pSW321 and pSW196 as previously described[33]. The primers used are listed in Supplementary Table 2. The fraction of Enterobacteriaceae as part of the entire bacterial population for each sample was calculated by dividing the gene-copy number of the *Enterobacteriacaea* by the gene-copy number determined using the eubacterial primers.

Quantification of mRNA levels in intestinal tissue. The relative transcription levels of mRNAs for iNOS, CXCL1, CXCL2, IL-17, IL-6, IFN-γ, LCN2 and TNF-α, encoded by the *Nos2*, *Cxcl1*, *Cxcl2, Il17, Il6*, *Ifng*, *Lcn2* and *Tnf* genes, respectively, were determined by qRT–PCR as described previously[31]. In brief, colonic or caecal tissue was homogenized in a Mini Beadbeater (Biospec Products) and RNA was extracted using the TRI-reagent method (Molecular Research Center). To remove residual DSS contaminants, RNA was further purified using the Dynabeads mRNA Direct Kit (Life Technologies) per the manufacturer`s instructions. cDNA was generated with TaqMan reverse-transcription reagents (Life Technologies). Real-time PCR was performed using SYBR Green (Life Technologies), and data were acquired in a QuantStudio 6 Flex instrument (Life Technologies) and analysed using the comparative C_t method. The primers listed in Supplementary Table 2 were added at a final concentration of 250 nM. Target-gene transcription of each sample was normalized to the respective levels of *Gapdh* mRNA.

Histopathology. Mouse caecal and colonic tissue was fixed in phosphate-buffered formalin and 5-μm sections of the tissue were stained with haematoxylin and eosin. The fixed and stained sections were blinded and evaluated by an experienced veterinary pathologist according to the criteria described previously[12]. Images were taken at a magnification of 10×, and the contrast for the images was uniformly (linear) adjusted using Adobe Photoshop CC.

Measurement of succinate and butyrate concentrations in bacterial culture using GC–MS. Bacterial cultures were cleared by centrifugation at 13,200*g* at 4 °C for 30 min and then passed through a 0.22-μm filter. The supernatant was dried using a SpeedVac concentrator. The pellet was then dissolved in pyridine at 80 °C for 20 min before derivatization with *n-tert*-butyldimethylsilyl-*n*-methyltrifluoroacetamide with 1% t-BDMCS sylilation reagent (Cerilliant) at 80 °C for 1 h. Derivatized samples were transferred to autosampler vials for gas chromatography–mass spectrometry (GC–MS) analysis (Shimadzu, TQ8040). The injection temperature was 250 °C and the injection split ratio was set to 1:100 or 1:1,000 with an injection volume of 1 μL. The gas chromatography oven temperature started at 130 °C for 4 min, rising to 230 °C at 4 °C min^{-1}, and to 280 °C at 20 °C min^{-1} with a final hold at this temperature for 2 min. The gas chromatography flow rate of the helium carrier gas was kept constant at a linear velocity of 50 cm s^{-1}. The column used was a 30 m × 0.25 mm × 0.25 μm Rtx-5Sil MS (Shimadzu). The interface temperature was 300 °C. The electron-impact ion-source temperature was 200 °C, with 70 V ionization voltage and 150 μA current. To measure succinate, Q3 scans (range of 50–500 *m/z*, 1000 *m/z* per second) were first performed to determine the retention time for succinate and succinate-2,2,3,3-d_4 (CDN Isotopes), which was 11.0 and 10.9 min respectively. Multiple-reaction-monitoring mode was then used (target ion *m/z* 289→147, reference ion *m/z* 331→189) to measure succinate quantitatively. To measure butyrate, Q3 scans were performed as described above, and the retention time for butyrate and butyrate-d_7 (CDN Isotopes) was 6.1 and 6.2 min, respectively. Q3-selected ion monitoring (single-quadrupole mode) with an event time of 0.05 s was performed to quantitatively measure butyrate. The target and reference (qualifier) ions for butyrate were *m/z* = 145 and *m/z* = 75, respectively; target and reference ions for deuterated butyrate were *m/z* = 152 and *m/z* = 76.

Strain isolation and identification. Tenfold serial dilutions of the faecal content of C57BL/6 mice (Charles River) were plated on MacConkey agar (10 g l^{-1} pancreatic digest of gelatin, 3 g l^{-1} peptone, 10 g l^{-1} lactose, 1.5 g l^{-1} bile salts, 5 g l^{-1} sodium chloride, 13.5 g l^{-1} agar, 30 mg l^{-1} neutral red, 1 mg l^{-1} crystal violet) and incubated aerobically at 37 °C overnight. To isolate mouse–commensal *E. coli* and *Proteus* strains, single colonies were isolated and identified using the EnteroPluri Test (Liofilchem) per the manufacturer`s recommendations.

Nitrate reductase activity assays. Overnight cultures of *E. coli* or *Proteus* strains were diluted 1:100 in fresh LB broth containing 40 mM sodium nitrate to induce the expression of nitrate reductases, in the presence or absence of sodium tungstate at the indicated concentrations. Cultures were incubated aerobically for 3 h at 37 °C and the relative nitrate reductase activity was measured as described previously[34]. The experiment was repeated three times and representative results are shown.

NF-κB activation in epithelial cells. HeLa57A cells, stably transfected with an NF-κB–luciferase reporter construct[35,36], were maintained in Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum at 37 °C in a 5% CO_2 atmosphere. For the NF-κB activation assays, cells were seeded in a 48-well plate to reach 80% confluency within 24 h. Cells were treated with 0.1, 1 or 10 ng ml^{-1} of phorbol 12-myristate 13-acetate (PMA, dissolved in DMSO) or DMSO alone. At the same time, sodium tungstate with a final concentration of 0.02% or 0.002% (w/v) in water was added to the cells. After 5 h, cells were washed in DPBS and lysed in 0.1 ml of reporter lysis buffer (Promega). Firefly luciferase activity was measured with a commercial luciferase assay system (Promega). The experiment was repeated three times and representative results are shown. HeLa57A cells were generated by R. T. Hay (University of Dundee). These cells have not been authenticated or tested for mycoplasma contamination.

LDH-release assay. The MODE-K cell line was maintained in DMEM (Sigma) supplemented with 10% FBS at 37 °C in 5% CO_2. Bone-marrow-derived macrophages (BMDMs) were differentiated from bone-marrow cells collected from femurs and tibias of SPF C57BL/6 mice. In brief, bone-marrow cells were collected with 10 ml cold RPMI-1640 medium (Sigma) and then pelleted at 1,000 r.p.m. for 5 min at 25 °C. The cells were resuspended in BMM medium (RPMI-1640 supplemented with 10% heat-inactivated FBS, 1 mM glutamine, 1% antibiotics–antimycotics, and 30% L-cell conditioned medium) and allowed to differentiate for seven days. MODE-K experiments were performed in triplicate. Plates were seeded with cells to a final confluency of 80% before treatment. Two days after seeding, MODE-K cells were treated for 24 h with 2–4% DSS (Alfa Aesar), with and without 0.002–0.2% sodium tungstate dihydrate (Sigma). For BMDM experiments, plates were seeded with 1×10^5 cells per well for 48 h. After 24 h the medium was replaced with RPMI supplemented with 2% FBS and glutamine. On the day of the experiment, culture medium was replaced with medium supplemented with 4 or 6% DSS, with and without 0.2% sodium tungstate dehydrate, for 24 h. Cytotoxicity was determined using the LDH-release assay CytoTox 96 non-radioactive cytotoxicity assay (Promega), per the manufacturer's recommendations. Absorbance readings were corrected based on the absorbance of the medium alone. Five-minute treatment with 10% Triton X-100 was used as the total LDH-release control. The experiment was repeated three times, and representative results are shown. MODE-K cells were generated by D. Kaiserlian (Institut Pasteur de Lyon). These cells have not been authenticated or tested for mycoplasma contamination.

Statistics and reproducibility. No statistical methods were used to predetermine sample size. The investigators were not blinded to allocation during experiments and outcome assessment, except for histology analysis. Nitrate reductase activities, fold changes in mRNA levels, competitive indices, relative abundance of Enterobacteriaceae and bacterial numbers were transformed logarithmically and the statistical significance of differences between groups was determined using a two-sided Student's *t*-test or PERMANOVA (using distance matrices). Cumulative histopathology scores were analysed using the Mann–Whitney *U* test. Details regarding the statistics of each experiment are reported in Supplementary Table 5.

Data availability. The bacterial 16S-ribosomal DNA and metagenomics-sequencing reads generated and analysed during the current study are available at the European Bioinformatics Institute repository under accession numbers PRJEB15095 and PRJEB19192. All data generated or analysed during this study are included in this published article (and its Supplementary Information files).

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