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Reporting Summary

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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	Flow cytometry: BD LSRFortessa™ (BD Biosciences), Cytek® Aurora (Cytek) spectral cytometer. Cell sorting: BD Influx™ cell sorter (BD Biosciences). Conventional immunofluorescence microscopy: Leica Aperio® AT2 (Leica), PhenoImager® HT 2.0 (Akoya Biosciences). Xenium spatial transcriptomics: We used the Xenium in situ platform for FFPE targeting 380 genes from the predesigned Xenium Human Immuno-Oncology Profiling Panel (10x Genomics). For sc-RNAseq data analysis, we used the publicly available NSCLC dataset GSE131907, HGSOC GSE180661, and ovarian metastatic dataset GSE286057. For the Visium spatial transcriptomics analysis, we used the publicly available datasets GSE263920 for HGSOC and E-MTAB-13530 for NSCLC. For the deconvolution of Visium spots, published scRNAseq datasets for HGSOC (GSE180661) and NSCLC (E-MTAB-13526) were respectively annotated and used as deconvolution references.
Data analysis	Flow cytometry: FlowJo software (v.10.9.0, TreeStar, Inc.). Immunostaining: Halo AI software (v.3.6.4134, Indica Labs), Visiopharm software (v. 2025.08.1). Statistical analysis: Prism (v. 8.4.2, GraphPad), R software (v.4.4.2, http://www.r-project. org/). Next-generation sequencing analysis: R packages; ComplexHeatmap (v.3.20), Pheatmap (v.1.0.12), MCPcounter (v.1.2.0), CellChat (v.1.6.1), ProjecTILs (v.3.5.0), and ggplot2 (v.3.5.2). sc-RNAseq analysis: R packages; Seurat (v.5.1.0), SingleR (v.2.6.0), celldex (v.1.16.0), and ClusterProfiler (v.4.4). Xenium spatial transcriptomics analysis: R packages; Seurat (v.5.1.0), Harmony (v.1.2.1), SingleR (v.2.6.0), and dbscan (v.1.2.0). Visium spatial transcriptomics analysis: R packages; Seurat (v.5.3.0), spacexr (v.2.2.1), tidyverse (v.2.0.0), and pheatmap (v.1.0.13).

All analyses reported in this study used the statistical software R (v.4.4.2). All codes employed or generated during the current study are available publicly at https://github.com/HenslerM/Lanickova_NK .

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

Data availability. The raw data and datasets generated in this study, including Xenium in situ analyses of patients from Study Cohort 9 and 10, have been deposited in the Gene Expression Omnibus (GEO) database under accession code: GSE320142.
The ovarian and lung cancer publicly available data used in this study are available in the TCGA database via the Xena browser.

