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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	Methods for data generation and collection are included in detail in the methods
Data analysis	All data analysis programs and versions are included in detail in the methods

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 data will be uploaded to the European Genome-Phenome Archive (EGA) under accession number EGAS00001006555, where all the matching patient data is already uploaded for earlier publications. A data transfer agreement is required to access this data.

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	This is a study of ovarian carcinosarcoma, which only occurs in the female sex. As such, tumours were collected from females only and only female mice were used to develop PDX models.
Reporting on race, ethnicity, or other socially relevant groupings	The WEHI-Stafford Fox Rare Cancer Program is accessible by anyone of any sex, race and ethnicity and from any social group.
Population characteristics	There were no human participants included in this research, the research solely used models generated from patient material.
Recruitment	As above, not relevant.
Ethics oversight	Ethics approval for the WEHI-SFRCP was obtained from the Royal Melbourne Hospital Human Research Ethics Committee (Project number 2015.300) and governance review by the WEHI HREC (Project number G16/02).

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	In most experiments sample size calculations were not required. The number of tumours was selected to ensure there was enough material for each type of experiment. For the proteomics experiments, a minimum of 3 tumours were included per model and two models per group. This was sufficient to determine significant similarities and differences between groups.
Data exclusions	For the snRNA-seq and spatial transcriptomics, some nuclei and barcoded spots were removed prior to analysis based on the following criteria. Nuclei (snRNA-seq) or barcoded spots (ST) were filtered based on the number of features, unique molecular identifier counts (UMIs), and percentage of UMI counts from mitochondrial genes. Thresholds for each metric varied with the technology used and the sequencing depth (Supplementary Table S3). For the creation of EMT bins nuclei with less than 3,000 UMIs were then removed.
Replication	Western blotting was repeated with different tumours from the same models to ensure results were consistent. No other replication was performed due to the precious nature of the samples and the cost of each method. Instead sufficient replicate numbers of tumours were included where possible (ie proteomics analysis).
Randomization	Tumours were allocated to one of three groups (epithelial-like, mesenchymal-like and mixed) for proteomic analysis based on histological analysis of the epithelial, mesenchymal and mixed components present in each model.
Blinding	No blinding was included as it was not relevant for most of the study as individual tumours were characterised by the different methods. For proteomics, all samples were included in a batch for analysis using standard software and so blinding was not required.

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

For immunohistochemistry (IHC) the following antibodies were used: anti-p53 (mouse, DO-7, Dako; #M700101), anti-PAX8 (rabbit, poly, Proteintech; #10336-1-AP), anti-WT-1 (rabbit, poly, Abcam; #AB15249), anti-Ki67 (mouse, MIB-1, Dako; #M7240), anti-pan-cytokeratin (mouse, AE1/3, Dako; #M3515), anti-vimentin (rabbit, D21H3, Cell Signaling Technology; #5741), and anti-HMGA2 (rabbit, D1A7, Cell Signaling Technology; #8179).

For western blotting the following antibodies were used: anti-ZEB1 (Novus Biologicals, #NBP1-05987, polyclonal), anti-E-cadherin (Cell Signaling Technology, #3195, 24E10), anti-cytokeratin-18 (Santa Cruz Biotechnology, #SC-51582, C-04), anti-N-cadherin (Abcam, #AB18203, polyclonal), anti-vimentin (Cell Signaling Technology#, 5741, D21H3), anti-N-MYC (Cell Signaling Technology, #51705, D4B2Y), anti-HMGA2 (Cell Signaling Technology, #8179, D1A7), and anti-β-actin (Sigma Aldrich, #A5441, AC-15).

For flow cytometric analysis the following antibodies were used: BV421-MHC class 1 (H-2k[d]) (BD Biosciences, #742431, SF1-1.1), Alexa Fluor 647-E-cadherin (BioLegend, #324112, 67A4), and PE-Cy7-N-cadherin (BioLegend, #350811, 8C11).

Validation

Suppliers of antibodies provide a performance guarantee where all antibodies have been validated to ensure optimal performance. We also included samples with known low and high expression of each protein as controls.

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

PDX models were grown in female NOD-SCID-IL-2Rγ mice with mice being transplanted with tumour fragments between 6-12 weeks of age.

Wild animals

The study did not involve any wild animals.

Reporting on sex

This is a study of ovarian carcinosarcoma, which only occurs in the female sex. As such, tumours were collected from females only and only female mice were used to develop PDX models.

Field-collected samples

The study did not involve samples collected from the field.

Ethics oversight

All animal experiments were conducted according to the National Health and Medical Research Council Australian Code for the Care and Use of Animals for Scientific Purposes 8th Edition, 2013 (updated 2021), and under the approval of the WEHI Animal Ethics Committee (AEC 2019.024, 2022.030, and 2022.038).

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	PH PDX models were established through transplanting fragments of cryopreserved tumour tissue subcutaneously from PDXs generated in the Mayo Clinic (USA). The remaining PDX models (#105, #177, #233, #264, #436, and #718) were established through transplanting fragments of tumour tissue obtained from patients consented to the WEHI-Stafford Fox Rare Cancer Program (Melbourne, Australia). Tumour fragments (1-4 mm^3) were transplanted subcutaneously into NOD-SCID-IL-2Rγ mice under anaesthesia. Tumour growth was monitored twice weekly and once a volume > 700 mm3 was reached the mice were euthanised and tumours excised. Tumours from OCS PDX models were mechanically digested using surgical blades and enzymatically digested using the human Tumour Dissociation Kit in gentleMACSTM C tubes on a gentleMACS Dissociator (Miltenyi Biotec) according to manufacturer's instructions. The single-cell suspension was then filtered through a 100 µm cell strainer (Corning) before red blood cells were depleted via hypotonic lysis, using red blood cell lysis buffer (WEHI).
Instrument	Cytek® Aurora Spectral Cytometers (5L 16UV-16V-14B-10YG-8R)
Software	FlowJo software (v1.0.7.1)
Cell population abundance	No fluorescence-activated cell sorting was performed for the purposes of this manuscript.
Gating strategy	Forward scatter area (FSC-A) and side scatter area (SSC-A) were used to eliminate cell debris, whilst FSC-A and forward scatter height (FSC-H) allowed for the exclusion of doublets. PI and BV421-MHC1 were then used to select for viable human cells in the tumour. These cells were then segregated into four populations based on AF647-E-cadherin and PE-Cy7-N-cadherin and assessed for their expression of 354 different PE-conjugated cell surface markers (CSM) included in the LEGENDScreen Human PE kit. All data analysis was carried out using FlowJo (v.1.0.7.1) software, with population gating set according to fluorescence minus one (FMO) controls, allowing for a 0.5% false positive rate.

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