Growth rate alterations of human colorectal cancer cells by 157 gut bacteria

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ABSTRACT

Several bacteria in the human gut microbiome have been associated with colorectal cancer (CRC) by high-throughput screens. In some cases, molecular mechanisms have been elucidated that drive tumorigenesis, including bacterial membrane proteins or secreted molecules that interact with the human cancer cells. For most gut bacteria, however, it remains unknown if they enhance or inhibit cancer cell growth. Here, we screened bacteria-free supernatants (secretomes) and inactivated cells of over 150 cultured bacterial strains for their effect on CRC cell growth. We observed family-level and strain-level effects that often differed between bacterial cells and secretomes, suggesting that different molecular mechanisms are at play. Secretomes of *Bacteroidaceae*, *Enterobacteriaceae,* and *Erysipelotrichaceae* bacteria enhanced CRC cell growth, while most *Fusobacteriaceae* cells and secretomes inhibited growth, contrasting prior findings. In some bacteria, the presence of specific functional genes was associated with CRC cell growth rates, including the virulence genes TcdA in *Clostridiales* and FadA in *Fusobacteriaceae*, which both inhibited growth. *Bacteroidaceae* cells that enhanced growth were enriched for genes of the cobalamin synthesis pathway, while *Fusobacteriaceae* cells that inhibit growth were enriched for genes of the ethanolamine utilization pathway. Together, our results reveal how different gut bacteria have wide-ranging effects on cancer cells, contribute a better understanding of the effects of the gut microbiome on the human host, and provide a valuable resource for identifying candidate target genes for potential microbiome-based diagnostics and treatment strategies.

INTRODUCTION

Over the past few decades, thousands of microbial species have been identified in the human gut microbiome. Each person harbors an estimated 3.8 x 10^{13} bacteria in their guts with a relatively stable species composition (1-3). Changes in the composition of the gut microbiome have been linked with various diseases including colorectal cancer (CRC), the third leading cancer worldwide with an incidence that is estimated to rise in the coming decennium (4, 5). Besides important environmental and genetic factors, the initiation and development of CRC is affected by the human gut microbiome. During tumorigenesis, the bacterial composition on the affected intestinal mucosa changes in a process that is described by the bacterial driver-passenger model (6, 7). Bacterial drivers may facilitate the acquisition of hallmarks of cancer (8) in mucosal cells by generating DNA-damage, reducing the epithelial barrier function, and stimulating pro-carcinogenic immune responses. As the tumor microenvironment changes in the transition from adenoma to carcinoma, bacterial passengers compete with the drivers, further shifting the microbiome towards a CRC signature (9, 10). The newly acquired bacteria may in turn affect tumor development, by potential inhibiting, enhancing, or neutral effects on tumor cell growth (6). These CRC-specific changes offer the opportunity to use the bacterial community for diagnostic, prognostic, preventive, and treatment measures (11-20).

In faeces of CRC patients, the genera *Fusobacterium*, *Peptostreptococcus, Ruminococcus*, and *Escherichia/Shigella* are enriched, while *Bacteroides* and *Lachnospiraceae* (*Roseburia, Lachnospira, Anaerostipes*) have a lower relative abundance (5, 9, 11, 21-25). Even though phyla such as *Bacteroidetes* are depleted,

single species like enterotoxigenic *Bacteroides fragilis* may be enriched in some CRC patients (25-27). Comparing tumor tissue with adjacent normal tissue on the intestinal mucosa of CRC patients revealed that *Fusobacterium, Prevotella, Streptococcus*, and *Peptostreptococcus* were enriched in tumors while *Blautia, Escherichia, Pseudomonas*, and *Faecalibacterium* were enriched in the normal mucosa (5, 7, 9, 11, 22-24, 28).

Many different bacteria have been associated with CRC tumors (10), but we are only beginning to understand the different mechanisms that are involved. The effect of bacteria on CRC cell growth may be driven by direct bacterial-to-epithelial cell-cell contact or by secreted products present in the secretome (29, 30). Membrane-bound bacterial proteins that require cell-cell contact can activate epithelial cell signalling. For example, the passenger bacterium *Fusobacterium nucleatum* encodes the membrane protein *Fusobacterium* adhesin A (FadA) that binds to E-cadherin, activating β-catenin signaling and resulting into increased tumor growth (31-33). Specific *E. coli* species with *eae* gene express the adhesin protein intimin on their membrane surface which bind and cause lesions to gut epithelial cells, allowing bacteria to breach the colonic barrier. Once the bacteria are bound to the epithelial cells, this allows them to inhibit DNA repair proteins, further contributing to lasting DNA damage (34-36). Several secreted bacterial toxins are known that can bind to receptors or pass through the cell membrane into the cytoplasm. The driver bacterium enterotoxigenic *B. fragilis* secretes the metalloprotease *B. fragilis* toxin (BFT) which leads to E-cadherin cleavage and increased wnt-signalling in colon epithelial cells and to tumor formation in mice and increased cell proliferation *in vivo*

(37, 38). Bacteria such as *Escherichia coli* containing the *pks* island are able to produce a genotoxin called colibactin. Upon mucosal breach, colibactin reaches the epithelial cells and alkylates DNA, ultimately leading to tumorigenesis (39-41). These examples show that taxonomically diverse bacteria may lead to the acquisition of hallmark capabilities via diverse mechanisms.

The aim of this study was to examine the effects of bacterial cells and their secretomes on the growth rates of epithelial cells. We tested the effect of 157 different gut bacteria on the growth rates of five CRC cell lines and one non-cancerous kidney cell line. Our results revealed that different bacterial families specifically inhibit or enhance CRC cell growth, although contrasting effects could be observed between some closely related strains. Both known virulence genes and novel microbial pathways were associated with the different growth rate changes. These results provide the first large-scale *in vitro* analysis of the effects of different microbial strains on epithelial cell growth.

MATERIALS AND METHODS

Bacterial strains

We selected 116 different gut bacteria, including species that are depleted or enriched in CRC patients whose genome sequences were available in the PATRIC database (42). Additionally, we selected specific bacteria without sequenced genomes (n=39) that were strongly linked to CRC or were isolated from CRC tissue, including *Streptococcus bovis* (43, 44), *Clostridium septicum* (44-46), *Clostridioides*

difficile (47, 48), *Bacteroides* sp. (27), and the two potentially beneficial bacteria *Lactobacillus casei Shirota* (49-51) and *Akkermansia muciniphila* ATCC BAA-835™ (52-55). Together, we analysed 157 bacterial strains isolated from the human gut microbiome (Supplementary Table S1).

We purchased 96 bacterial strains from the reference catalogue of the Human Microbiome Project (HMP, Prof. Dr. Emma Allen-Vercoe from the University of Guelph in Guelph, Canada); 24 bacteria were kindly provided by Prof. Dr. Cynthia L. Sears from Johns Hopkins Medical Institutions, Baltimore, MD, USA; five strains were purchased from DSMZ (*Clostridium septicum* (Macé 1889) Ford 1927 DSM7534, *C. difficile* (Hall and O'Toole 1935) Lawson et al. 2016 DSM27543 (known as *Clostridium difficile* 630, PMID: 6870225), *Fusobacterium nucleatum* Knorr 1922 DSM15643, *Fusobacterium nucleatum* subsp. *polymorphum* (ex Knorr 1922) Dzink et al. 1990 DSM20482, and *Peptostreptococcus stomatis* Downes and Wade 2006 DSM17678); one strain from ATCC (*Streptococcus agalactiae* ATCC13813); and 31 bacteria were in stock at the Radboud University Medical Center in Nijmegen, The Netherlands (56-58). Information about the bacterial strains, their origin, growth media, and their genome sequence is provided in Supplementary Table S1.

Bacteria were cultured in their respective media under anaerobic conditions at 37°C aired with nitrogen gas (N_2, see Supplementary Table S1). Alternatively, *Ralstonia* sp. 5_2_56FAA, *Ralstonia* sp. 5_7_47FAA and *Pseudomonas* sp. 2_1_26 were grown aerobically at 37°C, and *Bacillus smithii* was grown anaerobically at its preferred temperature of 50°C. Eight media were prepared to culture bacteria

(Supplementary Table S1): brain heart infusion-supplemented (BHI-S, ATCC Medium 1293), BHI-S supplemented with 0.1% Tween 80 at pH 8.0 (BHI-T((59), NADC - 99X medium (ATCC Medium 1804), Desulfovibrio medium (ATCC Medium 2755), Modified Reinforced Clostridial Medium (RCM, ATCC Medium 2107), Reinforced Clostridial medium with sodium lactate (60% solution) at a concentration of 1.5% (RCM+, from ATCC Medium 1252), differential RCM (DRCM), and nutrient broth (NB, ATCC Medium 3). Bacteria were grown until the medium was turbid and the optical density (OD) was at least 1.0. Absorbance was obtained by measuring OD at 600nm.

Obtaining secretomes and bacterial cells

To investigate the effect of secreted molecules, we obtained secretomes from 154 bacterial cultures as follows. After culturing, bacteria were centrifuged at 4,700 rpm for 10 minutes and some bacteria subsequently at a higher speed to settle them down (see Supplementary Table S1). Next, supernatants were spun at 4,700 rpm for 10 minutes to pellet any remaining bacteria and filter-sterilized using 0.2 µm filters (Sigma-Aldrich, USA). Molecules larger than 10 kDa were concentrated using amicon ultra-15 centrifugal filters (Merck Millipore, Merck, USA). Concentrated supernatants were frozen at -80°C until further use and are further referred to as secretomes.

To investigate the effect of bacterial surface-bound molecules, 145 bacteria were inactivated to allow cellular growth rates to be assessed by measuring metabolic activity (see the section “MTT assay” below). Cells of twelve spore-forming bacteria under our experimental conditions were excluded from this analysis (see Supplementary Table S1). Pelleted bacteria were resuspended in 70% ethanol and

incubated for 5 minutes according to our inactivation protocol (60). After centrifugation at 20,000 rcf for 30 seconds, bacteria were washed in PBS twice and inactivated bacteria were frozen at -80°C until further use.

Culturing of cell lines and identification of their mutational landscapes

Five CRC cell lines (Caco-2, HCT15, HCT116, HT29, and SW480) and one non-cancerous embryonic kidney cell line (HEK293T) were selected based on their differences in mutational landscapes (61). Known oncogenes and tumor suppressor genes were confirmed with targeted single molecule molecular inversion probe (smMIP) mutation analysis as described (62), with additional smMIPs targeting CXCR4 (NM_001008540.1) codons 281-357, EZH2 (NM_00004456.4) codons 471-502, 618-645, 679-704, and SF3B1 (NM_012433.2) codons 603-471, 833-906 (smMIP sequences are available upon request), at the Radboud Diagnostics Department, Nijmegen, The Netherlands (Supplementary Table S2). Cells were split twice a week using Dulbecco's Modified Eagle Medium (DMEM, Lonza, Switzerland) supplemented with 10% fetal bovine serum (FBS, Thermo Fisher Scientific, USA) and 1% Penicillin/Streptomycin (Pen/Strep, Thermo Fisher Scientific, USA). Cells used for this study were not split for more than 25 passages.

For MTT assays, optimal cell seeding in 96 well plates (Greiner Bio-One, Austria) was defined at 5,000 cells/well for Caco-2, 4,000 cells/well for HCT15, 1,500 cells/well for HCT116, 10,000 cells/well for HT29, 6,000 cells/well for SW480, and 20,000 cells/well for HEK293T. Cells were incubated overnight to attach before addition of secretomes or bacterial cells.

MTT assay

Secretomes were diluted to their original concentrations in DMEM supplemented with 10% FBS and 1% Pen/Strep. Inactivated bacteria were diluted with DMEM supplemented with 10% FBS and 1% Pen/Strep to an OD of 0.2 and incubated on cell lines up to 72 hours. For secretomes, filter sterilized bacterial culture media used to generate secretomes served as a control for cell growth in the assay, while for bacterial cells, DMEM supplemented with 10% FBS and 1% Pen/Strep served as control for cell growth. MTT assays were performed to measure the cell metabolic activity every 24 hours. These assays involve the conversion of the water-soluble yellow dye MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] to the insoluble purple formazan by the action of mitochondrial reductase. At 24, 48 and 72 hours 10 µl of MTT (5 mg MTT dissolved per mL PBS) dye was added to the wells and cells were incubated for 3 hours. Formazan was then solubilized with 150 µL MTT solvent (0.5 mL of 10% Nonidet (dissolved in water), 50 mL isopropanol (2-propanol) and 16,7 µL hydrochloric acid fuming 37% together) and the concentration determined by optical density at 570 nm (BioRad microplate reader model 680). Metabolic activity of cell lines was used as a measure for cell growth (63). All experiments were performed in quadruplicate.

Cell growth analysis

Absorbances at optical density of 570 nm were measured by MTT assays at four time points (0, 24, 48, and 72h). Growth rates per hour were calculated by dividing the difference in absorbance by the time interval between measurements (24 h). Results

from four independent experimental replicates were averaged. Growth rates between 24-48 h were selected for comparative analysis because that time window captured the optimal growth for most cell lines (Supplementary Figure S1).

A growth rate score was defined by subtracting the growth of negative controls (cells cultured without bacterial products) from those cultured with bacterial products (secretomes or bacterial cells). Scores greater than 0 refer to enhanced growth, while scores lower than 0 refer to inhibited growth (see Supplementary Tables S3 and S4). To allow comparability between cell lines, normalized growth rate scores were calculated by dividing per cell line the scores (g) of each of the n bacteria by the norm (|g|) of the experimental condition ($|g| = \sqrt{\sum_{n}^{i=i} g_i^2}$). The normalized growth rate scores were used to evaluate whether the enhancing or inhibiting effect of a bacteria is significantly stronger than the mean effect observed for all other bacteria. For this purpose, growth rate scores were transformed into z-scores and p-values were computed by separate one tailed z-tests for enhancing or inhibiting effects. Based on these p-values, strains were identified as significant enhancers or inhibitors of growth by using a significance cut-off of $p<0.05$.

The overall effects of bacterial secretomes and inactivated cells were visualized by projecting their normalized growth scores in a two-dimensional space with the t-SNE algorithm (64). To evaluate if bacteria of the same family have a similar overall effect on cell growth relative to bacteria from other families, we applied unsupervised nearest neighbour clustering (65) and evaluated how often bacteria from the same

family were nearest neighbours compared to a random sample without replacement. For this analysis, we only used bacteria from families with more than four representatives. Random groups were evaluated per family and were defined to contain the same number of strains as the family. Fisher's exact test was used to evaluate if the nearest neighbour groups were enriched for bacteria of the same family compared to 1,000 random groups of the same size. The harmonic means of p-values from this comparison are reported.

Association of bacterial virulence genes to growth rate changes

Bacterial genomes were screened for 35 known virulence genes that may be associated with cancer or epithelial cell changes (Supplementary Table S5). The virulence factors Map (Mitochondrial associated protein), Type-3 secretion system (T3SS) effector protein of *Citrobacter rodentium*, Shiga toxin 2A (Stx2A), Shigella enterotoxin 1 (ShEt1), and colibactin (cyclomodulin toxin on polyketide synthase (pks) island of *Enterobacteriaceae*) were identified in the *Enterobacteriaceae* family, *B. fragilis* toxin (BFT) in *B. fragilis* species, FadA in the *Fusobacteriaceae* family and *Clostridium difficile* toxin A (TcdA) in the *Clostridiales* order (Supplementary Table S5). Growth rate changes of strains containing virulence genes (if present in ≥3 strains) were compared to those of their non-virulent counterparts within the family or species (in case of *B. fragilis).* Groups were compared using Mann-Whitney U-test of aggregate data of all cell lines. $P<0.05$ was considered significant.

Genes and subsystems identification

To identify genes that are associated with the inhibiting/enhancing effects of bacterial strains within families, we sorted all strains based on their effect on growth rate scores and used a normalized Kolmogorov-Smirnov statistic to quantify the association of a gene with the observed effect. Significance of the rank-based statistic was estimated by comparing its value to values obtained from 10^3 random permutations of the same list. This provided all genes encoded by the genomes from a family with a p-value which quantified the association of the gene to the inhibiting/enhancing effect. We evaluated genes that belong to the same functional subsystems (42, 66) were more often found to be significantly associated to the inhibiting/enhancing effect than to 103 random groups of genes We defined this association by modeling the average count of genes belonging to a functional susbsystem within the random groups as Poisson distributed variables. We then tested if the count of genes with significant p-values was statistically higher than expected from the Poisson model, with a significance level of 0.05 after Benjamini/Hochberg correction for multiple tests. We used the Poisson distribution as the null distribution since (i) the labels for functional subsystem within the random groups are independent; (ii) Counts are expressed as averages from many random samples; (iii) the mean and variance are equivalent, all features consistent with a Poisson distribution(67)

RESULTS

Reproducibility of growth rate alterations by bacterial cells and secretomes

To identify alterations in the growth rates of CRC cell lines by bacterial cells or their secreted products, inactivated cells or secretomes were added to five CRC cell lines with different mutational landscapes and one non-cancerous kidney cell line (see Methods and Supplementary Table S2). Cell culture and bacterial culture media served as a control for cell growth for cells and secretomes respectively. A total of 7,176 experiments were conducted where we measured the bacterial effect on cell growth. Each experiment was repeated four times. We evaluated reproducibility of these replicates by performing linear regression over all pairwise combinations of replicates. As shown in Supplementary Figure S2, we found high reproducibility between replicates (regression coefficient: 0.87 ± 0.05, intercept: 0.04 ± 0.02). Based on this reproducibility, we averaged the four experimental replicates for further analysis.

Contrasting effects between bacterial cells and secretomes

Figure 1A summarizes the effect of bacterial cells and secretomes on the growth of human cell lines. Overall, bacterial cells exhibit a stronger inhibiting effect than secretomes (p=1.02e-75, Wilcoxon signed rank test, Figure 1B). There was a low correlation between the effects of secretomes and inactivated bacteria on CRC cell growth (Supplementary Table S6), indicating that specific factors within the two compartments (cell wall attached or secreted molecules) are of importance for the observed effects.

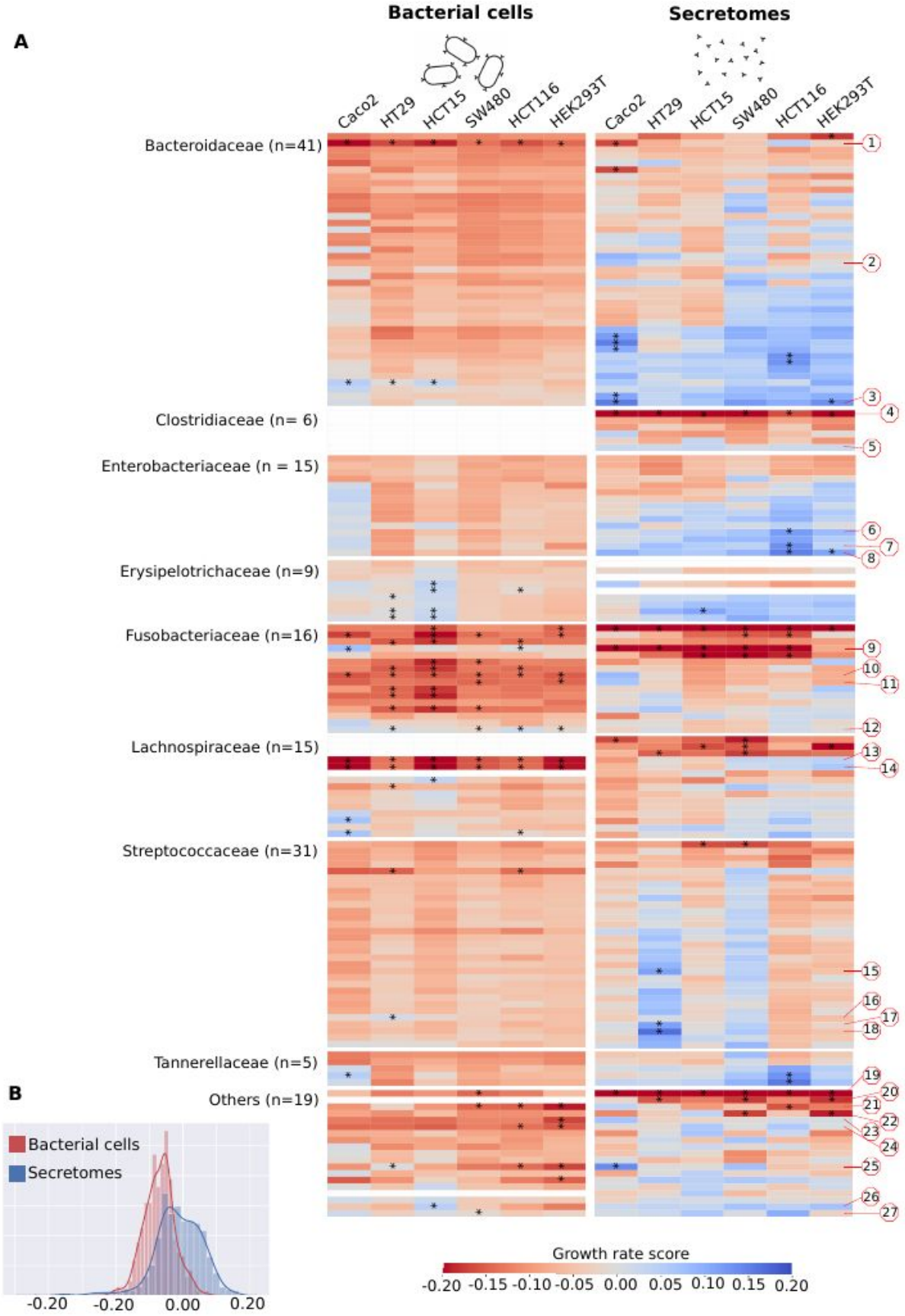
A
Bacterial cells
Secretomes
Caco2
HT29
HCT15
SW480
HCT116
HEK293T
Bacteroidaceae (n=41)
Clostridiaceae (n= 6)
Enterobacteriaceae (n = 15)
Erysipelotrichaceae (n=9)
Fusobacteriaceae (n=16)
Lachnospiraceae (n=15)
Streptococcaceae (n=31)
Tannerellaceae (n=5)
Others (n=19)
B
Bacterial cells
Secretomes
-0.20
-0.20
0.00
0.20
Growth rate score
-0.20 -0.15 -0.10 -0.05 0.00 0.05 0.10 0.15 0.20

FIGURE 1. Growth rate scores of six human cell lines upon treatment with bacterial cells and secretomes. (A) Heatmap indicating low and high growth rate scores, respectively red and blue. Bacteria are sorted within bacterial families by the average growth rate score. Red numbered octagons highlight the strains discussed in the text: *Bacteroides sp.* 2_1_22 (1)*, B. fragilis* K570 clinda R (ETBF) (2), *B.* sp. 4_1_36 (3), *Clostridium septicum* (Mace 1889) Ford 1927 (4), *C.* sp. D5 (5), *Escherichia coli* D9 (6), *Klebsiella* sp. 1_1_55 (7), *E. coli* 4_1_47FAA (8), *F. nucleatum* DSM 15643 (ATCC 25586) (9), *F. nucleatum* DSM 20482 (ATCC 10953) (10), *F. necrophorum subsp. funduliforme* 1_1_36S (11), *F. nucleatum subsp. animalis* 11_3_2 (12), *Lachnospiraceae bacterium* 8_1_57FAA (13), *L. bacterium* 3_1_46FAA (14), *Streptococcus bovis* 1212 (15), *S. bovis* 1459 (16), *S. bovis* 1417 (17), *S. bovis* 207 (18), *Pediococcus acidilactici* 7_4 (19), *Pseudomonas* sp. 2_1_26 (20), *D.* sp. 6_1_46AFAA (21), *Ralstonia* sp. 5_2_56FAA (22), *Ruminococcaceae bacterium* D16 (23), *Synergistes* sp. 3_1_syn1 (24), *Desulfovibrio sp.* 3_1_syn3 (25)*, Propionibacterium sp.* 5_U_42AFAA (26), and *Eubacterium sp.* 3_1_31 (27). Highlighted with asterisks are cases that correspond to the 5% extremes of the z-score distribution. (B) Distribution of the growth rate scores for bacterial cells and secretomes.

Difference in growth rate alterations between CRC cell lines

Growth rates were significantly enhanced or inhibited ($p<0.05$) in one or more cell lines in 35 out of 145 (24.1%) inactivated bacterial strains (Figure 2A, Supplementary Table S3) and 33 out of 154 (21.4%) secretomes (Figure 2B, Supplementary Table S4). Growth rates of HEK293T cells were affected by the lowest number of bacteria (n=21, n=3 enhanced and n=18 inhibited growth). On the other end of the spectrum were HCT116 cells that were affected by 28 different bacteria (n=11 enhanced and n=17 inhibited growth) and HCT15 cells that were affected by 27 different bacteria (n=8 enhanced and n=19 inhibited; Figure 2C). These two cell lines had microsatellite instability (MSI) and harbored the greatest number of pathogenic mutations in known tumor suppressor and oncogenes (n=3 and n=4 respectively, see Supplementary Table S2). In general, the number of pathogenic mutations of a cell line correlated with the number of bacteria that significantly affected its growth (Pearson r=0.931,

$p<0.01$, see Figure 2D), suggesting that acquiring hallmark mutations might make cells more susceptible to growth rate changes by bacteria.