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 participants involved in this study were women with high grade serous ovarian carcinoma (HGSOC) and patients with non-small cell lung carcinoma (NSCLC), where results apply to all sex and genders. Sex and gender were not considered in the study design. Sex and gender was determined on self-reporting. No sex or gender-based analyses were performed.
Reporting on race, ethnicity, or other socially relevant groupings	All participants were of European ancestry and Czech, or French ethnicity; race or ethnicity was not analyzed as a study variable.
Population characteristics	Study cohort 1: Stage III-IV chemo-naïve high grade-serous ovarian cancer (HGSOC). Study cohort 2: Stage III-IV chemo-naïve non-small cell lung carcinoma (NSCLC). Study cohort 3: Stage III-IV chemo-naïve HGSOC who underwent primary surgery. Study cohort 4: Stage I-IIIA chemo-naïve NSCLC who underwent primary surgery. Study cohort 5: Stage III-IV HGSOC who underwent primary surgery after neoadjuvant chemotherapy (3-4 cycles of CBDCA +PTX). Study cohort 6: Stage III-IV chemo-naïve primary HGSOC who underwent primary surgery. Study cohort 7: Stage III-IV chemo-naïve primary NSCLC who underwent primary surgery. Study cohort 8: Metastatic chemo-naïve HGSOC who underwent primary surgery. Study cohort 9: Stage III-IV chemo-naïve HGSOC who underwent primary surgery. Study cohort 10: Stage III-IV chemo-naïve NSCLC who underwent primary surgery. Study cohort 11: Stage III-IV chemo-naïve primary HGSOC. Study cohort 12: Stage III-IV chemo-naïve primary NSCLC.
Recruitment	Patients from study cohort 3 were randomly recruited at the Obstetrics and Gynecology department at University Hospital Kralovske Vinohrady, Prague, Czech Republic. Patients from study cohort 4 were randomly recruited at the Pneumology department at Institut Mutualiste Montsouris, Hotel Dieu and University Hospital Motol. Patients from study cohort 5 were randomly recruited at the Obstetrics and Gynecology department at University Hospital Kralovske Vinohrady, Prague, Czech Republic. Patients from study cohorts 9 and 10 were randomly recruited at the Obstetrics and Gynecology, and Pneumology departments respectively at University Hospital Hradec Kralove, Czech Republic. The histology of HGSOC and NSCLC was approved by pathologists at the institutes where the samples were collected from. Potential biases applicable to the study were the relatively subjective resectability/operability of the disease prior to enrollment and the self-selection bias. The impact of both biases on the results of our study were minimized by presenting and discussing eligible patients at multidisciplinary tumor board meetings before enrollment.
Ethics oversight	This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the local Ethical Committees (EK-VP/60/0/2020; EK-410/23; 202504P19; 201607S14P; Progress UK, Q40/11). Written informed consent was obtained from the patients before inclusion in the study. The recruitment of the patients from cohort 4 was with the consent of patients and the agreement of the French ethic committee (number 2008-133) in application with the article L. 1121-1 of French law.

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 were determined based on prior experience from similar human studies, as well as available resources and sample availability. No statistical methods were used to predetermine sample size number. Human participants: Study cohort 1: RNAseq data from 280 chemo-naïve patients with stage III-IV HGSOC, identified in The Cancer Genome Atlas (TCGA) database (https://cancergenome.nih.gov/). Study cohort 2: RNAseq data from 110 chemo-naïve patients with stage III-IV HGSOC, identified in The Cancer Genome Atlas (TCGA) database (https://cancergenome.nih.gov/). Study cohort 3: 42 chemo-naïve patients with stage III-IV HGSOC, collected at University Hospital Kralovske Vinohrady, Prague, Czech Republic Study cohort 4: 26 chemo-naïve patients with stage I-IIIA NSCLC collected at Institut Mutualiste Montsouris and Hotel Dieu (n=22) and University Hospital Motol (n=4). Study cohort 5: 18 patients with stage III-IV HGSOC after neo-adjuvant chemotherapy, collected at University Hospital Kralovske Vinohrady, Prague, Czech Republic. Study cohort 6: Publicly available pre-processed scRNAseq data from tumor samples of 5 patients with stage III-IV primary HGSOC (GSE180661). Study cohort 7: Publicly available pre-processed scRNAseq data from tumor samples of 5 patients with stage III-IV primary NSCLC (GSE131907). Study cohort 8: Publicly available pre-processed scRNAseq data from tumor samples of 15 patients with metastatic HGSOC (GSE286057). Study cohort 9: A retrospective series of formalin-fixed paraffin-embedded (FFPE) tumor samples were obtained from 24 chemo-naïve stage III-IV patients with HGSOC at University Hospital Hradec Kralove, Czech Republic. Study cohort 10: A retrospective series of formalin-fixed paraffin-embedded (FFPE) tumor samples were obtained from 24 chemo-naïve stage III-IV patients with NSCLC at University Hospital Hradec Kralove, Czech Republic. Study cohort 11: Publicly available spatially resolved transcriptomic data generated by 10x Visium Technology from tumor samples of chemo-naïve patients with stage III-IV primary HGSOC (GSE263920). Study cohort 12: Publicly available spatially resolved transcriptomic data generated by 10x Visium Technology from tumor samples of chemo-naïve patients with stage III-IV primary NSCLC (E-MTAB-13530). For animal experiments, groups of at least 6 animals were used, and whenever possible, larger groups were used to improve statistical power.
Data exclusions	Outliers or mice with symptoms non attributable to cancer were excluded as a predetermined criterion.
Replication	Unless otherwise noted, results always include data from at least 2 independent experiments as a measure of reproducibility. In each individual experiment, each technical replicate was measured once.
Randomization	Human participants: Patients were randomly recruited at the Obstretics and and Gynecology, and Pneumology departments at University Hospital Kralovske Vinohrady, University Hospital Hradec Kralove, University Hospital Motol, and Institut Mutualiste Montsouris, and Hotel Dieu, France. In murine experiments, mice were randomly allocated to a treatment group.
Blinding	Blinding was not implemented as assessments were strictly quantitative and not applicable for further clinical validation. Non-blinded confirmation by independent operators was implemented for immunostaining.

