

Reporting Summary

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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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give <i>P</i> values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	Flow cytometry (FACS): BD FACS Diva Software (LSRII Fortessa, BD machine), Cytek Aurora Flow Cytometer (Cytek Biosciences) Immunofluorescence: Images were acquired with Nikon Eclipse Ni microscope (Nikon) on NIS Elements BR software (v. 4.12.01) and were merged with ImageJ software (v. 1.54g). Immunohistochemistry: Whole slides were scanned using the NanoZoomer S210 platform (Hamamatsu) Single cell RNA sequencing: 10x Genomics Chromium X, Illumina NovaSeq X TCR sequencing: MiSeq platform (v. 2)
Data analysis	Flow cytometry files were furthered analyzed with FlowJo (v. 10) software. Immunofluorescence and Immunohistochemistry: Images were further analyzed with QuPath software (v. 0.6.0). single cell RNA sequencing: R Version (4.2.0), Python (v3.8.16), Cell Ranger (v. 5.0), Seurat (v. 5.1.0), SoupX (v. 1.6.2), scDbfFinder (v. 1.12.0), Harmony (v .1.2.4), clusterProfiler (v. 4.12.6), msigdb (v. 25.1.1), compositions (v. 2.0.8), emmeans (v1.10.4), ggplot2 (v. 4.0.1), CellChat (v. 2.1.2), ComplexHeatmap (v. 2.14.0), svglite (v. 2.1.3), statsmodels (v.0.14.0), SciPy (v. 1.10.1), matplotlib (v.3.7.1). Plots, Mann Whitney tests, and Kruskal-Wallis tests of data generated by flow cytometry, immunohistochemistry, and immunofluorescence were performed with Graphpad Prism software (v. 11). Clinical data as well as flow cytometry data were managed with Microsoft Excel (v. 16.111.1).

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 Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

All data supporting conclusions in this study are available in the main text, Extended Data, Source Data, and Supplementary Information. Individual-level clinical data are subject to restricted access to protect patient privacy and to comply with data protection regulations. All requests will be reviewed by the corresponding author and the study team with responses within 2 weeks. Raw scRNA-seq data are available at the Gene Expression Omnibus (GEO) under accession number GSE322796. Per-sample CellChat ligand–receptor interactions across all samples (prior to modeling) are available at Figshare under DOI <https://doi.org/10.6084/m9.figshare.32600346>.

Github: <https://github.com/saumyapo/CART-Enterocolitis-Analysis-Scripts/tree/main>

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

Sex was considered in our study and was not an exclusionary factor in our study. The described syndrome in this study was not specific to a certain sex and thus we did not constrain the methodology specifically for sex. We provide patient-level data on sex (as assigned in their medical records) as well as assay-specific data in Supplementary Table 1 and an Extended Data Figure.

Reporting on race, ethnicity, or other socially relevant groupings

Race and ethnicity classifications, as self-reported by study participants in their medical records, are provided in Supplementary Table 1 and an Extended Data Figure. The described syndrome was not specific to a certain race or ethnicity.

Population characteristics

Adult patients (age >18) were recruited based on diagnosis of myeloma, receipt of ciltacabtagene autemcelt CAR-T therapy, and presence of clinically defined enterocolitis. Patients were not excluded by race, ethnicity or sex. Further population characteristics are provided in Supplementary Table 1.

Recruitment

Participants were recruited for this study from 3 large academic centers (Mount Sinai Hospital, Weill Cornell Medical Center, and Johns Hopkins University Hospital). Retrospective recruitment after receiving the therapy of interest (CAR-T therapy) introduces potential bias.

Ethics oversight

Informed patient consent was provided to all study participants prior to enrollment. Participants were not financially compensated. This study was principally conducted at the Mount Sinai Hospital, and institutional review board (IRB) approval was obtained. Respective, local IRBs approved and oversaw this study at each collaborating institution.

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

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](https://www.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

Sample size was not pre-determined. Study participants were recruited retrospectively according to CAR-T therapy status and clinical symptoms consistent with the syndrome described in our study. In total, we describe 43 patients, of which 26 are health controls, 10 myeloma CAR-T patients experiencing enterocolitis, and 7 myeloma CAR-T patients not experiencing enterocolitis. Participants were recruited to maintain group size comparability between CAR-T enterocolitis and CAR-T without enterocolitis groups, although exact group size matching could not be achieved due to the relative rarity of the treatment conditions.

Data exclusions

Data was not excluded from this study

Replication	All data are from individual patients, representing biological replicates. Longitudinal sampling was performed as described in the manuscript. Reproducibility of the data was observed by the consistency of data findings among patients within each treatment group.
Randomization	Participants were not randomized for this study. Participant groups were determined by clinical status.
Blinding	Participants were allocated to groups by clinical status, which preempted randomization and blinding. In cases of manual quantification of immunohistochemistry data, positive cell data collection was completed blindly. Where possible, automated quantification protocols were used as described in Methods.

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
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☐	☐ ChIP-seq
☐	☒ Flow cytometry
☐	☐ MRI-based neuroimaging

Antibodies

Antibodies used

Flow Cytometry antibodies:

CD3, BV605, UCHT1, Mouse, IgG1, κ , Biolegend, 1:200
 CD3, PB, UCHT1, Mouse IgG1, κ , Biolegend, 1:200
 CD19, BV605, HIB19, Mouse IgG1, κ , Biolegend, 1:200
 CD19, PE-Cy7, SJ25C1, Mouse IgG1, κ , Biolegend, 1:200
 CD66b, PB, G10F5, Mouse IgM, κ , Biolegend, 1:200
 CD16, A700, 3G8, Mouse IgG1, κ , Biolegend, 1:200
 BDCA1 (CD1c), APC-Cy7, L161, Mouse IgG1, κ , Biolegend, 1:200
 BDCA3 (CD141), PE-Cy7, M80, Mouse IgG1, κ , Biolegend, 1:200
 CD14, FITC, 63D3, Mouse IgG1, κ , Biolegend, 1:200
 HLADR, PerCP-Cy5.5, L243, Mouse IgG2a, κ , BD Biosciences, 1:33
 CD206, PE, 19.2, Mouse IgG1, κ , Invitrogen, 1:200
 CD45, PE/Dazzle 594, HI30, Mouse IgG1, κ , Biolegend, 1:200
 CD4, A700, RPA-T4, Mouse IgG1, κ , Biolegend, 1:200
 Ki67, PE, Ki-67, Mouse IgG1, κ , Biolegend, 1:200
 CD8, APC-Cy7, SK1, Mouse IgG1, κ , Biolegend, 1:100
 CD45RA, PE-Cy7, HI100, Mouse IgG2b, κ , Invitrogen, 1:200
 CCR7, A488, G043H7, Mouse IgG2a, κ , Biolegend, 1:200
 IgA1, A488, B3506B4, Mouse IgG1, κ , Southern Biotech, 1:200
 IgA2, PE, IS11-21E11, Mouse IgG1, κ , Miltenyi Biotec, 1:11
 CD27, PerCP-Cy5.5, O323, Mouse IgG1, κ , Biolegend, 1:100
 CD10, APC-Cy7, HI10a, Mouse IgG1, κ , Biolegend, 1:200
 CD38, APC, HB-7, Mouse IgG1, κ , Biolegend, 1:200
 IgD, PB, IA6-2, Mouse IgG2a, κ , Biolegend, 1:200
 IgM, A700, MHM-88, Mouse IgG1, κ , Biolegend, 1:100
 CD3, BV805, UCHT1, Ms IgG1 κ , BD Biosciences 1:25
 CAR, FITC, Acrobiosystems, 1:100
 CD45, NFB585, 30-F11, Rat IgG2b κ , Thermo Fisher 1:25
 CD14, NFB660-40S MEM-15, Ms IgG1, Thermo Fisher 1:25
 CD19, BB755 SJ25C1, Ms IgG1 κ , BD Biosciences 1:25
 CD66b, PE-Dazzle594 G10F5, Ms IgG1 κ , BioLegend 1:25
 CD38, APC-FIRE810 HIT2, Ms IgG1 κ , BioLegend 1:25
 CD20, BV480 2H7, Ms IgG2b κ , BD Biosciences 1:25
 CD16, NFR685, 3G8 Ms IgG1 κ , Thermo Fisher 1:25

Immunofluorescence antibodies:

Anti-human IgA1 IgG, Rabbit, 1:500, Abcam, ab193187
 Anti-human IgA2 IgG1, Mouse, 1:50, Miltenyi Biotec, 130-093-081
 Anti-human STAT1 IgG, Rabbit, 1:200, Sigma Aldrich, HPA000931
 Anti-human CD3 IgG1, Mouse, 1:10, Abcam, ab17143
 Anti-human CD68 IgG2, Mouse, 1:50, Invitrogen, MA1-80133

Anti-rabbit IgG, A488, Goat, 1:1000, Abcam, ab150077
 Anti-mouse IgG, A594, Goat, 1:1000, Abcam, ab150116
 Anti-mouse IgG1, A594, Goat, 1:500, Jackson Immuno, 115-585-205
 Anti-mouse IgG2a, Cy5, Goat, 1:200, Jackson Immuno, 115-175-206

Immunohistochemistry antibodies:
 CD3, PA0122, LN10, Leica
 CD4, PA0427, 4B12, Leica
 CD8, PA0183, 4B11, Leica
 CD20, PA0359, L26, Leica
 MUM1, PA0129, EAU32, Leica
 Ki67, GA62661-2, MIB-1, Dako / Agilent

Validation

Antibodies were validated by the manufacturer for use. Additional information is available on respective manufacturer websites.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration N/A

Study protocol N/A

Data collection Patients were recruited from November 2021 to May 2026 through the Inflammatory Bowel Disease Center and endoscopy unit in conjunction with the Department of Oncology at Mount Sinai Hospital in addition to 2 patients from the Jill Roberts Inflammatory Bowel Disease Center at Weill Cornell Medical Center and 1 patient from Department of Gastroenterology and Hepatology at Johns Hopkins Hospital.

Outcomes N/A

Plants

Seed stocks N/A

Novel plant genotypes N/A

Authentication N/A

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication. N/A

Files in database submission N/A

Genome browser session
 (e.g. [UCSC](#)) N/A

Methodology

Replicates N/A

Sequencing depth	N/A
Antibodies	N/A
Peak calling parameters	N/A
Data quality	N/A
Software	N/A

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 is described in Methods.
Instrument	Fortessa LSR II (BD Bioscience)
Software	BD FACS Diva Software, with Quantification performed using FlowJo v10
Cell population abundance	Abundance of cells was confirmed post-acquisition to determine inclusion in study
Gating strategy	Gating strategies for flow cytometry data are provided in supplementary figures

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

Magnetic resonance imaging

Experimental design

Design type	N/A
Design specifications	N/A
Behavioral performance measures	N/A

Acquisition

Imaging type(s)	N/A
Field strength	N/A
Sequence & imaging parameters	N/A
Area of acquisition	N/A
Diffusion MRI	☐ Used ☐ Not used

Preprocessing

Preprocessing software	N/A
Normalization	N/A
Normalization template	N/A

Noise and artifact removal	N/A
Volume censoring	N/A

Statistical modeling & inference

Model type and settings	N/A
Effect(s) tested	N/A
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	N/A
(See Eklund et al. 2016)	
Correction	N/A

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis