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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	For flow cytometry, cytoflex software was used for data collection.
Data analysis	For flow cytometry, kaluza software was used for data analysis.

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

All relevant data are available from the authors upon reasonable request.

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	For small and robust in vitro experiments: n = 3. For non-efficacy animal studies (e.g. CD45 silencing): n = 5. For the efficacy studies: n = 12 because of the higher level of variation between disease severity. When n was set to 12, the standard deviations were deemed small enough.
Data exclusions	No data was excluded
Replication	All experiments were carried out at least 3 times successfully.
Randomization	Samples and mice were randomized in the experiments
Blinding	Investigators were blinded during randomization and during data acquisition

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

Rat anti-mouse α4β7 integrin (Clone DATK32, Biolegend)
Rat anti-mouse β7 integrin (Clone FIB504, BioXCell)
Mouse anti-rat IgG2a (Clone RG7/1.30, BioXCell)
Rat IgG2a isotype control (Clone 2A3, BioXCell)
PE-conjugated donkey anti-mouse IgG (Polyclonal, Jackson Immuno Research)
AlexaFluor 647-conjugated goat anti-rat IgG (Polyclonal, Biolegend)
AlexaFluor 647-conjugated mouse anti-human IgG (Polyclonal, Biolegend)
AlexaFluor 647-conjugated rat anti-mouse CD45 (Clone 30-F11, Biolegend)
AlexaFluor 488-conjugated rat anti-mouse CD45 (Clone 30-F11, Biolegend)
BV650-conjugated rat anti-mouse/human CD11b (Clone M1/70, Biolegend)
PE/Cy5-conjugated rat anti-mouse CD19 (Clone 6D5, Biolegend)
BV421-conjugated hamster anti-mouse CD3ε (Clone 145-2C11, Biolegend)
APC/Cy7-conjugated rat anti-mouse CD4 (Clone GK1.5, Biolegend)
AlexaFluor 488-conjugated rat anti-mouse CD8a (Clone 53-6.7, Biolegend)
PE-conjugated rat anti-mouse CD8a (Clone 53-6.7, Biolegend)
PE/Dazzle 594 rat anti-mouse CD25 (Clone PC61, Biolegend)
BV510 armenian hamster anti-mouse CD69 (Clone H1.2F3, Biolegend)
PE-conjugated rat anti-mouse FOXP3 (Clone MF-14, Biolegend)
HRP-conjugated donkey anti-rat IgG (Polyclonal, Jackson Immuno Research)

Validation

Every antibody was validated for the specific assay it was used for. Antibodies were also checked for cross-reactivity.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	American Type Culture Collection
Authentication	None of the cell lines used were authenticated
Mycoplasma contamination	Cell lines were tested negative for mycoplasma contamination every 2 months.
Commonly misidentified lines (See ICLAC register)	No misidentified cell lines were used in the study.

Animals and other organisms

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

Laboratory animals	C57BL/6J wild type and C57BL/6J IL-10KO mice were used in this study.
Wild animals	This study did not use wild animals
Field-collected samples	This study did not involve samples collected from the field
Ethics oversight	The Tel Aviv Institutional Animal Care and Use Committee approved the animal protocols for all in vivo studies in accordance with current regulations and standards of the Israel Ministry of Health.

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	Cells were either taken from cell culture or animal tissues. For tissue appropriate tissue dissociation techniques were used. Single cell suspensions were used for the flow cytometry
Instrument	Beckman Coulter CytoFLEX LX
Software	Kaluza
Cell population abundance	Cells were collected to obtain at least 3000 events in the smallest subpopulation.
Gating strategy	Live cells were gated with DAPI-negative staining. Singlets were gated with SSC-H vs. SSC-A plots. Different cell types were gated with FSC/SSC plots and specific cell populations were gated with the corresponding labeled antibody.

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