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	Flow cytometry: anti-Annexin V (catalog number: EXB0027, Exbio, 2:100)

anti-CALR (clone: FMC75, Enzo Life eciences, Ing, 2.4:100)
anti-CD3 (clone: MEM-57, catalog number: A7-202-T100, Exbio, 5:100)
anti-CD3 (clone: 17A2, catalog number: 100218, BioLegend, 1:100)
anti-CD3 (clone: 17A2, catalog number: 15-0032-82, Invitrogen, 0.125:100)
anti-CD3 (clone: SK7, catalog number: 344861, BioLegend, 5:100)
anti-CD8 (clone: RPA-T8, catalog number: 560774, BD Biosciences, 5:100)
anti-CD8a (clone: 53-6.7, catalog number: 563152, BD Biosciences, 1:100)
anti-CD8a (clone: 53-6.7, catalog number: 612898, BD Biosciences, 0.25:100)
anti-CD8a (clone: RPA-T8, catalog number: 301026, BioLegend, 0.5:100)
anti-CD16 (clone: 3G8, catalog number: 302012, BioLegend, 5:100)
anti-CD16/CD32 (Fc Block) (clone: 2.4G2, catalog number: 553142, BD Biosciences, 1:20)
anti-CD44 (clone: IM7, catalog number: 562464, BD Biosciences, 1:100)
anti-CD45 (clone: HI30, catalog number: 560777, BD Biosciences, 5:100)
anti-CD45 (clone: HI30, catalog number: MHCD4517, Thermo Fisher Scientific, 6:100)
anti-CD45 (clone: 30-F11, catalog number: 69-0451-82, Invitrogen, 0.5:100)
anti-CD45 (clone: 30-F11, catalog number: 746947, BD Biosciences, 0.125:100)
anti-CD45 (clone: HI30, catalog number: 304095, BioLegend, 0.25:100)
anti-CD56 (clone: MEM-188, catalog number: 304626, BioLegend, 6:100)
anti-CD56 (clone: HCD-56, catalog number: 318328, BioLegend, 6:100)
anti-CD56 (clone: 5.1H11, catalog number: 362553, BioLegend, 0.3:100)
anti-CD62L (clone: MEL/14, catalog number: 612833, BD Biosciences, 1:100)
anti-CD107a (clone: 1D4B, catalog number: 121645, BioLegend, 0.25:100)
anti-Epcam (clone: 9C4, catalog number: 324204, BioLegend, 2:100)
anti-Granzyme B (clone: GB11, catalog number: 560213, BD Biosciences, 0.03125;100)
anti-IFNG (clone: XMG1.2, catalog number: 12-7311-82, Invitrogen, 1:100)
anti-IFNG (clone: XMG1.2, catalog number: 567061, BD Biosciences, 0.25:100)
anti-NK1.1 (clone: PK136, catalog number: 108733, BioLegend, 1:100)
anti-NK1.1 (clone: PK136, catalog number: 17-5941-82, Invitrogen, 1:100)
anti-NK1.1 (clone: PK136, catalog number: 25-5941-82, Invitrogen, 1:100)
anti-NKG2A (clone: S19004C, catalog number: 375108, BioLegend, 6:100)
anti-NKG2A (clone: S19004C, catalog number: 375104, BioLegend, 6:100)
anti-NKG2A (clone: REA1161, catalog number: 130-120-371, MACS Miltenyi Biotec, 1:100)
anti-NKG2A (clone: 20d5, catalog number: 741125, BD Biosciences, 0.25:100)
anti-NKG2A (clone: 131411, catalog number: 747919, BD Biosciences, 2.5:100)
anti-NKG2D (clone: 1D11, catalog number: 320812, BioLegend, 1:100)
anti-NKG2D (clone: CX5, catalog number: 25-5882-82, Invitrogen, 1:100)
anti-NKG2D (clone: CX5, catalog number: 46-5882-82, Invitrogen, 5:100)
anti-NKp46 (clone: 9E2, catalog number: 331919, BioLegend, 2:100)
anti-NKp46 (clone: 29A1.4, catalog number: 562850, BD Biosciences, 1:100)
anti-NKp46 (clone: 29A1.4, catalog number: 756928, BD Biosciences, 1:100)
anti-PD1 (clone: EH12.2H7, catalog number: 329904, BioLegend, 6:100)
anti-PD1 (clone: RMP1-30, catalog number: 109112, BioLegend, 1:100)
anti-PD1 (clone: 29F.1A12, catalog number: 135214, BioLegend, 1:100)
anti-PD1 (clone: RMP1-30, catalog number: 569780, BD Biosciences, 1:100)
anti-TCF1 (clone: C63D9, catalog number: 2203S, Cell Signaling, 0.167:100)
anti-TIM3 (clone: F38-2E2, catalog number: 345006, BioLegend, 3:100)
anti-TIM3 (clone: 5D12/TIM-3, catalog number: 747626, BD Biosciences, 4:100)
anti-TIM3 (clone: RMT3-23, catalog number: 119745, BioLegend, 2:100)
anti-rabbit IgG (catalog number: 79408S, Cell Signaling, 1:600)

Immunohistochemistry/Immunofluorescence:
anti-CD3 (clone:SP162, catalog number: ab135372, Abcam, 1:100)
anti-CD4 (clone:RBT-CD4, catalog number: LS-C312222, LSBio, 1:50)
anti-CD4 (clone:EPR19514, catalog number: ab183685, Abcam, 1:150)
anti-CD8 (clone:CAL38, catalog number: ab237723, Abcam, 1:250)
anti-CD8 (clone:SP16, catalog number: ab101500, Abcam, 1:60 in panels 1 and 2, 1:50 in panel 3)
anti-CD20 (clone:SP32, catalog number: ab64088, Abcam, 1:100)
anti-CD20 (clone:L26, catalog number: M0755, DAKO, 1:300)
anti-CD21/CR2 (clone:2G9, catalog number: 76069, Cell Signaling, 1:50)
anti-CD23 (clone:SP23, catalog number: ab16702, Abcam, 1:200)
anti-CD45 (clone: 998215, catalog number: MAB14302, R&D Systems, 1:100)
anti-CD57 (clone:NK/804, catalog number: ab220187, Abcam, 1:50)
anti-DC-LAMP (clone: 1010E1.01, catalog number: DDX0191P-100, Dendritics, 1:350)
anti-Granzyme B (clone: EPR8260, catalog number: ab134933, Abcam, 1:250)
anti-HLA-E (clone:MEM-E/06, catalog number: MA1-19356, Invitrogen, 1:100)
anti-NCR1 (clone: EPR23097-35, catalog number: ab233558, Abcam, 1:500)
anti-NKG2A (clone:EPR23737-127, catalog number: 260035, Abcam, 1:500 in immunohistochemistry, 1:400 in immunofluorescence)
anti-NKp46 (clone:EPR22403-57, catalog number: ab224703, Abcam, 1:100)
anti-PanCK (clone:AE1/AE3, catalog number: ab80826, Abcam, 1:100 in immunohistochemistry, 1:200 in immunofluorescence)

