

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	MinKNOW (Oxford Nanopore Technologies, multiple versions, updated frequently, from 18.12 to 22.10.10) was used for data collection during ONT RNA sequencing. Guppy (Oxford Nanopore Technologies, versions 4.0.11, 4.4.1, 5.0.11, 6.0.0) was used for basecalling of RNA sequencing data. Dorado (Oxford Nanopore Technologies, version 0.7.0) was used for basecalling of RNA and cDNA sequencing data.
Data analysis	Minimap 2.17, Nanopolish 0.13.2, Samtools 1.9, Guppy (versions 4.0.11, 4.4.1, 5.0.11, 6.0.0), Subread 2.0.1 R 4.1.2 with the following packages: base, datasets, graphics, grDevices, grid, methods, stats, stats4, utils (all of them have the same version number as R) Other R packages loaded via namespace: BiocGenerics 0.40.0, biomaRt 2.50.3 dplyr 1.1.0, forcats 1.0.0, ggplot2 3.4.1, gprofiler2 0.2.1, Gviz 1.38.4, IRanges 2.28.0, nanotail 0.1.0, purrr 1.0.1, S4Vectors 0.32.4, stringr 1.5.0, tibble 3.1.8, tidyr 1.3.0, tidyverse 2.0.0, Biostrings 2.62.0, data.table 1.14.8, foreach 1.5.2, GenomicAlignments 1.30.0, GenomicFeatures 1.46.5, gridExtra 2.3, knitr 1.42, magrittr 2.0.3, plyr 1.8.8, rlang 1.1.1, rmarkdown 2.20, rstudioapi 0.14, scales 1.2.1, stringi 1.7.12, SummarizedExperiment 1.24.0, vroom 1.6.1, protti 0.9.1

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](#)

The raw sequencing data (fast5 and pod5 files) were deposited at the European Nucleotide Archive (ENA) (<https://www.ebi.ac.uk/ena/browser/home>) under the project numbers PRJEB75356 and PRJEB80123 with sample numbers listed in Supplementary Data 5.

MS/MS data was deposited to PRIDE with following reviewer access details:

Username: reviewer_pxd072661@ebi.ac.uk
Password: sXOFClwz3bC0

Data underlying figures are provided in Supplementary Datasets and are also publicly available from Zenodo along with additional raw data: <https://zenodo.org/records/17716349>

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 [Not applicable.](#)

Reporting on race, ethnicity, or other socially relevant groupings [Not applicable.](#)

Population characteristics [Not applicable.](#)

Recruitment [Not applicable.](#)

Ethics oversight [Not applicable.](#)

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 [No statistical method was used to predetermine sample size. For in vivo animal experiments, we estimated the sample size based on previous studies, our pilot experiments.](#)

Data exclusions [There was no formal criteria of sample exclusions. All attempts to repeat the experiments were successful.](#)

Replication [We used at least two biological replicates for statistical analysis, precise replicate number is denoted within each figure caption. Below mentioned experiments were performed in stated number of biological replicates, which can vary between experimental groups:](#)

Figure 1A: blood indices: n (WT) = 7; n (Tent5c^{cat}) = 6 | plasma albumins: n (WT) = 4; n (Tent5c^{cat}) = 4 | RBC/Ret-He: n (WT) = 5; n (Tent5c^{cat}) = 5
Figure 1B: n (WT) = 8; n (Tent5c^{ko}) = 9
Figure 1C: n (WT) = 5; n (Tent5c^{cat}) = 5
Figure 2A: n (WT) = 6–9; n (Tent5c^{ko}) = 6–12
Figure 2B: n (WT) = 5–9; n (Tent5c^{ko}) = 12
Figure 2C: n (WT) = 6–8; n (Tent5c^{ko}) = 9–12
Figure 2D: n (WT) = 6; n (Tent5c^{ko}) = 7
Figure 2E: bone marrow: n (WT) = 8; n (Tent5c^{cat}) = 7 | spleen: n (WT) = 6; n (Tent5c^{cat}) = 7
Figure 2F: n (WT) = 10; n (Tent5c^{ko}) = 11

