ABclonal Technology, China) was used for Western blot, (https://abclonal.com.cn/catalog/AC002), PMID:34379783.
Rabbit polyclonal anti-β-ACTIN (#20536-1-AP, Proteintech, China) was used for Western blot, (https://www.ptgcn.com/products/ACTB-Antibody-20536-1-AP.htm), PMID: 36477541.
Rabbit monoclonal anti-E-cad (#3195S, Cell Signaling Technology, USA) was used for Western blot, (https://www.cellsignal.cn/products/primary-antibodies/e-cadherin-24e10-rabbit-mab/3195?site-search-type=Products&N=4294956287&Ntt=3195s&fromPage=plp&_requestid=1614421), PMID:36646679.
Rabbit monoclonal anti-SNAIL (#3879S, Cell Signaling Technology, USA) was used for Western blot, (https://www.cellsignal.cn/products/primary-antibodies/snail-c15d3-rabbit-mab/3879?site-search-type=Products&N=4294956287&Ntt=3879s&fromPage=plp&_requestid=1614668), PMID: 36470928.
Mouse monoclonal anti-STAT3 (#60199-1-Ig Proteintech, USA) was used for Western blot and Immunoprecipitation, (https://www.ptgcn.com/products/STAT3-Antibody-60199-1-Ig.htm), PMID: 34853180, PMID: 36640665.
Rabbit monoclonal anti-p-STAT3Y705 (#9145S, Cell Signaling Technology, USA) was used for Western blot, Immunoprecipitation and Chromatin Immunoprecipitation, (https://www.cellsignal.cn/products/primary-antibodies/phospho-stat3-tyr705-d3a7-xp-rabbit-mab/9145?site-search-type=Products&N=4294956287&Ntt=9145s&fromPage=plp&_requestid=1615496), PMID: 35606353, PMID: 34440089, PMID: 25040935
Rabbit monoclonal anti-HA (#3724S, Cell Signaling Technology, USA) was used for Western blot and Immunoprecipitation, (https://www.cellsignal.cn/products/primary-antibodies/ha-tag-c29f4-rabbit-mab/3724?site-search-type=Products&N=4294956287&Ntt=3724s&fromPage=plp&_requestid=1616236), PMID: 35618710, PMID: 36130923.
Mouse monoclonal anti-FLAG (#8146S, Cell Signaling Technology, USA) was used for Western blot, (https://www.cellsignal.cn/products/primary-antibodies/dykddddk-tag-9a3-mouse-mab-binds-to-same-epitope-as-sigma-s-anti-flag-m2-antibody/8146?site-search-type=Products&N=4294956287&Ntt=8146s&fromPage=plp&_requestid=1616568), PMID: 32002546, PMID: 34463618, PMID: 31300647.
Rabbit monoclonal anti-FLAG (#14793S, Cell Signaling Technology, USA) was used for Western blot and Immunofluorescence, (https://www.cellsignal.cn/products/primary-antibodies/dykddddk-tag-d6w5b-rabbit-mab-binds-to-same-epitope-as-sigma-s-anti-flag-m2-antibody/14793), PMID: 32413996, PMID: 35396552.
Rabbit monoclonal anti-GST (#AF2299, Beyotime, China) was used for Western blot and Pulldown, (https://www.beyotime.com/product/AF2299.htm)
Rabbit polyclonal anti-L3MBTL3 (#ab99928, Abcam, UK) was used for Western blot, Immunoprecipitation and Immunohistochemistry, (https://www.abcam.cn/products/primary-antibodies/l3mbtl3-antibody-ab99928.html). Data provided in the manuscript.
Rabbit polyclonal anti-L3MBTL3 (#A7289, ABclonal Technology, China) was used for Western blot, (https://abclonal.com.cn/catalog/A7289)
Rabbit polyclonal anti-L3MBTL3(#a302-854a, Bethyl, USA) was used for Chromatin Immunoprecipitation, (https://www.biomol.com/products/antibodies/primary-antibodies/general/anti-l3mbtl3-a302-854a-t?number=A302-854A), PMID: 29030483.
Rabbit polyclonal anti-SNAIL (#A5544, ABclonal Technology, China) was used for Immunohistochemistry, (https://abclonal.com.cn/

