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Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	FACS Diva Software version 7 (BD)
Data analysis	FlowJo v10.0.6 (Tree Star Inc.), GraphPad Prism v6.0e (GraphPad Software Inc.), RStudio v1.0.136, GSEA (http://broadinstitute.org/gsea), TCR analysis (R package tcR [ID: 26017500]), HALO™ image analysis software v.2.0.1145.19 (Indica Labs).

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

RNA sequencing data are available at NCBI GEO: (GSE99531)

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences

Study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No expected effect size was pre-specified as this study was exploratory. Generally accepted samples sizes were used, with a significant difference between conditions indicating that the sample size is sufficient. No conclusion was derived from an experiment in the case the difference between conditions was not significant.
Data exclusions	No data were excluded.
Replication	Every figure states how many times each experiment had been repeated. To ensure experiments could be reliably reproduced, fully independent experiments were performed as defined by commonly accepted standards.
Randomization	Not applicable for this study as no treatment strategies are compared.
Blinding	Pathologists were blinded to the clinical outcome for PD-1T TIL quantification by IHC.

Materials & experimental systems

Policy information about availability of materials

n/a	Involved in the study
☒	☐ Unique materials
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Research animals
☐	☒ Human research participants

Antibodies

Antibodies used

Antibodies used for flow cytometry (clone, dilution, supplier-ID):
Anti-CD19 APC-eFluor780 (SJ25C1, 1:50, 47-0198-42), -CD45 PerCP-Cy5.5 (2D1, 1:100, 45-9459-42), -CD56 PE (CMSSB, 1:50, 12-0567-42), -CD3 APC-eFluor780 (SK7, 1:100, 47-0036-42), -Lag-3 FITC (3DS223H, 1:20, 11-2239-42), -TIGIT PE (MBSA43, 1:20, 12-9500-42), -2B4 FITC (eBioDM244, 1:20, 11-5837-42), -CD137 FITC (4B4, 1:20, 11-1379-42), -IL-2 PE (MQ1-17H12, 1:20, 12-7029-42), -TNFa APC (MAb11, 1:20, 17-7349-82), -CD26 FITC (2A6, 1:20, 11-0269-42), -CXCR5 Biotin (MU5UBEE, 1:20, 13-9185-82), -ICOS FITC (ISA-3, 1:20, 11-9948-42), -CD38 APC (HIT2, 1:20, 17-0389-42), -Eomes eFluor660 (WD1928, 1:20, 50.4877-42), -T-bet PE (eBio4B10, 1:20, 12-5825-82), -pSTAT3 PE (LUVNKLA, 1:20, 12-9033-42) were purchased from eBioscience.
Anti-CD4 BV711 (SK3, 1:50, 563028), -PD-1 PE-Cy7 (EH12.1, 1:20, 561272), -PD-1 AlexaFluor647 (EH12.1, 1:20, 560838), -BTLA PE (J168-540, 1:20, 558485), -IFNg BV421 (4S.B3, 1:20, 564791), -CD27 BV711 (M-T271, 1:20, 564893), -CD28 PE-Cy7 (CD28.2, 1:50, 560684), -Ki67 BV421 (B56, 1:25, 565929), -CD20 BV711 (2H7, 1:20, 563126), and Streptavidin BV711 (1:200, 563262) and Streptavidin BV605 (1:200, 563260) were purchased from BD.
Anti-CD8 BV605 (RPA-T8, 1:100, 301040), -CD8 BV711 (SK1, 1:100, 344734), -CD8 PE-Cy7 (SK1, 1:100, 344750), -CD4 PE (SK3, 1:100, 344606), -CD11b PE (ICRF44, 1:100, 301306), -CD11c PE (3.9, 1:100,301606), -CD14 PerCP-Cy5.5 (HCD14, 1:100, 325622), -CD45 APC-eFluor780 (HI30, 1:100, 304014), -Tim-3 BV421 (F38-2E2, 1:20, 345008), -IL10 PE (JES3-9D7, 1:20, 501404), -CD200 BV421 (OX-104, 1:20, 329210), -CD109 PE (W7C5, 1:20, 323305), -GITR APC (621, 1:20, 311610), -CD39 FITC (A1, 1:20, 328206), -CD127 BV605 (A019D5, 1:100, 351334), -CCR7 PE (G043H7, 1:100, 353204), -CD45RA BV421 (HI100, 1:100, 304130), -CD62L BV421 (DREG-56, 1:50, 304828), -KLRG1 BV421 (2F1/KLRG1, 1:50, 138414), -CD36 APC (5-271, 1:50, 336208), -CCR6 PE-Cy7 (G034E3, 1:50, 353418), -CCR4 PE-Cy7 (TG6/CCR4, 1:50), -CXCR3 PE (G025H7, 1:50, 353706), -HLA ABC APC-Cy7 (W6/32, 1:100, 311426), and Streptavidin PE-Cy7 (1:200, 405206) were purchased from Biolegend.
Anti-CXCL13 APC (53610, 1:20, IC801A) was purchased from R&D Systems.

Antibodies used for IHC:
Anti-CD4 (4B12, RTU, PA0427), -CD8 (4B11, RTU, PA0183) were purchased from Novocastra, -CD19 (LE-CD19, RTU, IR65661-2), -Bcl-6 (PG-B6p, RTU, IS62530-2), -CD21 (1F8, RTU, IR60861) were purchased from DAKO, and -PD-1 (NAT105m RTU, 760-4895) was purchased from Roche Diagnostics.