Some strains significantly enhanced or inhibited the growth rate of specific cell lines (Figure 1). *Streptococcaceae* cells generally had a neutral effect on cell growth, however, some *Streptococcaceae* secretomes specifically enhanced growth of HT29 and SW480 cells (Figure 1). Three *Streptococcus bovis* secretomes (strains 207, 1212 and 1417) and one inactivated bacterium (strain 1459) selectively enhanced growth in HT29 cells, while no effects were observed in other cell lines (Figure 1 and Figure 2C). The genomes of these enhancing *Streptococcus bovis* strains cluster together in a phylogenetic tree with *Streptococcus gallolyticus* subsp. *gallolyticus* (SGG) and subsp. *pasteurianus* (SGP) (Supplementary Figure 3). These effects of *Streptococcus bovis* may be cancer-specific since HEK293T was not affected. Other notable cell-line specific effects include *Erysipelotrichaceae* cells, and *Tannerellaceae* secretomes that significantly enhance growth of HCT15 and HCT116 cells, respectively.

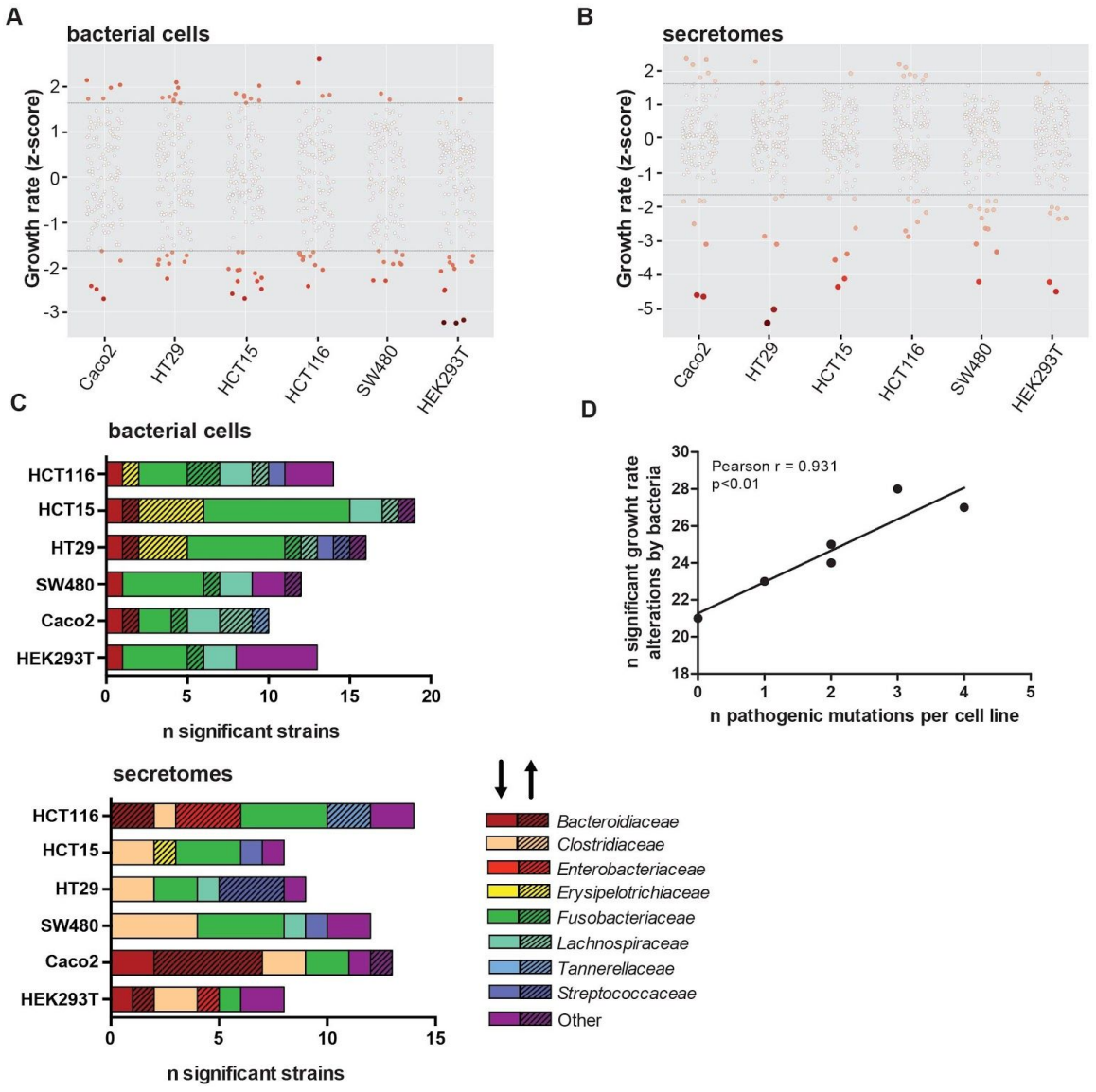

FIGURE 2: Growth rate alterations of cells lines upon incubation with bacterial cells and secretomes. Distribution plots illustrating effects of (A) bacterial cells and (B) secretomes on cell lines. Negative numbers indicate growth inhibition whereas positive numbers show growth enhancement. The color intensity of the circles represents significance of the effect on growth. (C) Overview of the number of bacterial cells and secretomes significantly enhancing or inhibiting cell growth per tested cell line, sorted by bacterial family. The shading of the bar (arrow pointing upwards) highlights enhancing and unshaded bar (arrow pointing downwards) highlights inhibiting strains. (D) Correlation of number of strains significantly altering growth rates to the number of pathogenic mutations present in cell lines. HEK293T, Caco-2, HT29, SW480, HCT116, and HCT15 were shown to possess 0, 1, 2, 2, 3, and 4 pathogenic mutations, respectively.

Bacterial family-level and strain-level effects on CRC cell growth rates

To assess the overall effect of the different bacterial secretomes and cells on our six cell lines, we projected the growth rate scores into a two-dimensional t-SNE plot. Figure 3 shows this lower dimensional space overlayed with family specific colors and a shade corresponding to the average growth effect. We observed a clear clustering of bacterial families, i.e. cells or secretomes from the same families tend to have similar effects on the different cell lines (see also Figure 1, Table 1). For bacterial cells, the most striking effect was observed for *Fusobacteriaceae* that generally inhibited growth of the cancer cells. Most *Bacteroidaceae*, *Enterobacteriaceae,* and *Erysipelotrichaceae* secretomes enhanced cell growth, although not always significantly (Figure 1). Contrastingly, *Clostridiaceae* secretomes generally inhibited growth rates. The effect of bacterial cells and secretomes was significantly clustered for five and three bacterial families, respectively (Supplementary Table S7).

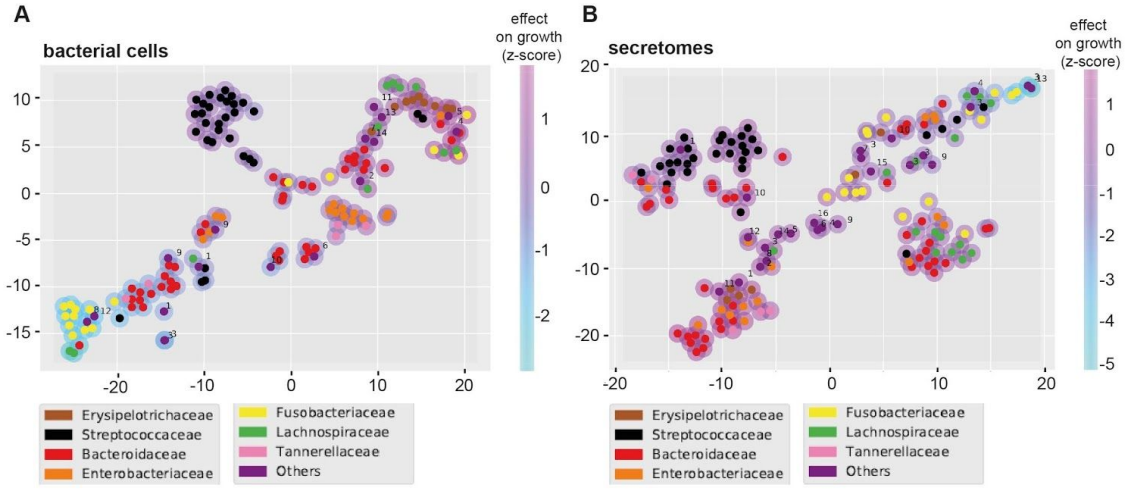

FIGURE 3. t-SNE plots summarizing the overall growth effects of bacterial cells (A) and secretomes (B) on six human cell lines. Coloured circles correspond to strains belonging to particular bacterial families. Magenta and light blue shading around the

circles indicate enhancing and inhibiting effect of strains, respectively. Families labelled as "Others" contains the following strains for bacterial cells (A): *Lactobacillaceae* (1), *Peptostreptococcaceae* (2), *Desulfovibrionaceae* (3), *Eubacteriaceae* (4), *Bifidobacteriaceae* (5), *Enterococcaceae* (6), *Veillonellaceae* (7), *Synergistaceae* (8), *Burkholderiaceae* (9), *Pseudomonadaceae* (10), *Propionibacteriaceae* (11), *Ruminococcaceae* (12), *Akkermansiaceae* (13), *Acidaminococcaceae* (14). And the following strains for secretomes (B): *Lactobacillaceae* (1), *Eubacteriaceae* (2), *Clostridiaceae* (3), *Peptostreptococcaceae* (4), *Bifidobacteriaceae* (5), *Enterococcaceae* (6), *Veillonellaceae* (7), *Synergistaceae* (8), *Burkholderiaceae* (9), *Desulfovibrionaceae* (10), *Propionibacteriaceae* (11), *Ruminococcaceae* (12), *Pseudomonadaceae* (13), *Akkermansiaceae* (14), *Acidaminococcaceae* (15), *Bacillaceae* (16).

In the *Bacteroidaceae* family (n=41 strains tested), secretomes and bacterial cells of seven and one strains significantly enhanced cell growth, respectively. The effects were most prominently observed in Caco-2 cells, while the growth of non-cancerous cell line HEK293T was only significantly enhanced by the secretome of *Bacteroides* sp. 4_1_36 (Figure 2C & Table 1). Only three *Enterobacteriaceae* secretomes (n=15) significantly enhanced growth of HEK293T cells (*Escherichia coli* 4_1_47FAA) and HCT116 (*Escherichia coli* 4_1_47FAA and D9, and *Klebsiella* sp. 1_1_55) while no effects were observed for bacterial cells.

Growth inhibiting effects were mainly observed within the family *Fusobacteriaceae* (Figure 1, Table 1). From the 12 out of 16 significant *Fusobacteriaceae* (81.3%) cells, two enhanced and ten inhibited cellular growth. *Fusobacterium necrophorum* subsp. *funduliforme* 1_1_36S cells enhanced growth in HCT116, SW480, and HEK293T cells. Strikingly, while *Fusobacterium nucleatum* subsp. *animalis* 11_3_2 cells enhanced growth of Caco-2 and HCT116, its secretome inhibited growth in those same cell lines. Especially the cell line HCT15 was sensitive for *Fusobacteriaceae* growth inhibition where 11 out of 16 strains significantly reduced growth rates.

Alternatively, HEK293T and Caco-2 were less sensitive to *Fusobacteriaceae* with only four out of 16 strains inhibiting cell growth. Notably, the effect of *Fusobacteriaceae* secretomes on cell growth may be cancer specific, since most secretomes that inhibited cancer cell growth did not inhibit growth of HEK293T cells.

Families with fewer than 5 strains tested

Among strains from families with less than five tested strains (n=18), *Eubacterium sp.* 3_1_31 and *Propionibacterium sp.* 5_U_42AFAA cells increased cell growth rates in SW480 and HCT15 cells, respectively (Table 1). Interestingly, *Pseudomonas* sp. 2_1_26 secretomes significantly inhibited the growth rates of all cell lines while the cells specifically inhibited SW480. *Pediococcus acidilactici* 7_4 and *Ruminococcaceae bacterium* D16 cells selectively inhibited the non-cancerous cell line, HEK293T, while *Synergistes sp.* 3_1_syn1 also inhibited HCT116. Aerobically cultured *Ralstonia* sp. 5_2_56FAA secretomes inhibited 2 cell lines, SW480 and HEK293T. For *Desulfovibrio* sp. 3_1_syn3, the secretome increased Caco-2 growth while the bacterial cells increased HT29 growth. Contrastingly, these same bacterial cells decreased growth of HCT116 and HEK293T. Similarly, *Desulfovibrio* sp. 6_1_46AFAA cells decreased the growth rates of HCT116, SW480 and HEK293T cells.

Strain-specific effects that contrast their family

While strains from the same bacterial families tend to have similar effects on the growth rates of cell lines (Supplementary Table S7), large variations were observed within certain families. For instance, within the *Clostridiaceae* family, the secretome

of *Clostridium septicum* (Mace 1889) Ford 1927 strongly inhibited growth of all tested cell lines, while the *Clostridium* sp. D5 secretome enhanced growth, although the significance threshold was not reached (Figure 1 and Supplementary Table S4). Similarly, *Bacteroides* sp. 2_1_22 cells strongly inhibited the growth rates of all cell lines while *B. fragilis* K570 cells enhanced growth in most cell lines (Figure 1 and Supplementary Table S3). A large growth rate variation was also observed in cell lines exposed to *Lachnospiraceae* cells (n=11). For this family, the cells of *L. bacterium* 3_1_46FAA and *L. bacterium* 8_1_57FAA significantly inhibited the growth rates of all cell lines, while most of the other strains showed weak or low inhibition.

The observed variations in growth effect within bacterial families might either be explained by the phylogenetic distances between the strains or by characteristics with a non-phylogenetic distribution, such as accessory functions. To evaluate this, we measured the distances on a phylogenomic tree and compared them with the differences in growth rate effects over the cell lines. For most bacterial families, there is no association between the growth rate effects and phylogenetic distances (Supplementary Table S8, Supplementary Figure S4), suggesting that these effects may be associated with accessory functions that are independently gained or lost in different lineages. For *Erysipelotrichaceae* secretomes and cells, *Fusobacteriaceae* cells, and *Lachnospiraceae* secretomes, we found that the phylogenetic distance was significantly correlated with the growth rate effects, suggesting that these effects may be associated to variations in universally shared genes or to accessory functions with phylogenetically consistent dynamics.

The presence of virulence genes is associated with growth rate inhibition

To explain the complex, sometimes strain-dependent patterns of growth enhancement or inhibition, we analyzed the genome sequences of 144/157 tested gut bacteria. First, we checked whether 35 known bacterial family-specific virulence genes were present within the genomes of the tested strains (Supplementary Table S9), because some of the encoded virulence factors have been linked to cell proliferation changes. Seven toxin genes were found, including TcdA (68); FadA (31); colibactin present on the pks-island (69, 70); Shiga toxin ShEt1; *Shigella* enterotoxin Stx2A; effector protein Map secreted by T3SS of *Citrobacter rodentium* and *Escherichia coli* (71, 72); and BFT (38).

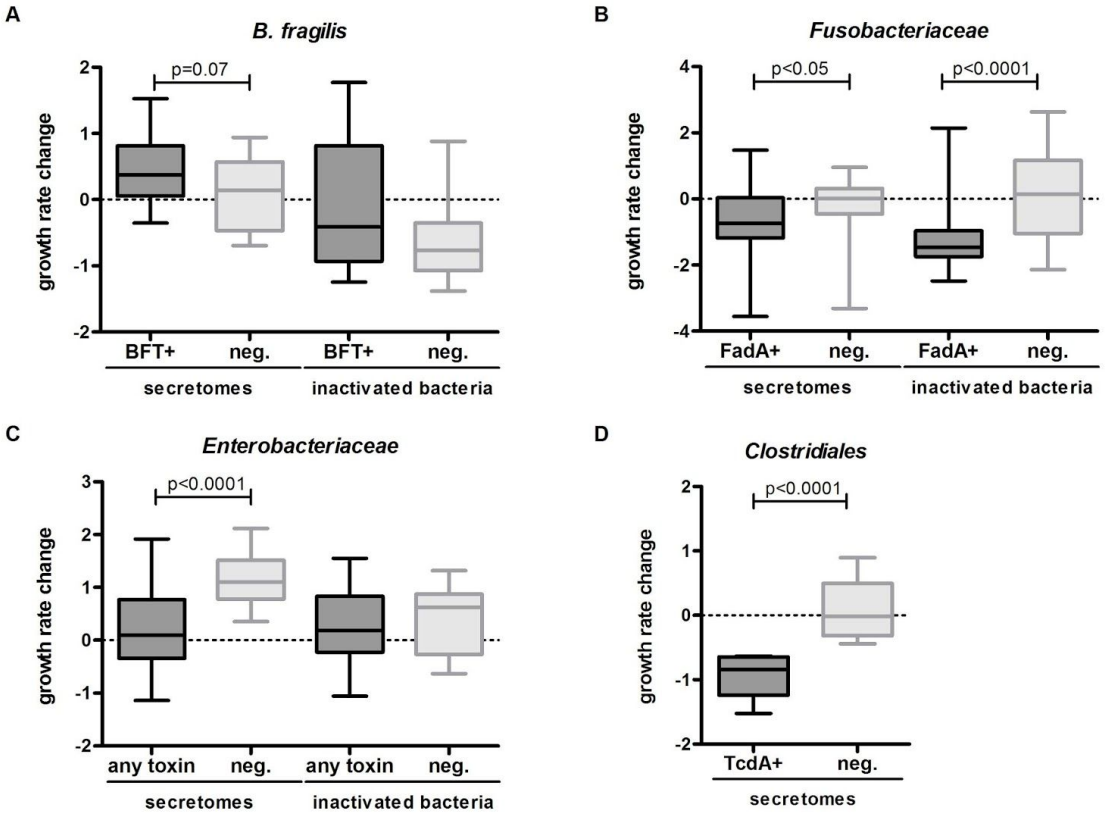

FIGURE 4. Influence of strains with and without encoded virulence factors on cellular growth rates. *B. fragilis* (A), *Fusobacteriaceae* (B), *Enterobacteriaceae* (C) and

Clostridiaceae (D) encoding the virulence factors *bft*, *fadA*, any toxin (*Map*, *pks*, *ShEt1*, *Stx2A*), and *TcdA*, respectively, were compared to strains without these encoded virulence factors (Mann-Whitney U test). A trend towards cell growth enhancement was observed for *B. fragilis bft*+ secretomes (p=0.07) (A), while significant inhibition of cell growth was observed for *fadA*+ *Fusobacteriaceae* cells (p<0.0001), and secretomes (p<0.05) (B), for *Enterobacteriaceae* secretomes encoding toxins (p<0.0001) (C), and *TcdA*+ *Clostridiales* secretomes (p<0.0001) (D).

As shown in Figure 4, strains containing virulence genes tend to change growth rates, relative to related strains without those virulence genes. For example, the secretomes of *Clostridiales* strains significantly inhibited growth rate if their genomes contained *TcdA* (Figure 4A, p<0.0001). Similarly, *Fusobacteria* strains encoding the membrane protein *fadA*, that might be responsible for growth rate changes of epithelial cells (31), inhibited growth rates significantly (Figure 4B, p<0.0001 and p<0.05 for bacterial cells and secretomes respectively). Within the *Enterobacteriaceae* family, multiple secreted toxins were identified in the genomes, including colibactin, *ShEt1*, *Stx2A*, and *Map*. Secretomes of *Enterobacteriaceae* possessing any of these toxins inhibited cell growth relative to strains without these toxins (Figure 4C, p<0.0001). No differences were observed between bacterial cells of *Enterobacteriaceae* with or without the toxin genes. The secretomes of three *B. fragilis* strains encoding the secreted enterotoxin *bft* enhanced the growth rates of CRC cells, while the five *B. fragilis* strains without the toxin did not, although this trend was not significant (Figure 4A, p=0.075). The trend was not observed for bacterial cells, where only *B. fragilis* K570 significantly enhanced growth rates (Table 1).

Functional categories associated with differential effects within families

Beside the toxin genes described above, other genes might also play a role in the observed effects. Thus, we next performed an unbiased comparative genome analysis where we associated all annotated bacterial genes to the effect of the strain on cell growth. We next grouped the genes by functional category and assessed whether genes within a category were significantly associated with cell growth alterations. Based on the PATRIC (42) annotations we evaluated genes in two hierarchical levels of functions, namely 'Subsystems' and 'Superclass'. All functional categories found to be significantly associated with cell growth alterations are listed in Supplementary Table S10.

The "Membrane transport" superclass was significantly associated with inhibiting *Enterobacteriaceae* cells and secretomes, and with enhancing *Fusobacteriaceae* secretomes. Other enriched superclasses included: "Cell envelope", "Metabolism", "Cellular processes", "Protein processing", "Energy", and "Stress response, defense and virulence" (Supplementary Table S10). Subsystems including "Cobalamin synthesis", "Ethanolamine utilization", and the "Dpp dipeptide ABC transport system" were consistently found to be associated with growth enhancement or inhibition in multiple bacterial families and in multiple cell lines (Supplementary Table S10). The significant effects of other subsystems including "Vir-like type 4 secretion system", "Glutamate fermentation", "Flagellum", "Branched-chain amino acid biosynthesis", and others were associated with specific bacterial families. We expect that these statistical associations will provide valuable leads for future experiments.

DISCUSSION

Over 150 human gut bacteria belonging to taxonomic groups that have previously been associated with CRC were tested for their effects on cell growth of five CRC cell lines (HT29, Caco-2, HCT116, SW480 and HCT15) with different mutation landscapes representing commonly mutated genes in CRC, and one non-cancerous kidney cell line (HEK293T). Our results show that cell growth enhancing and inhibiting effects of gut bacteria depend both on the mutational landscape of the cancer cells and on the identity and functional content of the bacteria, including secreted or cell wall attached factors. CRC is a heterogeneous disease, as is reflected in the five different CRC cell lines with mutations in key CRC related genes (*KRAS*, *APC, BRAF*, *TP53*, *CTNNB1* and *PIK3CA*). As expected, the growth rate of non-cancerous HEK293T kidney cells was affected by the lowest number of gut bacterial strains, with only small differences.

Closely related bacteria may have distinct effects on cell growth

A striking observation was that the effects of bacterial cells and secretomes were strongly associated to bacterial families, although exceptions to this general pattern were observed. Previous studies have found that *Fusobacteria*, *Streptococcus, Peptostreptococcus, Ruminococcus* and *Escherichia/Shigella* tend to be enriched in tumors, while *Bacteroides, Pseudomonas, Lachnospira* and *Anaerostipes* are depleted (5, 7, 9, 22-24, 28, 31, 41, 73-76). Regardless of the enrichment or depletion on CRC tumors *in vivo,* our *in vitro* results indicate that closely related bacteria may have distinct effects on cancer cell growth. For example, we observed that different *Fusobacteria* strains, which were all cultured in the same media under

the same conditions, may have opposing effects on cancer cell growth, while these bacteria are consistently enriched in patients (24, 28, 77). This suggests that specific bacterial factors play a role in CRC.

***Fusobacteriaceae*: enhancing or inhibiting growth?**

Previous studies indicated that *Fusobacteriaceae* enhanced growth of HCT116, SW480, and HT29 cells (31, 76). *F. nucleatum* ATCC25586was shown to enhance CRC cell growth via interaction with Toll like receptors TLR4, TLR2, and myeloid differentiation primary response protein 88 (MYD88) (76), and the *F. nucleatum* strain Fn12230 was previously shown to enhance cell growth through the cell-wall attached adhesin FadA (31). Our results showed that most *Fusobacteriaceae* significantly inhibited cellular growth, including *Fusobacterium nucleatum* ATCC25586, contrasting previous observations (76, 78), and that the presence of the *FadA* gene was significantly linked to growth inhibition by cells and secretomes (Table 1). Notably, the secretomes showed less pronounced inhibition than bacterial cells. While FadA is membrane-bound, secretomes likely include outer membrane vesicles (OMVs) that are 40-110 nm in size and express FadA (32, 79). To rule out the possibility that these contrasting results were due to differences in methods, we compared our high-throughput MTT-based assay, used in this study, with the cell counting assay, that was employed in the referred studies, on 6 cell lines, using 6 different secretomes, and found a high correlation (Pearson's r=0.813, Supplementary Figure S5). These results confirm that the observed inhibitory effects by *Fusobacteriaceae* strains do not depend on the applied experimental techniques, but may partly be due to use of different *Fusobacteriaceae* strains(Fn12230,

ATCC25586, ATCC23726) isolated from extra-intestinal sites(80). Specifically HCT15 cell growth was significantly inhibited by 11/16 *Fusobacteriaceae* strains (nine cells and three secretomes). HCT15 cells contain a missense mutation in MYD88 (p.Arg264Ter) resulting in a MYD88 deficiency, and may thus explain the insensitivity of this cell line to *F. nucleatum* subsp. *animalis* 11_3_2 and *F. necrophorum* subsp. *funduliforme* 1_1_36S, the two *Fusobacteriaceae* strains that promoted growth of the other CRC cell lines, but not of HCT15.

Virulence factors are associated to cell growth inhibition

The growth-inhibiting properties of *Clostridiaceae* secretomes may result from toxins encoded by this family. We observed that the presence of the *TcdA* gene in *Clostridiaceae* was significantly associated with cell growth inhibition. *Clostridium septicum* (Mace 1889) Ford 1927 secretomes inhibited cell growth in all of our cell lines. This strain produces multiple exotoxins (alpha toxin, lethal toxin and hemolytic toxin) and has been associated to CRC (14, 15).

Enterobacteriaceae strains encoding the toxins colibactin, *Stx2A*, *ShEt1*, and *Map* inhibited cell growth relative to non-toxigenic *Enterobacteriaceae* strains. Colibactin (present in four of our *Escherichia* strains) is a genotoxic compound that alkylates DNA and generates DNA double strand breaks (41, 74). The DNA damaging effect of colibactin may not directly affect cell growth in our experimental setup, although colibactin may induce cell cycle arrest via SUMOylation of TP53 causing inactivation (69, 70). Cell cycle arrest would stall cell growth, which can only happen in *TP53* wildtype cell lines with active TP53 protein. Indeed, the only cell lines that were

relatively inhibited by strains encoding colibactin were the wildtype *TP53* cell lines HEK293T and HCT116.

An important virulence factor of *B. fragilis* is BFT (81). While in previous research BFT was shown to enhance cell growth of HT29/c1 cells via β-catenin nuclear signalling (38), enterotoxigenic *B. fragilis* secretomes (VPI13784 (*bft1*), 86-5443-2-2 (*bft2),* and K570 (*bft3*)) only marginally enhanced CRC cell growth in our assay compared to the other *B. fragilis* secretomes in our screen. The mild effects as observed may depend on the level of toxin production and secretion under our experimental conditions. Interestingly, enterotoxigenic *B. fragilis* str. Korea 570 cells significantly enhanced growth, which might be independent of BFT and related to other cell-wall attached factors.

***Streptococcus bovis* strains specifically enhance growth of HT29 cells**

Streptococcus bovis infections have been linked to colorectal neoplasia (43, 82, 83). Our results demonstrate that secretomes of *Streptococcus bovis* strains that are closely related to known *S. gallolyticus* and *S. pasteurianus* strains (Supplementary Figure S3), selectively enhance growth of HT29 cells. This is in line with a previous study showing cell growth enhancing effects in HT29 and HCT116 cells that was mediated through *β*-catenin, while no effect was observed in SW480 and HEK293T cells (84). An intact *β*-catenin pathway may therefore be required to observe the specific effect of *S. gallolyticus* on cell growth as is the case in HT29 cells (85), which may thus be sensitive to the effects of *S. gallolyticus* in our assay. HCT116 cells have a mutation in *CTNNB1 (p.Ser45del)* that interferes with *β*-catenin degradation, which

may explain its insensitivity to *S. gallolyticus*. Alternatively, mutations in the *APC*-gene in the other CRC-cells (86) may interfere with *β*-catenin signalling depending on the specific mutation.

Bacterial functions associated with cell growth alterations

Several functional categories were significantly associated with CRC cell growth. Most of these functions were identified in specific bacterial families and consistently inhibited or enhanced cell growth in different cell lines. These functions may reflect novel pathways of bacterial interference with CRC cell growth that, to our knowledge, have not been previously identified. Most functions are related to cell metabolism, secretion, and transport systems. For example, secretomes of *Enterobacteriaceae* that encode the "Vir-like type 4 secretion system" inhibited growth of all cell lines. Similarly, the gene superclass "Membrane transport" was mostly associated to secretomes that inhibited cell growth (Supplementary Table S10). Molecules that are secreted by these bacterial transport systems may be responsible for the inhibiting effect. For example, the Vir-like type 4 secretion system allows bacteria to secrete proteinaceous effectors that kill competitors (87). Here, we report an important first step in understanding the cell growth enhancing or inhibiting effects of human gut bacteria by identifying putative transport systems for effector molecules.

While the growth effects of secretomes were mostly associated with membrane transport functions, effects on CRC cell growth by bacterial cells were associated with metabolic pathways (Supplementary Table S10). It is possible that these associations may be attributed to metabolic enzymes that may still be, although the

bacterial cells were inactivated. In other ecosystems, metabolic enzymes of dead bacteria have been shown to remain active for up to 96 hours (88). Our experiment was performed within 72 hours. The synthesis of cobalamin (vitamin B12), which is important for human cell proliferation *in vitro* (89) and a common addition to cell culturing media, was significantly associated with the cell growth enhancing effect of *Bacteroidaceae* and *Enterobacteriaceae* cells. Several possible scenarios can be envisioned to explain this observation. First, it remains to be tested whether vitamin B12 was retained in the bacterial fraction after washing, stimulating human cell growth on those cells. Second, different human gut-associated *Bacteroides* strains contain surface-exposed lipoproteins with high affinity for cobalamin (90). Such molecules may remove cobalamin directly from the media, making it unavailable to the human cells and impeding their growth.

The “Ethanolamine utilization” pathway was another metabolic process that we found to be associated to the inhibiting effect of *Fusobacteriaceae* cells on the growth rate of CRC cell lines. Ethanolamine (EA) is the basal component of phosphatidylethanolamine, a major phospholipid in animal cell membranes and is utilized by bacteria including *Fusobacteria* as a carbon source in the gut (91-93). EA sensing regulators have been proposed to regulate virulence in *Enterobacteriaceae* (93, 94). It remains to be tested if the EA in human cell membranes triggers virulence factors in *Fusobacteria* that encode EA utilization genes, or perhaps if inactivated *Fusobacteria* cells retain the capacity to digest and kill human cells by the activity of EA utilization enzymes.

Overall, the statistical associations found in this exploratory analysis provide valuable clues about the possible functions and mechanisms that drive the interactions of bacteria with human cells in the gut. Future experiments are needed to confirm whether these factors are causal and to further clarify the molecular mechanisms involved.

Outlook

Our broad screen revealed many significant associations between gut bacteria, their encoded functions, and growth enhancement or inhibition of human CRC cell lines. Many growth rate effects remain elusive and need to be further examined. Moreover, it will be important to investigate the growth rate effects of living bacterial communities or mock communities, which are thought to synergize in affecting tumorigenesis (53), but fall outside the scope of our present study. Bacterial effects should be examined in more natural environments that mimic the conditions in the human gut, *e.g.* in co-culture with mucus, immune cells, and/or within organoid cultures (95). Our study forms an important baseline for such further research by identifying important traits in individual bacterial strains that are associated to enhancing or inhibiting cancer cell growth, as well as important host factors that determine sensitivity to those bacterial traits.

CONCLUSIONS

Above, we presented the results of the first large-scale analysis of the effects of gut bacteria on CRC cell growth. Our results with bacterial cells and secretomes reflect the complexity of the microbe-host interactions in the human gut. First, bacterial

families tend to have consistent effects on cell growth, although these effects are not universal. This may partially be explained by the presence of virulence genes in some strains. Second, there are cell line dependent effects in CRC cells due to their mutational landscape heterogeneity. Notably, these cell lines have acquired several different cancer hallmarks, yet their growth can still be influenced by specific bacteria. Our results suggest that the response of CRC cells to gut bacteria may differ between patients due to differences in their gut bacteria, although the relevance of our *in vitro* results for patients remains to be studied. Cell growth enhancing and inhibiting bacterial traits could be important for determining risk for cancer or its progression, and these consequences could potentially be counteracted by microbiome modulation. Currently, microbiome medicine applications have already been adapted to some other diseases. For instance, *Akkermansia muciniphila* was demonstrated to improve diabetes type 2 and obesity in mice (17, 18). Resistant life-threatening *Clostridium difficile* infections and ulcerative colitis were successfully treated with faecal microbiota transplants (FMT) (19, 20). Our study highlights the complex processes at play at the gut-microbiome interface and contributes to a better understanding of the role of different bacterial strains in altering colonic epithelial cell proliferation.

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Supplementary Figure captions

S1. Average growth of human cell lines exposed to bacterial cells and secretomes. Colored lines and error bars show the average and standard deviation of MTT measurements for 6 human cell lines exposed to cells and secretomes of 145 and 154 bacteria, respectively. Measurements were recorded at the incubation times of 0, 24, 48, and 72h. The dark lines show the average of the cell line without bacterial products (negative controls).

S2. Reproducibility of four experimental replicates. Scatter plots of the pairwise combinations of four experimental replicates of MTT measurements at incubation times of 0, 24, 48, and 72h. Individual plots exhibit replicates of one cell line exposed to the cells or secretomes of, respectively 145 and 154 bacterial strains. Lines show the best fit to a linear model. The specific linear regression coefficients, intercepts, R^2, and p-values are shown on the top of each plot.

S3. Cell growth rate alterations ordered by phylogenomic distances. Heatmaps show the growth rate alterations of six cell lines incubated with the cells and secretomes of strains from seven bacterial families. Rows of the heatmap are ranked according to the tips of the phylogenomic trees shown on the left.

S4. *Streptococcus* phylogenomic tree. Genome-based phylogenetic reconstruction of 238 Streptococcus genomes confirms that the genome sequences of the *S. bovis* strains reported in this study are closely related to previously sequenced genomes of *S. gallolyticus* and *S. pasteurianus*. The taxa names of strains used in our study are highlighted red. Monophyletic branches containing strains from a single species are collapsed and highlighted with blue triangles.

S5. Linear relation between cell counts and MTT measurements.

Cell growth was recorded by two different methods (MTT assay and cell counting) and plotted on a linear x-y graph. Both methods were significantly correlated ($p<0.0001$, Pearson $r=0.813$).

Supplementary Table captions

S1. Bacterial strains used in this study.

S2. Cancer mutational profile of six human cell lines used in this study.

S3. Growth rate scores, z-scores, and p-values measured from human cells incubated with bacterial cells.

S4. Growth rate scores, z-scores, and p-values measured from human cells incubated with bacterial secretomes.

S5. Literature summary of microbial virulence factors potentially associated to cancer.

S6. Correlation between growth rate scores of cells and secretomes.

S7. Statistical significance analysis of family-specific clustering of the growth rate scores.

S8. Correlation between the pairwise phylogenetic distance between bacterial strains used in this study and the pairwise Euclidean distance of the growth rate scores.

S9. Distribution of genes coding for virulence factors in the genomes of the bacteria used in this study. The TcdA toxin was present in bacteria of the *Clostridiales* order while other toxins were present within bacterial families.

S10. Functional genomic terms significantly associated to growth rate scores within bacterial families.

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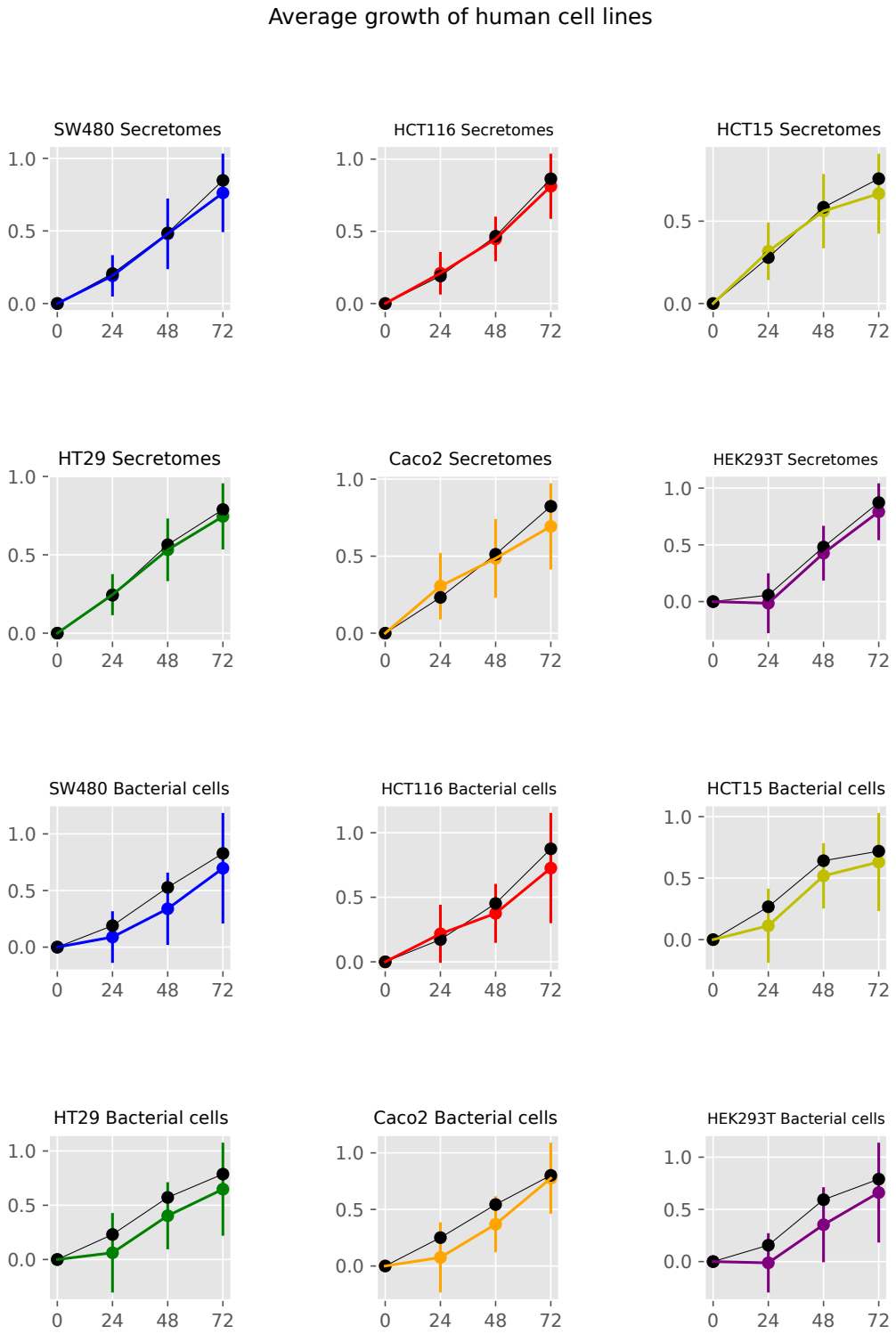
Table 1: Secretomes and bacteria significantly enhancing or reducing cell growth rate (z-scores).

Family	Bacteria	Caco-2	HT29	HCT15	SW480	HCT116	HEK293 T
Bacteroidaceae	*B. dorei* 5_1_36/D4	0.89	0.82	1.36	0.90	1.87	1.38
	B. eggerthii 1_2_48FAA	1.82	0.59	1.51	1.16	1.21	1.48
	B. fragilis K570 clinda R (ETBF)	1.74	1.71	1.77	0.71	1.15	0.36
	B. massiliensis 3972 T(B)2	-0.44	-1.63	-0.83	-0.51	-1.45	-2.01
	B. ovatus 3_8_47FAA	1.96	0.17	1.17	1.27	1.24	1.42
	Bacteroides sp. 1_1_6	2.36	-0.21	0.63	0.86	1.27	0.93
	Bacteroides sp. 2_1_16	1.15	0.51	0.98	0.53	1.87	1.17
	Bacteroides sp. 2_1_22	-1.83	-0.73	-0.05	-0.49	0.82	-0.08
	Bacteroides sp. 2_1_22	-2.49	-2.26	-2.31	-1.64	-2.42	-1.78
	Bacteroides sp. 4_1_36	2.39	0.67	1.34	1.58	1.50	1.93
	Bacteroides sp. 9_1_42FAA	1.71	-0.06	0.71	1.09	1.46	0.87
	Bacteroides sp. D2	-1.82	-0.64	-0.04	-0.17	0.45	0.04
Clostridiaceae	*C. septicum* (Mace 1889) Ford 1927	-4.64	-5.02	-4.11	-2.63	-1.84	-4.49
Enterobacteriaceae	*E. coli* 4_1_47FAA	1.63	1.05	1.26	1.17	2.12	1.65
	E. coli D9	0.48	0.64	1.12	0.88	1.75	1.28
	Klebsiella sp. 1_1_55	0.77	1.15	1.19	0.57	1.92	0.70
Erysipelotrichaceae	*Coprobacillus* sp. 29_1	-0.06	1.32	1.94	1.03	0.81	0.91
	Coprobacillus sp. 29_1	0.40	1.84	1.64	1.15	0.72	0.21
	Coprobacillus sp. 8_2_54BFAA	0.68	1.78	1.59	1.15	0.82	0.46
	Coprobacillus sp. D7	1.02	1.64	1.74	1.18	0.80	0.58
	Erysipelotrichaceae bacterium 2_2_44A	1.07	1.26	1.70	0.95	1.82	0.68
	Erysipelotrichaceae bacterium 21_3	1.19	1.51	1.85	1.13	1.47	1.10
Fusobacteriaceae	*F. gonidiaformans* 3-1-5R	-0.43	-1.52	-2.62	-3.32	-2.16	-1.16
	F. necrophorum subsp. *funduliforme* 1_1_36S	1.18	1.98	1.12	1.71	2.63	1.72
	F. nucleatum subsp. *animalis* 11_3_2	-2.50	-2.86	-3.56	-3.09	-2.70	-0.77
	F. nucleatum subsp. *animalis* 11_3_2	2.15	0.48	1.11	0.96	2.09	1.20
	F. nucleatum subsp. *animalis* 21_1A	-1.45	-1.74	-2.31	-1.33	-1.47	-1.03
	F. nucleatum subsp. *animalis* 3_1_33	-0.66	-1.74	-2.07	-1.24	-1.60	-1.25
	F. nucleatum subsp. *animalis* 7_1	0.14	-0.72	-1.49	-1.83	-1.81	0.10
	F. nucleatum subsp. *animalis* 7_1	-1.86	-1.40	-2.48	-1.73	-1.30	-1.75
	F. nucleatum subsp. *nucleatum* ATCC 25586	-1.64	-1.67	-1.67	-1.89	-1.67	-2.04
	F. nucleatum subsp. *polymorphum* ATCC 10953	-1.51	-1.39	-1.33	-1.94	-1.60	-1.88
	F. nucleatum subsp. *vincentii* 3_1_27	-0.48	-1.88	-2.13	-1.65	-1.56	-1.20
	F. nucleatum subsp. *vincentii* 3_1_36A2	-0.95	-1.62	-2.24	-1.72	-1.17	-1.26
	F. nucleatum subsp. *vincentii* 4_1_13	-0.97	-1.92	-2.06	-1.52	-1.76	-1.45
	F. periodonticum 1_1_41FAA	-0.83	-1.94	-2.04	-1.27	-1.69	-1.48
	F. periodonticum 2_1_31	-3.10	-3.10	-3.38	-2.64	-2.44	-2.35
	F. periodonticum 2_1_31	-1.08	-1.32	-1.66	-0.86	-0.97	-1.90
Lachnospiraceae	*Anaerostipes* sp. 3_2_56FAA	-0.51	-1.67	-1.39	-2.08	-1.54	-1.47
	C. symbiosum WAL-14163	-1.01	-1.27	-1.75	-1.82	-0.70	-2.33
	C. symbiosum WAL-14673	-1.80	-1.20	-1.56	-2.32	-1.14	-1.14
	Lachnospiraceae bacterium 1_1_57FAA	2.04	0.78	0.80	1.62	0.60	0.81

	Lachnospiraceae bacterium 3_1_46FAA	-2.41	-1.37	-2.59	-2.30	-1.84	-3.22
	Lachnospiraceae bacterium 4_1_37FAA	1.98	0.93	1.19	1.46	1.80	1.23
	Lachnospiraceae bacterium 5_1_63FAA	0.50	1.68	1.81	1.04	0.09	1.04
	Lachnospiraceae bacterium 8_1_57FAA	-2.70	-1.52	-2.70	-2.30	-1.95	-3.24
Tannerellaceae	*Parabacteroides* sp. 2_1_7	0.06	0.17	0.56	0.88	1.89	0.73
	Parabacteroides sp. 2_1_7	1.73	-0.64	0.92	-0.04	0.32	0.41
	Parabacteroides sp. D13	0.86	0.56	1.04	1.22	2.21	1.10
Streptococcaceae	*S. bovis* 1212	0.23	1.64	0.40	0.62	-0.66	-0.41
	S. bovis 1417	0.49	1.65	0.39	0.67	-0.51	-0.02
	S. bovis 1459	0.63	2.10	0.84	1.13	0.94	0.53
	S. bovis 207	0.35	2.29	0.45	0.81	-0.59	-0.42
	S. salivarius NTB2	-0.98	-0.89	-1.73	-1.98	-1.52	-0.86
	S. sp. 2_1_36FAA	-1.57	-1.84	-0.52	-0.51	-1.73	-1.54
Other	*C. difficile* (Prévot 1938) Lawson et al. 2016	0.13	-1.75	-1.26	-2.10	-1.22	-2.04
	Desulfovibrio sp. 3_1_syn3	2.20	0.17	0.41	0.99	-0.37	-0.17
	Desulfovibrio sp. 3_1_syn3	-0.77	1.76	-0.40	-1.47	-1.77	-2.52
	Desulfovibrio sp. 6_1_46AFAA	0.90	0.06	-0.87	-0.55	-1.75	-1.35
	Desulfovibrio sp. 6_1_46AFAA	-0.78	1.17	-0.69	-1.93	-2.06	-3.17
	Eubacterium sp. 3_1_31	1.25	1.02	1.24	1.85	0.96	1.43
	P. acidilactici 7_4	-1.58	-0.82	0.71	0.33	-1.39	-1.95
	Propionibacterium sp. 5_U_42AFAA	0.20	0.20	2.02	0.96	-0.31	-1.33
	Pseudomonas sp. 2_1_26	-4.60	-5.41	-4.35	-4.20	-2.87	-4.21
	Pseudomonas sp. 2_1_26	-0.02	-1.26	-0.72	-1.91	-1.45	0.35
	Ralstonia sp. 5_2_56FAA	-1.12	-0.28	0.99	-2.05	-0.36	-2.18
	Ruminococcaceae bacterium D16	-1.14	-1.53	-1.34	-1.23	-1.22	-2.50
	Synergistes sp. 3_1_syn1	-1.40	-1.60	-1.57	-1.34	-1.68	-2.09

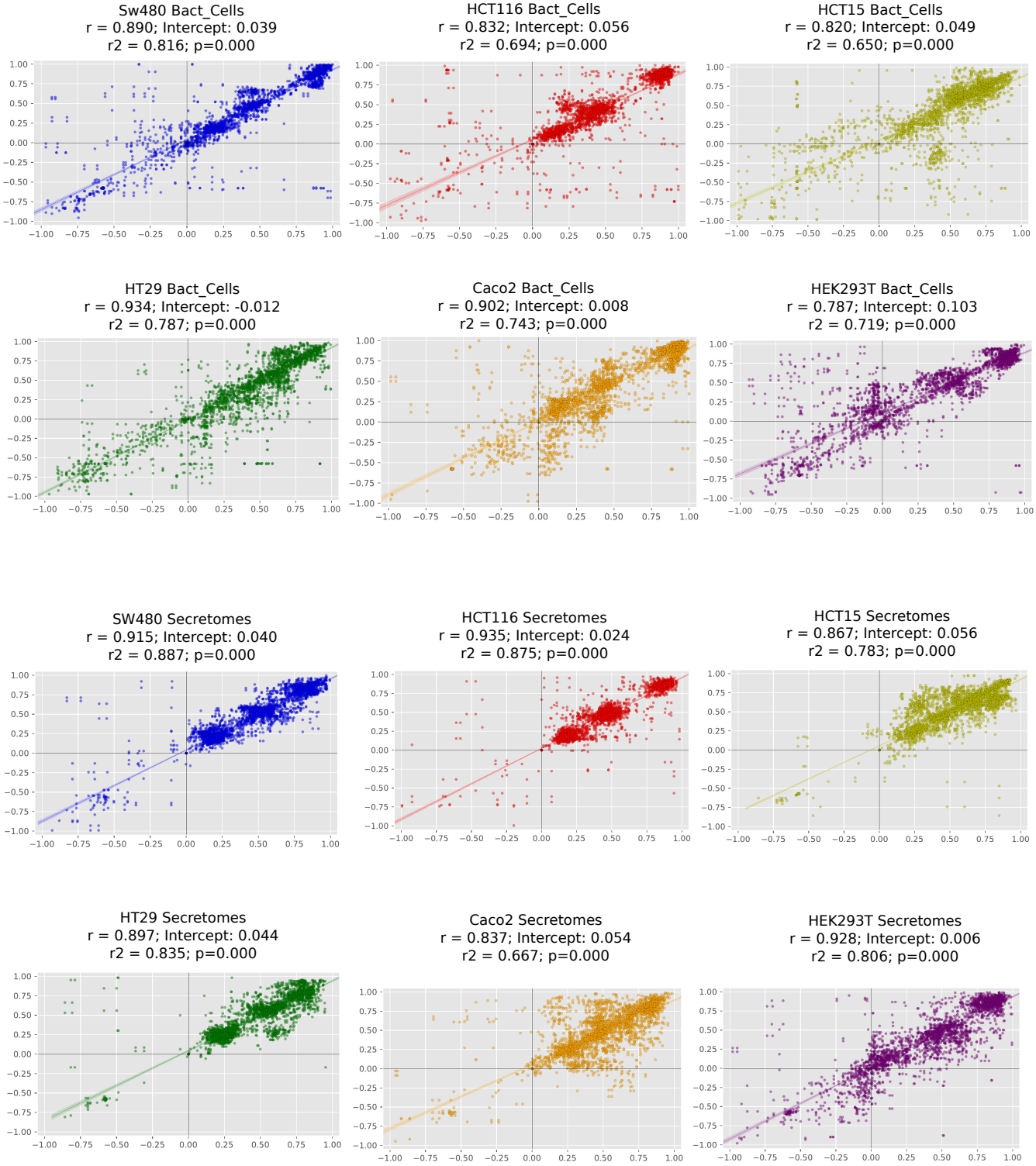
Secretomes are highlighted in grey, green represents significant enhancement ($p<0.05$) in cell growth rate and red represents significant reduction ($p<0.05$) in cell growth rate.