catalog/A5544), PMID:27874055.
Mouse monoclonal anti-E-cad (#610181, BD Biosciences, USA) was used for Immunofluorescence, (https://www.bdbiosciences.com/zh-cn/products/reagents/microscopy-imaging-reagents/immunofluorescence-reagents/purified-mouse-anti-e-cadherin.610181).
All antibodies were verified when they were arrived.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Human breast cell lines MCF7, T47D, ZR75, SUM149PT, MDA-MB-157, SUM159PT, MDA-MB-231, Bt549, Hs578t, HMLE, Human embryonic kidney cell line HEK-293T and mouse breast cancer cell line 4T1 were used in the manuscript. MCF7(HTB-22), T47D(HTB-133),MDA-MB-157(HTB-24),MDA-MB-231(HTB-26), BT549(HTB-122), Hs578T(HTB-126), HEK-293T(CRL-3216) and 4T1(CRL-2539) were acquired from the American Type Culture Collection (ATCC).
Authentication	None of the cell lines used were authenticated.
Mycoplasma contamination	All the cell lines were tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None of the cell lines used in this study were found in the commonly misidentified cell lines database.

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	Wild-type BALB\c mice (6-week-old, female) were purchased from Shanghai Lingchang Biotechnology (Shanghai, China). Mice were housed in air-filtered flow cabinets with a 12-hours light cycle at 22±2°Cand 55±5% humidity, and allowed free access food and water.
Wild animals	This study did not involve wild animals.
Reporting on sex	BALB\c mice (6-week-old, wild-type female) were used in allograft model, as the breast cancer are mainly a female disease and rarely diagnosed in male.
Field-collected samples	This study did not involve samples colected from the field.
Ethics oversight	All the experimental protocols for mice were approved by the Ethics Committee of East China Normal University.

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://dataview.ncbi.nlm.nih.gov/object/PRJNA934165?reviewer=lso5hn8gfi4f0uh2ahcnbsq7o3
Files in database submission	1.159_1.input.1.fq.gz, 1.159_1.input.2.fq.gz, 1.159_2.lgG.1.fq.gz, 1.159_2.lgG.2.fq.gz, 1.159_3.L3_ChIP.1.fq.gz, 1.159_3.L3_ChIP.2.fq.gz, 2.159_4.input.1.fq.gz, 2.159_4.input.2.fq.gz, 2.159_5.1gG.1.fq.gz, 2.159_5.lgG.2.fq.gz, 2.159_6.L3_ChIP.1.fq.gz, 2.159_6.L3_ChIP.2.fq.gz
Genome browser session (e.g. UCSC)	https://genome-idx.s3.amazonaws.com/bt/hg19.zip

Methodology

Replicates	Two biological replicates for ChIP-seq.
Sequencing depth	A minimum of 17 million reads of paired-end sequences were used. An average of 10% of reads were mapped uniquely. Fragment lengths were 150bp.
Antibodies	Rabbit polyclonal anti-L3MBTL3(#a302-854a, Bethyl, USA) and Rabbit monoclonal anti-p-STAT3Y705 (#9145S, Cell Signaling Technology, USA).
Peak calling parameters	Peak calling was carried out by the MACS2 tool.

Data quality	The quality of the ChIP-seq data was assessed as described by the encode project (http://www.encodeproject.org/data-standards/terms/).
Software	ChIP-seq were mapped to the Homo sapiens reference genome (hg19) by Bowtie2. Normalized genome-wide signal-coverage tracks from raw-read alignment files were built by Samtools, deeptools, and MACS2. Visualization of the ChIP-seq signal at enriched genomic regions (Profile and Heatmap) was achieved by using deepTools. Peak-associated genes and motif were identified by using the annotate Peaks function of HOMER.