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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	Fungal microbiome was analyzed using the Illumina MiSeq Next generation sequencing platform. All flow cytometry data were collected by FACS Diva Software V9.0. Whole genomic sequencing data were collected by Illumina HiSeqX platform by Novogene. Co., Ltd.
Data analysis	Fungal microbiome analysis performed with QIIME v1.6, R packages Phyloseq (1.26.1), Vegan (2.5-5) in R version 3.5.2, and ggplot2 (v3.3.3). The dendrogram performed by SNPRelate R package and circlize R package . Flow cytometry data analyzed by FlowJo V10. Statistical analysis analyzed by R , Graphpad Prism V9 and JMP softwarev16.1. Fluorescence In Situ Hybridization (FISH) Images were merged by Fiji ImageJ 2.1.0/1.53c software.

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

ITS sequencing data are publicly available in NCBI Sequence Read Archive (SRA) under the Bioproject ID PRJNA610042. The data from whole-genome sequencing of human gut-derived C. albicans isolates are publicly available in the NCBI Sequence Read Archive (SRA) under Bioproject ID PRJNA702809. Raw sequencing data for representative C. albicans strains were downloaded from the NCBI Sequence Read Archive under BioProject ID PRJNA43288443.

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.

- [x] 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 human sample studies, we chose our sample size for 38 non-inflammatory bowel disease individuals (PMID: 26843508) to give sufficient data values to conduct standard statistical tests. Seventy-eight colonic mucosa-enriched lavage samples (38 non-inflammatory bowel disease individual and 40 patients with ulcerative colitis) were obtained following Institutional Review Board-approved protocols from the Center for Advanced Digestive Diseases and the JRI IBD Live Cell Bank Consortium at Weill Cornell Medicine. No statistical analysis was used to determine the appropriate sample size for mice. The group sizes of mice and samples were chosen based on our experience with similar studies (PMID: 29326275), common practice in the field, resource availability and animal welfare guidelines. Four or more mice per group were used in each experiment to give sufficient data values to conduct standard statistical tests.
Data exclusions	Based on quality control, one non-IBD sample was excluded from further mycobiome sequencing and analysis. No mice or other data were excluded for analysis.
Replication	All attempts at replication of experiments were successful and were performed at least two to three times.
Randomization	Age and sex matched groups of mice were randomly allocated to the experimental groups. For all other experiments, samples/animals were randomly allocated to experimental groups and processed.
Blinding	The investigators were blinded during sample and data collection. The investigators were not blinded for performing experiments, since different treatments are required for separate groups. For colon histological evaluation, the investigators were blinded to group allocation during the data collection and/or analysis.

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	
[ ]	[x]	Antibodies
[ ]	[x]	Eukaryotic cell lines
[x]	[ ]	Palaeontology
[ ]	[x]	Animals and other organisms
[ ]	[x]	Human research participants
[x]	[ ]	Clinical data

Methods

n/a	Involved in the study	
[x]	[ ]	ChIP-seq
[ ]	[x]	Flow cytometry
[x]	[ ]	MRI-based neuroimaging

Antibodies

Antibodies used

The staining antibodies for flow cytometry were purchased from Thermo Fisher Scientific, Biolegend or BD Biosciences. Dead cells were excluded with eBioscience Fixable Viability Dye eFluor 506 (Thermo Fisher Scientific, Cat # 65-0866-14, 1:1000 dilution) during surface staining. All antibodies used at 1:200 unless otherwise noted.
Fluorophore-conjugated antibodies against mouse antigens:
anti-CD16/CD32 (clone 92),Cat # 14-0161-81, RRID: AB_467132.
anti-CD45 (clone 30-F11), Cat # 103151, RRID:AB_2565884.
anti-CD45 (clone 30-F11), Cat # 103155, RRID:AB_2650656.
anti-I-A/I-E (clone M5/114.15.2), Cat # 107639, RRID: AB_2565894.
anti-CD11b (clone M1/70), Cat # 25-0112-82, RRID: AB_469588.
anti-Ly6G (clone 1A8-Ly6g), Cat # 127624, RRID: AB_10640819.
anti-CD11c (clone N418),Cat # 117319, RRID: AB_528735.
anti-CD4 (clone RM4-5), Cat # 100548, RRID: AB_2563054.
anti-CD4 (clone RM4-5),Cat #100526, RRID:AB_312727.
anti-TCRβ (clone H57-597),Cat # 109206, RRID: AB_313429.
anti-TCRβ (clone H57-597),Cat # 109228, RRID: AB_1575173.
anti-FOXP3 (clone FJK-16S),Cat # 17-5773-82, RRID: AB_469457.

anti-IL-17A (clone eBio 17B7) Cat#12-7177-81; RRID:AB_763582.
anti-IFNγ (clone XMG1.2) Cat#505824; RRID:AB_2561300,
anti-RORγt (clone B2D) Cat # 12-6981-82; RRID: AB_10807092,
anti-IL-17F (clone 9D3.1C8) Cat # 517006; RRID:AB_10661903.
For IL-1 R blockade in vivo antibodies: InVivoMab anti-IL-1R1 IgG (JAMA147; BioXCell) Cat#BE0256,
1 mg of InVivoMAb Armenian hamster IgG (BioXcell) Cat#BE0091.

Validation

All antibodies used in this study are commercially available. All antibodies have been validated by the manufacturer. Data are available on the manufacturer's websites.
Fluorophore-conjugated antibodies against mouse antigens:
anti-CD16/CD32 (clone 92), Cat # 14-0161-81. https://www.thermofisher.com/antibody/product/CD16-CD32-Antibody-clone-93-Monoclonal/14-0161-82
anti-CD45 (clone 30-F11), Cat # 103151. https://www.biolegend.com/en-us/products/brilliant-violet-650-anti-mouse-cd45-antibody-11987?GroupID=BLG6837
anti-CD45 (clone 30-F11), Cat # 103155. https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-mouse-cd45-antibody-8721
anti-I-A/I-E (clone M5/114.15.2), Cat # 107639.https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-mouse-i-a-i-e-antibody-11988
anti-CD11b (clone M1/70), Cat # 25-0112-82.https://www.thermofisher.com/antibody/product/CD11b-Antibody-clone-M1-70-Monoclonal/25-0112-82
anti-Ly6G (clone 1A8-Ly6g), Cat # 127624.https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-ly-6g-antibody-6755?GroupID=BLG5803
anti-CD11c (clone N418), Cat # 117319.https://www.biolegend.com/en-us/products/alexa-fluor-700-anti-mouse-cd11c-antibody-3429?GroupID=BLG11937
anti-CD4 (clone RM4-5), Cat # 100548.https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-mouse-cd4-antibody-7627
anti-CD4 (clone RM4-5), Cat #100526. https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-cd4-antibody-1937?GroupID=BLG4211
anti-TCRβ (clone H57-597), Cat # 109206. https://www.biolegend.com/de-at/products/fitc-anti-mouse-tcr-beta-chain-antibody-270
anti-TCRβ (clone H57-597), Cat # 109228. https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-tcr-beta-chain-antibody-5603?GroupID=BLG6996
anti-FOXP3 (clone FJK-16S), Cat # 17-5773-82. https://www.thermofisher.com/antibody/product/FOXP3-Antibody-clone-FJK-16s-Monoclonal/17-5773-82
anti-IL-17A (clone eBio 17B7), Cat#12-7177-81. https://www.thermofisher.com/antibody/product/IL-17A-Antibody-clone-eBio17B7-Monoclonal/12-7177-81
anti-IFNγ (clone XMG1.2), Cat#505824. https://www.biolegend.com/en-us/products/alexa-fluor-700-anti-mouse-ifn-gamma-antibody-12538
anti-RORγt (clone B2D), Cat # 12-6981-82.https://www.thermofisher.com/antibody/product/ROR-gamma-t-Antibody-clone-B2D-Monoclonal/12-6981-82
anti-IL-17F (clone 9D3.1C8), Cat # 517006. https://www.biolegend.com/en-us/search-results/alexa-fluor-488-anti-mouse-il-17f-antibody-6963
For IL-1 R blockade in vivo antibodies: InVivoMab anti-IL-1R1 IgG (JAMA147; BioXCell) Cat#BE0256, https://bxcell.com/product/anti-m-il-1-r/
1 mg of InVivoMAb Armenian hamster IgG (BioXcell) Cat#BE0091. https://bxcell.com/product/polyclonal-3/

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Caco2 cell line ATCC HTB-37™
Authentication	Caco2 cell line HTB-37™ was obtained from commercial sources, manufacturing companies have authentication information.
Mycoplasma contamination	All cell lines used in this work were tested negative in mycoplasma contamination assay
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other organisms

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

Laboratory animals

8-12-week-old wild-type SPF C57BL/6 mice (JAX:000664) were purchased from Jackson laboratory. Germ free (GF) mice were bred and maintained within sterile vinyl isolators at Weill Cornell Medical College Gnotobiotic Mouse Facility. Altered Schaedler flora (ASF) mice were generated from germ-free wild-type C57BL/6 mice upon inoculation with ASF community. As specified in the “Methods” section of the manuscript, all laboratory animal experimental groups included equal mixes of male and female mice between 8-16 weeks of age. All mice used in these experiments were housed with a 12-hr light/dark cycle per day at a temperature of 72±2°F, and 30-70% relative humidity.

Wild animals

No wild animals used in the study.

Field-collected samples	No field-collected samples used in the study.
Ethics oversight	All animal experiments were approved and are in accordance with the Institutional Animal Care and Use Committee guidelines at Weill Cornell Medicine.

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	Seventy-eight colonic mucosa-enriched lavage samples (38 non-inflammatory bowel disease individual and 40 patients with ulcerative colitis) were from de-identified individuals following informed consent and Institutional-Review-Board-approved protocols at Weill Cornell Medicine.
Recruitment	Colonic mucosa-enriched lavage samples were obtained from de-identified individuals following informed consent and Institutional-Review-Board-approved protocols from the Center for Advanced Digestive Diseases and the JRI IBD Live Cell Bank Consortium at Weill Cornell Medicine. Ulcerative colitis patients were recruited and enrolled from the EPIC electronic medical record system by physicians or study coordinators after obtaining informed consent and collecting disease history, surgical history, disease phenotype, extraintestinal manifestations of disease, mediations, and other clinical data. If patient did not have current IBD diagnosis, their reasons for undergoing endoscopy or colonoscopy was noted. Healthy individuals were identified through their medical chart and health history. Recruitment was kept broad to limit selection bias, recruiting any adults undergoing colonoscopy regardless of visit reason, age, gender, or race.
Ethics oversight	Mucosal washings were obtained following Institutional Review Board-approved protocols from the Center for Advanced Digestive Diseases and the JRI IBD Live Cell Bank Consortium at Weill Cornell Medicine.

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	Colonic lamina propria cells (cLP) were isolated as below. Colons were excised, opened longitudinally, washed of fecal contents and then cut into 1 cm pieces. Intestinal pieces were transferred into Hank's Balanced Salt Solution (HBSS) medium (Thermo Fisher Scientific), supplemented with 2 mM EDTA, and were shaken for 8 min at 37°C. The remaining tissue was washed, minced and subsequently incubated in digestion medium consisting of RPMI 1640 (Thermo Fisher Scientific), 5% FBS, 0.5 mg/ml collagenase type VIII (Sigma-Aldrich), 5 U/ml DNase (Sigma-Aldrich), 100 IU/ml penicillin and 100 µg/ml streptomycin (Thermo Fisher Scientific), for 25 min at 37°C by gentle shaking. The cell suspensions were filtered through a 100 µm mesh and centrifuged at 1700 rpm. The obtained cells were filtered through a 70 µm filter, washed twice with PBS and used as cLP cells.
Instrument	BD LSRFortessa (BD Biosciences)
Software	Flow cytometry data were collected by BD Diva and further analyzed by FlowJo V10 (TreeStar)
Cell population abundance	No cells were sorted in this study. Additionally, no cell population abundances were reported.
Gating strategy	All gating were determined after FSC/SSC gating on lymphocytes population. FSA-A vs FSC-H and SSC-A vs SSC-W gates were used to gate singlets. Only CD45 positive viable cells (Fixable Viability Dye 506, eBioscience) were included for further analysis.

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