Supplementary Figure S1

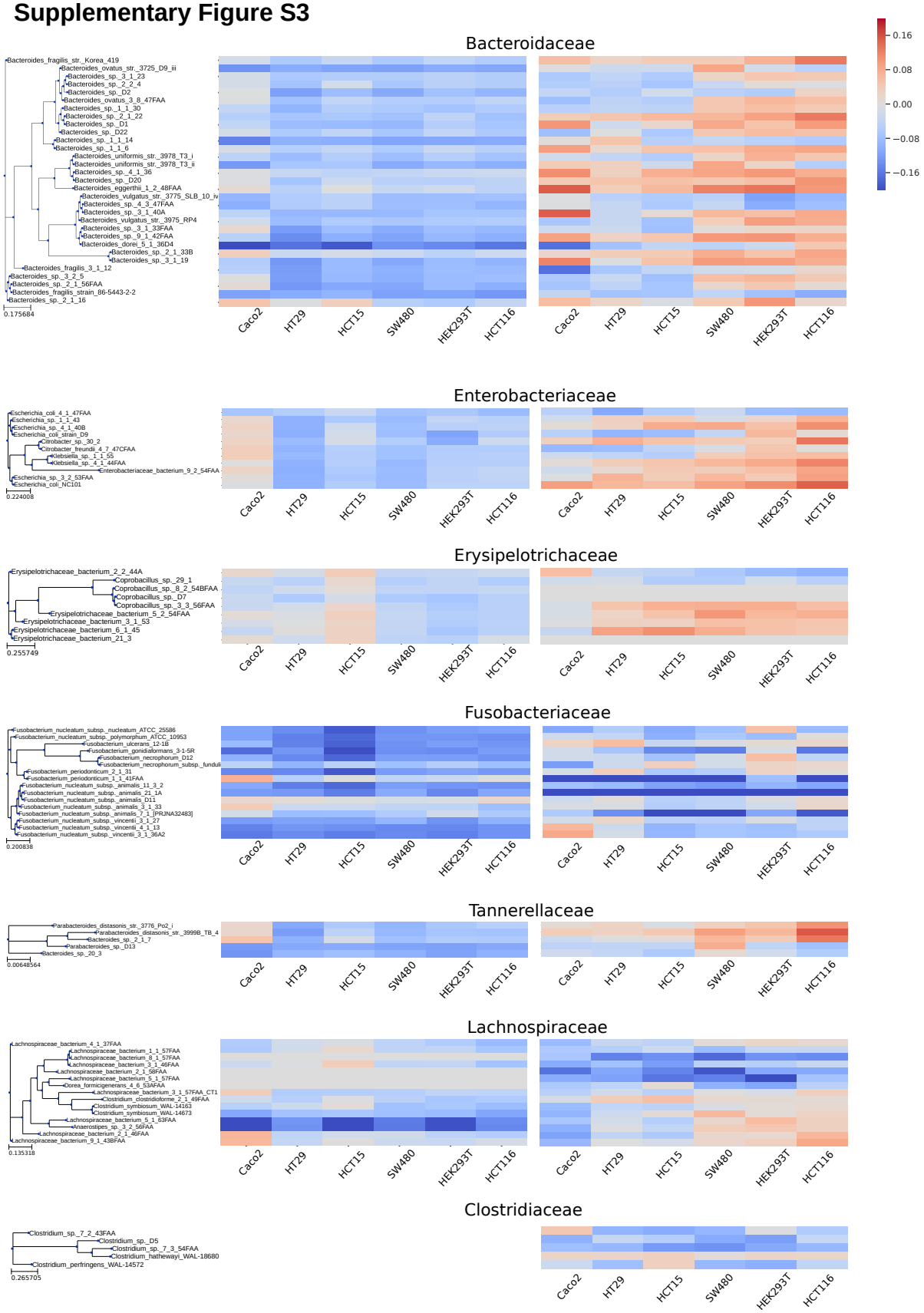


Supplementary Figure S2

Reproducibility of experimental replicates

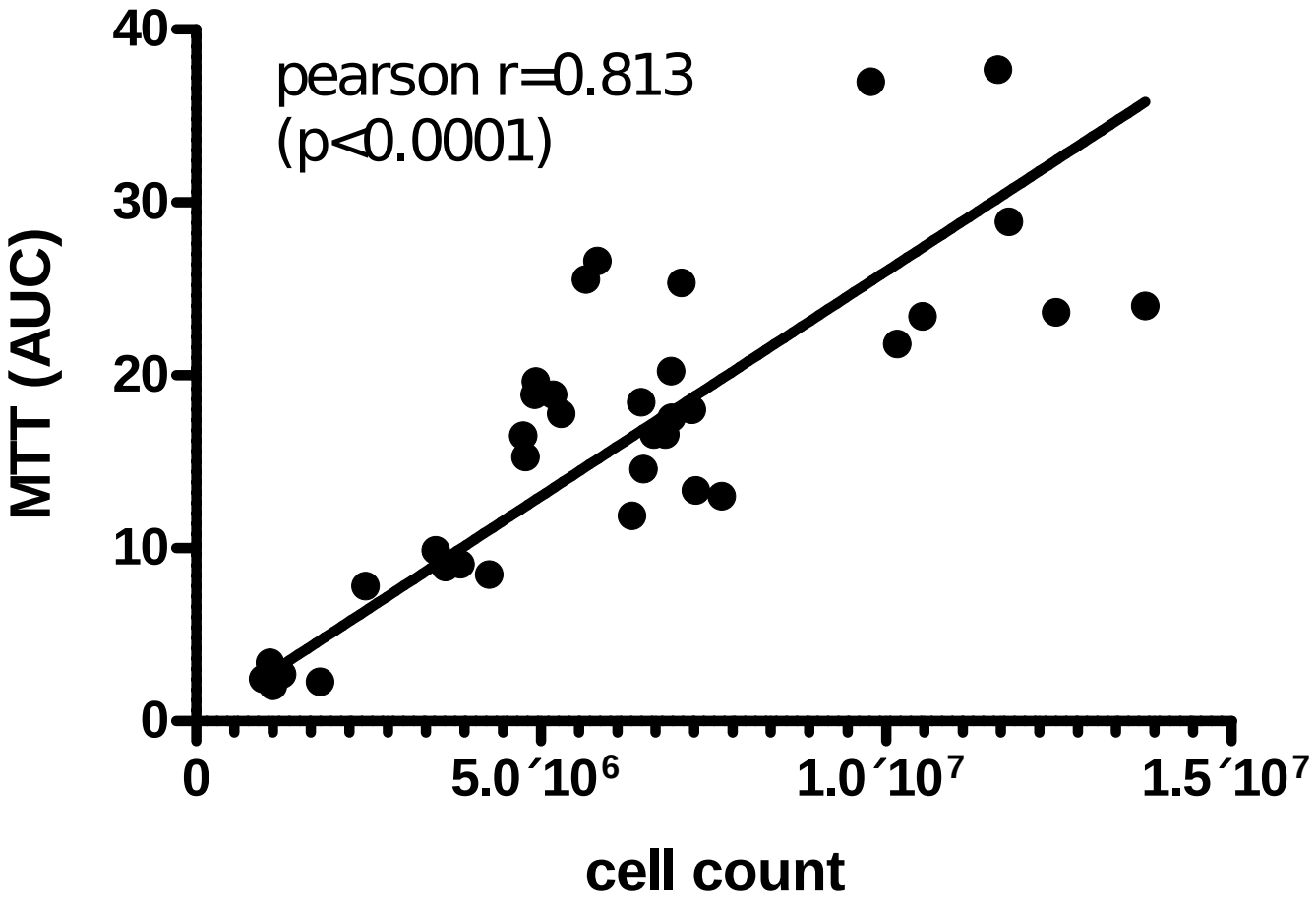


Supplementary Figure S3



Supplementary Figure S4

Supplementary Figure S5



Supplementary Table S1

Bacterial strain	Phylum	Family	Genome ID	Known Toxins	NCBI Taxon ID	Genome Status	GenBank Accessions	RefSeq Accessions	Contigs	Genome Length	GC Content	Isolation Source	Collection	Isolation Country	Host Name	Host Gender	Host Age	Host Health	Body Sample Site	Sporulation	Temperature	Growth condition	Medium
Citrobacter freundii 4_7_47CFAA	Proteobacteria	Enterobacteriaceae	742730.3	Map	742730	WGS	ADLG00000000	-	36	5120174	52.1		University of Guelph, Canada							No	37 ºC	Anaerobic	BHI-S
Citrobacter sp. 30_2	Proteobacteria	Enterobacteriaceae	469595.3	Map	469595	WGS	ACDJ00000000	NZ_ACDJ00000000	18	5125150	51.9	isolated from an intestinal biopsy specimen	University of Guelph, Canada		Human, Homo sapiens	female	23	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis 86-5443-2-2 (ETBF)	Bacteroidetes	Bacteroidaceae	817.96	BFT	817	WGS	LIDS00000000		156	5258210	43.3	Stool sample	JHMI, USA	United States	Pig, Sus scrofa			Diarrheal disease		No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis K570 clinda R (ETBF)	Bacteroidetes	Bacteroidaceae		BFT									JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis VPI clinda R (ETBF)	Bacteroidetes	Bacteroidaceae		BFT									JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum DSM 15643 (ATCC 25586)	Fusobacteria	Fusobacteriaceae	190304.8	FadA	190304	Complete	AE009951	NC_003454	1	2174500	27.2		DSMZ							No	37 ºC	Anaerobic	DRCM
Fusobacterium nucleatum DSM 20482 (ATCC 10953)	Fusobacteria	Fusobacteriaceae	393480.8	FadA	393480	WGS	AARG00000000	NZ_AARG00000000	2	2441632	26.8		DSMZ							No	37 ºC	Anaerobic	DRCM
Fusobacterium nucleatum subsp. animalis 11_3_2	Fusobacteria	Fusobacteriaceae	457403.8	FadA	457403	WGS	ACUO00000000	NZ_ACUO00000000	81	2702139	26.9	healthy biopsy tissue from a 60 year old male	University of Guelph, Canada		Human, Homo sapiens	male	60		Gastrointestinal tract; Colon	No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. animalis 21_1A	Fusobacteria	Fusobacteriaceae	469601.8	FadA	469601	WGS	ADEE00000000	NZ_ADEE00000000	49	2128810	26.8	healthy biopsy tissue from a 49 year old female.	University of Guelph, Canada		Human, Homo sapiens	female	49		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. animalis 3_1_33	Fusobacteria	Fusobacteriaceae	469603.3	FadA	469603	WGS	ACQE00000000	NZ_ACQE00000000	40	2307769	26.9	inflamed biopsy tissue from a 54 year old female with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	54	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. animalis 7_1	Fusobacteria	Fusobacteriaceae	457405.3	FadA	457405	WGS	ACDF00000000	NZ_ACDF00000000	18	2510873	26.8	inflamed biopsy material from a 45 year old male patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	male	45	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. animalis D11	Fusobacteria	Fusobacteriaceae	556264.3	FadA	556264	WGS	ACDS00000000	NZ_ACDS00000000	76	2446817	26.9	healthy biopsy tissue from a 19 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	19	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. vincentii 4_1_13	Fusobacteria	Fusobacteriaceae	469606.3	FadA	469606	WGS	ACDE00000000	NZ_ACDE00000000	12	2268505	26.9	healthy biopsy tissue from a 59 year old female	University of Guelph, Canada		Human, Homo sapiens	female	59		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium periodonticum 1_1_41FAA	Fusobacteria	Fusobacteriaceae	469621.8	FadA	469621	WGS	ADGG00000000		80	2454647	27.9		University of Guelph, Canada							No	37 ºC	Anaerobic	BHI-S
Fusobacterium periodonticum 2_1_31	Fusobacteria	Fusobacteriaceae	469599.3	FadA	469599	WGS	ACDC00000000	NZ_ACDC00000000	35	2532453	28.0	inflamed biopsy tissue from a 25 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	25	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Fusobacterium sp. 3_1_36A2	Fusobacteria	Fusobacteriaceae	469604.7	FadA	469604	WGS	CP003700.1	NC_022196.1	51	2236033	26.9		University of Guelph, Canada							No	37 ºC	Anaerobic	BHI-S
Klebsiella sp. 1_1_55	Proteobacteria	Enterobacteriaceae	469608.3	Map	469608	WGS	ACXA00000000	NZ_ACXA00000000	19	5459739	57.5	healthy biopsy tissue from a 40 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	40	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Klebsiella sp. 4_1_44FAA	Proteobacteria	Enterobacteriaceae	665944.3	Map	665944	WGS	ACWO00000000	-	195	5478883	57.1		University of Guelph, Canada							No	37 ºC	Anaerobic	BHI-S
Escherichia coli DH5 alpha pks	Proteobacteria	Enterobacteriaceae	668369.7	pks	668369	WGS	JRYM01000000		89	4507030	50.7	common laboratory strain	JHMI, USA	South Korea						No	37 ºC	Anaerobic	BHI-S
Escherichia coli NC101	Proteobacteria	Enterobacteriaceae	753642.3	pks, ShEt1	753642	WGS	AEFA00000000	NZ_AEFA00000000	27	5021144	50.6		JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Escherichia coli Nissle 1917	Proteobacteria	Enterobacteriaceae	316435.10	pks, ShEt1	316435	Complete	CP007799	NZ_CP007799.1	1	5441200	50.6	feces	Radboudumc, Netherlands		Human, Homo sapiens	male		dysentery		No	37 ºC	Anaerobic	BHI-S
Escherichia sp. 3_2_53FAA	Proteobacteria	Enterobacteriaceae	469598.5	pks, Stx2A	469598	WGS	ACAC00000000	NZ_ACAC00000000	56	5175730	50.5	inflamed biopsy tissue from a 52 year old male patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	male	52	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Escherichia coli NC101 delta pks	Proteobacteria	Enterobacteriaceae		ShEt1									JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Escherichia sp. 4_1_40B	Proteobacteria	Enterobacteriaceae	457401.3	ShEt1, Stx2A	457401	WGS	ACDM00000000	NZ_ACDM00000000	33	4934999	50.5	inflamed biopsy tissue from a 38 year old female with ulcerative colitis	University of Guelph, Canada		Human, Homo sapiens	female	38	ulcerative colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Clostridium clostridioforme 2_1_49FAA	Firmicutes	Lachnospiraceae	742735.4	TcdA	742735	WGS	ADLL00000000	-	148	5455952	48.9		University of Guelph, Canada							Yes	37 ºC	Anaerobic	RCM
Clostridium hathewayi WAL-18680	Firmicutes	Clostridiaceae	742737.3	TcdA	742737	WGS	ADLN00000000	-	142	5654180	50.0		University of Guelph, Canada							Yes	37 ºC	Anaerobic	RCM
Clostridium perfringens WAL-14572	Firmicutes	Clostridiaceae	742739.3	TcdA	742739	WGS	ADLP00000000	-	35	3462156	28.1		University of Guelph, Canada							Yes	37 ºC	Anaerobic	RCM
Clostridium sp. 7_3_54FAA	Firmicutes	Clostridiaceae	665940.3	TcdA	665940	WGS	ACWK00000000	-	172	5432458	48.1		University of Guelph, Canada							Yes	37 ºC	Anaerobic	RCM
Clostridium symbiosum WAL-14163	Firmicutes	Lachnospiraceae	742740.3	TcdA	742740	WGS	ADLQ00000000	NZ_ADLQ00000000	52	5352498	47.4		University of Guelph, Canada		Human, Homo sapiens				Gastrointestinal tract	Yes	37 ºC	Anaerobic	RCM
Clostridium symbiosum WAL-14673	Firmicutes	Lachnospiraceae	742741.3	TcdA	742741	WGS	ADLR00000000	NZ_ADLR00000000	55	4916964	47.6		University of Guelph, Canada		Human, Homo sapiens				Gastrointestinal tract	Yes	37 ºC	Anaerobic	RCM
Acidaminococcus sp. D21	Firmicutes	Acidaminococcaceae	563191.3		563191	WGS	ACGB00000000	NZ_ACGB00000000	79	2238973	50.2	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	55	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Akkermansia muciniphila	Verrucomicrobia	Akkermansiaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacillus smithii 7_3_47FAA	Firmicutes	Bacillaceae	665952.3		665952	WGS	ACWF00000000	-	175	3224201	40.7	inflamed biopsy tissue from a patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens			Crohn's disease		Yes	50 ºC	Anaerobic	NB
Bacteroides dorei 5_1_36/D4	Bacteroidetes	Bacteroidaceae	556260.3		556260	WGS	ACDI00000000	NZ_ACDI00000000	42	5530727	41.7	inflamed biopsy tissue from a 45 year old male patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	male	45	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides eggerthii 1_2_48FAA	Bacteroidetes	Bacteroidaceae	665953.3		665953	WGS	ACWG00000000	NZ_ACWG00000000	41	4586481	44.5	inflamed biopsy tissue from a 25 year old male patient with irritable bowel syndrome symptoms	University of Guelph, Canada		Human, Homo sapiens	male	25	irritable bowel syndrome	Gastrointestinal tract; Terminal ileum	No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis 3_1_12	Bacteroidetes	Bacteroidaceae	457424.5		457424	WGS	ABZX00000000	NZ_ABZX00000000	33	5530115	43.6	healthy biopsy tissue from a 52 year old female	University of Guelph, Canada		Human, Homo sapiens	female	52		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis 9343 delta cap	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis 9343 delta cap delta pilus 77	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis 9343 delta tsr 15 M4	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides fragilis NCTC 9343 (NTBF)	Bacteroidetes	Bacteroidaceae	272559.47		272559	WGS	OCGB01000000		3523	4438570	50.9		JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides massiliensis 397 T(B)2	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides ovatus 3_8_47FAA	Bacteroidetes	Bacteroidaceae	665954.3		665954	WGS	ACWH00000000	NZ_ACWH00000000	42	6545234	42.0	inflamed biopsy tissue from a 25 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	25	Crohn's disease	Gastrointestinal tract; Sigmoid colon	No	37 ºC	Anaerobic	BHI-S
Bacteroides ovatus 3725 D9 iii	Bacteroidetes	Bacteroidaceae	1339347.3		1339347	WGS	JNHG00000000	-	556	6980703	42.4	tissue	JHMI, USA	United States	Human, Homo sapiens				Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides ovatus S47R17	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 1_1_14	Bacteroidetes	Bacteroidaceae	469585.3		469585	WGS	ACRP00000000	NZ_ACRP00000000	57	6446424	42.9	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	male	40	microscopic colitis	Gastrointestinal tract; Transverse colon	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 1_1_30	Bacteroidetes	Bacteroidaceae	457387.3		457387	WGS	ADCL00000000	NZ_ADCL00000000	171	6441725	42.2	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens				Gastrointestinal tract; Colon	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 1_1_6	Bacteroidetes	Bacteroidaceae	469586.3		469586	WGS	ACIC00000000	NZ_ACIC00000000	71	6855195	43.1	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	male	56		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 2_1_16	Bacteroidetes	Bacteroidaceae	469587.3		469587	WGS	ACPP00000000	NZ_ACPP00000000	18	5236303	43.2	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	58		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 2_1_22	Bacteroidetes	Bacteroidaceae	469588.3		469588	WGS	ACPQ00000000	NZ_ACPQ00000000	36	6003748	41.9	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	54		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 2_1_33B	Bacteroidetes	Bacteroidaceae	469589.3		469589	WGS	ACPR00000000	NZ_ACPR00000000	24	4927045	44.9	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	54	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 2_1_56FAA	Bacteroidetes	Bacteroidaceae	665938.3		665938	WGS	ACWI00000000	NZ_ACWI00000000	96	5632316	43.5	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	29	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 2_2_4	Bacteroidetes	Bacteroidaceae	469590.5		469590	WGS	ABZZ00000000	NZ_ABZZ00000000	64	7101224	42.1	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	43	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 3_1_19	Bacteroidetes	Bacteroidaceae	469592.4		469592	WGS	ADCJ00000000	NZ_ADCJ00000000	36	5250116	44.8	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	59		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 3_1_23	Bacteroidetes	Bacteroidaceae	457390.3		457390	WGS	ACRS00000000		20	6520178	41.5	gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens				gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 3_1_33FAA	Bacteroidetes	Bacteroidaceae	457391.3		457391	WGS	ACPS00000000	NZ_ACPS00000000	35	5419714	42.0	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	54	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 3_1_40A	Bacteroidetes	Bacteroidaceae	469593.3		469593	WGS	ACRT00000000	NZ_ACRT00000000	73	5505782	42.1	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	38	ulcerative colitis	Gastrointestinal tract; Rectal	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 3_2_5	Bacteroidetes	Bacteroidaceae	457392.3		457392	WGS	ACIB00000000	NZ_ACIB00000000	48	5157255	43.2	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	male	27	ulcerative colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 4_1_36	Bacteroidetes	Bacteroidaceae	457393.3		457393	WGS	ACTC00000000	NZ_ACTC00000000	38	4638757	45.8	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	male	45	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 4_3_47FAA	Bacteroidetes	Bacteroidaceae	457394.3		457394	WGS	ACDR00000000	NZ_ACDR00000000	88	5452289	42.7	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	25	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. 9_1_42FAA	Bacteroidetes	Bacteroidaceae	457395.6		457395	WGS	ACAA00000000	NZ_ACAA00000000	50	5622644	42.3	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	47	microscopic colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. D1	Bacteroidetes	Bacteroidaceae	556258.5		556258	WGS	ACAB00000000	NZ_ACAB00000000	58	5986762	41.9	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	54		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. D2	Bacteroidetes	Bacteroidaceae	556259.3		556259	WGS	ACGA00000000	NZ_ACGA00000000	20	6943133	41.7	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	44		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. D20	Bacteroidetes	Bacteroidaceae	585543.3		585543	WGS	ACPT00000000	NZ_ACPT00000000	15	4487454	46.4	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	59	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides sp. D22	Bacteroidetes	Bacteroidaceae	585544.3		585544	WGS	ADCK00000000	NZ_ADCK00000000	94	6344045	41.6	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	55	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Bacteroides stercoris 3972 D14 (B)	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides thetaiotaomicron VPI5482	Bacteroidetes	Bacteroidaceae	226186.12		226186	Complete	AE015928,AY171301	NC_004663,NC_004703	2	6293399	42.9	the feces of a healthy adult	JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bacteroides uniformis 3978 T3i	Bacteroidetes	Bacteroidaceae	1339348.3		1339348	WGS	JNHO00000000	-	47	5047633	46.4	tissue	JHMI, USA	United States	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Bacteroides uniformis 3978 T3ii	Bacteroidetes	Bacteroidaceae	1339349.3		1339349	WGS	JNHN00000000	-	185	4973014	46.3	tissue	JHMI, USA	United States	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Bacteroides vulgatus 3775 SL(B)10iv	Bacteroidetes	Bacteroidaceae	1339350.3		1339350	WGS	JNHI00000000	-	134	5443924	42.3	tissue	JHMI, USA	United States	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Bacteroides vulgatus 3975 RP4	Bacteroidetes	Bacteroidaceae	1339352.3		1339352	WGS	JNHM00000000	-	184	4989697	42.2	tissue	JHMI, USA	United States	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Bacteroidse stercoris 4009 N(B)17	Bacteroidetes	Bacteroidaceae											JHMI, USA							No	37 ºC	Anaerobic	BHI-S
Bifidobacterium sp. 12_1_47BFAA	Actinobacteria	Bifidobacteriaceae	469594.3		469594	WGS	ADCN00000000	NZ_ADCN00000000	61	2405990	60.0	inflamed biopsy tissue from a 25 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	25	Crohn's disease	Gastrointestinal tract; Sigmoid colon	No	37 ºC	Anaerobic	BHI-S
Ralstonia sp. 5_2_56FAA	Proteobacteria	Burkholderiaceae	658080.3		658080	WGS	ACTT00000000	-	121	5218704	63.7		University of Guelph, Canada							No	37 ºC	Aerobic	NB
Ralstonia sp. 5_7_47FAA	Proteobacteria	Burkholderiaceae	658664.3		658664	WGS	ACUF00000000	NZ_ACUF00000000	32	5249816	63.5	inflamed biopsy tissue from a 25 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	25	Crohn's disease	Gastrointestinal tract; Sigmoid colon	No	37 ºC	Aerobic	NB
Clostridioides difficile (Prévot 1938) Lawson et al. 2016	Firmicutes	Peptostreptococcaceae	272563.8										University of Guelph, Canada							Yes	37 ºC	Anaerobic	DRCM
Clostridium septicum (Mace 1889) Ford 1927	Firmicutes	Clostridiaceae											University of Guelph, Canada							Yes	37 ºC	Anaerobic	DRCM
Clostridium sp. 7_2_43FAA	Firmicutes	Clostridiaceae	457396.3		457396	WGS	ACDK00000000	NZ_ACDK00000000	29	3835902	27.8	inflamed biopsy tissue from a 59 year old female patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	female	59	Crohn's disease	Gastrointestinal tract	Yes	37 ºC	Anaerobic	RCM
Clostridium sp. D5	Firmicutes	Clostridiaceae	556261.3		556261	WGS	ADBG00000000	NZ_ADBG00000000	47	5427315	45.0	healthy biopsy tissue from a 44 year old female	University of Guelph, Canada		Human, Homo sapiens	female	44		Gastrointestinal tract	Yes	37 ºC	Anaerobic	RCM

