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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	In the Supplementary Materials section, "Table of Resources" lists all versions of software used with links. Computational methods section states the datasets used in generating IBD network or querying it systematically for the generation of Target Report Cards.
Data analysis	Within the manuscript (main text) we have revealed that the codes are publicly available at the following links: https://github.com/sahoo00/BoNE; https://github.com/sahoo00/Hegemon

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

RNA Seq data his being deposited for public release (with embargo at NCBI GEO). Github link is posted within 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

Life sciences study design

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

Sample size	Sample size for animal colitis models were chosen based on numerous prior examples of studies in these models. Sample size for patient PBMC bacterial clearance assays were determined based on prior study on IBD patients evaluating bacterial clearance in vivo. That study has been cited.
Data exclusions	no data was excluded
Replication	All attempts at replication were successful. Two models of colitis were studied in mice.
Randomization	Mice ordered from Jackson were randomly assigned to treatment or control arm for the therapeutic agent.
Blinding	All histology slides, bacterial colony counting, qPCR and ELISA studies were analyzed in a blinded manner.

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	A detailed Table of Resources is provided with Cat# and vendor information for all reagents, including antibodies.
Validation	Each antibody was validated by manufacturer using gene depletion techniques.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Murine primary peritoneal macrophages, and human PBMCs
Authentication	None of the cells were authenticated because they are primary cells and not passaged.
Mycoplasma contamination	All primary cells were used fresh for studies and not cultured/passages. Hence, mycoplasma contamination was not measured. However, the media used to cultivate was tested periodically and determined to be negative.
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	Adult C57BL/6 mice were acquired from Jackson Laboratories. All animals were maintained in an institutional animal care. Provided with standard light–dark cycle, fed with standard laboratory chow and clean drinking water.
Wild animals	n/a
Field-collected samples	n/a
Ethics oversight	All animal studies were approved by the University of California, San Diego Institutional Animal Care and Use Committee (IACUC). Protocol # S17223; PI: Ghosh, Pradipta

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	Blood samples were obtained from either healthy volunteers or from IBD patients undergoing colonoscopies a part of their routine care and follow-up at UC San Diego's Inflammatory Bowel Disease (IBD) Center.
Recruitment	Consecutive patients presenting to the IBD clinic were recruited and consented using a study proposal approved by the Institutional Review Board of the University of California, San Diego.
Ethics oversight	UCSD HRPP (IRB # 160246);PI: Ghosh, Pradipta

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