## METHODS

**Bacterial strains.** The *E. coli*, *Proteus*, and *E. cloacae* strains used in this study are listed in Supplementary Table 1. All strains were routinely grown aerobically in LB broth (10 g $l^{-1}$ tryptone, 5 g $l^{-1}$ yeast extract, 10 g $l^{-1}$ NaCl) or on LB agar plates (10 g $l^{-1}$ tryptone, 5 g $l^{-1}$ yeast extract, 10 g $l^{-1}$ NaCl, 15 g $l^{-1}$ agar) at 37 °C. When appropriate, antibiotics were added to the medium at the following concentrations: 30 μg $ml^{-1}$ chloramphenicol, 100 μg $ml^{-1}$ carbenicillin, 50 μg $ml^{-1}$ kanamycin.

**Plasmids.** All primers and plasmids are listed in Supplementary Tables 2 and 3. pWZ5 was constructed with standard molecular cloning techniques[23] using the Gibson Assembly Cloning Kit (New England Biolab) according to the recommendations of the manufacturer. The flanking regions of the *moaA* gene from the *E. coli* strain NRG857c were amplified and ligated into pGP706 to make pWZ5. Plasmid inserts were verified by Sanger sequencing.

**Construction of mutants by allelic exchange.** pWZ5 was propagated in DH5α λ*pir* and conjugated into the *E. coli* strains NRG857c or NC101 using S17-1 λ*pir* as the conjugative donor strain. Exconjugants that had the suicide plasmid integrated into the recipient chromosome (single crossover) were recovered on LB plates containing appropriate antibiotics. Sucrose plates (8 g $l^{-1}$ nutrient broth base, 5% sucrose, 15 g $l^{-1}$ agar) were used to select for the second crossover event, thus creating WZ12 and WZ245, respectively. Deletion of the target gene was confirmed by PCR.

**Anaerobic growth assays.** Anaerobic growth assays were performed in mucin broth. Mucin broth contained hog mucin (Sigma–Aldrich) at a final concentration of 0.5% (w/v) in no-carbon E medium[24] and was supplemented with trace elements[25]. Sodium formate, sodium nitrate, DMSO and trimethylamine-N-oxide (TMAO, Sigma–Aldrich) were added to a final concentration of 40 mM, in the absence or presence of sodium tungstate (Sigma–Aldrich) at the indicated final concentrations. A volume of 2 ml of mucin broth was inoculated with the indicated strains at a concentration of $1 \times 10^4$ colony-forming units (CFU) per ml and incubated anaerobically (Bactron EZ Anaerobic Chamber, Sheldon Manufacturing) for 18 h at 37 °C. Bacterial numbers were counted as described[12].

**DSS-induced-colitis model and sodium tungstate treatment.** All experiments involving mice were approved by the Institutional Animal Care and Use Committee at UT Southwestern Medical Center (APN#T-2013-0159) and UC Davis (APN#16196). Studies involving animals were performed with compliance to all relevant ethical regulations. Female 9–12-week-old C57BL/6J wild-type mice were obtained from Jackson Laboratory (Bar Harbour) and bred at UT Southwestern (essentially devoid of endogenous Enterobacteriaceae) or Charles River Laboratories (Morrisville) (harbouring endogenous Enterobacteriaceae), as indicated. Mice were randomly assigned into cages before the experiment. The drinking water was replaced with either filter-sterilized water (mock treatment), a filter-sterilized solution of 0.2% (w/v) sodium tungstate (Sigma), a filter-sterilized solution of 2% or 3% (w/v) DSS (relative molecular mass 36,000–50,000; MP Biomedicals) in water, or a filter-sterilized solution of DSS and 0.2% (w/v) sodium tungstate. In one experiment, tungsten was administered in a sodium tungstate-fortified diet (1,000 parts per million (p.p.m.)). At the indicated time points, animals were inoculated orally with either 0.1 ml LB broth or 0.1 ml LB broth containing $1 \times 10^9$ CFU *E. coli*, or remained uninfected. In the competitive colonization experiments, mice were inoculated with $5 \times 10^8$ CFU of each *E. coli* or *E. cloacae* strain. One day before the end of the experiment, the drinking water was switched to regular, filter-sterilized water for 24 h to reduce the amount of DSS present in the samples. After euthanization, colonic and caecal tissue were collected, flash frozen and stored at −80 °C for subsequent mRNA and protein expression analysis. Faecal material, caecal content, and colonic content were collected in sterile PBS and the bacterial loads for the *E. coli* strains or Enterobacteriaceae were quantified by plating serial tenfold dilutions on LB plates supplemented with appropriate antibiotics or MacConkey agar plates, respectively. *E. coli* NC101 and Nissle 1917 strains were differentially marked with the low-copy number plasmids pWSK29 and pWSK129 to facilitate bacterial recovery from biological samples[12]. For the competitive colonization experiments involving NRG857c, animals were inoculated with an equal mixture of the NRG857c Δ*lacZ* mutant (LB33) and the Δ*moaA* mutant (WZ12) as described above. The bacterial load in the luminal content of the indicated organs was determined by plating serial tenfold dilutions on LB plates supplemented with the appropriate antibiotics and 40 mg $l^{-1}$ 5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside. Germ-free C57BL/6 mice were maintained in plastic gnotobiotic isolators on a 12-h light cycle. DSS-mediated colitis was induced in 8–12-week-old germ-free mice, following the protocol described above.

**Piroxicam-accelerated colitis model in conventional *Il10*$^{-/-}$ mice.** Conventional *Il10*$^{-/-}$ mice (7–12 weeks old, males only) on a C57BL/6 background were randomly assigned into cages before oral inoculation with $1 \times 10^9$ CFU of mouse AIEC NC101. Regular mouse chow was replaced with piroxicam-fortified diet (100 p.p.m.; Teklad custom research diets, Envigo) and changed daily. Drinking water was replaced with either filter-sterilized water (mock treatment) or a filter-sterilized solution of 0.2% (w/v) sodium tungstate. After 14 days, mice were euthanized and the samples were collected as described above.

**Faecal transplant into gnobiotic mice.** All procedures involving human subjects were reviewed and approved by the institutional review board at the University of Texas Southwestern Medical Center (IRB#112010-130). Studies involving human samples were performed with compliance to all relevant ethical regulations. Written informed consent was obtained from all participants or parents or legal guardians of participating minors. Except for E.B. and S.F.-D., none of the investigators handling the samples had access to personally identifiable information. Patients were considered for faecal donation if they had an established diagnosis of inflammatory bowel disease, had active disease at the time of collection and were free from antibiotic use over the past three months. Characteristics of patients from whom samples were taken are summarized in Supplementary Table 4. Human faecal samples were obtained during colonoscopy by direct endoscopic aspiration of faecal contents from patients with active colonic disease. A total of 10 ml of liquid faecal material was collected from each patient and aliquoted into 1-ml cryovials. The samples were then snap-frozen in liquid nitrogen and stored at −80 °C until use.

Germ-free Swiss–Webster mice (7–12 weeks old, mix of male and female) were maintained in plastic gnotobiotic isolators on a 12-h light cycle. Mice were randomized, paired and orally gavaged with endoscopy samples from the patients listed in the table at the end of this section. Colonization was allowed to proceed for three days before mice received DSS or DSS plus sodium tungstate for seven days. Mice were euthanized and the samples were collected as described above.

**16S RNA pyrosequencing and analysis.** Caecal contents were collected and DNA was extracted from faecal samples using the MoBio PowerFecal kit (MoBio Laboratories) according to the recommendations of the manufacturer. The extracted DNA was subjected to KCl precipitation to remove residual DSS contaminants. In brief, DNA was incubated with excess KCl on ice to precipitate DSS. The samples were then cleared by centrifugation and the resulting supernatant was subsequently subjected to ethanol precipitation to recover the DNA. The purified DNA was subjected to paired end library construction to facilitate assemblies and longer accurate reads. The 16S rRNA coding sequences used to identify the bacteria were amplified using primers 515F and 806R that flank the V3–V4 hypervariable region, and barcoded before pyrosequencing. The barcoded amplicons were purified and quantified on an Invitrogen Qubit system (Life technology). Libraries were sequenced using an Illumina MiSeq system (Illumina). 16S-sequencing data was subjected to a standard workflow for processing and quality assessment of the raw 16S-sequence data and the downstream phylogenetic analysis. The pipeline consists of an initial customized Linux-based command script for trimming, demultiplexing and quality filtering the raw paired end-sequence data generated by the Illumina system. Sequence alignment, operational taxonomic units (OTUs) picking against the Greengenes reference collection, clustering, phylogenetic and taxonomic profiling, permutational multivariate analysis of variance (PERMANOVA), and the analysis of beta diversity (principle component analysis) on the demultiplexed sequences were performed with the Quantitative Insights into Microbial Ecology (QIIME) open source software package[26].

**Metagenomics.** Groups of randomized Charles River C57BL/6 mice were treated as described in Extended Data Fig. 2b. Sample collection, shotgun metagenomics sequencing and data analysis were performed as previously described[11].

Reads that mapped to the SEED database were exported from MEGAN5 into BIOM tables, which were subjected to analysis of similarity (ANOSIM) in Qiime[26] and principal component analysis (PCA) using STAMP[27]. To map reads to bacterial metabolic genes, a total of 100 of each of the butyrate production operons (*bcdAB, but* and *ato*) and succinate dehydrogenase operons (*sdhABC*) were downloaded from the KEGG database. Sequences were clustered to remove redundancy using cdhit-est[28,29] with a sequence identity threshold of 0.9. Paired end reads were mapped to these gene clusters using the BBmap tool with the following settings: 'qtrim = lr, minid = 0.90, ambig = random, covstats = true'. Coverage statistics for each gene cluster were tallied from the percentage of unambiguous and ambiguous mapped reads and used to determine the absolute number of reads that mapped to a particular gene set. A similar strategy was used to map reads to fumarate respiration and butyrate production pathways.

**Abundance of Enterobacteriaceae.** The relative abundance of endogenous Enterobacteriaceae as part of the bacterial microbiota was analysed as described previously[30–32]. In brief, the caecum or colon content was extracted using the PowerFecal DNA Isolation Kit (MoBio Laboratories) according to the manufacturer's instructions, and the resulting DNA was further purified using the KCl method as described above. A 2-μl sample of the bacterial DNA was used as the template for SYBR Green-based real-time PCR reactions as described above. The gene copy number in the sample was determined based on a standard curve generated using