Desulfovibrio sp. 3_1_syn3	Proteobacteria	Desulfovibrionaceae	457398.5	457398 WGS	ADDR00000000	NZ_ADDR00000000	58	3725567	59.1	healthy biopsy tissue from a 60 year old female	University of Guelph, Canada	Human, Homo sapiens	female	60		Gastrointestinal tract	No	37 ºC	Anaerobic	Desulfo medium (ATCC Medium: 2755 Desulfovibrio Medium)
Desulfovibrio sp. 6_1_46AFAA	Proteobacteria	Desulfovibrionaceae	665942.3	665942 WGS	ACWM00000000	-	97	3826115	61.1		University of Guelph, Canada						No	37 ºC	Anaerobic	Desulfo medium (ATCC Medium: 2755 Desulfovibrio Medium)
Enterobacteriaceae bacterium 9_2_54FAA	Proteobacteria	Enterobacteriaceae	469613.3	469613 WGS	ADCU00000000	NZ_ADCU00000000	38	4679347	47.9	inflamed biopsy tissue from a 74 year old male patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	male	74	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Escherichia coli 4_1_47FAA	Proteobacteria	Enterobacteriaceae	1127356.4	1127356 WGS	ACTQ00000000	-	109	5256230	50.6		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Escherichia coli D9	Proteobacteria	Enterobacteriaceae	56,213,757	562 Complete	CP010152,CP010153,CP010154,CP010155,CP010156	NZ_CP010152.1,NZ_CP010153.1,NZ_CP010154.1,NZ_CP010155.1,NZ_CP010156.1					University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Escherichia coli PL1	Proteobacteria	Enterobacteriaceae									JHMI, USA						No	37 ºC	Anaerobic	BHI-S
Escherichia sp. 1_1_43	Proteobacteria	Enterobacteriaceae	457400.3	457400 WGS	ACID00000000	NZ_ACID00000000	43	2235585	51.1	inflamed biopsy tissue from a 59 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	59	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Enterococcus saccharolyticus 30_1	Firmicutes	Enterococcaceae	742813.4	742813 WGS	ADLY00000000	-	61	3119200	40.7		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Coprobacillus sp. 29_1 (D6)	Firmicutes	Erysipelotrichaceae	469596.3	469596 WGS	ADKX00000000	NZ_ADKX00000000	38	3857363	31.1		University of Guelph, Canada	Human, Homo sapiens				Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Coprobacillus sp. 3_3_56FAA	Firmicutes	Erysipelotrichaceae	665941.3	665941 WGS	ACWL00000000	-	106	3952410	31.3		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Coprobacillus sp. 8_2_54BFAA	Firmicutes	Erysipelotrichaceae	469597.4	469597 WGS	ACTG00000000	-	21	3785849	31.8		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Coprobacillus sp. D7	Firmicutes	Erysipelotrichaceae	556270.3	556270 WGS	ACDT00000000	NZ_ACDT00000000	95	3561737	31.4	intestinal biopsy specimen taken from the transverse colon of a patient with active Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	59	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Erysipelotrichaceae bacterium 2_2_44A	Firmicutes	Erysipelotrichaceae	457422.3	457422 WGS	ADCZ00000000		89	4966377	43.34		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI w/ 0.1% Tween 80, pH 8.0
Erysipelotrichaceae bacterium 21_3	Firmicutes	Erysipelotrichaceae	658657.3	658657 WGS	ACTI00000000	-	37	4403767	43.7		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI w/ 0.1% Tween 80, pH 8.0
Erysipelotrichaceae bacterium 3_1_53	Firmicutes	Erysipelotrichaceae	658659.3	658659 WGS			85	4486197			University of Guelph, Canada	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI w/ 0.1% Tween 80, pH 8.0
Erysipelotrichaceae bacterium 5_2_54FAA	Firmicutes	Erysipelotrichaceae	552396.3	552396 WGS			48	3193878			University of Guelph, Canada	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI w/ 0.1% Tween 80, pH 8.0
Erysipelotrichaceae bacterium 6_1_45	Firmicutes	Erysipelotrichaceae	469614.3	469614 WGS	ACTK00000000	-	91	4835437	44.0		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI w/ 0.1% Tween 80, pH 8.0
Eubacterium sp. 3_1_31	Firmicutes	Eubacteriaceae	457402.3	457402 WGS	ACTL00000000	-	45	3065786	37.9	fecal sample	University of Guelph, Canada	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Fusobacterium gonidiaformans 3-1-5R	Fusobacteria	Fusobacteriaceae	469605.7	469605 WGS	ACDD00000000		99	1848430	32.3		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Fusobacterium necrophorum D12	Fusobacteria	Fusobacteriaceae	556263.8	556263 WGS	ACDG00000000		118	1950825	35.2		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Fusobacterium necrophorum subsp. funduliforme 1_1_36S	Fusobacteria	Fusobacteriaceae	742814.3	742814 WGS	ADLZ00000000	-	39	2300242	34.6		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Fusobacterium nucleatum subsp. vincentii 3_1_27	Fusobacteria	Fusobacteriaceae	469602.7	469602 WGS	CP007064.1,CP007065.1,CP007066.1	NZ_CP007064.1,NZ_CP007065.1,NZ_CP007066.1	77	2197574	27.0		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Fusobacterium ulcerans 12-1B	Fusobacteria	Fusobacteriaceae	457404.5	457404 WGS	AGWJ00000000		38	3677742	30.3		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Anaerostipes sp. 3_2_56FAA	Firmicutes	Lachnospiraceae	665937.3	665937 WGS	ACWB00000000	NZ_ACWB00000000	13	3286322	44.0	inflamed biopsy tissue from a 29 year old female with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	29	Crohn's disease	Gastrointestinal tract	Yes	37 ºC	Anaerobic	RCM
Dorea formicigenerans 4_6_53AFAA	Firmicutes	Lachnospiraceae	742765.5	742765 WGS	ADLU00000000	-	143	3825700	40.3		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 1_1_57FAA	Firmicutes	Lachnospiraceae	658081.3	658081 WGS	ACTM00000000	NZ_ACTM00000000	92	2910479	41.9	inflamed biopsy tissue from a 22 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	22	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 2_1_46FAA	Firmicutes	Lachnospiraceae	742723.3	742723 WGS	ADLB00000000	NZ_ADLB00000000	46	2204631	38.8		University of Guelph, Canada	Human, Homo sapiens				Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 2_1_58FAA	Firmicutes	Lachnospiraceae	658082.3	658082 WGS	ACTO00000000		90	3437939	42.4	feces	University of Guelph, Canada	Human, Homo sapiens					No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 3_1_46FAA	Firmicutes	Lachnospiraceae	665950.3	665950 WGS	ACWP00000000	NZ_ACWP00000000	80	3092386	42.0	healthy biopsy tissue from a 46 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	46	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 3_1_57FAA_CT1	Firmicutes	Lachnospiraceae	658086.3	658086 WGS	ACTP00000000	NZ_ACTP00000000	145	7693209	46.8	inflamed biopsy tissue from a 22 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	22	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 5_1_57FAA	Firmicutes	Lachnospiraceae	658085.3	658085 WGS	ACTR00000000	NZ_ACTR00000000	64	3336973	46.3	inflamed biopsy tissue from a 22 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	22	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 5_1_63FAA	Firmicutes	Lachnospiraceae	658089.3	658089 WGS	ACTS00000000	NZ_ACTS00000000	48	3041190	37.1	healthy biopsy tissue from a 51 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	51	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 6_1_37FAA	Firmicutes	Lachnospiraceae	552395.3	552395 WGS	ADCR00000000	NZ_ADCR00000000	15	3067358	40.9	human fecal sample	University of Guelph, Canada	Human, Homo sapiens	female	71	colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 8_1_57FAA	Firmicutes	Lachnospiraceae	665951.3	665951 WGS	ACWQ00000000	NZ_ACWQ00000000	51	2927350	41.6	inflamed biopsy tissue from a 22 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	22	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lachnospiraceae bacterium 9_1_43BFAA	Firmicutes	Lachnospiraceae	658088.3	658088 WGS	ACTX00000000	NZ_ACTX00000000	26	2840852	41.4	inflamed biopsy tissue from a 59 year old female patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	female	59	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Lactobacillus casei Shirota	Firmicutes	Lactobacillaceae									Radboudumc, Netherlands						No	37 ºC	Anaerobic	BHI-S
Pediococcus acidilactici 7_4	Firmicutes	Lactobacillaceae	563194.3	563194 WGS	ACXB00000000	NZ_ACXB00000000	9	2017988	42.0	the human gastrointestinal tract	University of Guelph, Canada	Human, Homo sapiens	male	45	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Peptostreptococcus stomatis DSM17678	Firmicutes	Peptostreptococcaceae	596315.3	596315 WGS	ADGQ00000000	NZ_ADGQ00000000	74	1988044	36.7	the human oral cavity	DSMZ	Human, Homo sapiens				Oral	No	37 ºC	Anaerobic	BHI-S
Propionibacterium sp. 5_U_42AFAA	Actinobacteria	Propionibacteriaceae	450748.3	450748 WGS	ACUE00000000	-	14	2530254	60.1		University of Guelph, Canada						No	37 ºC	Anaerobic	BHI-S
Pseudomonas sp. 2_1_26	Proteobacteria	Pseudomonadaceae	665948.3	665948 WGS	ACWU00000000	-	293	6282392	66.4	gastrointestinal tract	University of Guelph, Canada	Human, Homo sapiens					No	37 ºC	Aerobic	NB
Ruminococcaceae bacterium D16	Firmicutes	Ruminococcaceae	552398.3	552398 WGS	ADDX00000000	NZ_ADDX00000000	104	3210947	56.8	healthy biopsy tissue from a 57 year old male	University of Guelph, Canada	Human, Homo sapiens	male	57		Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Streptococcus agalactiae ATCC 13813	Firmicutes	Streptococcaceae	888745.3	888745 WGS	AEQQ00000000	-	134	2114958	35.3	oral cavity	ATCC	Human, Homo sapiens				Oral	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1067	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Bacteremia, HCV cirrhosis	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1212	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, Colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1293	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, no underlying disease	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1294	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, HCV fibrosis, Advanced colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1361	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, Advanced colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1364	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1365	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, Advanced colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1417	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1445	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, colon cancer, alcoholic liver disease	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 1459	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, Advanced colon adenoma, HCV hepatitis	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 207	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis 992	Firmicutes	Streptococcaceae	this study							Blood	Radboudumc, Netherlands	Italy, Napoli	Human, Homo sapiens		Endocarditis, Advanced colon adenoma	Blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis NCTC8133	Firmicutes	Streptococcaceae								faeces; infant faeces	Radboudumc, Netherlands		Human, Homo sapiens			faeces; infant faeces	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis NTB22	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens			blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus bovis NTB7	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens		endocarditis	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus 9L-1503 1121 L	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Weert	Human, Homo sapiens			blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus NTB1	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens		spondylodiscitis	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus NTB11	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Amsterdam	Human, Homo sapiens		endocarditis, Colon cancer	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus NTB12	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens			blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus NTB4	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens			blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus subsp. macedonicus NTB3	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens		endocarditis	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus UCN34	Firmicutes	Streptococcaceae	637909.5	637909 Complete	FN597254	NC_013798	1	2350911	37.6	responsible for endocarditis in a patient also suffering from colon cancer, blood	Radboudumc, Netherlands	France, Institut Pasteur	Human, Homo sapiens		endocarditis	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus gallolyticus UCN50	Firmicutes	Streptococcaceae									Radboudumc, Netherlands	France, Institut Pasteur					No	37 ºC	Anaerobic	BHI-S
Streptococcus macedonicus 19AS	Firmicutes	Streptococcaceae	59310.16	59310 WGS	PEBN01000000		98	2249955	37.3	Asiago cheese	Radboudumc, Netherlands	Italy, Thiene					No	37 ºC	Anaerobic	BHI-S
Streptococcus macedonicus 33MO	Firmicutes	Streptococcaceae	59310.8	59310 WGS	JNCV00000000	-	76	2223217	37.4	curd of Morlacco cheese	Radboudumc, Netherlands	Italy, Thiene					No	37 ºC	Anaerobic	BHI-S
Streptococcus macedonicus 8SP	Firmicutes	Streptococcaceae	this study							Spressa cheese	Radboudumc, Netherlands	Italy, Thiene					No	37 ºC	Anaerobic	BHI-S
Streptococcus macedonicus ACA-DC 205	Firmicutes	Streptococcaceae	this study							Greek Kasseri cheese	Radboudumc, Netherlands	Greece, Athens					No	37 ºC	Anaerobic	BHI-S
Streptococcus macedonicus CIP105685T	Firmicutes	Streptococcaceae	this study								Radboudumc, Netherlands	France, Institut Pasteur					No	37 ºC	Anaerobic	BHI-S
Streptococcus salivarius NTB2	Firmicutes	Streptococcaceae	this study							blood	Radboudumc, Netherlands	Netherlands, Nijmegen	Human, Homo sapiens		COPD/AAA/pneumoniae	blood	No	37 ºC	Anaerobic	BHI-S
Streptococcus sp. 2_1_36FAA	Firmicutes	Streptococcaceae	469609.3	469609 WGS	ACOI00000000	NZ_ACOI00000000	10	2229964	40.5	inflamed biopsy tissue from a 45 year old male patient with Crohn's disease	University of Guelph, Canada	Human, Homo sapiens	male	45	Crohn's disease	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S

Synergistes sp. 3_1_syn1	Synergistetes	Synergistaceae	457415.3	457415	WGS	ACUH00000000	-	65	3281561	56.1	University of Guelph, Canada							No	37 ºC	Anaerobic	Synergistes medium
Parabacteroide distasonis 3999B T(B)4	Bacteroidetes	Tannerellaceae	1339344.3	1339344	WGS	JNHP00000000	-	180	5315679	44.9	tissue	JHMI, USA	United States	Human, Homo sapiens				Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Parabacteroides distasonis 3776 Po2 i	Bacteroidetes	Tannerellaceae	1339341.3	1339341	WGS	JNHL00000000	-	172	5288232	44.9	tissue	JHMI, USA	United States	Human, Homo sapiens				Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Parabacteroides sp. 2_1_7	Bacteroidetes	Tannerellaceae	457388.5	457388	WGS	ABZY00000000	NZ_ABZY00000000	38	5180144	45.1	inflamed biopsy tissue from a 37 year old female patient with ulcerative colitis	University of Guelph, Canada		Human, Homo sapiens	female	37	ulcerative colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Parabacteroides sp. 20_3	Bacteroidetes	Tannerellaceae	469591.4	469591	WGS	ACRQ00000000	NZ_ACRQ00000000	61	5749901	45.0	the human gastrointestinal tract	University of Guelph, Canada		Human, Homo sapiens	female	49		Gastrointestinal tract; Colon	No	37 ºC	Anaerobic	BHI-S
Parabacteroides sp. D13	Bacteroidetes	Tannerellaceae	563193.3	563193	WGS	ACPW00000000	NZ_ACPW00000000	22	5370710	45.2	inflamed biopsy tissue from a 27 year old male patient with ulcerative colitis	University of Guelph, Canada		Human, Homo sapiens	male	27	ulcerative colitis	Gastrointestinal tract	No	37 ºC	Anaerobic	BHI-S
Veillonella sp. 3_1_44	Firmicutes	Veillonellaceae	457416.3	457416	WGS	ADCV00000000	NZ_ADCV00000000	16	2163458	38.6	healthy biopsy tissue from a 25 year old male patient with Crohn's disease	University of Guelph, Canada		Human, Homo sapiens	male	25	Crohn's disease	Gastrointestinal tract; Descending colon	No	37 ºC	Anaerobic	RCM+ (ATCC 1252)

Supplementary Table S2: smMIP mutation analysis

			Mutations confirmed from Ahmed et al.(2013)						From Ahmed et al. (2013)[b]		additional variants detected with smMIP panel													
Cel Lines	**gender**	MSI/MSS[a]	KRAS	%	BRAF	%	PIK3CA	%	PTEN	TP53	*CTNNB1*	%	CXCR4	%	EGFR	%	HRAS	%	MYD88	%	PDGFRA	%	SF3B1	%
HCT116	*F*	*MSI*	c.38G>A (p.Gly13Asp)	51	--	--	c.3140A>G (p.His1047Arg)	51	--	--	c.133_135delTCT (p.Ser45del)	54	c.1002C>A p.=	58%	c.2361G>A p.=	100	--	--	c.510G>A (p.Met170Ile)	50	c.1701A>G p.=	100	c.2631T>C p.=	52
CACO-2	*F*	*MSS*	--	--	--	--	--	--	--	c.610G>T (p.Glu204*)	--	--	--	--	c.2361G>A p.=	49	c.81T>C p.=	100	--	--	c.1701A>G p.=	100	c.2631T>C p.=	21
HCT15	*M*	*MSI*	c.38G>A (p.Gly13Asp)	51	--	--	c.1633G>A (p.Glu545Lys) & c.1645G>A (p.Asp549Asn)	52	--	c.722C>T (p.Ser241Phe)	--	--	--	--	c.2361G>A p.=	51	c.81T>C p.=	46	c.790C>T (p.Arg264Ter)	49	c.1701A>G p.=	100	c.2631T>C p.=	52
HT29	*F*	*MSS*	--	--	c.1799T>A (p.Val600Glu)	24	--	--	--	c.818G>A (p.Arg273His)	--	--	--	--	c.2361G>A p.=	68	c.81T>C p.=	81	--	--	c.1701A>G p.=	100	c.2631T>C p.=	100
SW480	*F*	*MSS*	c.35G>T (p.Gly12Val)	100	--	--	--	--	--	c.818G>A (p.Arg273His) & c.925C>T (p.Pro309Ser)	--	--	--	--	c.2361G>A p.=	100	c.81T>C p.=	100	--	--	c.1701A>G p.= c.2472C>T p.=	100	c.2631T>C p.=	34
HEK293T	*F*	*MSS*	--	--	--	--	--	--	ND	ND	--	--	--	--	c.2361G>A p.=	100	--	--	--	--	c.1701A>G p.=	100	c.2631T>C p.=	100

green cells represent pathogenic mutations, ND = not done, [a]MSI (based on BAT25, NR21, NR22, NR24, NR27), [b]not tested with smMIP panel
no variants detected in *CHEK2, ERBB2, EZH2, GNA11, GNAQ, GNAS, H3F3A, H3F3B, IDH1, IDH2, JAK2, MPL, and NRAS*

Supplementary Table S3: Growth rate change of cell lines by bacterial cells

Bacterial cells		growth rates							growth rates (z-scores)												
Bacteria	Family	Caco2	HT29	HCT15	SW480	HEK293T	HCT116	Average	Caco2-z	HT29-z	HCT15-z	SW480-z	HEK293T-z	HCT116-z	Average	Caco2-p	HT29-p	HCT15-p	SW480-p	HEK293T-p	HCT116-p
Acidaminococcus sp. D21	Acidaminococcaceae	0.00090994	-0.0606662	-0.0145831	-0.06540314	-0.06935158	-0.07794683	-0.04784119	9.92019957	2.28967998	28.88679472	0.2814403	0.13366262	-0.07725262	0.4057541	0.1779022	0.3856465	0.1867682	0.3888123	0.4466515	0.4691048
Akkermansia muciniphila	Akkermansiaceae	-0.00018865	-0.04916758	0.02541875	-0.0486173	-0.08405504	-0.05172841	-0.03472304	0.90238776	0.5721116	1.8216296	0.75897711	-0.26179321	0.66510685	0.70973662	0.1825961	0.2829519	0.051842	0.223147	0.3963907	0.2522544
Bacteroides dorei 5_1_36/D4	Bacteroidaceae	-0.05304268	-0.06879688	-0.06417141	-0.075207	-0.04094717	-0.07562955	-0.06296578	0.04544173	0.08997242	-0.02388812	0.00253233	0.89761139	-0.01164004	0.16667162	0.4818148	0.4640307	0.4904379	0.4989862	0.1838679	0.4953403
Bacteroides eggerthii 1_2_48FAA	Bacteroidaceae	-0.00324026	0.03402886	-0.04159951	-0.03785342	-0.0292293	-0.02544378	-0.02857647	0.85291051	0.94395205	0.39069384	1.06519655	1.21105507	1.40934096	0.97885816	0.1960357	0.1717623	0.3475114	0.1425599	0.1121348	0.0786478
Bacteroides fragilis 3_1_12	Bacteroidaceae	-0.00153136	0.11856753	-0.08230502	-0.10633468	-0.07536663	-0.09098983	-0.07918256	0.88061777	-1.13250526	-0.35695116	-0.88302119	-0.02811476	-0.4465577	-0.32775538	0.1884371	0.1278882	0.3601012	0.1877867	0.4887464	0.3270385
Bacteroides fragilis 86-5443-2-2 (ETBF)	Bacteroidaceae	-0.1326289	0.10465352	-0.11250656	-0.11724431	-0.10420269	-0.11016812	-0.11356735	-1.24492504	-0.79074629	-0.91166803	-1.19337873	-0.80367255	-0.98957991	-0.98899509	0.1057886	0.213747	0.1801409	0.1155529	0.2099893	0.1603525
Bacteroides fragilis 9343 delta cap	Bacteroidaceae	-0.13205927	0.10374633	-0.11770571	-0.12352809	-0.10207235	-0.11745102	-0.11609379	-1.23568929	-0.76846372	-1.00716163	-1.37214468	-0.74637639	-1.19579087	-1.05427109	0.1074928	0.2203157	0.1560913	0.0842715	0.2269396	0.1150821
Bacteroides fragilis 9343 delta cap delta plus 77	Bacteroidaceae	-0.12172445	0.09957326	-0.10392585	-0.12390628	-0.10495457	-0.11334611	-0.11123842	-1.06812632	-0.66596388	-0.75406478	-1.38290374	-0.82389472	-1.07956287	-0.96241938	0.1418985	0.2519799	0.2246212	0.0826146	0.2041892	0.1393366
Bacteroides fragilis 9343 delta tsr 15 M4	Bacteroidaceae	-0.11757425	0.07458701	-0.07036389	-0.10985508	-0.08870557	-0.09992793	-0.09350228	-1.00083726	-0.0522461	-0.13762543	-0.98316322	-0.38687109	-0.6996348	-0.54339648	0.1576155	0.4790942	0.4450793	0.1619265	0.3489296	0.2413209
Bacteroides fragilis K570 clinda R (ETBF)	Bacteroidaceae	0.05144474	0.00276486	0.0336613	-0.05045007	-0.0609138	-0.03471292	-0.0106226	1.73954289	1.71186523	1.77302188	0.70683704	0.36060035	1.14689064	1.23979301	**0.0404426**	**0.0429166**	**0.0376061**	0.2390732	0.358732	0.1248937
Bacteroides fragilis NCTC 9343 (NTBF)	Bacteroidaceae	-0.10992486	-0.08378818	-0.08173438	-0.11468426	-0.08599044	-0.10204659	-0.09636145	-0.87681427	-0.2782471	-0.34647015	-1.12054816	-0.31384658	-0.75962344	-0.61592495	0.1894693	0.3900412	0.3640436	0.1304149	0.3764057	0.2229535
Bacteroides fragilis VPI clinda R (ETBF)	Bacteroidaceae	-0.08616292	-0.08603347	-0.08080445	-0.11360787	-0.08319177	-0.10540114	-0.0925336	-0.49155139	-0.33339647	-0.32939	-1.08992622	-0.23857516	-0.85460546	-0.55624078	0.3109161	0.3689815	0.3704991	0.1370424	0.4053969	0.1955656
Bacteroides massiliensis 3972 (T)b2	Bacteroidaceae	-0.12937384	-0.1035649	-0.09365437	-0.12061894	-0.10482925	-0.1059308	-0.10966202	-1.1921493	-0.7640072	-0.56540669	-1.28938267	-0.82052436	-0.86960262	-0.91684547	0.1157934	0.2216432	0.2852326	0.0978583	0.2051492	0.191436
Bacteroides ovatus 3_8_47FAA	Bacteroidaceae	-0.05682669	0.12782086	-0.0850314	-0.10969958	-0.08296899	-0.09529336	-0.09283515	-0.01591006	-1.35978751	-0.40702707	-0.96081748	-0.2325834	-0.56840964	-0.59075586	0.4936311	0.086205	0.3414761	0.1674859	0.4077295	0.28421
Bacteroides ovatus 3725 D9 iii	Bacteroidaceae	-0.11667911	-0.10587823	-0.09268217	-0.11631338	-0.11284932	-0.12694085	-0.11189051	-0.98632393	-0.82082777	-0.54755017	-1.16689489	-1.03622754	-1.46449	-1.00371905	0.1611499	0.2050627	0.291349	0.1208115	0.1492119	0.0708396
Bacteroides ovatus S47R17	Bacteroidaceae	-0.09373093	0.09605791	-0.07518261	-0.10854594	-0.09279915	-0.10297351	-0.09488167	-0.61425498	-0.57961891	-0.22613269	-0.94592032	-0.49696959	-0.78586847	-0.60812749	0.2688205	0.2804086	0.4102443	0.1712597	0.3089981	0.2151751
Bacteroides sp. 1_1_14	Bacteroidaceae	-0.01935281	-0.08424177	-0.05903567	-0.06871958	-0.05966006	-0.05676023	-0.05796179	0.59167061	-0.28938839	0.07044052	0.18709161	0.39430397	0.52263382	0.24612542	0.2763492	0.3857584	0.4718242	0.4255402	0.346174	0.2999844
Bacteroides sp. 1_1_30	Bacteroidaceae	0.03398848	-0.02797338	0.01300421	0.02586789	-0.04433063	0.02272825	0.01665261	1.456533	1.09268822	0.91593662	1.40617804	0.80661165	1.48620141	1.13401882	0.0719279	0.1364353	0.179026	0.0791149	0.2091404	0.0679344
Bacteroides sp. 1_1_6	Bacteroidaceae	-0.04400989	-0.08808598	-0.08744076	-0.08707638	-0.06956044	-0.07125981	-0.07457221	0.1918944	-0.3838108	-0.4512802	-0.33513668	0.12804535	0.11208654	-0.12303356	0.423652	0.3500664	0.3253304	0.368323	0.4488809	0.4552234
Bacteroides sp. 2_1_16	Bacteroidaceae	-0.01434816	-0.06243522	-0.03227909	-0.06290126	-0.03952695	-0.05715748	-0.04477469	0.6728133	0.24622897	0.56188358	0.35261563	0.93580883	0.51138595	-0.54678938	0.2497917	0.4024222	0.2864345	0.3617302	0.1738519	0.3039202
Bacteroides sp. 2_1_22	Bacteroidaceae	-0.2091635	-0.16423885	-0.11888751	-0.13301194	-0.14065502	-0.16064075	-0.1661081	-2.48541456	-2.22554698	-2.31145695	-1.64194883	-1.78407346	-2.41869437	-2.15010635	**0.006308**	**0.0118066**	**0.0101005**	**0.0497133**	**0.0367063**	**0.0076107**
Bacteroides sp. 2_1_33B	Bacteroidaceae	-0.03717427	0.09250853	-0.05383652	-0.06121385	-0.07311099	0.05781956	-0.06261064	0.30272345	-0.49243834	0.16593451	0.4006176	0.03255176	0.4926395	0.15033808	0.3806505	0.3106018	0.4338779	0.3438397	0.486971	0.3105305
Bacteroides sp. 2_1_56FAA	Bacteroidaceae	-0.01459229	-0.06311561	-0.05599227	-0.05591929	-0.04575085	-0.05523744	-0.04843462	0.66885512	0.22951704	0.12633961	0.55124446	0.76841417	0.56575066	0.48502018	0.251055	0.4089244	0.4495582	0.2900786	0.2203305	0.2851154
Bacteroides sp. 2_2_4	Bacteroidaceae	-0.00177549	-0.11945204	-0.08725055	-0.09850934	-0.08380442	-0.08052895	-0.07855346	0.87665959	-1.15423077	-0.44778653	-0.66039138	-0.25505248	-0.15036378	-0.29852756	0.1895114	0.1233848	0.3265937	0.2537676	0.3989999	0.4400332
Bacteroides sp. 3_1_19	Bacteroidaceae	-0.0031182	-0.07573687	-0.03633696	-0.05446471	-0.05464812	0.03954612	-0.04397516	0.8548896	-0.08048927	0.48735199	0.59262547	0.52911845	1.01004155	0.56558963	0.1954869	0.4678131	0.3124062	0.2760288	0.2977259	0.1554005
Bacteroides sp. 3_1_23	Bacteroidaceae	0.01055305	0.12676625	-0.10823734	-0.11046598	-0.08576766	-0.1004576	-0.08685696	1.07654769	-1.33388402	0.83325459	-1.00054325	-0.30785482	-0.71463196	-0.51893682	0.1400089	0.0903655	0.2015373	0.1576866	0.3786905	0.2366534
Bacteroides sp. 3_1_33FAA	Bacteroidaceae	-0.01471435	-0.05981571	-0.04007781	-0.06813775	-0.03718776	-0.06199087	-0.04698734	0.66687603	0.3105699	0.41864318	0.20364401	0.99872225	0.37453686	0.49549871	0.2516879	0.3776546	0.3372083	0.41904	0.1581274	0.3535198
Bacteroides sp. 3_1_40A	Bacteroidaceae	-0.01215099	-0.05195718	-0.03716121	-0.06063212	-0.03083854	-0.04868284	-0.04023715	0.70843693	0.50359269	0.47221276	0.41717	1.16948727	0.75134052	0.67037336	0.2385754	0.3066606	0.3178036	0.3377484	0.1202895	0.2254412
Bacteroides sp. 3_2_5	Bacteroidaceae	-0.01324957	-0.07495442	-0.01604761	-0.0662177	-0.04992797	-0.05543607	-0.04597222	0.69062511	-0.06127055	0.86000993	0.25826694	0.65606876	0.56012672	0.49397115	0.2441488	0.4754873	0.1940712	0.3977551	0.2551589	0.2870348
Bacteroides sp. 4_1_36	Bacteroidaceae	0.01201783	-0.04852121	-0.0009574	-0.03267876	-0.02085522	-0.04219444	-0.02223153	1.10029677	0.58798794	1.13717427	1.20671959	1.43799279	0.93505575	1.06753785	0.1347726	0.2775866	0.1269108	0.1129664	0.0745134	0.1740459
Bacteroides sp. 4_3_47FAA	Bacteroidaceae	-0.04523054	0.08390157	-0.0534561	-0.08044348	-0.05214185	-0.07298122	-0.06469248	0.1721035	-0.28103243	0.17292185	-0.14643929	0.5965257	0.06334577	0.09623752	0.4314436	0.3889692	0.4311209	0.441587	0.274722	0.4746582
Bacteroides sp. 9_1_42FAA	Bacteroidaceae	-0.03668601	0.08135011	-0.08471438	-0.0879491	-0.0538127	-0.06894253	-0.06890914	0.31063981	-0.21836269	-0.40120429	-0.35996528	0.55158754	0.17769912	0.0100657	0.377628	0.4132784	0.3436231	0.3589701	0.2899607	0.4292378
Bacteroides sp. D1	Bacteroidaceae	-0.04889248	-0.13765252	-0.10069224	-0.11320059	-0.08556633	-0.09992793	-0.09815535	0.11273079	-1.6012749	-0.69467242	-1.07833954	-0.38312624	-0.6996348	-0.72405285	0.4549671	0.0540464	0.2428763	0.1396091	0.3503209	0.2413209
Bacteroides sp. D2	Bacteroidaceae	-0.05084552	-0.12179939	-0.08484119	-0.09769478	-0.08175763	-0.08516352	-0.087017	0.08106535	-1.21188693	-0.4035334	-0.63721802	-0.20000323	-0.28158893	-0.44219419	0.4675833	0.1119758	0.3427637	0.2612727	0.420468	0.3887552
Bacteroides sp. D20	Bacteroidaceae	-0.00458298	-0.07036178	-0.02631909	-0.04841366	-0.05084694	-0.04338619	-0.04065177	0.83114051	0.05153498	0.67135185	0.76477045	0.63135277	0.90131213	0.64191045	0.2021345	0.4793784	0.2502577	0.2214155	0.2631901	0.1828821
Bacteroides sp. D22	Bacteroidaceae	0.01580184	-0.12288802	-0.08021268	-0.10409482	-0.08021209	-0.08787805	-0.07658066	1.16164857	-1.23862602	-0.31852081	-0.81929444	-0.15843543	-0.35844938	-0.28661292	0.1218729	0.1069488	0.3746264	0.2055002	0.4368405	0.3595388
Bacteroides stercoris 3972 D14 (B)	Bacteroidaceae	-0.11969004	-0.08812	-0.08985012	-0.11872798	-0.10278247	-0.11118331	-0.10505899	-1.03514149	-0.38464639	-0.49553333	-1.23558736	-0.76547511	-1.01832446	-0.82245136	0.1494653	0.3497559	0.309506	0.1075117	0.2212054	0.153425
Bacteroides stercoris 4009 N(B)17	Bacteroidaceae	-0.12180583	-0.08022746	-0.07966317	-0.10997142	-0.09229789	-0.11471441	-0.09978003	-1.06944571	-0.190788	-0.30842799	-0.98647371	-0.48348814	-1.11830554	-0.69282152	0.1416013	0.4240868	0.3784717	0.1611132	0.31378	0.1308926
Bacteroides thetaiotaomicron VPI5482	Bacteroidaceae	-0.12237546	-0.0699989	-0.06651737	-0.10784774	-0.08849672	-0.10663702	-0.09364553	-1.07868147	0.06044801	-0.0669767	-0.92605744	-0.38125382	-0.88959883	-0.54702004	0.1395329	0.475816	0.4732077	0.1763753	0.3510173	0.1860136
Bacteroides uniformis 3978 T3i	Bacteroidaceae	-0.10097344	-0.05788793	-0.04665071	-0.0800362	-0.07876403	-0.09189468	-0.0760345	-0.731681	0.35792037	0.29791754	-0.13485261	-0.11948902	-0.47217785	-0.1337271	0.2314082	0.3597373	0.382489	0.4461794	0.4522799	0.3178161
Bacteroides uniformis 3978 T3ii	Bacteroidaceae	-0.08941798	0.05689002	-0.04550943	-0.08242171	-0.08118676	-0.07503367	-0.07174326	-0.54432713	0.3824312	0.31887954	-0.20271746	-0.18464936	0.00523177	-0.03752524	0.2924595	0.3505794	0.3744899	0.4194033	0.426501	0.4979056
Bacteroides vulgatus 3775 SL(B)10iv	Bacteroidaceae	-0.12514226	-0.0693616	-0.06626375	-0.1052295	-0.08640816	-0.10089898	-0.09221738	-1.12354085	0.07610152	-0.06231847	-0.85157163	-0.32508112	-0.72712959	-0.50225669	0.1297792	0.4695642	0.4750686	0.1964075	0.3721335	0.2328021
Bacteroides vulgatus 3975 RP4	Bacteroidaceae	-0.14866007	-0.0983032	-0.09995252	-0.11235693	-0.10934054	-0.10606322	-0.11244608	-1.50484555	-0.63476828	-0.68108593	-1.05433855	-0.9418574	-0.87335191	-0.9483746	0.0655138	0.2620727	0.2471623	0.1450293	0.1722983	0.190412
Bifidobacterium sp. 12_1_47BFAA	Bifidobacteriaceae	0.01616803	0.01137182	0.02358003	-0.0375916	-0.03618525	-0.02928386	-0.01244741	1.16758584	1.50045931	1.58785747	1.07264513	1.02568515	1.30061154	1.27580741	0.1206722	0.0660772	0.0555396	0.1408824	0.1516834	0.095926
Ralstonia sp. 5_2_56FAA	Burkholderiaceae	-0.08746494	-0.10672872	-0.05928828	-0.11058234	-0.09608515	-0.10740945	-0.09459331	-0.51266169	-0.84171768	0.06578269	-1.00385373	-0.58534798	-0.91146965	-0.63154468	0.3034727	0.1991573	0.4736846	0.1568873	0.2784753	0.1801932
Ralstonia sp. 5_7_47FAA	Burkholderiaceae	-0.07769976	-0.07570285	-0.0354493	-0.08681453	-0.08664488	-0.09549199	-0.07630055	-0.35433448	-0.07965367	0.50365577	-0.3276881	-0.33144736	-0.57403357	-0.1939169	0.361084	0.4681466	0.3066384	0.3711444	0.3697195	0.2822997
Desulfovibrio sp. 3_1_syn3	Desulfovibrionaceae	-0.1032113	-0.00089379	-0.08446076	-0.12690272	-0.16801515	-0.13779898	-0.10354712	-0.76796432	1.75782304	-0.39654606	-1.46814861	-2.51993587	-1.7719318	-0.86111727	0.2204642	**0.0388731**	0.3453444	0.0703435	**0.0057248**	**0.0376959**
Desulfovibrio sp. 6_1_46AFAA	Desulfovibrionaceae	-0.10382162	-0.02477554	-0.10069224	-0.14319399	-0.19215891	-0.14792883	-0.11876185	-0.77785977	1.17123429	-0.69467242	-1.93161587	-3.16929232	-2.0587525	-1.2434931	0.2175318	0.1199385	0.2428763	**0.0262926**	**0.0007357**	**0.0194195**
Citrobacter freundii 4_7_47CFAA	Enterobacteriaceae	0.03337918	-0.09397137	-0.0520612	-0.07578883	-0.05489875	-0.05775335	-0.05018239	1.44663755	-0.52836899	0.19854208	-0.01402007	0.52237773	0.49451414	0.35328041	0.0732992	0.2979865	0.4210413	0.4943876	0.3000738	0.3098667
Citrobacter sp. 30_2	Enterobacteriaceae	0.03606459	-0.08611285	-0.05409014	-0.07645793	-0.05406332	-0.05113254	-0.04763203	1.49017753	-0.3353462	0.16127629	-0.03305534	0.54484681	0.68197865	0.41831296	0.0674125	0.3682437	0.4357178	0.4867695	0.2922803	0.2468794
Enterobacteriaceae bacterium 9_2_54FAA	Enterobacteriaceae	0.02544495	-0.09570637	-0.02162718	-0.07703977	-0.0477141	-0.04259169	-0.04320569	1.31799669	-0.57098441	0.757529	-0.04960774	0.71561183	0.92380787	0.51572554	0.09299	0.2833347	0.223581	0.480149	0.2363502	0.1769607
Escherichia coli 4_1_47FAA	Enterobacteriaceae	-0.00177549	-0.09597853	-0.05523141	-0.08364355	-0.04437241	-0.04504139	-0.05434046	0.87665959	-0.57766918	0.14031428	-0.2374775	0.80548815	0.85444601	0.31029356	0.1895114	0.2810681	0.4440137	0.405824	0.2094647	0.1956098
Escherichia coli D9	Enterobacteriaceae	-0.00128723	-0.09822382	-0.05180759	-0.08611633	-0.05272665	-0.0516622	-0.05697064	0.88457595	-0.63281855	0.20320031	-0.30782521	0.58079734	0.66698149	0.23248522	0.1873667	0.2627103	0.419214	0.3787018	0.2800104	0.2516542
Escherichia coli DH5 alpha pks	Enterobacteriaceae	-0.09747425	-0.06961335	-0.05358291	-0.08134532	-0.07078573	-0.0931747	-0.07766271	-0.67494708	0.06991811	0.17059274	-0.17209552	0.0950907	-0.50842099	-0.16997701	0.2491121	0.472033	0.4320395	0.4314468	0.4619905	0.3049615
Escherichia coli NC101	Enterobacteriaceae	-0.06980624	-0.05328395	-0.0285171	-0.07354878	-0.06447828	-0.08284623	-0.0620801	-0.22635332	0.47100443	0.63098057	0.04970667	0.26473226	-0.21597636	0.16234904	0.4101583	0.3182361	0.2633121	0.4801094	0.3952544	0.4142113
Escherichia coli NC101 delta pks	Enterobacteriaceae	-0.08404713	-0.07074734	-0.0444527	-0.07957073	-0.07558941	-0.09449887	-0.0748177	-0.45724717	0.04206489	0.33828881	-0.12161089	-0.03410652	-0.5459139	-0.12975409	0.3231774	0.4831654	0.3671311	0.4514368	0.486349	0.2919125
Escherichia coli Nissle 1917	Enterobacteriaceae	0.02141682	0.01892417	0.02174131	-0.05254468	-0.0510558	-0.035375	-0.01912359	1.25268671	1.31495689	1.55408534	0.64724839	0.6257355	1.12814419	1.08714284	0.1043716	0.0934985	0.0594423	0.2580102	0.2650333	0.1288057
Escherichia coli PL1	Enterobacteriaceae	-0.0564605	0.06432897	-0.03020788	-0.0886473	-0.07596536	-0.07485712	-0.06507785	-0.00997279	0.19971409	0.59992574	-0.37982816	-0.0442176	0.01023082	0.06264202	0.4960077	0.4205814	0.2735853	0.3515479	0.4823044	0.4959044
Escherichia sp. 1_1_43	Enterobacteriaceae	0.00444982	-0.09754343	-0.06588332	-0.0848654	-0.04733816	-0.04060545	-0.05529766	0.97759318	-0.61610662	-0.05533114	-0.27223755	0.72572292	0.98004723	0.289948	0.1633009	0.2682079	0.4778609	0.392357	0.2332338	0.1626944
Escherichia sp. 3_2_53FAA	Enterobacteriaceae	0.01604597	-0.09567235	-0.06296673	-0.08535995	-0.03831558	-0.04868284	-0.05249191	1.16560675	-0.57014881	-0.00176156	-0.28630709	0.96838899	0.75134052	0.33785313	0.1210715	0.2836186	0.4992948	0.3869415	0.1655886	0.2254412
Escherichia sp. 4_1_40B	Enterobacteriaceae	0.02373605	-0.09887019	-0.05966971	-0.08390538	-0.04725462	-0.03623571	-0.05036659	1.29028943	-0.64869489	0.05879536	-0.24492609	0.72796982	1.10377381	0.38120124	0.0977012	0.2575415	0.4764764	0.4029282	0.2325444	0.1340174
Klebsiella sp. 1_1_55	Enterobacteriaceae	0.02361398	-0.0855005	-0.01395527	-0.0562102	-0.10314448	-0.02398721	-0.04319728	1.28831034	-0.32030546	0.89844028	0.54296826	-0.77521171	1.45058315	0.51413081	0.0980443	0.3739477	0.1836468	0.2929282	0.2183143	0.0727501
Klebsiella sp. 4_1_44FAA	Enterobacteriaceae	0.017999	-0.09846196	-0.01604761	-0.08079258	-0.11354551	-0.05907752	-0.05832103	1.19727219	-0.63866773	0.86000993	-0.15637073	-1.05495177	0.45702124	0.11071885	0.1147937	0.2607998	0.1940712	0.4376568	0.1448891	0.3232588
Enterococcus saccharolyticus 30_1	Enterococcaceae	0.0076235	-0.11240999	-0.08490459	-0.11427697	-0.06408841	-0.09343953	-0.076916	1.02904953	-0.98126229	-0.40469796	-1.10896148	0.27521784	-0.51591957	-0.28442899	0.1508917	0.1623947	0.3423343	0.132896	0.3912081	0.3023311
Coprobacillus sp. 29_1 (D6)	Erysipelotrichaceae	-0.03143722	0.00250817	0.02668684	-0.03474062	-0.06663645	-0.04980838	-0.02557128	0.39574068	1.84138269	1.64492072	1.1537519	0.20668714	0.71947156	0.99365911	0.3456423	**0.0323182**	**0.0494079**	0.1234828	0.4178474	0.2351579
Coprobacillus sp. 3_3_56FAA	Erysipelotrichaceae	-0.02985038	0.01565829	0.0195216	-0.03863889	-0.06187454	-0.04782213	-0.02905368	0.42146886	1.39517416	1.51332588	1.04285081	0.3347609	0.77571091	0.91388192	0.3361733	0.0807551	0.0644352	0.1476731	0.3684651	0.2181667
Coprobacillus sp. 8_2_54BFAA	Erysipelotrichaceae	-0.01373783	-4.3298E-05	0.02345322	-0.03471153	-0.05732148	-0.04623314	-0.02143234	0.68270875	1.77871295	1.58552836	1.15457952	0.45721739	0.82070239	1.07990823	0.2466482	**0.0371405**	0.0558021	0.1233134	0.3231881	0.2050985
Coprobacillus sp. D7	Erysipelotrichaceae	0.0072573	-0.00569055	0.03169577	-0.03392609	-0.05276842	-0.04696143	0.01673223	1.02311226	1.64000393	1.73692065	1.17692526	0.57967389	0.8000813	1.15945288	0.1522906	**0.049914**	**0.0406719**	0.1188004	0.2803901	0.2110294
Erysipelotrichaceae bacterium 2_2_44A	Erysipelotrichaceae	0.01030892	-0.02120348	0.02947662	-0.04192624	-0.04888369	-0.010878	-0.0385098	1.07258951	1.25897193	1.69616118	0.94932973	0.68415512	1.82176289	1.24716173	0.1408949	0.1032343	**0.0443739**	0.1703912	0.2461906	**0.033769**
Erysipelotrichaceae bacterium 21_3	Erysipelotrichaceae	0.01726661	-0.01103162	0.03803619	-0.0355261	-0.03330304	-0.02332512	-0.00798051	1.18539765	1.50881528	1.85337625	1.13140616	1.10320348	1.4693296	1.37525474	0.1171202	0.0650072	**0.0314569**	0.128119	0.134141	0.0701839
Erysipelotrichaceae bacterium 3_1_53	Erysipelotrichaceae	-0.03961556	0.01940044	0.0081094	-0.03779524	-0.0400282	-0.0329253	-0.02694256	0.26314164	1.30325854	1.30370579	1.06685179	0.92232738	1.19750606	1.0094652	0.3958693	0.0954747	0.0953986	0.142186	0.1773466	0.1147482
Erysipelotrichaceae bacterium 5_2_54FAA	Erysipelotrichaceae	-0.02692083	-0.06022394	-0.0128774	-0.05952664	-0.06989461	-0.04947734	-0.04648679	0.46896702	0.30054274	0.91823773	0.44861957	0.11905772	0.72884478	0.49737826	0.3189659	0.3814844	0.1784155	0.3262923	0.4524513	0.2322763
Erysipelotrichaceae bacterium 6_1_45	Erysipelotrichaceae	-0.03094896	-0.04675219	0.01432301	-0.05210829	-0.03873329	-0.0564954	-0.03511919	0.40365704	0.63143895	1.41783228	0.6596627	0.95715445	0.5301324	0.76664631	0.3427181	0.2631619	0.0774048	0.2540019	0.1684088	0.2973734
Eubacterium sp. 3_1_31	Eubacteriaceae	0.02105062	-0.03110318	0.00462217	0.01027461	-0.02127293	-0.04120132	-0.01302988	1.24674944	1.01581334	1.23965521	1.84978041	1.42675825	0.96317542	1.29032201	0.1054543	0.1540221	0.1067586	**0.0317131**	0.0761143	0.1668935
Fusobacterium gonidiaformans 3-1-5R	Fusobacteriaceae	-0.01520261	-0.0816903	-0.08110034	-0.05853753	-0.02177419	-0.06106376	-0.05322812	0.65895967	-0.22671865	-0.33482459	0.47675865	1.4132768	0.40078189	0.39803896	0.254228	0.4100157	0.368441	0.3161788	0.0780698	0.3437791
Fusobacterium necrophorum D12	Fusobacteriaceae	0.03765143	-0.02545593	-0.02543143	-0.03881344	-0.04169905	-0.07913858	-0.0288145	1.5159057	1.15452236	0.68765563	1.03788509	0.87738921	-0.11099623	0.86039363	0.0641098	0.1233251	0.2450848	0.1488258	0.1893131	0.4556571
Fusobacterium necrophorum subsp. funduliforme 1_1_36S	Fusobacteriaceae	0.01690042	0.0081214	-0.00209868	-0.05101654	-0.01020356	0.01765771	0.00256012	1.17946038	1.97925611	1.11621226	1.71487834	1.72447358	2.62973493	1.7240026	0.1182959	**0.0235102**	0.1313396	**0.0426415**	**0.0417749**	**0.0041594**
Fusobacterium nucleatum subsp. animalis 11_3_2	Fusobacteriaceae	0.07646802	-0.05287571	-0.00228889	-0.04166442	-0.02954363	-0.00154255	-0.00857455	2.14525637	0.48103158	1.1127186	0.95677831	1.20431435	2.08608785	1.33103118	**0.0156714**	0.3146548	0.1320879	0.1685038	0.1134297	**0.0181604**
Fusobacterium nucleatum subsp. animalis 21_1A	Fusobacteriaceae	-0.14507951	-0.14333379	-0.1888241	-0.12221897	-0.112543	-0.12727189	-0.13987854	-1.44679223	-1.74081951	-2.31340535	-1.33490177	-1.02798888	-1.47386323	-1.55629516	0.0732776	**0.0403314**	**0.010132**	0.0901993	0.151141	0.0695739
Fusobacterium nucleatum subsp. animalis 3_1_33	Fusobacteriaceae	-0.09649773	-0.14329977	-0.17538241	-0.11896072	-0.12085547	-0.13184025	-0.13113939	-0.65911436	-1.73998392	-2.06651946	-1.24220832	-1.25155624	-1.60321374	1.42709934	0.2541782	**0.0404042**	**0.0190544**	0.1062879	0.1045771	0.0538332
Fusobacterium nucleatum subsp. animalis 7_1	Fusobacteriaceae	-0.17034691	0.12931772	-0.19801772	-0.1362702	-0.13940188	-0.12098212	-0.14905609	-1.85646389	-1.39555375	-2.48226598	-1.73464229	-1.75036984	-1.29577194	-1.75287795	**0.0312383**	0.0805481	**0.0063715**	**0.040872**	**0.0395069**	0.0967554
Fusobacterium nucleatum subsp. animalis D11	Fusobacteriaceae	-0.04254511	0.09359716	-0.04996886	-0.07791251	-0.05406332	-0.07960204	-0.0662815	0.21564348	-0.51917743	0.23697243	-0.07443634	0.54484681	-0.12411874	0.0466217	0.4143415	0.3011914	0.4060205	0.4702289	0.2922803	0.4504403
Fusobacterium nucleatum subsp. Nucleatum ATCC 25586	Fusobacteriaceae	-0.15716392	-0.14047615	-0.15

Supplementary Table S4: Growth rate change of cell lines by bacterial secretomes

Secretomes		growth rates																													
Bacteria	Family	Caco2	HT29	HCT15	SW480	HEK293T	HCT116	Average	Caco2-z	HT29-z	HCT15-z	SW480-z	HEK293T-z	HCT116-z	Average	Caco2-p	HT29-p	HCT15-p	SW480-p	HEK293T-p	HCT116-p
Acidaminococcus sp. D21	Acidaminococcaceae	-0.04775969	0.02130444	-0.01527376	-0.11193937	-0.03707053	-0.05956672	-0.0417176	-0.25762916	0.46851739	0.25493289	-1.32632857	-0.24139431	-0.52653839	-0.27140669	0.3980222	0.3191611	0.3990663	0.0916511	0.4043196	0.2986607
Akkermansia muciniphila	Akkermansiaceae	0.00467111	-0.03307343	0.03833069	-0.00703726	0.01757804	-0.03977281	-0.0032172	0.4348652	-0.21747398	0.98610038	-0.02634433	0.45219688	-0.27529247	0.22567528	0.3313153	0.4136431	0.1612539	0.4894571	0.3250324	0.3912008
Bacillus smithii 7_3_47FAA	Bacillaceae	-0.0371782	-0.01683738	0.05582822	-0.06080194	-0.02889065	-0.01535415	-0.01720568	-0.11787121	-0.01265191	1.2247675	-0.69261532	-0.13757653	0.03465576	0.04978472	0.4529325	0.4949363	0.1095802	0.2435668	0.4451102	0.486132
Bacteroides massiliensis 3972 T(B)2	Bacteroidaceae	-0.06123917	-0.14484208	-0.09507927	-0.04609619	-0.17602937	-0.13194483	-0.10920515	-0.43566316	-1.62746554	-0.83361848	-0.51037652	-2.00503829	-1.44524033	-1.14290038	0.331025	0.0512581	0.2014823	0.3043109	**0.0221321**	0.0735354
Bacteroides ovatus 3725 D9 iii	Bacteroidaceae	-0.03836028	-0.07251007	-0.07014969	-0.03962191	-0.07647947	-0.10216147	-0.06654698	-0.13348381	-0.71497781	-0.4935777	-0.43014493	-0.74155373	-1.06719741	-0.59682287	0.4467332	0.2365913	0.3102337	0.3330349	0.2284464	0.1421568
Bacteroides stercoris 4009 N(B)17	Bacteroidaceae	0.08957086	0.06828823	0.00136192	0.03534838	-0.03320051	-0.09161705	0.01162531	1.55620242	1.06123048	0.48184444	0.49891358	-0.19227665	-0.93335612	0.41209302	0.0592289	0.1435075	0.3144	0.308347	0.4235171	0.1745333
Bacteroides uniformis 3978 T3ii	Bacteroidaceae	-0.00041945	-0.04785533	-0.05493445	-0.04816046	-0.11302688	-0.08773226	-0.05868814	0.36763029	-0.40395171	-0.28604108	-0.5359576	-1.20542044	-0.88404618	-0.49129779	0.3561273	0.3426397	0.387066	0.2953899	0.1132636	0.1875582
Bacteroides uniformis 3978 T3i	Bacteroidaceae	-0.00232602	-0.03144748	-0.06265911	-0.03230316	-0.1027005	-0.07959271	-0.05183816	0.34244868	-0.19696221	-0.39140583	-0.33944835	-1.07435969	-0.7807301	-0.40674292	0.3655864	0.4216771	0.3472769	0.366719	0.140547	0.2167321
Bacteroides stercoris 3972 D14 (B)	Bacteroidaceae	-0.02062913	-0.05094791	-0.0562219	-0.05144451	-0.0765945	-0.0616487	-0.05291444	0.10070519	-0.44296544	-0.30360187	-0.57665478	-0.74302633	-0.55296511	-0.41975139	0.4597618	0.3283728	0.3803383	0.2814511	0.2279997	0.2895263
Bacteroides fragilis 9343 delta tsr 15 M4	Bacteroidaceae	0.0083508	0.04071272	-0.06476584	0.03459774	0.03968425	-0.05961381	-0.00017569	0.48346571	0.71335808	-0.42014167	0.48961137	0.73251157	-0.52713609	-0.24527816	0.3138229	0.2370928	0.3366905	0.3116394	0.2311997	0.2984527
Bacteroides ovatus S47RT17	Bacteroidaceae	-0.04617723	-0.06409138	-0.05669006	-0.03544227	-0.01962539	-0.05924383	-0.03506429	-0.42672842	-0.60877378	-0.30998751	-0.50007636	-0.0199633	-0.5224399	-0.19963944	0.4061342	0.2706792	0.3779007	0.3079365	0.4920323	0.300089
Bacteroides thetaiotaomicron VPI5482	Bacteroidaceae	-0.04179211	-0.01229066	-0.02380174	0.04857843	0.01622686	-0.05924383	-0.01205384	-0.17881071	0.04470615	0.13861079	0.62686508	0.43504785	-0.5224399	0.09666321	0.4288141	0.4821126	0.4447002	0.2530164	0.3312428	0.300089
Bacteroides vulgatus 3975 RP4	Bacteroidaceae	0.00587225	0.05076361	-0.05025284	-0.03389827	-0.04607947	-0.05887385	-0.0220781	0.45072961	0.8401527	-0.22218365	-0.35921556	-0.35573444	-0.51774372	-0.02733251	0.3255624	0.1996439	0.4118033	0.3592787	0.3605852	0.3017294
Bacteroides fragilis 9343 delta cap delta pilus 77	Bacteroidaceae	-0.01815059	-0.07096378	-0.02333358	0.04839077	0.05614004	-0.05572902	-0.01060769	0.13344129	-0.69547095	0.14499653	0.66053953	0.94161974	-0.47782614	0.11788333	0.4467501	0.2426699	0.4421701	0.2537631	0.1724081	0.3158323
Bacteroides fragilis NCTC 9343 (NTBF)	Bacteroidaceae	0.01635841	0.03504299	-0.06172279	0.03206432	-0.01243173	-0.05498906	-0.00761298	0.58922848	0.64183292	-0.37863434	0.4582164	0.07131744	-0.46843377	0.15225452	0.2772096	0.2598114	0.3520211	0.3228617	0.47148	0.319191
Bacteroides vulgatus 3775 SL(B)10iv	Bacteroidaceae	0.04019059	0.03057593	-0.02497214	0.08714262	0.02539297	-0.05313917	0.0175318	0.90399864	0.58547976	0.12264643	1.14076627	0.55138267	-0.44495284	0.47655349	0.1822171	0.2784709	0.4510351	0.1262106	0.2900695	0.3276525
Bacteroides fragilis VPI clinda R (ETBF)	Bacteroidaceae	0.0701238	-0.0093574	-0.02941967	-0.0522378	0.00218763	-0.04610955	0.00972957	1.29934997	0.31780224	0.06198188	0.70821337	0.25686413	-0.35572532	0.38141438	0.0961868	0.3749243	0.4752081	0.2386896	0.3983184	0.3605886
Bacteroides fragilis 86-5443-2-2 (ETBF)	Bacteroidaceae	0.00244042	-0.02397374	-0.02052461	0.08686113	-0.01544843	-0.04555458	-0.00269997	0.40540271	0.10267904	0.18331086	1.13727794	0.03303003	-0.34868104	-0.2179436	0.3421048	0.4589759	0.4270424	0.1269374	0.4867823	0.3632374
Bacteroides fragilis 9343 delta cap	Bacteroidaceae	-0.01262152	-0.06830073	-0.03222864	0.0631221	0.02655324	-0.04296473	-0.01107338	0.20646797	-0.6618758	0.02366742	0.84309546	0.5661086	-0.31580775	0.11027598	0.4179496	0.2533339	0.4905281	0.1988193	0.2850326	0.3756832
Bacteroides sp. 3_2_5	Bacteroidaceae	-0.05593889	-0.04740863	-0.06944745	-0.0293006	0.00829837	-0.00393187	0.03295485	-0.36565828	-0.3983164	-0.48399909	-0.3022395	0.33442068	0.17963981	-0.17269213	0.356865	0.3447197	0.3136331	0.380859	0.3686195	0.4284876
Bacteroides sp. 3_1_23	Bacteroidaceae	-0.07083559	-0.04144109	-0.06968153	0.01736426	0.04504016	0.01111396	-0.01807331	-0.56241061	-0.32303435	-0.48719196	0.27604806	0.8007417	0.37061801	0.01246181	0.2862935	0.3729356	0.3124982	0.3909097	0.210885	0.3550108
Bacteroides sp. D2	Bacteroidaceae	-0.16610076	-0.06641081	-0.03667617	-0.01832247	-0.01498432	0.01771193	-0.04746377	-1.82065187	-0.63803407	-0.03699713	-0.16619464	0.03892041	0.45436665	-0.36143178	**0.0338806**	0.2610487	0.4851955	0.4337885	0.4844263	0.3242492
Bacteroides fragilis K570 clinda R (ETBF)	Bacteroidaceae	0.06015242	0.02267892	-0.00860246	0.04316187	0.10239356	0.01849898	0.03971388	1.16765013	0.48585683	0.34592972	0.59574116	1.52866213	0.46435672	0.76469945	0.120707	0.3129726	0.3642737	0.2750251	0.0625579	0.3206536
Bacteroides sp. D22	Bacteroidaceae	-0.02192561	-0.02417992	-0.07756224	0.00735572	0.02160276	0.02295331	-0.01195933	0.0835817	-0.10527996	-0.59468529	0.15201856	0.50327797	0.52089595	0.09330149	0.4665861	0.4579406	0.2753787	0.4393906	0.3068075	0.3006279
Bacteroides fragilis 3_1_12	Bacteroidaceae	-0.03473778	-0.05687536	-0.01958829	-0.04834812	-0.05536161	0.0238166	-0.03184909	-0.08563874	-0.51774175	0.19608247	-0.53828315	-0.47354186	0.53185371	-0.14787822	0.4657657	0.3017301	0.4220225	0.2945849	0.3173625	0.296813
Bacteroides sp. 2_1_56FAA	Bacteroidaceae	-0.06117562	-0.04023842	-0.05867974	0.02455791	0.04573632	0.03947907	-0.00838675	-0.43482377	-0.30786235	-0.33712702	0.36519427	0.80957726	0.73065889	0.13760288	0.3313304	0.3787114	0.3675961	0.3570386	0.2083331	0.2317662
Bacteroides sp. 2_1_33B	Bacteroidaceae	-0.0478296	-0.03794762	0.04307437	0.04670183	0.05764839	0.04071233	0.00270183	-0.25855248	-0.27896329	-0.12426894	0.63960955	0.96076344	0.74631284	0.28081685	0.3976648	0.3897873	0.4503907	0.2605352	0.1675485	0.2270046
Bacteroides sp. 2_2_4	Bacteroidaceae	-0.06282798	-0.02889896	-0.07756224	0.05789889	0.06731728	0.04354885	-8.7362E-05	-0.45664784	-0.16481201	-0.59468529	0.77836756	1.0834795	0.78231693	0.23800314	0.3234268	0.4343344	0.2753787	0.2174286	0.1385152	0.2162651
Bacteroides sp. 4_3_47FAA	Bacteroidaceae	-0.01918014	-0.03479777	0.05337392	0.02275637	0.07466564	0.04515209	0.00587038	0.11984322	-0.23922709	-0.26475527	0.34286896	1.17674371	0.80266707	0.32302343	0.4521488	0.4051622	0.3952663	0.3654278	0.1188842	0.2103274
Bacteroides sp. 2_1_22	Bacteroidaceae	-0.16686339	-0.07345503	0.03761249	-0.04462619	-0.0240344	0.04620037	0.05006519	-1.83072451	-0.72689867	-0.04976861	-0.49215968	-0.07594183	0.81597293	-0.3932534	**0.0331273**	0.2329182	0.4800887	0.3107359	0.4696341	0.2064973
Bacteroides sp. 3_1_33FAA	Bacteroidaceae	-0.0788432	-0.00067631	-0.06367346	0.04663927	0.05950482	0.05415493	0.00285101	-0.66817339	0.19122437	-0.4052416	0.63883436	0.98432493	0.91694091	0.27631826	0.2513163	0.4239305	0.3421642	0.2607878	0.1616899	0.178804
Bacteroides sp. 3_1_19	Bacteroidaceae	-0.07846189	-0.04373189	-0.05352997	0.04438735	0.06832285	0.05649813	-0.0010859	-0.66313706	-0.35193341	-0.26688385	0.61092773	1.09624197	0.94668342	0.2286498	0.2529291	0.3620136	0.3944441	0.2699643	0.1357056	0.171114
Bacteroides eggerthii 1_2_48FAA	Bacteroidaceae	0.10958889	0.03057593	0.07685291	0.08855007	0.09883787	0.07690868	0.08021923	1.82060935	0.58547976	1.51154538	1.15520792	1.48353388	1.20575631	1.29418876	**0.0338838**	0.2784709	0.0646994	0.1226204	0.0683261	0.1131989
Bacteroides sp. D1	Bacteroidaceae	0.08957086	0.02636659	0.04607131	0.09915289	0.10313086	0.07801861	0.07371852	1.55620242	0.53237774	1.09168283	1.28960167	1.53801979	1.21984487	1.20462159	0.0592289	0.2966311	0.1367047	0.0978657	0.0614108	0.1105092
Bacteroides sp. 1_1_14	Bacteroidaceae	-0.06702244	-0.03164792	-0.07444117	0.03675583	0.09469958	0.0782039	0.00609125	-0.51204739	-0.19949098	-0.55213367	0.16353523	1.43101138	1.22219296	0.31765127	0.3037246	0.4206849	0.2898185	0.3022152	0.0755467	0.1100654
Bacteroides ovatus 3_8_47FAA	Bacteroidaceae	-0.1168854	-0.00241159	0.05215741	0.09753303	0.09394675	0.07931354	0.07347377	1.95656036	0.16933333	0.17469746	1.27448558	1.42168496	1.23928152	1.20593126	**0.0248246**	0.43255	0.1192927	0.1005113	0.0768875	0.1074294
Bacteroides sp. 1_1_6	Bacteroidaceae	0.10358124	-0.03247834	0.01248075	0.06481104	0.05497978	0.08208839	0.05541048	2.36201403	-0.20996679	0.63350582	0.86402543	0.92689381	1.27150291	0.97466253	**0.0089008**	0.4165795	0.2625275	0.1930136	0.1762068	0.1010394
Bacteroides sp. 1_1_30	Bacteroidaceae	0.01940893	0.03890872	0.03998522	0.07907323	0.05022268	0.08634316	0.05232365	0.62951906	0.60600001	0.08866818	1.04076748	0.86651751	1.32550904	0.92693022	0.263833	0.2442008	0.1557788	0.148205	0.1922293	0.0917865
Bacteroides sp. 3_1_40A	Bacteroidaceae	0.0943373	0.01511303	0.04852916	0.05486505	0.08038962	0.08763809	0.06347871	1.61915645	0.39041112	1.12520797	0.74077111	1.24939162	1.34194569	1.07781399	0.0521411	0.3476455	0.1294744	0.2286839	0.1050177	0.089099
Bacteroides sp. 9_1_42FAA	Bacteroidaceae	0.10158228	-0.02062345	0.01833276	0.08292026	0.05045474	0.09725756	0.05498736	1.71484659	-0.06041417	0.71332759	1.08844132	0.8694827	1.46404651	0.96495175	**0.0426761**	0.4758344	0.2371022	0.1374182	0.1915225	0.0709404
Bacteroides sp. 4_1_36	Bacteroidaceae	0.15305979	0.03736243	0.0643296	0.12261042	0.13387793	0.10021739	0.10190959	2.39475013	0.67109321	1.34072678	1.58029582	1.92825686	1.50161599	1.56945646	**0.0081403**	0.2503837	0.0892963	0.0564319	**0.0265229**	0.0659675
Bacteroides sp. D20	Bacteroidaceae	0.04171585	0.04973275	0.05438117	0.04473139	0.0585766	0.10576709	0.05915081	0.92414394	0.82714812	1.20502975	0.61519124	0.97254419	1.57205877	1.01935267	0.176922	0.2033127	0.1133388	0.2685519	0.1646023	0.0573762
Bacteroides sp. 2_1_16	Bacteroidaceae	0.05906567	0.0249062	0.03752737	0.03797562	0.07435624	0.12926079	0.06051532	1.15329661	0.51395459	0.97514303	0.53147132	1.17281679	1.87026654	1.03615815	0.123624	0.3030559	0.1639569	0.2969457	0.119669	**0.0303023**
Bacteroides dorei 5_1_36/D4	Bacteroidaceae	0.03885599	0.04913141	0.0655	0.06781361	0.09094805	0.12926079	0.07358498	0.88637152	0.81956212	1.35669113	0.90123429	1.38339755	1.87026654	1.20292052	0.1869308	0.2054713	0.0867383	0.1829514	0.0825821	**0.0303023**
Bifidobacterium sp. 12_1_47BFAA	Bifidobacteriaceae	-0.02526211	0.01726691	0.00684686	0.01079047	-0.01061644	-0.01183935	-0.00213561	0.03951388	0.4175828	0.55665921	0.19458323	0.09435683	0.07926952	0.23032758	0.484189	0.3376281	0.2882599	0.4226111	0.4622906	0.4683063
Ralstonia sp. 5_2_56FAA	Burkholderiaceae	-0.11325052	-0.03805592	0.03827217	-0.17067704	-0.18958762	-0.04680242	-0.08668356	-1.12261758	-0.29234093	0.98530216	-0.05422673	-2.17711743	-0.36452	-0.83558483	0.1300235	0.3892616	0.1614498	**0.0196549**	**0.014473**	0.357291
Ralstonia sp. 5_7_47FAA	Burkholderiaceae	-0.10753079	-0.00042953	0.06753225	-0.06530579	-0.11927544	0.0253436	-0.03327762	-1.04707272	0.19433759	-1.38441106	-0.7484286	-1.28472625	0.55123615	-0.1583738	0.1467467	0.4227076	0.0824273	0.2263653	0.0987133	0.2901198
Clostridium septicum (Mace 1889) Ford 1927	Clostridiaceae	-0.37978961	-0.41354668	-0.33543746	-0.21684148	-0.37186556	-0.16316102	-0.3134403	-4.64300704	-5.01724613	-4.11211664	-2.62631282	-4.49056099	-1.8414703	-3.78845223	**1.595E-06**	**2.407E-07**	**1.849E-05**	**0.0042083**	**3.315E-06**	**0.0323389**
Clostridium sp. 7_3_54FAA	Clostridiaceae	-0.07950415	-0.08805263	-0.12499903	-0.13239434	-0.10686059	-0.08639024	-0.1030335	-0.67690301	-0.91105135	-1.24172547	-1.57981387	-1.12715883	-0.86701183	-1.06727739	0.2485336	0.1803522	0.1064232	0.0564868	0.129062	0.1921938
Clostridium perfringens WAL-14572	Clostridiaceae	0.04404187	-0.09372236	-0.10439994	-0.08970162	-0.0034808	-0.05919674	-0.0510766	0.9548655	-0.98257651	-0.96075281	-1.05075052	0.18492128	-0.52184221	-0.39602254	0.1690362	0.16212	0.1675512	0.1459005	0.4264088	0.3002976
Clostridium sp. 7_2_43FAA	Clostridiaceae	-0.02631073	-0.07834536	0.03183496	-0.08726204	-0.10152336	-0.0381079	0.04995241	0.02566399	-0.78859159	0.89749821	-1.02051833	-1.05941956	-0.25415964	-0.36658782	0.4897293	0.214424	0.1839467	0.1529536	0.1439191	0.3993658
Clostridium hathewayi WAL-18680	Clostridiaceae	-0.09685398	-0.03144123	-0.05313629	-0.10584041	-0.11973955	-0.03385314	-0.07347743	-0.90605569	-0.1968834	-0.26151402	-1.25074809	-1.29061662	-0.20015351	-0.68432856	0.1816719	0.4217081	0.3965192	0.1047704	0.0976899	0.4204249
Clostridium sp. D5	Clostridiaceae	0.02478547	0.02259302	0.0313668	0.06638045	0.02204507	0.02145882	0.02143827	0.70053121	0.48477311	0.89111247	0.13993273	0.50889168	0.5019262	0.53786123	0.241085	0.3133578	0.1856556	0.4441762	0.3048324	0.307284
Desulfovibrio sp. 6_1_46AFAA	Desulfovibrionaceae	0.0398474	-0.01108175	-0.09807976	-0.04954232	-0.12449664	-0.1563164	-0.0666115	0.89946595	0.05995697	-0.87454528	-0.55308213	-1.35099292	-1.75459087	-0.59563138	0.1834221	0.4760171	0.1901351	0.2894861	0.087641	**0.0391772**
Desulfovibrio sp. 3_1_syn3	Desulfovibrionaceae	-0.13801585	-0.00206172	0.00397937	0.07497029	-0.03155926	-0.0471724	0.02137225	-2.19511182	0.17374701	-0.40898892	0.98692243	-0.17144616	-0.36921618	0.53805251	**0.0137803**	0.4308094	0.3407844	0.1603179	0.4317166	0.3555345
Escherichia coli NC101	Enterobacteriaceae	-0.04827446	-0.10622878	-0.0556367	-0.02723653	-0.07994324	-0.08366249	-0.06682066	-0.26442819	-1.14087767	-0.29561969	-0.27665442	-0.78425882	-0.83238814	-0.59903051	0.3953927	0.1261875	0.383392	0.3906747	0.2156943	0.2018296
Escherichia coli NC101 delta pks	Enterobacteriaceae	-0.04943744	-0.10266273	-0.05961607	-0.04498837	-0.09979983	-0.08366249	-0.06682066	-0.2439444	-1.09826165	-0.34936485	-0.42923487	-1.03754487	-0.72407127	-0.71830108	0.2926296	0.1358981	0.3627791	0.3104613	0.148954	0.2139762
Escherichia coli PL1	Enterobacteriaceae	-0.07439453	-0.11408809	-0.0568071	-0.0361502	-0.09005359	-0.0725631	-0.07400943	-0.60941629	-1.2394957	-0.31158405	-0.3871222	-0.91384708	-0.69150258	-0.69216131	0.2704659	0.1068345	0.377292	0.3488655	0.1796162	0.2439168
Escherichia coli DH5 alpha pks	Enterobacteriaceae	-0.04579592	-0.03067433	-0.07448018	0.05711697	-0.01045928	-0.03242031	-0.02278551	-0.2316921	-0.18720878	-0.55264582	0.76867775	0.09635152	-0.18196646	-0.04808065	0.408095	0.425509	0.2896358	0.2202984	0.4614959	0.4275716
Citrobacter freundii 4_7_47CFAA	Enterobacteriaceae	-0.08735924	-0.0821028	-0.03906379	-0.00771966	0.04692752	0.00445433	-0.02747727	-0.78065126	-0.83599262	-0.06956441	-0.03480088	0.82469588	0.28608668	-0.10170444	0.2167554	0.2008132	0.4721799	0.486074	0.204009	0.3870485
Klebsiella sp. 4_1_44FAA	Enterobacteriaceae	-0.04846512	-0.09212505	-0.08200977	-0.03536828	0.06406853	0.01136062	-0.03042318	-0.26694635	-0.96242599	-0.65534984	-0.37743239	1.04224691	0.3737488	-0.14102648	0.39442	0.1671307	0.2554336	0.3524688	0.1478619	0.3538421
Escherichia coli Nissle 1917	Enterobacteriaceae	0.07082924	-0.02860637	0.02838227	0.01219792	-0.00075417	0.04273265	0.02079662	1.30866716	-0.16112082	0.85040336	0.12102488	0.21952721	0.77195686	0.53357644	0.0946021	0.4357921	0.1967803	0.415774	0.4128408	0.2193248
Citrobacter sp. 30_2	Enterobacteriaceae	-0.02101045	-0.04006661	-0.05313984	0.03888265	0.0533322	0.05955663	0.0062591	0.09566887	-0.30569492	-0.2615624	0.5427115	0.905983	0.98550522	0.32710188	0.4617678	0.3795388	0.3965005	0.2930549	0.1816912	0.1613999
Escherichia sp. 3_2_53FAA	Enterobacteriaceae	-0.01910387	0.03152089	0.03822961	-0.01466309	0.02005574	0.07357886	0.02160302	0.12085048	0.59740062	0.98472164	-0.12084635	0.4836434	1.16349064	0.53821007	0.4517486	0.2744698	0.1615924	0.4517502	0.3137597	0.1215473
Escherichia sp. 4_1_40B	Enterobacteriaceae	-0.02158242	0.01708885	0.04373051	0.03459774	0.05753236	0.08819305	0.03659335	0.08811439	0.41533656	1.05975411	0.48961137	0.95929085	1.34898997	0.72684954	0.4647786	0.338452	0.143843	0.3116394	0.1679192	0.0879653
Escherichia sp. 1_1_43	Enterobacteriaceae	-0.00156339	0.07232576	0.03846369	0.06603084	0.04094055	0.09263281	0.05147171	0.35252132	1.11216507	0.98791451	0.87914153	0.74871009	1.40534419	0.91429944	0.3617926	0.1322552	0.1608092	0.1888857	0.2262803	0.0792803
Enterobacteriaceae bacterium 9_2_54FAA	Enterobacteriaceae	0.00911343	0.02765516	0.07977891	0.08329558	0.05393554	0.10946688	0.06054092	0.49353836	0.5463346	1.55145627	1.09309243	0.91364048	1.61902063	1.0365636	0.3102476	0.2910145	0.0597925	0.1363953	0.1796705	0.0521556
Escherichia coli D9	Enterobacteriaceae	0.00777882	0.0352148	0.04782692	0.06612467	0.08271016	0.11982631	0.05991361	0.47591123	0.64400035	-1.1562936	0.88030431	1.27884347	1.75051382	1.02420042	0.3165159	0.2591068	0.1315126	0.1885705	0.0997433	**0.039525**
Klebsiella sp. 1_1_55	Enterobacteriaceae	0.02989509	0.07507473	0.05309373	0.04125968	0.03722769	0.13296059	0.06158525	0.76801794	1.14684394	1.18746896	0.57216851	0.70158713	1.9172284	1.04888581	0.2204946	0.1249514	0.1167594	0.28292	0.2407549	**0.0272097**
Escherichia coli 4_1_47FAA	Enterobacteriaceae	0.09509953	0.06760099	0.05836054	0.08911308	0.11194888	0.14868472	0.09513469	1.6292291	1.05256077	1.25930856	1.16518458	1.64963683	2.11681627	1.47883939	0.0510723	0.1454853	0.1032196	0.1212046	**0.0489298**	**0.0168467**
Enterococcus saccharolyticus 30_1	Enterococcaceae	-0.05876062	0.00068099	0.02582334	-0.01072223	-0.04758782	0.01197725	-0.01309818	-0.40292706	0.20834706	0.81549947	-0.07200973	-0.37487815	0.38157578	0.09260123	0.3430175	0.4172136	0.2066329	0.4712036	0.3534208	0.3509263
Erysipelotrichaceae bacterium 21_3	Erysipelotrichaceae	0.05805519	-0.03152714	-0.04359751	-0.06202173	-0.08440942	-0.09563974	0.04319006	1.13995039	-0.19796711	-0.13140452	-0.70773142	-0.84221214	-0.98441647	-0.28729688	0.1263803	0.4212827	0.4475581	0.2388395	0.1990666	0.1616674
Erysipelotrichaceae bacterium 6_1_45	Erysipelotrichaceae	-0.01935173	-0.01125356	-0.05658898	-0.05648575	-0.0160697	-0.04828234	-0.03467201	0.11757687	0.05778954	-0.30860887	-0.6391276	0.02514497	-0.38330474	-0.18842164	0.4530495	0.476883	0.3784266	0.2606922	0.4899369	0.3502834
Coprobacillus sp. 29_1	Erysipelotrichaceae	-0.03250709	0.08908349	0.10855487	0.07853584	0.0538944	0.0455075	0.05717817	-0.05617625	1.32356824	1.94396173	1.03410794	0.91311838	0.80717825	0.99429305	0.4775277	0.0921078	**0.0255699**	0.1497557	0.1798079	0.2090242
Coprobacillus sp. 8_2_54BFAA	Erysipelotrichaceae	-0.00409913	0.02972313	0.02931859	0.05498447	0.05343029	0.04772737	0.03518079	0.31902978	0.57472143	0.86317484	0.74225101	0.90722801	0.83535537	0.70696007	0.3744574	0.282106	0.1932475	0.2282348	0.1813617	0.2009927
Coprobacillus sp. 3_3_56FAA	Erysipelotrichaceae	-0.01020017	0.0498249	0.07344278	0.07675306	0.07721577	0.05901175	0.05434135	0.23844862	0.82831065	1.46503106	1.01201518	1.20910961	0.97558902	0.95525067	0.4054649	0.2029831	0.0708065	0.1549774	0.1125545	0.1631037
Coprobacillus sp. D7	Erysipelotrichaceae	-0.00741228	0.02268654	0.05642257	0.10168337	0.09984324	0.07510587	0.05499373	0.26560665	0.52378684	1.17026926	1.32205209	1.0692423	1.18287308	0.99076846	0.3937559	0.2996193	0.1183815	0.0919401	0.1417025	0.1176666
Eubacterium sp. 3_1_31	Eubacteriaceae	0.01063868	0.02275858	0.06327623	0.00316464	-0.02832739	0.09984741	0.02855969	0.51368365	0.48686172	-1.32635886	0.1000812	-0.13042776	1.49691981	0.63224625	0.3031509	0.3126155	0.0916461	0.4603103	0.4479457	0.0665739
Fusobacterium nucleatum subsp. animalis 11_3_2	Fusobacteriaceae	-0.21715882	-0.24234426	-0.29478901	-0.25408011	-0.0784896	-0.23060609	-0.21957798	-2.49501546	-2.85748166	-3.55766972	-3.08778714	-0.76707867	-2.69755643	-2.57709818	**0.0061546**	**0.0020732**	**0.000179**	**0.0009746**	0.2207741	**0.0034013**
Fusobacterium periodonticum 2_1_31	Fusobacteriaceae	-0.26263697	-0.26132927	-0.28183656	-0.21827452	-0.20310227	-0.21023252	-0.23956868	-3.09568087	-3.0969826	-3.38099752	-2.64407159	-2.34864325	-2.43895315	-2.8342215	**0.0009489**	**0.0009447**	**0.0003469**	**0.0039926**	**0.0092289**	**0.0072043**
Fusobacterium gonidiaformans 3-1-5R	Fusobacteriaceae	-0.06085785	-0.1365093	-0.22604735	-0.27278984	-0.10977813	-0.18818173	-0.16569403	-0.43062684	-1.52234522	-2.62002989	-3.3196448	-1.16418784	-2.1590605	-1.86931585	0.3328591	0.0633417	**0.0042871**	**0.0004335**	0.1214062	**0.0151516**
Fusobacterium nucleatum subsp. animalis 7_1	Fusobacteriaceae	-0.01776927	-0.07271052	-0.14341691	-0.15221809	-0.00997197	-0.16080324	-0.092815	0.13847761	-0.71750648	-1.49294637	-1.82547686	0.10253641	-1.81154279	-0.93440975	0.444753	0.2358095	0.0670904	**0.033518**	0.4590327	**0.0345739**
Fusobacterium periodonticum 1_1_41FAA	Fusobacteriaceae	-0.07611045	-0.08556763	0.11415684	-0.12397522	-0.09307029	-0.10919108	0.10034525	-0.63207974

