nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies 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	All data needed to evaluate the conclusions in the paper are presented in the main text and the supplementary materials. Additional data related to this paper can be requested from the authors. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD050734. Data is now publicly available. The Single cell RNA-seq data is uploaded to the GEO - GSE272861 You may view our GSE272861 study at: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE272861 Data is now publicly available.
Data analysis	Code availability statement: No original code was generated for this project. Any code referenced or utilized is either in the public domain or has been appropriately cited from external sources. References that were used for the code:27,63–66

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 and material availability:
All data needed to evaluate the conclusions in the paper are presented in the main text and the supplementary materials.
Data availability statement:
All data needed to evaluate the conclusions in the paper are presented in the main text and the supplementary materials. Source data are provided with this paper.
The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD050734.
The Single cell RNA-seq data is uploaded to the GEO - To view our GSE272861 study at: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE272861.
All data is now publicly available.

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	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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 size was above 6 repeats or 6 mice in each condition to allow statistical significance.
Data exclusions	No data was excluded
Replication	We are presenting one representative experiment out of at least three independent experiments performed.
Randomization	not relevant
Blinding	not relevant

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: The following antibodies were used: CD4-FITC, mouse (IgG2bκ, Miltenyi Biotec), CD8-APC-VIO770 APC (REA734, Miltenyi Biotec), CD11b-PE (REA592, Miltenyi Biotec), Ly6c-APC (REA796, Miltenyi Biotec), Ly6g-FITC (REA526, Miltenyi Biotec), CD3-VioBlue (BW264/56, Miltenyi Biotec), CD45 APC (REA737, Miltenyi Biotec), Ly6A-PE (REA422, Miltenyi Biotec), CD44 APC (REA664, Miltenyi Biotec), MHC2 APC (M5/114.15.2, Biolegend), CD11c (N418, Biolegend), FoxP3 Alexa fluor 647 (MF-14, Biolegend), CD25 BV650 (PC61, Biolegend), REA control antibody- PE (isotype control, REA293, Miltenyi Biotec), CD69 (clone REA937), CD62L (clone MEL14-H2.100), anti-phopho-Erk1/2 (clone 6B8B69, Biolegend) and cMyc (clone 9E10, Abcam).

Validation: We have used commercial antibodies as detailed.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): B16F10 purchased directly from ATCC
B16F10-OVA a gift from Lea Eizenbach
Ret melanoma a gift from Viktor Umansky, German Cancer Research Center, Heidelberg, Germany.
MC38 purchased directly from ATCC

Authentication: Cell line were authenticated by the companies or the donors.

Mycoplasma contamination: Cell line were tested for mycoplasma and were negative

Commonly misidentified lines (See ICLAC register): No commonly misidentified lines were used.

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: gp100
OT1
C57blk

Wild animals: n/a

Reporting on sex: All experimental models encompass both male and female mice as well as cell lines.

Field-collected samples: n/a

Ethics oversight: All the animal experiments were conducted according to the guidelines of the Tel Aviv University Institutional Animal Care and Use Committee (#01-21-046).

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

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	Intracellular flow cytometry as performed using Miltenyi Biotec fixation buffer and permeabilization buffer according to the manufacture protocol.
Instrument	Cells were analyzed using flow cytometry (CytoFLEX, Beckman Coulter) and sorted by FACS (BD FACSAria III, BD Biosciences)
Software	Kaluza
Cell population abundance	At least 300 cells were recorded in each gate
Gating strategy	Gating strategy appear in Extended data of relevant Figures.

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