Figure 2G: n (WT) = 8; n (Tent5c^{cat}) = 7
 Figure 2H: n (WT) = 6; n (Tent5c^{cat}) = 7
 Figure 3A: n (Tent5c-Egfp) = 5–10
 Figure 3B: n (Tent5c-Egfp) = 5
 Figure 3C: n (WT) = 2; n (Tent5c^{ko}) = 2
 Figure 3D: n (WT) = 2; n (Tent5c^{ko}) = 2
 Figure 3E: n (WT) = 3; n (Tent5c^{cat}) = 3
 Figure 3F: n (WT) = 3; n (Tent5c^{cat}) = 3
 Figure 4A-C: n (WT) = 3; n (Tent5c^{cat}) = 3
 Figure 5B-C: n (Tent5c-Egfp) = 3
 Figure 5D: n = 3
 Figure 6A-D: n = 3
 Figure 7E: n (Tent5c-Egfp erythroblasts) = 3; n (Tent5c-Egfp b-cells) = 3
 Supplementary Figure 1A: n (WT) = 7; n (Tent5c^{ko}) = 4
 Supplementary Figure 1B: n (WT) = 33-46; n (Tent5c^{ko}) = 11–15
 Supplementary Figure 1C: n (WT) = 7-8; n (Tent5c^{cat}) = 7-8
 Supplementary Figure 1D: n (WT) = 4–6; n (Tent5c^{ko}) = 4–6
 Supplementary Figure 1E: n (WT) = 7–12; n (Tent5c^{ko}) = 6–7
 Supplementary Figure 2A: n = 2
 Supplementary Figure 2C: n = 2
 Supplementary Figure 2D: n (WT) = 3; n (Tent5c^{cat}) = 3
 Supplementary Figure 3B: n (Tent5c-Egfp) = 3
 Supplementary Figure 3E: n = 2
 Supplementary Figure 5A-B: n = 3
 Supplementary Figure 6A: n = 3
 Supplementary Figure 6B: n = 1
 Supplementary Figure 6C: n = 3

Randomization	Mice of different genotypes were assigned with individual numerical tags in the database and they were used for the tissue collection and throughout subsequent processing as the only identifiers.
Blinding	Individual mice had an assigned numerical tag and mice with different genotypes were indistinguishable by the experimenter. Blinding was not relevant for the experiments performed on cultured cells.

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
☐	☐ Clinical data
☐	☐ Dual use research of concern
☐	☐ Plants

Methods

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

Antibodies

Antibodies used

Hamster Anti-Mouse CD3-BV421 (BD Biosciences, Cat# 562600), Rat Anti-Mouse CD11b-BV421 (BD Biosciences, Cat# 562605), Rat Anti-Mouse CD41-BV421 (BD Biosciences, Cat# 747729), Rat Anti-Mouse CD45R-BV421 (BD Biosciences, Cat# 562922), Rat Anti-Mouse Ly6G/Ly6C-BV421 (BD Biosciences, Cat# 562709), Rat Anti-Mouse CD71-PE (Southern Biotech, Cat# 1720-09), Rat Anti-Mouse TER-119-Alexa Fluor 647 (BioLegend, Cat# 116218), Rat Anti-Mouse CD44-PE-CF594 (BD Biosciences, Cat# 562464), Rat Anti-Mouse CD11b-BV786 (BD Biosciences, Cat# 740861), Rat Anti-Mouse F4/80-Like Receptor-BUV395 (BD Biosciences, Cat# 744341), Rat Anti-Mouse Ly6C-PE-Cy7 (BD Biosciences, Cat# 560593), Rat Anti-Mouse VCAM1-BV650 (BD Biosciences, Cat# 740471), Rat Anti-Mouse CD169-BV421 (BD Biosciences, Cat# 566604), Rat Anti-Mouse TER-119-Biotin (Invitrogen, Cat# 13-5921-82), Rat Anti-Mouse CD71-FITC (Southern Biotech, Cat# 1720-02), Mouse Anti-Transferrin Receptor (H68.4) (Invitrogen, Cat# 13-6800), Goat Anti-Rabbit IgG-HRP (Sigma-Aldrich, Cat# 401393), Goat Anti-Mouse IgG-HRP (Sigma-Aldrich, Cat# 401215), Rabbit Anti-GFP (ChromoTek, Cat# pabg1), Rabbit Anti-DYKDDDDK Tag (ChromoTek, Cat# 20543-1-AP), Mouse Anti-HA Tag (6E2) (Cell Signaling Technology, Cat# 2367), Mouse Anti- α -Tubulin (DM1A) (Sigma-Aldrich, Cat# T9026), Rabbit Anti-GAPDH (Proteintech, Cat# 10494-1-AP), Rabbit Anti-DBC1/p30 DBC (Bethyl Laboratories, Cat# A300-434A), Rabbit Anti-SQSTM1/p62 (Cell Signaling Technology, Cat# 5114), Rabbit Anti-FNDC3A (Proteintech, Cat# 25240-1-AP), Rabbit Anti-FNDC3B (Proteintech, Cat# 22605-1-AP), Rabbit Anti-LARP4 (Proteintech, Cat# 16529-1-AP), Rabbit Anti-LARP5 (Novus Biologicals, Cat# NBP3-05086), Rabbit Anti-Hemoglobin subunit alpha (Abcam, Cat# ab82811), Rabbit Anti-Hemoglobin subunit beta (Abcam, Cat# EPR20614).

Validation

Pre-validated antibodies were purchased from commercial vendors and specific clones were chosen based on the literature, our own pilot studies, or by the product data sheets provided by companies.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

HEK293T cell line was obtained from ATCC (CRL-3216, ATCC). Primary culture of murine erythroblasts were of mixed sex as we used random pooling of the livers (further described in relevant section of the methods). B-cells for primary culture were obtained from adult female mice.

