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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	BD FACS Diva software version 8.0.1, Quant Studio RT-PCR version 1.3, ELISA Ascents software version 2.6.
Data analysis	All software used throughout this work is publicly available: FlowJoV8.8.7/10, ImageJ, Graph Pad Prism 7, Illustrator, Alakazam from the Change-O toolkit (http://clip.med.yale.edu/changeo.) and BRepertoire (http://mabra.biomed.kcl.ac.uk/BRepertoire/).

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

The data supporting the findings of this study are available from the corresponding author upon request. RNA sequencing data is available from the public

repository on the National Center for Biotechnology Information's Sequence Read Archive in raw format (BioProject: PRJNA417372; BioSample accession: SAMN07985450, SAMN07985451, SAMN07985452, SAMN07985453, SAMN07985454, SAMN07985455).

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	No statistical method was used to predetermine sample size. Sample sizes were chosen based on previous experience with the experimental protocols. The antibody responses examined in this work were highly reproducible with little variability. Carcinogenesis experiments have a greater biological variation, however the protocols are well-known, and much previous experience guided us to increase our samples sizes to minimum 10 animals per experimental group to ensure statistical power in these longitudinal studies.
Data exclusions	No data points were excluded from data sets.
Replication	All the experimental data provided are based on biological replicates and are representative of independent experiments. All experiments were reliably reproduced.
Randomization	For animal work, mice of a particular genotype were randomly selected for experiment from a larger cohort - other than that, no randomization was used. For human tissue, individual SSC tumours were graded by an experienced dermatopathologist as low risk or high risk based on the Scottish Intercollegiate Guidelines Network for cutaneous SCC, as outlined in the materials and methods.
Blinding	For reporting on tumour development following chemically induced carcinogenesis, back skin and tumours were evaluated by an observer blinded to the experimental groups. For most other experiments, the investigators were not blinded to group allocation.

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	For all flow cytometry staining, cell suspensions were incubated with 2% Rat Serum (Sigma) and Fc block (clone 93, BD Bioscience) for 30mins on ice, prior to staining. The following antibodies were then used: eBioscience: anti-CD45 (30-F11), B220 (RA3-6B2),), CD95 (Jo2), GL7 (GL-7), IgE (23G3), IgG1 (M1-14D12), TCRβ (H57-597), TCRγδ (eBioGL3), Vγ5 (536), CD117 (2B8), IL-4 (11B11); BD Biosciences: CD38 (90/CD38), CD138 (281-2), IgG2a (R19-15); Biolegend: CD41 (MWReg30), FcεRI (MAR-1), IL-6 (MP5-20F3), CD63 (NVG-2), Vγ4 (UC3-10Ab), CD3 (145-2C11); Millipore:, γH2AX (JBW301). All antibodies were used at a dilution of 1:100-1:200 as per respective manufacturers recommendation. OVA-loaded tetramers were provided by the NIH tetramer facility - Emory University Vaccine Center 954 Gatewood Road Atlanta, GA 30329. Reagents are provided to qualified investigators at no cost.
Validation	All antibodies were validated by the manufacturers and by our own and colleagues' labs where they are used extensively. All antibodies were titrated to determine optimal staining concentration.

Animals and other organisms

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

Laboratory animals

Only mice were used in this study and groups were age- and sex-matched for all experiments. In general females mice at 7-9 weeks were used throughout . Tcrd-/-, Tcrb-/-, IL4-/-, Langerin-DTA (LC-deficient) and Vg5Vd1-/- were on the FVB/N background after >10 backcrosses; Igh-7-/-, FceR1a-/- and Cpa3Cre/+ were on the BALB/c background after >10 backcrosses; and OTII Tg, Tcrb-/-, CD19-Cre and Bcl6fl/fl were on the C57BL/6 background. Genetic backgrounds of individual strains and controls are indicated where appropriate. Humoral responses were also examined in male animals and were comparable.
All mouse studies were approved by Imperial College AWERB (Animal Welfare and Ethical Review Body) and by the UK Home Office. Experiments involving cancer studies strictly adhered to the guidelines set out by the National Cancer Research Institute (NCRI) and Workman et al. in 'Guidelines for the Welfare and Use of Animals in Cancer Research'. All studies using mice were conducted following the Animal Research: Reporting In Vivo Experiments (ARRIVE) guidelines.

Wild animals

n/a

Field-collected samples

n/a

Human research participants

Policy information about studies involving human research participants

Population characteristics

Two cohorts of human research participants were involved in this study:
A: freshly excised SSC tumour tissue and peri-lesional skin for flow cytometric analysis from 12 patients: All tumor tissue used in the study was confirmed SSCs with a diameter > 8mm. Non-lesional skin was histopathologically normal and > 6mm away from the tumor edge.
B: For SSC tumor gene expression, fixed frozen paraffin embedded skin samples from 56 patients obtained from the University of Dundee, Tayside NHS Trust and Greater Glasgow and Clyde NHS Trust were analyzed.

Recruitment

In A: freshly excised SCC tissue and peripheral blood were obtained from 12 patients during surgery at the Dermatology Department, University Hospital Southampton NHS Foundation Trust. Ethics were provided by the South Central Hampshire B NRES Committee (reference number 07/H0504/187). All participants recruited to the study provided informed consent for blood and tissue samples to be used for research purposes.
In B: The study was conducted according to the Declaration of Helsinki Principles and all patients donating samples to this study provided written, informed consent in accordance with ethical approval from the East of Scotland Research Ethics Service (EoSRES) REC 1. SSC tumors were graded by an experienced dermatopathologist as low risk or high risk based on the Scottish Intercollegiate Guidelines Network for cutaneous SCC. In addition, peri-lesional skin (histopathologically normal looking skin > 4 mm away from the tumor edge) and abdominal non-UV exposed skin were also analyzed.

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

Tumour tissue, skin, skin-draining LNs, spleens and blood were collected and processed using standard methods as detailed in the Material and Methods section.

Instrument

BD FACSVerse and BD LSRFortessa X-20

Software

BD FACS DIVA software version 8.0.1 and FlowJo software, version 8.8.7 and version 10

Cell population abundance

For cell sorting: 10,000 to 200,000 cells were collected for each population. The purity of each population was over 95% and was determined by rerunning the sorted population on a FACS.
For FACS analysis: the population abundance varied in different tissues and in different analysis - the relevant cell abundance is indicated within the results section.

Gating strategy

Flow cytometric analysis focused around identifying activated B cells, mainly germinal center B cells (GC B cells) and antibody-secreting plasma cells (PCs). In all experiments, cells were first gated on singlets (FSC-H vs FSC-A) before setting a lymphocyte gate based on SSC-A vs FSC-A. Dead cells and T cells were excluded from the analysis by using a Live/Dead dye (Invitrogen) and pan CD3 antibody respectively. GC B cells were gated as B220+, CD95+ GL7+. PCs were identified as FSChi, CD95+, CD138+. Additional intracellular staining was carried out to assess isotype class switching. Isotype control antibodies were used to

determine if the staining was specific. Fluorescence Minus One (FMO) controls were used to determine the gating boundaries.

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