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	NA
Data analysis	Cell Profiler StarDist QuPath Proteome Discoverer v2.3 Mascot (version 2.4) AlphaFold2 R package cutoff v0.1.0 (R v4.1.0)

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

Mass Spectrometry data have been deposited in PRIDE, accession number PXD023666. The publicly available TCGA data were downloaded from gdac.broadinstitute.org (release 28 January 2016). All other data are provided in the manuscript or Supplementary Information. Source data for all Figures are provided in the Source Data file accompanying the manuscript.

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	Human breast tumour samples were obtained from adult female patients for generation of patient derived xenograft (PDX) and patient derived organoid (PDO) models which were subsequently used for experimental investigation. As this research focuses on female breast cancer, only female tumour tissue from female patients was used.
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable
Population characteristics	Not applicable
Recruitment	Human breast tumour samples were obtained from adult female patients after informed consent as part of a non-interventional clinical study (BTBC study REC no.: 13/LO/1248, IRAS ID 131133; Principal Investigator: Prof. Andrew Tutt; Study Title: "Analysis of functional immune cell stroma and malignant cell interactions in breast cancer in order to discover and develop diagnostics and therapies in breast cancer subtypes"). This study had local research ethics committee approval and was conducted adhering to the principles of the Declaration of Helsinki. Specimens were collected from surgery and transported immediately to cut up. A clinician histopathologist or pathology-trained technician identified and collected tumour material into basal culture media. Tumour material was used for generation of PDX and PDO models.
Ethics oversight	King's College London and GSTT Foundation NHS Trust research ethics committee

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 animal studies, sample sizes were selected using statistical power calculations performed using NC3R EDA assistant.
Data exclusions	Some animals were excluded from tumour specific survival where death was not due to tumour limit being reached. Analysis without exclusion of these animals is also presented.
Replication	All in vitro experiments were carried out with biological replicates as noted.
Randomization	For animal studies, once tumour volumes reached a range of 45-95 mm3 in volume, mice were randomised to treatment groups using a random number generator.
Blinding	Blinding was not used.

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used: HORMAD1 - Abcam (ab250052), B-ACTIN-Sigma (A5441), HISTONE H3 - CST (5192), MAD2L1-Bethyl (A310-082A), GFP - Sigma (g1544), CDC20 - Abcam (ab26483), BUBR1-Bethyl (A300-386A), CYCLIN B1 - CST (4135), CREST (ACA) - Immunovision (HCT-0100), HA-TAG - MERCK (11867423001), B-TUBULIN - Abcam (ab6046), AURORA B - Novus Biologicals (NB100-294), INCENP - CST (2786), MCHERRY - Abcam (ab213511), BUB1 -Abcam (ab54893), P-CENPA - CST (2187), P-AURORA B - CST (2914), P-H3 - CST (9706), P-DSN1 - Iain Cheeseman Lab, MYC - Sigma (SAB4301136), HORMAD1 - ProteinTech (13917-1-AP), HORMAD1 - ProteinTech (67091-1), Aurora B - Abcam (ab3609) SNAP - NEB (P9310S)

Validation: HORMAD1 antibodies were validated by knockdown by RNAi or over-expression of the protein of interest (e.g. Figure 1A, Figure 2D).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): Cell lines obtained from ATCC:
RPE1 hTERT (CRL-4000), HeLa (CCL-2), MCF10A (CRL-10317), MDA-MB-436 (HTB-130) NCI-H1299 (CRL-5803)
Cell lines obtained BioIVT/Asterand:
SUM159PT (HUMANSUM-0003006), SUM149PT (HUMANSUM-0003004)

Authentication: cell lines regularly tested by STR

Mycoplasma contamination: cell lines regularly tested for Mycoplasma contamination

Commonly misidentified lines (See ICLAC register): *Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

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: NOD.Cg-PrkdcscidIl2rgtm1Wjl/SzJ (NSG) mice purchased from Charles River UK used for all experiments

Wild animals: Not applicable

Reporting on sex: Only female mice were used for the animal studies detailed in this paper as studies utilised patient derived xenograft (PDX) models or cell line xenografts derived from female breast cancer patients.

The number of female NSG mice used in each study and ages at time of tumour implantation are detailed below:
- KCL010 PDX response to AZD2811 NPs = 25 mice; 22-26 days old
- KCL003 PDX response to AZD2811 NPs = 30 mice; all 45 days old
- KCL625OX PDX response to AZD2811 NPs = 30 mice; all 39 days old
- KCL002 PDX response to AZD2811 NPs = 25 mice; all 33 days old
- SUM159 tumour xenograft response to AZD2811 NPs: 50 mice; all 47 days old

Field-collected samples: Not applicable

Ethics oversight: All animal studies were conducted under PPL PF642A32A Protocol 3 (Subcutaneous or Mammary Fad Pad Models) which received ethical approval from King's College London (KCL) Animal Welfare Ethical Review Body (AWERB) and the Home Office.

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

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA