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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	No software was used
Data analysis	GraphPad Prism version 6

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

The source data underlying subpanels of Figs. 1, 2 and 5, and Supplementary Figs. 6 and 8 are provided as a Supplementary Source Data file. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Field-specific reporting

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Not appropriate
Data exclusions	No data were excluded
Replication	Regulatory T cell functional assay was performed once for each patient due to the lack of primary cells available
Randomization	No randomization
Blinding	Blinding no relevant for this study

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

Antibody Source Clone
anti-CD45-PerCP-Cy5.5 Beckton Dickinson 2D1 (HLe-1)
anti-CD3-FITC Beckton Dickinson SK7
anti-CD4-PE-Cy7 Beckton Dickinson SK3
anti-CD8-APC-Cy7 Beckton Dickinson SK1
anti-CD19-APC Beckton Dickinson SJ25C1
anti-CD16-PE Beckton Dickinson B73.1
anti-CD56-PE Beckton Dickinson NCAM16.2
anti-CD4-PerCP-Cy5.5 Beckton Dickinson SK3
anti-CD8-APC-H7 Beckton Dickinson SK1
anti-CD45RA-FITC Beckton Dickinson L48
anti-CD45RO-PE Beckton Dickinson UCHL1
anti-CCR7-PE-Cy7 Beckton Dickinson 3D12
anti-CD31-AF647 Beckton Dickinson M89D3
anti-CD19-V500 Beckton Dickinson HIB19
anti-CD27-V450 Beckton Dickinson M-T271
anti-CD24-FITC Beckton Dickinson ML5
anti-IgD-PE Beckton Dickinson IA6-2
anti-CD38-PE-Cy7 Beckton Dickinson HIT2
anti-CD21-APC Beckton Dickinson B-ly4
anti-CD14-FITC Beckman Coulter RMO52
anti-CD14- APC BD Pharmingen M5E2
anti-CD3-PerCP BD Pharmingen SK7
anti-CD45RO PE-CF 594 Beckton Dickinson UCHL1
anti-CD4 PE-Cy7 Beckman Coulter SFCI 12T4D11
anti-TNF-a-PE BD Pharmingen MAb11
anti-IL4-APC eBioscience 17-7049-42
anti-IFNg-FITC BD Bioscience B27
anti-IL17A-PE Invitrogen 12-7179-42
anti-CTLA4-PE BD Pharmingen BNI3
anti-CD25-PE-Cy7 BD Pharmingen M-A251

anti-Foxp3-APC Invitrogen PCH101
anti-Helios-eF450 Invitrogen 22F6
anti-P-STAT1-AF647 BD phosflow 4a
anti-CD11c PE Cy5 BD Bioscience BU.15
anti-CD14 VioBlue Beckman Coulter TUK4
anti-CD16 BV510 Sony 3G8
anti-CD33-PerCP-Cy5.5 Beckton Dickinson P.67.6
anti-pSTAT1-BV421(pY701) Beckton Dickinson 4a

Validation: Data provided in the manuscript

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293T were provided by Sylvain Latour's lab
Authentication	None of the cell lines used were authenticated
Mycoplasma contamination	Cell lines were not tested for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

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	For surface staining, PBMCs (either freshly isolated or thawed after storage in liquid nitrogen) were washed with cold PBS and then incubated for 30 min at 4 °C (in the dark) with appropriate fluorochrome-labeled monoclonal antibodies. For intracellular staining, PBMCs were fixed and permeabilized after surface staining using the FoxP3 staining kit (eBioscience) according to the manufacturer's instructions, and then incubated with anti-FOXP3 and anti-CTLA4 for 30 min on ice. The antibodies used for flow cytometry are listed in Supplementary Table 2.
Instrument	Becton Dickinson LSRFortessa X-20
Software	FlowJo
Cell population abundance	Not available
Gating strategy	Data provided in the manuscript

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