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Corresponding author(s): Riakrd Holmdahl

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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 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	*Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.*
Data analysis	*Provide a description of all commercial, open source and custom code used to analyse the data in this study, specifying the version used OR state that no software was used.*

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

Proteomics dataset was deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD024126.

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	The sample size was chosen based on the studied effect size, incidence in the studied disease models, and our overall (extensive) experience with animal models. For enough statistical power, disease model experiments usually required 10 mice/group, whereas more controlled in vitro experiments usually required 5 mice/group.
Data exclusions	No data points were excluded from the presented data
Replication	Experiments were repeated either exactly, in a similar setup, or using alternative methods that give the same or similar information, for example evaluation of cytokine production by ELISA and flow cytometry in independent experiments; or evaluation of disease phenotypes using pathomechanistically similar disease models such as are CIA and EAE. Additionally, we exclusievly use biological replicates throughout the study.
Randomization	Mice of different genotypes were kept in mixed cages to avoid cage effects. Samples were also allocated randomly in culture plates to avoid plate effects.
Blinding	Animal disease model experiments such as CIA or EAE were scored in a blinded manner.

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	Antibodies are listed in the Materials and Methods section
Validation	All antibodies are commonly used in scientific publications and/or have been validated by the manufacturer

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	MCF-7 were originally obtained from ATCC
Authentication	Cell lines were not authenticated
Mycoplasma contamination	Cell lines were not tested for mycoplasma
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	species: Mus Musculus, strains: C57BL/10J and RIIIS/J, sex: female and male, age: 12 weeks
Wild animals	study did not involve wild animals
Field-collected samples	study did not involve field-collected samples
Ethics oversight	Jordbruksverket, regional ethic committee, Stockholm, Sweden

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	healthy volunteers, age: 28-48, gender: mixed female and male, no genotypic information, no known diagnosis
Recruitment	colleagues recruited on volunteer basis
Ethics oversight	Etikprövningsmyndigheten, Swedish ethical Review authority, Uppsala, Sweden

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 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	Mouse organs were harvested directly after termination of mice by CO2 and kept in PBS until mechanic dissociation on cell strainers. Cell suspensions were washed in PBS and red blood cells lysed if applicable. Thereafter cells were counted, and typically 1M cells were plated for staining. For more details on cell preparation and flow cytometry staining protocol please refer to Materials and Methods. Human PBMCs were prepared from blood of healthy donors using SepMate (Stemcell Technologies) as stated in Materials and Methods.
Instrument	LSR II (BD), Attune NxT (Thermo Scientific)
Software	BD FACSDiva v6.0 , Attune NxT Software v3.1, FlowJo v8.8.7
Cell population abundance	Only applicable to proteomic analysis in fig. 6h, the abundance of CD4+ cells afer enrichment was 85%. Cell frequencies in other experiments are stated in FACS plots.
Gating strategy	A typical gating strategy is as follows: Lymphocytes > singlets > viability > relevant markers (e.g. TCRb+ > CD4+ > CD44+). Figure exemplifying gating strategy will be added if manuscript is considered for revision.

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