Corresponding author(s): Thomas Gebhardt, Jason Waithman, Laura Mackay

Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

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, Olympus Fluoview, BioRad ddPCR System and C1000 Touch thermal cycler, Vectra 3.3, inForm 2.3.0
Data analysis	Graphpad Prism 6 and 7, Imaris 8 or 9, Adobe After Effects 11, Flowjo 9, QuantaSoft V1.7, Living Image v4.4

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

Raw data supporting the findings of this study are available from the corresponding authors upon request.

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 ☐ Ecological, evolutionary & environmental 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	Sample sizes were chosen based on prior research conducted in our laboratories to provide sufficient numbers of mice in each group to provide informative results and perform statistical testing, accounting for variability in possible disease outcomes using the epicutaneous melanoma model. For tumour challenge experiments, flow cytometric analysis experiments, ddPCR experiments, IVIS experiments and 2-PM experiments: sample sizes of n= 10 mice or more were pooled for each figure to account for the variance in disease outcomes in epicutaneously inoculated mice (60% anticipated developers, 40% anticipated non-developers). For sorting experiments: sample sizes of n= 15 B16.gB inoculated mice or more were chosen to allow enough cells to be isolated from tumours and peritumoural skins (~200/mouse) for subsequent PCR analysis.
Data exclusions	No data was excluded from analysis.
Replication	Experiments were reliably reproduced and the number of experiments performed stated in methods and legends. Culminated and pooled data is shown where possible. Where representative data is shown, relevant experiments were repeated successfully at least twice with the exact number of repeats indicated in each case. Most experiments were repeated at least twice if not 3 or more times to verify that experimental findings were reproducible. Attempts at data replication were successful within groups (i.e. developer vs. non-developer), accounting for variance in the exact proportion of mice developing (+/-60%) or not developing (+/-40%) macroscopic tumours in individual experiments.
Randomization	Animals of the same age and sex were randomly assigned to experimental groups.
Blinding	Blinding was not performed in this study. The experimental observations presented (presence or absence of a macroscopic tumour) would be consistent irrespective of blinding and therefore blinding was not relevant in this study.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☐	☒ Human research participants

Methods

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

Antibodies

Antibodies used

Antibodies used are described below:

MOUSE

Antibody, Supplier, Clone, Colour (Catalogue #) Dilution

Anti-mouse CD45.1, BD Biosciences, A20, FITC (550802); APC (561873); APCR-700 (561235); 1/200
Anti-mouse CD45.1, eBioscience, A20, PeCy7 (25-0453-82); APC-eFluor 780 (47-0453-82); 1/200

Anti-mouse CD45.2, BD Biosciences, 104, AF700 (560693); BUV737 (564880); BV786 (563686); 1/200
Anti-mouse CD45.2, eBioscience, 104, APC-eFluor 780 (47-0454-82); 1/100
Anti-mouse CD45.2, Biolegend, 104, BV785 (109839)

Anti-mouse CD8a, BD Biosciences, 53-6.7, APC (561093); BUV395 (563786); BUV805 (564920); FITC (553031); 1/200

Anti-mouse CD8a, eBioscience, 53-6.7, AF700 (56-0081-82); APC-eFluor 780 (47-0081-82); 1/200
Anti-mouse CD8a, Biolegend, 53-6.7, BV605 (100743); BV711 (100747); BV785 (100749); 1/200

Anti-mouse Va2, BD Biosciences, B20.1, BV421 (566241); PE (561078); PeCy7 (560624); AF700 (561239); 1/200

Anti-mouse CD69, BD Biosciences, H1.2F3, APC (560689), BUV737 (564684), PE (553237), 1/200
Anti-mouse CD69, Biolegend, H1.2F3, BV605 (104529), 1/200

Anti-mouse CD44, BD Biosciences, IM7, BUV395 (740215), BV510 (563114), FITC (561859), PeCy7 (561861), 1/200
Anti-mouse CD44, eBioscience, IM7, AF700 (56-0441-82), 1/100

Anti-mouse CD62L, BD Biosciences, MEL-14, BV605 (743209); 1/200
Anti-mouse CD62L, eBioscience, MEL-14, PerCP Cy5.5 (45-0621-82); 1/200

Anti-mouse PD-1, BD Biosciences, J43, PE (551892); 1/200
Anti-mouse PD-1, eBioscience, J43 (25-9985-82), PeCy7; 1/200
Anti-mouse PD-1, Biolegend, PeCy7 (135216), PE (135206) 29F.1A12; 1/200

Anti-mouse IFNg, BD Biosciences, XMG1.2, FITC (562019), PE (562020), PeCy7 (557649); 1/100

Anti-mouse TNF, BD Biosciences, MP6-XT22, APC (561062), APC Cy7 (560658); 1/100

Anti-mouse CD103, eBioscience, 2E7, APC (17-1031-82), FITC (HMCD10301); 1/200
Anti-mouse CD103, Biolegend, 2E7, PerCP Cy5.5 (121416); 1/200

Anti-mouse KLRG1, eBioscience, FITC (11-5893-82), APC (17-5893-82), 2F1; 1/200
Anti-mouse/human KLRG1, Biolegend, MAFA, BV711 (138427); 1/200

Anti-mouse Thy1.1, eBioscience, HIS57, purified (17-0900-82)
Anti-rat/mouse CD90.1 (Thy1.1), Biolegend, OX-7, AF700 (202520); 1/2500 (blood) and 1/3000 (spleen, LN, skin)

Anti-mouse CD16/CD32, BD Biosciences, 2.4G2, Purified (553142), 1/200

HUMAN

Anti-human CD8, Abcam, Ab4055, Purified, 1/800
Anti-human CD103, Abcam, Ab129202, Purified, 1/3000
Anti-human SOX10, Biocare Medical, BC34, Purified, 1/800

Validation

All antibodies were obtained from commercial vendors and we based specificity on descriptions and information provided in corresponding Data Sheets available and provided by the Manufacturers.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

Vero cells (CSL, Australia) were used to grow HSV viruses. B16 melanoma cells were generated by the laboratory of Dr Jason Waithman (corresponding author) or laboratories of Michel Holzel and Thomas Tuting (authors) and originally obtained from the ATCC.

Authentication

Vero cells and B16 cells were originally obtained from commercial sources (CSL or ATCC respectively) and were therefore authenticated by the manufacturer. B16 cells are true melanoma cells as they form distinctive melanoma tumours following injection to mice. Expression of relevant antigens (gB or Ova) by B16 melanoma cells has been confirmed using in vitro activation assays with transgenic T cells (gBT-I or OT-I respectively).

Mycoplasma contamination

Cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used in this study.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

Laboratory mouse (Mus musculus) strains C57BL/6, gBT-I, gBT-I × B6.SJL-PtprcaPep3b/BoyJ (gBT-I.CD45.1), gBT-I.Thy1.1, gBT-I.uGFP, OT-I × B6.SJL-PtprcaPep3b/BoyJ (OT-I.CD45.1), Rag1–/–, Rag2–/– × Il2rg–/–, Il15–/–, Itgae–/–, Cd69–/–, Perf1–/–, Ifng–/–, Tnfa–/–, gBT-I.CD45.1 × Cd69–/–, gBT-I.CD45.1 × Tnfa–/– and B6(Cg)-Tyrc-2J/J (B6 Albino) mice were bred in the Department of Microbiology and Immunology, The University of Melbourne. All transgenic strains were maintained on a C57BL/6 background. All mice were female and aged between 6 and 12 weeks of age at the time experiments commenced.

Wild animals

No wild animals were used in the study.

Field-collected samples

No field collected samples were included in the study.

Human research participants

Policy information about studies involving human research participants

Population characteristics	All melanoma samples analyzed were from lymph node (n = 68) or skin (n = 3) metastates. Patients were selected based on clinical and pathological confirmation of cutaneous melanoma (mucosal and acral melanomas excluded) and all patients had not received any systemic treatment or radiotherapy in the biopsied area prior to surgery. A detailed clinical overview of all the patients has been previously described in Edwards J et at. Clin Cancer Res 2018, 24(13):3036-3045 (Ref. 17). Images displayed in Fig. 2 were taken from two representative patient samples with the following characteristics: (1) age: 56, gender: male, site: lymph node; and (2) age: 77, gender: female, site: subcutaneous skin.
Recruitment	The archival human melanoma samples analysed were obtained from The Melanoma Institute Australia biospecimen bank with written informed patient consent and institutional review board approval. Patients were selected based on clinical and pathological confirmation of cutaneous melanoma (mucosal and acral melanomas excluded) and all patients had not received any systemic treatment or radiotherapy in the biopsied area prior to surgery. Only archival material was analysed, no patients were recruited specifically for the current study.

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	Sample preparation is described in the Materials & Methods section.
Instrument	BD Fortessa II
Software	BD FACS Diva for collection and Flowjo 9 (Treestar) for analysis.
Cell population abundance	No cell sorting was performed in this study.
Gating strategy	For spleen and LN samples, gBT-I cells were identified using the following gating strategy: FSCH lo/SSCH intermediate (lymphocytes) --> FSA/FSWlo (singlet gate) --> SSA/SSWlo (singlet gate #2) --> Live cells (negative for PI or LiveDead differentiator) --> +/- CD45.2+ (lymphocytes) where congenic marker expressed --> CD8+ (CD8+ T cells) --> Va2+ CD45.1+ or Va2 + Thy1.1+ (transgenic gBT-I) For skin and tumour samples, gBT-I cells were identified using the following gating strategy: FSCH lo/SSCH intermediate (lymphocytes) --> FSA/FSWlo (singlet gate) --> SSA/SSWlo (singlet gate #2) --> Live cells (negative for PI or LiveDead differentiator) --> +/- CD45.2+ (lymphocytes) where congenic marker expressed --> +/- CD3 intermediate (T cells) ---> Va2+ CD45.1+ or Va2+ Thy1.1+ (transgenic gBT-I) --> CD103+CD69+ (skin TRM cells)

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