Authentication

Cell lines were not authenticated.

Mycoplasma contamination

All cell lines tested negative for mycoplasma contamination by PCR.

Commonly misidentified lines
(See [ICLAC](#) register)

No commonly misidentified lines were used in this study.

Palaeontology and Archaeology

Specimen provenance

Not applicable.

Specimen deposition

Not applicable.

Dating methods

Not applicable.

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight

Not applicable.

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

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

The following mice strains were used in this study: B6CBAF1;B6-TENT5C KO/Tar; B6CBAF1;B6-TENT5C Cat (D90N;D92N)/Tar; B6CBAF1;B6-TENT5C-EGFP/GFP/Tar. Mice strains were generated and genotyped by Genome Engineering Unit, IIMCB (www.geu.iimcb.gov.pl) developed from Mouse Genome Engineering Facility (www.crisprpmice.eu). Mice of both sex were sacrificed at age 12-20 weeks for tissue collection. To perform experiments on fetal livers, pregnant females (12-20 weeks old) were sacrificed at embryonic development days E12.5-E15.5.

Wild animals

No wild animals were used in the study.

Reporting on sex

The sex of mice used to derive cell cultures was not considered in the study design or analysis, as these were not germ line cells, whose transcriptome vary significantly by sex.

Field-collected samples

No field collected samples were used in the study.

Ethics oversight

All procedures were approved by the I Local Ethical Committee in Warsaw affiliated at University of Warsaw, Faculty of Biology (approval number WAW/693/2018), with the requirements of the EU (Directive 2010/63/EU) and Polish (Act number 266/15.01.2015) legislation.

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration

Not applicable.

Study protocol

Not applicable.

Data collection

Not applicable.

Outcomes

Not applicable.

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

- | No | Yes |
|-------------------------------------|---|
| ☒ | ☐ Public health |
| ☒ | ☐ National security |
| ☒ | ☐ Crops and/or livestock |
| ☒ | ☐ Ecosystems |
| ☒ | ☐ Any other significant area |

Experiments of concern

Does the work involve any of these experiments of concern:

- | No | Yes |
|-------------------------------------|--|
| ☒ | ☐ Demonstrate how to render a vaccine ineffective |
| ☒ | ☐ Confer resistance to therapeutically useful antibiotics or antiviral agents |
| ☒ | ☐ Enhance the virulence of a pathogen or render a nonpathogen virulent |
| ☒ | ☐ Increase transmissibility of a pathogen |
| ☒ | ☐ Alter the host range of a pathogen |
| ☒ | ☐ Enable evasion of diagnostic/detection modalities |
| ☒ | ☐ Enable the weaponization of a biological agent or toxin |
| ☒ | ☐ Any other potentially harmful combination of experiments and agents |

Plants

Seed stocks	Not applicable.
Novel plant genotypes	Not applicable.
Authentication	Not applicable.

ChIP-seq

Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links <i>May remain private before publication.</i>	Not applicable.
Files in database submission	Not applicable.
Genome browser session (e.g. UCSC)	Not applicable.

Methodology

Replicates	Not applicable.
------------	--

Sequencing depth	Not applicable.
Antibodies	Not applicable.
Peak calling parameters	Not applicable.
Data quality	Not applicable.
Software	Not applicable.

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	Samples were prepared as described in the methods within "Flow cytometry" subsection.
Instrument	Samples were measured using CytoFLEX LX (Beckman Coulter Life Sciences) and sorted using CytoFLEX SRT (Beckman Coulter Life Sciences).
Software	CytExpert v2.2 software was used to control CytoFLEX LX instrument and analyse samples; CytExpert SRT v1.2 software was used to control CytoFLEX SRT and analyse sorted samples.
Cell population abundance	Purity of post-sort fractions for cells of interest was determined by sorting 1000 cells and re-acquiring at least 50% of each sample. The purity of sorted cells was at least 85% of phenotype intended for enrichment.
Gating strategy	Cell populations are described in the relevant figures and legends. Detailed gating strategy is described in Supplementary Figure 8 in Supplementary Information.

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

Magnetic resonance imaging

Experimental design

Design type	Not applicable.
Design specifications	Not applicable.
Behavioral performance measures	Not applicable.

Acquisition

Imaging type(s)	Not applicable.
Field strength	Not applicable.
Sequence & imaging parameters	Not applicable.
Area of acquisition	Not applicable.
Diffusion MRI	☐ Used ☒ Not used

Preprocessing

Preprocessing software	Not applicable.
Normalization	Not applicable.

Normalization template	Not applicable.
Noise and artifact removal	Not applicable.
Volume censoring	Not applicable.

Statistical modeling & inference

Model type and settings	Not applicable.
Effect(s) tested	Not applicable.
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	Not applicable.
(See Eklund et al. 2016)	
Correction	Not applicable.

Models & analysis

n/a	Involvement in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis