nature research

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Last updated by author(s): Aug 3, 2020

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.

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	BD FACSDiva v6, xPONENT v3.2, FastQC v0.11.9, nSolver v4.0 and Burrows-Wheeler Aligner-MEM v0.7.5a softwares
Data analysis	Prism v8, ImageJ v1.52a, FlowJo v10, Cluster v3.0, Java Treeview v1.1.6, Mutect v1.1.4, CellRanger Single-Cell Software Suite v3.1.0 and Seurat R toolkit v3.0 softwares

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. 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

10X Single-Cell RNA Sequencing Data have been deposited in the Gene Expression Omnibus (GEO) under accession ID GSE154654. Whole Exome sequencing generated in this study can be found in the GEO under accession ID GSE155556. Source data are available for this paper. All other data supporting the findings of this study are available from the corresponding author upon reasonable request.

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	The sample size was chosen in advance on the basis of common practice of the described experiment and is mentioned for each experiment. No statistical methods were used to predetermine sample size. Sample sizes were chosen based on past experience with tumor growth assays in wild type and Atg7-deficient host mice (Poillet-Perez et al, Nature, 2018).
Data exclusions	Outliers data were automatically excluded based on Grubb's test (Prism software). Outliers were removed from the Serum cytokine and chemokine profiling (Figure 1b).
Replication	Each experiment was conducted with biological replicates (at least 3 mice per group) and repeated multiple times (at least 2 independant experiments). All attempts at replication were successful.
Randomization	All experiments used mice that were randomly allocated into experimental groups.
Blinding	The investigators were not blinded during the experiments and outcome assessments. Blinding was not performed as the genotype and gender of the mice required identification for housing purposes.

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	
☐	☒	Antibodies
☐	☒	Eukaryotic cell lines
☒	☐	Palaeontology
☐	☒	Animals and other organisms
☒	☐	Human research participants
☒	☐	Clinical data

Methods

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

Antibodies

Antibodies used	For immunohistochemistry, the following antibodies were used: CD3 (1:100, Ab16669, Abcam), CD4 (1:1,000, Ab183685, Abcam), CD8 (1:100, 14-0808-82, Invitrogen), Foxp3 (1:75, 14-5773-80, Invitrogen), FIP200 (Proteintech, 17250-1-AP, 1:100), P62 (Enzo, P9860, 1:1000), B2m (1:5,000, Ab7585, Abcam), actin (1:5,000, A1978, Sigma) and peroxidase-conjugated antibody (1:5,000, NA934 and NA931, GE Healthcare). For flow cytometry, the following antibodies were used: CD11c (1:50, clone N418, 61-0114-82), CD4 (1:500, clone GK1.5, 17-0041-82), CD3 (1:300, clone 17A2, 56-0032-82), CD11b (1:300, clone M1/70, A15390), FoxP3-eFluor450 () (eBioscience); and CD45 (1:200, clone 30-F11, 103107), and CD8 (1:500, clone 53.67, 100749) (BioLegend). For T cell exhaustion, the following antibodies were used: CD45 (REA737, 1:50, 130-110-802), CD4 (REA604, 1:50, 130-118-852), CD8 (REA601, 1:10, 130-109-247) (Miltenyi Biotec Inc); CD3 (500A2, 1:500 152315), PD1 (29F.1A12, 1:300, 135213), TIM3 (RMT3-23, 1:100, 119721), LAG3 (C9B7W, 1:50, 125219) (BioLegend). For T cell and T reg depletion, the following antibodies were used: CD4 (clone GK1.5; BE003-1, BioXCell), CD8 (clone 2.43; BE0061, BioXCell) and CD25 (clone PC-61.5.3; BE0012, BioXCell).
Validation	Antibodies for flow cytometry and immunohistochemistry were validated with the use of positive and negative control (gene knock-outs and through the use of control tissues and cell lines) and following manufacturer's protocol. All the antibodies were validated as mouse specific and documented for use for these purposes (flow cytometry, Immunohistochemistry or Western blotting) on the manufacturer's website and datasheets.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	YUMM1.1 and YUMM1.3 were derived from BrafV600E/+;Pten-/-;Cdkn2-/- C57Bl/6J mouse melanomas and were generated previously in the Bosenberg laboratory. MB49 cell line was originally described by Summerhayes and Franks (1979) and provided by the Ratliff laboratory. UV YUMM1.1-9 were generated in our laboratory.
Authentication	YUMM1.1, YUMM1.3, UV YUMM1.1-9 and MB49 were authenticated using whole exome sequencing.
Mycoplasma contamination	Cells were tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No misidentified lines were used.

