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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.

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	No software was used for data collection. All data shown in the manuscript is already publicly available.
Data analysis	We wrote custom software code which is available online on Github (distributed under the MIT License, version 0.2.2, https://github.com/rajewsky-lab/novosparc). The code is written in python and uses commonly used python libraries (numpy, matplotlib, sklearn, scipy, ot). To calculate spatial autocorrelation we used the implementation of PySAL (version 2.0.0), a Python spatial analysis library. We also used an implementation of the Gromov-Wasserstein transport method by Erwan Vautier (distributed under the MIT License).

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

No datasets were generated during the current study. The single cell datasets analyzed for the current study were acquired from the GEO database with the following GEO accession numbers: GSE99457 for the intestinal epithelium, GSE84490 for the liver, GSE95025 for the Drosophila embryo, GSE66688 for the zebrafish embryo and GSE107585 for the kidney. The cerebellum Slide-seq datasets were acquired from the Broad Institute Single Cell Portal (https://portals.broadinstitute.org/single_ cell/study/slide-seq-study). The individual Drosophila embryos dataset (Petkova, M.D., et al., Cell 2019) is available as Supplemental Information files of the original manuscript. The BDTNP dataset was downloaded directly from the BDTNP webpage (http://bdtnp.lbl.gov).

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 sizes for Fig. 3c & Ext. Data Figs. 2c 6a-g, 11b,c, 17,18 were based on 100 instantiations, and for Figs. 2b,f, 3b, 5b & Ext. Data Figs. 10b, 16b,c,f,g there was no subsampling of the data.
Data exclusions	No data were excluded
Replication	Experimental replication was not attempted and is not applicable to this study
Randomization	Since the single cell transcriptomes are unique and technically not reproducible, randomization was not applicable to the study
Blinding	No datasets were generated during the current study, and therefore blinding was 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
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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