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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	Ribosomal Database Project database (trainset9_032012.pds), VFDB (http://www.mgc.ac.cn/VFs/), and NCBI Microbial proteins database at the NCBI website (http://www.ncbi.nlm.nih.gov/blast).
Data analysis	FlowJo (v.10.2), Mothur (v.1.36.1), QIIME (v.1.8.0), R package vegan (v.2.4.4), R package Indicspecies (v.1.7.6), MAFFT (v.7.305b), FastTree (v.2.1.10), Sickle (v.1.33), SPAdes (v.3.9.0), Prokka (v.1.11), khmer (v.1.4.1), FASTX Toolkit (v.0.0.13), KmerGenie (v.1.7.038), Velvet (v.1.2.10) and MetaVelvet (v.1.2.02), Prokka (v.1.12-beta), Roary (v.3.6.0), Bowtie2 (v.2.3.1), SAMtools (v.0.1.19), Prism (6.0e), ImageJ (1.8.0), and R (v.3.2.4.Revised).

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

The 16S rRNA sequence data, shotgun sequence data, and genome sequence data of OTU0001 and OTU0002 are available from the DDBJ Sequence Read Archive under DDBJ BioProject IDs PRJDB6615, PRJDB6620, and PRJDB6618-6619, respectively.

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 sample-size calculations were performed. Sample sizes were determined to be adequate based on previous experiments and preliminary studies
Data exclusions	No samples or animals were excluded from the analysis except for Extended Data Fig. 9a where outliers were detected prior to the analysis with two-tailed Grubbs' test (Prism).
Replication	Replicate experiments were successful at least two times. The sequencing studies (16S rRNA gene sequencing, , shotgun sequencing, and genome sequencing) and the studies in Extended Data Fig. 7 were performed one time each.
Randomization	Samples were not randomized for mouse experiments. Analyzed mice were age- and sex-matched whenever possible.
Blinding	Scoring of EAE severity and quantification of demyelinated regions in the white matter were done in blinded fashion.

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

Antibodies

Antibodies used	Following antibodies were used in the study (clone, supplier, catalogue number, dilution): anti-CD16/32 (clone 93, BioLegned, 1:100), APC-Cy7 anti-CD3 (clone 17A2, BioLegend, 100222, 1:100), PE-Cy7 anti-CD3e (clone 145-2C11, BD Biosciences, 552774, 1:200), FITC anti-TCRbeta (clone H57-597, BioLegend 109206, 1:100), APC anti-CD4 (clone GK1.5, BioLegend, 100412, 1:200), PerCP-Cy5.5 anti-CD4 (clone GK1.5, BioLegend, 100434, 1:100), PerCP-Cy5.5 anti-CD8alpha (clone 53-6.7, BioLegend, 100732, 1:100), PE-Cy7 anti-IL-17A (clone TC11-18H10.1, BioLegend, 506922, 1:100), FITC anti-IFN-gammna (clone XMG1.2, BioLegend, 505806, 1:100), PE anti-Foxp3 (clone FJK-16s, Thermo Fisher Scientific, 12-5773-82, 1:200), APC-Cy7 anti-CD44 (clone IM7, BioLegend, 103028, 1:100), Pacific Blue anti-CD62L (clone MEL-14, BioLegend, 104423, 1:200), PE anti-TCR Valpha3.2 (clone RR3-16, BioLegend, 135406, 1:100), Alexa Fluor 647 anti-TCR Vbeta11 (clone KT11, BioLegend, 125909, 1:200), FITC anti-Ki-67 (clone SolA15, Thermo Fisher Scientific, 11-5698-82, 1:200), eFlow 450 anti-MHC class II (clone AF6-120.1, Thermo Fisher Scientific, 48-5320-82, 1:100), FITC anti-CD11c (clone HL3, 553801, 1:100), anti-mouse I-A/I-E (clone M5/114.15.2, BioLegend, 107610, final conc. 10µg/ml), Purified Rat IgG2b, κ isotype control (clone RTK4530, BioLegend, 400621, final conc. 10ug/ml)
Validation	All antibodies were validated for use in flow cytometry and in vitro blocking assay (see manufacturer's website)

Animals and other organisms

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

Laboratory animals	SPF C57BL/6 mice (female) were purchased from CLEA Japan and 9-12 weeks age were used for experiments. C57BL/6-Tg(Tcra2D2,Tcrb2D2)1Kuch/J mice were obtained from The Jackson Laboratory and bred in the SPF and GF facility of the RIKEN Yokohama Branch. Both male and female mice at 6-8 weeks of age were used for experiments. GF C57BL/6 mice were originally

	purchased from Sankyo Labo Service Corporation and CLEA Japan, and bred in the GF facility of the RIKEN Yokohama Branch. Female mice at 5-7 weeks of age were used for gnotobiotic studies.
Wild animals	No wild animals were used in this study.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All experimental procedures were approved by, and performed in accordance with, the Institutional Animal Care and Use Committee of the RIKEN Yokohama Branch.

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	Sample preparation was described in Methods.
Instrument	FACS Canto II and FACS Aria III
Software	FACSDiva for collection and FlowJo (version 10.2) for analysis.
Cell population abundance	Approximately 1-3 x 10^7 of cells per mouse were harvested from lamina propria of the small intestine, of which CD4+ T cells and CD8alpha+ T cells constituted 20-30% and 5-10%, respectively. The purity of sorted cells was > 96% as determined by flow cytometry.
Gating strategy	RBCs, debris, and dead cells were gated out based on distinctive FSC and SSC profile. Zombie negative live cells were used for analyses. The detailed gating strategies were shown in Figure legends.

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