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| Last updated by author(s): | Mar 25, 2019 |

Reporting Summary

X Life sciences

Behavioural & social sciences

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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

| Statistics | | | | |
|---|--|--|--|--|
| For all statistical analys | es, confirm that the following items are present in the figure legend, table legend, main text, or Methods section. | | | |
| n/a Confirmed | | | | |
| ☐ ☐ The exact sam | pple size (n) for each experimental group/condition, given as a discrete number and unit of measurement | | | |
| A statement of | on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly | | | |
| The statistical Only common to | test(s) used AND whether they are one- or two-sided ests 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 descript AND variation | ion of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals) | | | |
| For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> values as exact values whenever suitable. | | | | |
| For Bayesian a | analysis, information on the choice of priors and Markov chain Monte Carlo settings | | | |
| For hierarchic | For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes | | | |
| Estimates of e | \square Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated | | | |
| 1 | Our web collection on <u>statistics for biologists</u> contains articles on many of the points above. | | | |
| Software and c | ode | | | |
| Policy information abou | ut <u>availability of computer code</u> | | | |
| Data collection | Zen | | | |
| Data analysis | Imaris, ImageJ, FSC Express Flow Cytometry Data Analysis, IDEAS®, Microsoft Excel and ZEN softwares. | | | |
| For manuscripts utilizing custo | om algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information. | | | |
| Data | | | | |
| - Accession codes, un - A list of figures that | ut <u>availability of data</u> include a <u>data availability statement</u> . This statement should provide the following information, where applicable: ique identifiers, or web links for publicly available datasets have associated raw data restrictions on data availability | | | |
| The authors declare that corresponding author up | all data supporting the findings of this study are available within this article and its supplementary information files or from the on reasonable request. | | | |
| | | | | |
| Field-speci | fic reporting | | | |
| Please select the one b | elow that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection. | | | |

Ecological, evolutionary & environmental sciences

Life sciences study design

| All studies must disclose on these points even when the disclosure is negative. | | |
|---|---|--|
| Sample size | At least three mice were analyzed in in vivo experiments. Organoid were grown from a mix of at least three mice and cultured in three independent biological repeats. | |
| Data exclusions | No data was excluded from any analyses. | |
| Replication | All experiments were repeated at least twice or three times as specified in the text. | |
| Randomization | Mice were randomized and sample sizes included mixed sex. Age was matched (8 weeks). | |
| Blinding | Investigators were blinded for statistical analyses of all microscopy quantifications. | |

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 | | Methods | | |
|----------------------------------|-----------------------------|-------------|------------------------|--|
| n/a | Involved in the study | n/a | Involved in the study | |
| | Antibodies | \boxtimes | ChIP-seq | |
| \boxtimes | Eukaryotic cell lines | | Flow cytometry | |
| \boxtimes | Palaeontology | \boxtimes | MRI-based neuroimaging | |
| | Animals and other organisms | | | |
| \boxtimes | Human research participants | | | |
| \boxtimes | Clinical data | | | |
| | | | | |

Antibodies

Antibodies used

Anti alpha human/mouse CD49f - (eBioscience, cat #12-0495-82, clone #eBioGoH3, lot #E01284-1632)

Anti Ly-6A/E - (BD Pharmigen, cat #558162, clone #D7, lot #5051949(

Anti Ki67 (eBioscience, cat #14-5698-80, clone #SolA15, lot #2002315)
Anti BrdU (Santa Cruz, cat #sc-32323, clone #IIB5, lot #F2016)

Anti keratin-5 (Abcam, cat #ab52635) Anti keratin-15 (Abcam, cat #ab77832)

Anti MCM2 (Abcam, cat #ab4461) Phalloidin (Life Technologies, cat #A22284, lot #1702518)

Validation

We rely on validation statements by manufacturers for all commercial antibodies.

Animals and other organisms

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research

Laboratory animals

Mus musculus - B6.Cg-Tg(Prdm1-EYFP)1Mnz/J mice. 8-week-old male and female mice were used randomly in this study.

Wild animals

Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Ethics oversight

All animal studies received institutional ethics approval by the Pre-Clinical Research Authority (PCRA) of the Technion-Israel Institute of Technology and were performed in agreement with this authority's guidelines (ethics #IL0040115).

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

Flow Cytometry

Plots

| Confirm that: | |
|---------------------------------|---|
| The axis labels state the i | marker and fluorochrome used (e.g. CD4-FITC). |
| The axis scales are clearly | y visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers). |
| All plots are contour plot | s with outliers or pseudocolor plots. |
| A numerical value for numerical | mber of cells or percentage (with statistics) is provided. |
| Methodology | |
| Sample preparation | Dorsal skin from 8-week-old mouse was shaved and harvested. Underlying adipose tissue was removed before incubating in trypsin overnight at 4oC or 2 hr at 37oC. Epidermis and hairs were collected and filtered before sorting. |
| Instrument | BD FACSAria IIIu |
| Software | FSC Express Flow Cytometry Data Analysis |
| Cell population abundance | Cells were sorted by setting a predefined purity mask (16/32) on Blimp1-EYFP positive cells, as determined by histogram for fluorescence intensity (see below). Purity was examined by fluorescence microscopy post sorting (>95%). |
| Gating strategy | Unstained cell sample was obtained by using littermates negative for Blimp1-EYFP. This sample was used to set PMT voltages, perform compensation and gate FSC-A/SSC-A. Dead cells and debris were gated out according to FSC and SSC properties and |

DAPI signal. Out of this parent population singlets were gated using FSC-W vs. FSC-H. Sorted cells were gated out of the singlets

according to Integrin alpha six positivity and from this parent population Sca1 negativity and EYFP positivity (Fig. 1b).

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