nature research

Corresponding author(s): AJ Radtke and RN Germain

Last updated by author(s): Aug 20, 2021

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 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	LASX software (v3.7.1.21655), Leica for microscopy acquisition.
Data analysis	Imaris and Imaris File Converter (x64, version 9.5.0 and higher, Bitplane, Oxford Instruments), Python (version 3.7.0 and higher), Custom SimpleITK Imaris Python Extension (code available at https://github.com/niaid/imaris_extensions).

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 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

See data availability statement in manuscript. The datasets generated during the current study are available in the Zenodo repository, [https://doi.org/10.5281/zenodo.5244551].

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	No sample size calculation was required for this work.
Data exclusions	Representative examples provided in the publication. No quantitative analyses are used so there is no risk of bias from exclusion.
Replication	All experiments and imaging panels were repeated at least three times on all tissue types to ensure reproducibility of the technique.
Randomization	Not applicable
Blinding	Not applicable

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 and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	See Supplementary Tables 1-2. Too extensive for inclusion here. Full antibody metadata (including lots) can be found here: https://doi.org/10.5281/zenodo.5244551
Validation	All antibodies use in the study have been used in our prior publications or underwent validation on human tissue individually to ensure expected distributions and co-localisation where appropriate. For further details of validations strategies see Hickey, J. et al. Spatial mapping of protein composition and tissue organization: a primer for multiplexed antibody-based imaging. arXiv:2107.07953 (2021).

Human research participants

Policy information about studies involving human research participants

Population characteristics	Human tissue was obtained at NIH at the time of risk-reducing surgery performed as a consequence of germline genetic mutation(s). All tissue procured, which included biopsies of lymph nodes, skin, spleen, liver and jejunum, was grossly normal as determined by the operative surgeon and histopathologically normal as determined by a board-certified pathologist. Human kidney samples were collected from patients undergoing elective renal surgery at Hannover Medical School. Samples were enrolled in this study after histologic assessment only after completion of routine diagnostics and written consent.
Recruitment	No recruitment or selection criteria was applied.
Ethics oversight	NIH Institutional Review Board (IRB)-approved protocol (13-C-0076) and the ethics committee of Hannover Medical School (ethics-vote number: 3381-16, 2893-15, 1741-13).

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