Validation	All antibodies are commercially available and were only used for applications validated by the manufacturer.

Human research participants

Policy information about studies involving human research participants

Population characteristics	Characteristics of patients for which freshly resected tumor material was obtained: BS-185, adenocarcinoma, IB; BS-191, large cell carcinoma, IIIA; BS-200, squamous cell carcinoma, IIB; BS-202, pleomorphic carcinoma, IV; BS-252, squamous cell carcinoma, IB; BS-253, adeno/sarcomatoid carcinoma, IV; BS-274, squamous cell carcinoma, IIA; BS-275, squamous cell carcinoma, IIIA; BS-278, squamous cell carcinoma, IB; BS-293, squamous cell carcinoma, IIB; BS-299, adenocarcinoma, IV; BS-300, adenocarcinoma, IV; BS-304, adenocarcinoma, IIIA; BS-319, large cell carcinoma, IV; BS-320, adenocarcinoma, IIIA; BS-321, adenocarcinoma, IB; BS-323, adenocarcinoma, IB; BS-327, adenocarcinoma, IB; BS-335, adenocarcinoma, IV; BS-342, squamous cell carcinoma, IIIA; BS-358, adenocarcinoma, IB; BS-360, adenocarcinoma, IIA; BS-369, adenocarcinoma, IA; BS-413, squamous cell carcinoma, IA; BS-416, adenocarcinoma, IA; BS-423, sarcomatoid carcinoma, IIIA; BS-430, squamous cell carcinoma, IIIA; BS-433, adenocarcinoma, IV; BS-447, adenocarcinoma, IA; BS-451, adenocarcinoma, IIA; BS-461, adenocarcinoma, IIIA; BS-469, squamous cell carcinoma, IIB; BS-474, adenocarcinoma, IIB; BS-447, adenocarcinoma, IA; BS-483, adenocarcinoma, IIA; BS-485, squamous cell carcinoma, IB; BS-488, sarcomatoid carcinoma, IV; BS-491, squamous cell carcinoma, IIIA; BS-515, squamous cell carcinoma, IIIB; BS-541, adenosquamous carcinoma, IIIA; BS-544, squamous cell carcinoma, IB; BS-548, adenocarcinoma, IIIA; BS-552, sarcomatoid carcinoma, IIB; BS-557, adenocarcinoma, IB; BS-562, adenocarcinoma, IIB; BS-585, squamous cell carcinoma, IA; BS-589, adenocarcinoma, IV; BS-704, adenocarcinoma, IIA; BS-719, squamous cell carcinoma, IIIB; BS-721, squamous cell carcinoma, IB; BS-723, adenocarcinoma, IIIA; LA-40, adenocarcinoma, IIB. Characteristics of patients included in PD-1T TIL predictive analysis: KSBL1, adenocarcinoma, IV; KSBL2, adenocarcinoma, IV; KSBL4, squamous cell carcinoma, IV; KSBL8, squamous cell carcinoma, IV; KSBL9, squamous cell carcinoma: USB1, adenocarcinoma, IV; UBS3, adenocarcinoma, IV; USB16, adenocarcinoma, IV: USB19, adenocarcinoma, IV; USB20, adenocarcinoma, IV; USB22, adenocarcinoma, IV; USB24, adenocarcinoma, IV; USB31, squamous cell carcinoma, IV; USB33, squamous cell carcinoma, IV; USB34, adenosquamous carcinoma, IV; USB35, adenocarcinoma, IV; USB37, squamous cell carcinoma, IV; USB39, adenocarcinoma, IV: USB42, adenocarcinoma, IV; USB43, adenocarcinoma, IV; USB45, adenocarcinoma, IV.

Method-specific reporting

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ Magnetic resonance imaging

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	Solid tumor lesions were mechanically dissociated and enzymatically digested using accutase (PAA), collagenase IV (Worthington), hyaluronidase (Sigma) and DNAse type IV (Sigma), directly after excision. Single cell suspensions were prepared and all samples were cryopreserved until further usage.
Instrument	BD LSR Fortessa Cell analyzer (BD Bioscience)
Software	FACS Diva Software version 7 (BD), FlowJo v10.0.6 (Tree Star Inc.)
Cell population abundance	Sorted PD-1 subsets hat a post-sort purity of >98%
Gating strategy	To identify the PD-1 subsets, the gating strategy was used as follows: identification of lymphocytes in the FSC/SSC plot, exclusion of doublets in FSC-A/FSC-H and SSC-A/SSC-H plots, live cells, identification of T cells by CD45/CD3/CD8, identification of PD-1 subsets as follows: We compared the PD-1 expression levels on NSCLC TILs with those of peripheral blood T cells from healthy donors. In peripheral blood of healthy donors, a clear population of PD-1-negative T cells and T cells with an intermediate level of PD-1 could be detected, with very few T cells displaying higher levels of PD-1 (average of 0.4%). In contrast, in TIL, sometimes sizable populations of T cells with bright PD-1 expression were detected (29.1±17.6%). Reflecting the definition of these cells on the basis of their tumor-associated level of PD-1 expression, we refer to these cells as 'PD-1T' ('tumor-associated') TILs. Remaining TILs were divided into those with a PD-1 level equal to that seen in peripheral blood ('PD-1Normal, PD-1N' TILs) and TILs with no detectable PD-1 expression ('PD-1-' TIL).

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