Validation	All antibodies were validated by immunohistochemistry and immunofluorescence prior to panel development. Antibody validation included the staining of known marker-positive and marker-negative tissue types (including tonsils, lymph node, spleen and different tumor types), assessment of staining pattern across the tissue compared to staining patterns published in the Human protein Atlas (proteinatlas.org), cell type specificity (assessed by co-staining with other markers) and intracellular localization.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Brca1-/-Trp53-/-/Myc/Hras SO1 cells were kindly provided by Dr. Sandra Orsulic, David Geffen School of Medicine, University of California, Los Angeles, California. Mouse Brca1-/-Trp53-/-/Myc/Akt BR5 cells were kindly provided by Dr. Sandra Orsulic, David Geffen School of Medicine, University of California, Los Angeles, California.
Authentication	The cell lines were used shortly after receipt from collaborators and hence were not authenticated.
Mycoplasma contamination	All cell lines were routinely confirmed to be Mycoplasma-free by PCR.
Commonly misidentified lines (See ICLAC register)	None.

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 C57BL/6 and FVB/NCrl mice, aged 8-12 weeks, were from the Institute of Microbiology, Czech Academy of Sciences and Velaz s.r.o. respectively (Prague, Czech Republic). Housing was in individually ventilated cages. Food and water were provided ad libitum, Teklad Global 18% Protein Rodent Diet, irradiated. Water in sterile prefilled bottles. Dark/Light cycle on a 12 h automated schedule. Temperature 21°C +/- 2°C and humidity 50 % +/- 10 %.
Wild animals	No Wild animals were used in this study.
Reporting on sex	Female mice were employed.
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	Animal experiments were approved by the Animal Care and Use Committee of the Institute of Molecular Genetics and were in agreement with local legal requirements and ethical guidelines.

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

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	Human tumor samples were mechanically minced in RPMI medium supplemented with 10% FBS and enzymatically digested using 1 mg/mL collagenase D and 0.1 mg/mL DNase I for 30 min at 37°C, followed by processing with the gentleMACS™ Dissociator (Miltenyi Biotec). RPMI supplemented with 10% FBS was then added to stop enzymatic activity, and tumors were filtered through a 100 µm cell strainer. After washing, cells were centrifuged for 10 min at 300 g and resuspended in RPMI medium supplemented with 10% FBS. Murine tumors were processed using the Tumor Dissociation Kit (Miltenyi Biotec) in combination with gentleMACS™ mechanical dissociation. RPMI medium was then used to stop enzymatic activity, and then tumors were filtered through a 100 µm cell strainer. After washing, cells were centrifuged for 10 min at 300 g and resuspended in RPMI medium.
Instrument	Flow cytometry data were acquired on BD LSRFortessa™ (BD Biosciences), and Cytek® Aurora (Cytek) spectral cytometer.
Software	Flow cytometry data were acquired with the FACSDiva sofware (BD) or the SpectroFlo® software (Cytek) and analyzed with FlowJo software (TreeStar, Inc.).
Cell population abundance	For NK cell isolation, CD45+ cells were isolated from murine tumor tissue using the EasySep Isolation kit (STEMCELL Technologies) following manufacturer recommendations, with Fc receptor blocking using purified anti-mouse CD16/CD32 (BD Biosciences). Isolated CD45+ cells were labeled with fluorochrome-conjugated antibodies against CD45, NK1.1, CD3, and NKG2A, together with a viability dye (Fixable Viability Dye 780 or propidium iodide) for live/dead discrimination. Flow cytometric analysis and cell sorting were performed on a BD Influx™ cell sorter (100 µm nozzle, single-cell mode).
Gating strategy	Gating strategy is fully described in Supplemental figures 3 and 4.

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