Animals and other organisms

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

Laboratory animals	For conditional whole-body Atg7: 8 to 10 weeks old male and female C57Bl/6J Ubc-CreERT2/+;Atg7flox/flox and Ubc-CreERT2/+;Atg7+/+ mice. For conditional whole-body Atg5: 8 to 10 weeks old male and femaleC57Bl/6J Ubc-CreERT2/+;Atg5flox/flox and Ubc-CreERT2/+;Atg5+/+ mice. For IFNgamma loss and whole-body Atg7 deletion : 8 to 10 weeks old male and female C57Bl/6J IFNg-/-;Ubc-CreERT2/+;Atg7flox/flox and IFNg-/-;Ubc-CreERT2/+;Atg7+/+ mice. For Sting loss and whole-body Atg7 deletion : 8 to 10 weeks old male and female C57Bl/6J Stinggt/gt;Ubc-CreERT2/+;Atg7flox/flox and Stinggt/gt;Ubc-CreERT2/+;Atg7+/+ mice. For liver-specific Atg7 deletion: 8 to 10 weeks old male and female C57Bl/6J Atg7flox/flox, Atg7+/+ mice and IFNg-/-;Atg7flox/flox, IFNg-/-;Atg7+/+ mice. For Fip200 deletion: 8 to 10 weeks old male C57Bl/6J mice or female Fip200flox/flox mice. Mice were housed in cages with corn cob in a temperature-controlled room (20–22°C) with a 12-h-light/-dark cycle, with a relative humidity of 30–70% in Rutgers Animal Care Facility.
Wild animals	The study did not involve wild animals
Field-collected samples	The study did not involve field-collected samples.
Ethics oversight	All animal care and treatments were carried out in compliance with Rutgers University Institutional Animal Care and Use Committee guidelines.

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

Flow Cytometry

Plots

Confirm that:

- [x] The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- [x] 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).
- [x] All plots are contour plots with outliers or pseudocolor plots.
- [x] A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Tumors were homogenized in RPMI media (Gibco, supplemented with 10% FBS) using a gentleMACS Octo Dissociator (Miltenyi Biotec Inc.) according to manufacturer's protocol, and passed through a 70 mm cell restrainer. Spleens were grounded with a rubber grinder through steel mesh, treated with ACK Lysis Buffer to remove erythrocytes and passed through a 70 mm cell restrainer. Non-specific binding of antibodies to cell Fc receptors was blocked using 10 uL/10^7 cells of FcR blocking reagent (Miltenyi Biotec Inc).
Instrument	Data were acquired using a LSR-II flow cytometer (BD Biosciences).
Software	Data were collected with BD FACSDiva v6 software and analyzed with FlowJo v10 software (Tree Star).
Cell population abundance	As we did flow analysis and no flow sorting, the cell population abundance is not applicable to our study.
Gating strategy	Live lymphocytes were gated using forward scatter area (FSC-A) versus side scatter area (SSC-A) for selection of lymphocytes, then forward scatter width versus height and side scatter width versus height for double exclusion, and finally the viability-dye

negative population was selected to exclude dead cells. Populations were gated as follows: CD45 (%CD45+ of total live lymphocytes), CD3 (%CD3+ of CD11b-, CD11c-, CD45+), CD8 (%CD8+ of CD3), CD4 (%CD4+ of CD3), PD1 (%PD1 of CD4 or CD8), TIM3 (%TIM3 of CD4 or CD8), LAG3 (%LAG3 of CD4 or CD8).

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