Supplementary Table S5: Screened microbial virulence factors in genomes

Genera	Species	virulence factors	Genbank ID	Pubmed ID	Reference
Citrobacter	*C. freundii*	slt-IicA	X67514.1	8423084	Schmidt, H. et al. (1993) Infect. Immun. 61, 534–43.
		slt-IicB	X67515.1	8423084	Schmidt, H.et al. (1993) Infect. Immun. 61, 534–43.
	C. rodentium	Map	FN543502.1	16759225	Ma, C.et al. (2006) Cell. Microbiol. 8, 1669–86.
Shigella	*S. flexneri*	ShET2 enterotoxin	NC_002698.1	11292750	Venkatesan, M. et al. (2001) Infect. Immun. 69, 3271–85.
		VirG	NC_002698.1	11292750	Venkatesan, M. et al. (2001) Infect. Immun. 69, 3271–85.
		ShET1 enterotoxin	DM147453.1	23768555	Dutilh, B. E., Backus, L., van Hijum, S. A. F. T., and Tjalsma, H. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
	S.dysenteriae	stxA stxB	M19437.1	2830229	Strockbine, N. A., Jackson, M. P., Sung, L. M., Holmes, R. K., and O'Brien, A. D. (1988) J. Bacteriol. 170, 1116–22.
		tox1	AB035142.1	23768555	Dutilh, B. E. et al. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
		tox2	AB035143.1	23768555	Dutilh, B. E. et al. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
Salmonella	*S. enterica*	enterotoxin stn	JX293348.1	23768555	Dutilh, B. E. et al. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
	S.typhimurium	typhoid toxin	DQ823381.1	23842500	Song, J. et al. (2013) Nature 499, 350–4.
Escherichia	*E.coli*	Colibactin	AM229678.1	16902142	Nougayrède, J.-P.et al. (2006) Science 313, 848–51.
		cdt-III	U89305.1	9220015	Pérès, S. Y.et al. (1997) Mol. Microbiol. 24, 1095–107.
		CNF1 cytotoxin	NC_007946.1	16585510	Chen, S. L.et al. (2006) Proc. Natl. Acad. Sci. U. S. A. 103, 5977–82.
		CIF	AY128544.1	14651638	Marchès, O.et al. (2003) Mol. Microbiol. 50, 1553–67.
		Intimin	M58154.1	2172966	Jerse, A. E. et al. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 7839–43.
		enteroaggregative heat-stable enterotoxin 1 astA	L11241.1	8385356	Savarino, S. J.et al. (1993) Proc. Natl. Acad. Sci. U. S. A. 90, 3093–7.
		heat-labile enterotoxin LT1	A16419.1	15364995	Reischl, U.et al. (2004) J. Clin. Microbiol. 42, 4092–100.
		pTC plasmid toxin	AJ555214.1	23768555	Dutilh, B. E. et al. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
		heat-labile enterotoxin LT87	X83966.1	23768555	Dutilh, B. E. et al. (2013) Best Pract. Res. Clin. Gastroenterol. 27, 85–99.
		heat-stable ST	AY342058.1	15364995	Reischl, U.et al. (2004) J. Clin. Microbiol. 42, 4092–100.
		subA subB	FJ664545.1	19940059	Tozzoli, R.et al. (2010) J. Clin. Microbiol. 48, 178–83.
Bacteroides	*B. fragilis*	bft1	AB026625.1	10655354	Scotto d'Abusco, A. S.et al. (2000) J. Clin. Microbiol. 38, 607–12.
		bft2	AB026626.1	10655354	Scotto d'Abusco, A. S.et al. (2000) J. Clin. Microbiol. 38, 607–12.
		bft3	AB026624.1	10655354	Scotto d'Abusco, A. S.et al. (2000) J. Clin. Microbiol. 38, 607–12.
		bft Korea	AF081785.2	10655354	Scotto d'Abusco, A. S.et al. (2000) J. Clin. Microbiol. 38, 607–12.
Clostridium	*C. difficile*	tcDA	AY238985.1	14550648	Letourneur, O.et al. (2003) Protein Expr. Purif. 31, 276–85.
		tcDB	AY238986.1	14550648	Letourneur, O.et al. (2003) Protein Expr. Purif. 31, 276–85.
	C. perfingens	enterotoxin cpe	U11259.1	7960138	Ladero, V.et al. (2013) Genome Announc. 1.
	C. botulinum	BtA (C2-toxin)	AJ224480.1	11741886	Barth, H. et al. (2002) J. Biol. Chem. 277, 5074–81.
	C. septicum	α-toxin	AY589051.1	16102005	Kennedy, C. L.et al. (2005) Mol. Microbiol. 57, 1357–66.
Fusobacterium	*F. nucleatum*	FadA	AY850357.1	16030227	Han, Y. W. et al. (2005)J. Bacteriol. 187, 5330–40.
Enterococcus	*E. faecalis*	Cytolysin	L37110.1	23628786	Van Tyne, D. et al.(2013) Toxins (Basel). 5, 895–911.
	E. faecium	Enterotoxin	NZ_LKPH01000073	24316578	Tatusova, T. et al. (2014) Nucleic Acids Res. 42, D553-9.
	E. durans	labile enterotoxin output A	NZ_AOSM0100009	23682153	Ladero, V. et al. (2013) Genome Announc. 1.

Supplementary Table S6: correlation of growth rates between bacterial cells and secretomes

Bacterial family	Cell line	R2	P-value	Benjamini-Hochberg adjusted P-value
Bacteroidaceae	HEK293T	0,36991	2,00E-05	0,00048
	HCT15	0,07469	0,08383	0,30953
	Caco2	0,04151	0,20137	0,43935
	HCT116	0,38997	1,00E-05	0,00048
	SW480	0,10675	0,03707	0,19771
	HT29	0,21012	0,00258	0,03096
Enterobacteriaceae	HEK293T	0,05259	0,41099	0,58022
	HCT15	0,00013	0,96774	0,98833
	Caco2	0,15732	0,14326	0,38203
	HCT116	0,74442	3,00E-05	0,00048
	SW480	0,00024	0,95618	0,99775
	HT29	0,191	0,10333	0,35427
Erysipelotrichaceae	HEK293T	0,80678	0,01501	0,1441
	HCT15	6,00E-05	0,98846	0,98846
	Caco2	0,65394	0,05141	0,22433
	HCT116	0,29054	0,26978	0,46248
	SW480	0,35235	0,21419	0,42838
	HT29	0,29737	0,26311	0,46775
Fusobacteriaceae	HEK293T	0,00822	0,73838	0,86444
	HCT15	0,00477	0,7994	0,9136
	Caco2	0,13257	0,16562	0,41841
	HCT116	0,03511	0,48709	0,6319
	SW480	0,05401	0,38639	0,59828
	HT29	0,01296	0,67465	0,80958
Lachnospiraceae	HEK293T	0,48532	0,01722	0,13776
	HCT15	0,00069	0,93869	1,00127
	Caco2	0,00094	0,92878	1,01321
	HCT116	0,06767	0,43981	0,58641
	SW480	0,12644	0,28318	0,46871
	HT29	0,22901	0,13647	0,38533
Streptococcaceae	HEK293T	0,02475	0,398	0,57891
	HCT15	0,16228	0,02464	0,16896
	Caco2	0,02491	0,39643	0,59465
	HCT116	0,02307	0,41466	0,56868
	SW480	0,08477	0,11204	0,33612
	HT29	0,11354	0,06379	0,25516
Tannerellaceae	HEK293T	0,83684	0,02947	0,17682
	HCT15	0,48796	0,18945	0,43303
	Caco2	0,34303	0,29944	0,4791
	HCT116	0,76745	0,0514	0,24672
	SW480	0,00314	0,92867	1,03665
	HT29	0,43883	0,22312	0,41191
others	HEK293T	0,02778	0,52259	0,66011
	HCT15	0,10305	0,20899	0,43615
	Caco2	0,02479	0,54619	0,67223
	HCT116	0,11267	0,18778	0,45067
	SW480	0,16597	0,10457	0,33462
	HT29	0,09869	0,21945	0,42134

Supplementary Table S7: Significance of family-specific clustering

Bacterial family	Bacterial Secretomes		Bacterial Cells	
	clustering p-value	B-H adjusted p-value	clustering p-value	B-H adjusted p-value
Bacteroidaceae	**0,047**	9,40E-02	**3,03E-06**	**1,06E-05**
Clostridiaceae	0,806	1	NA	NA
Enterobacteriaceae	0,178	2,85E-01	**1,62E-05**	**2,84E-05**
Erysipelotrichaceae	0,941	1	**0,006**	**8,40E-03**
Fusobacteriaceae	**0,009**	**2,40E-02**	**8,40E-06**	**1,96E-05**
Lachnospiraceae	**0,003**	**1,20E-02**	0,104	1,21E-01
Streptococcaceae	**3,24E-27**	**2,59E-26**	**5,35E-25**	**3,75E-24**
Tannerellaceae	1	1	0,883	8,83E-01

Reported p-values are derived from Fischer's exact test evaluating the likelihood that the strains from a family are nearest neighbors, compared to a random sampling with replacement of the same size. P-values reported are the harmonic mean of 103 iterations. For this calculation, only strains from families with more than four representatives were considered.

Supplementary Table S8: correlation between phylogentic distance and pairwise eucladian distance of growth rate changes

Bacterial family	Bacterial cells		Bacterial secretomes	
	Pearson R	P-value	Pearson R	P-value
Bacteroidaceae	-0,05729	0,0808	-0,05117	0,1189
Clostridiaceae			0,03481	0,8842
Enterobacteriaceae	-0,05052	0,6002	0,10128	0,2924
Erysipelotrichaceae	**0,53025**	**0,0026**	**0,96029**	**0,0000**
Fusobacteriaceae	**0,44857**	**0,0000**	-0,02809	0,6650
Lachnospiraceae	-0,03352	0,7281	**0,39881**	**0,0000**
Tannerellaceae	-0,18133	0,4442	-0,17130	0,4702

Correlation between the pairwise phylogenetic distance and and the pairwise euclidean distance of the effects of bacterial cells and secretomes on the growth rate of of six cell lines

Supplementary Table S9: Distribution of toxins in bacterial genomes

Bacterial strain	Bacterial family	Gene
Bacteroides fragilis K570 clinda R (ETBF)	Bacteroidaceae	BFT
Bacteroides fragilis VPI clinda R (ETBF)	Bacteroidaceae	BFT
Bacteroides fragilis 86-5443-2-2 (ETBF)	Bacteroidaceae	BFT
Bacteroides fragilis 9343 delta cap	Bacteroidaceae	
Bacteroides fragilis 3_1_12	Bacteroidaceae	
Bacteroides fragilis 9343 delta cap delta pilus 77	Bacteroidaceae	
Bacteroides fragilis 9343 delta tsr 15 M4	Bacteroidaceae	
Bacteroides fragilis NCTC 9343 (NTBF)	Bacteroidaceae	
Citrobacter freundii 4_7_47CFAA	Enterobacteriaceae	Map
Citrobacter sp. 30_2	Enterobacteriaceae	Map
Klebsiella sp. 1_1_55	Enterobacteriaceae	Map
Klebsiella sp. 4_1_44FAA	Enterobacteriaceae	Map
Escherichia coli DH5 alpha pks	Enterobacteriaceae	pks
Escherichia coli NC101	Enterobacteriaceae	pks, ShEt1
Escherichia coli Nissle 1917	Enterobacteriaceae	pks, ShEt1
Escherichia sp. 3_2_53FAA	Enterobacteriaceae	pks, Stx2A
Escherichia coli NC101 delta pks	Enterobacteriaceae	ShEt1
Escherichia sp. 4_1_40B	Enterobacteriaceae	ShEt1, Stx2A
Enterobacteriaceae bacterium 9_2_54FAA	Enterobacteriaceae	
Escherichia coli 4_1_47FAA	Enterobacteriaceae	
Escherichia coli D9	Enterobacteriaceae	
Escherichia sp. 1_1_43	Enterobacteriaceae	
Fusobacterium nucleatum subsp. animalis 11_3_2	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. animalis 21_1A	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. animalis 3_1_33	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. animalis 7_1	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. animalis D11	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. Nucleatum ATCC 25586	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. Polymorphum ATCC 10953	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. vincentii 3_1_36A2	Fusobacteriaceae	FadA
Fusobacterium nucleatum subsp. vincentii 4_1_13	Fusobacteriaceae	FadA
Fusobacterium periodonticum 1_1_41FAA	Fusobacteriaceae	FadA
Fusobacterium periodonticum 2_1_31	Fusobacteriaceae	FadA
Fusobacterium gonidiaformans 3-1-5R	Fusobacteriaceae	
Fusobacterium necrophorum D12	Fusobacteriaceae	
Fusobacterium necrophorum subsp. funduliforme 1_1_36S	Fusobacteriaceae	
Fusobacterium nucleatum subsp. vincentii 3_1_27	Fusobacteriaceae	
Fusobacterium ulcerans 12-1B	Fusobacteriaceae	
Clostridium hathewayi WAL-18680	Clostridiales	TcdA
Clostridium sp. 7_3_54FAA	Clostridiales	TcdA
Clostridium clostridioforme 2_1_49FAA	Clostridiales	TcdA
Clostridium perfringens WAL-14572	Clostridiales	TcdA
Clostridium symbiosum WAL-14163	Clostridiales	TcdA
Clostridium symbiosum WAL-14673	Clostridiales	TcdA
Clostridium sp. 7_2_43FAA	Clostridiales	
Clostridium sp. D5	Clostridiales	

Supplementary Table S10: Functional genomic terms significantly associated to growth rate scores within bacterial families

functional term	level	cell	effect	experiment type	family	Adjusted p-values
Multi-subunit cation antiporter	Subsystem	HCT116	enhancing	secretomes	Clostridiaceae	0,015602743
Flagellum	Subsystem	HEK293T	inhibiting	cells	Enterobacteriaceae	0,016628384
Flagellum	Subsystem	Caco2	enhancing	cells	Enterobacteriaceae	0,029933622
Flagellum	Subsystem	HCT15	enhancing	cells	Enterobacteriaceae	1,30E-05
Cell Envelope	SuperClass	HCT116	inhibiting	secretomes	Bacteroidaceae	0,005184393
Cell Envelope	SuperClass	Caco2	enhancing	cells	Bacteroidaceae	0,018445869
Cell Envelope	SuperClass	Caco2	enhancing	cells	Enterobacteriaceae	0,002175021
Cell Envelope	SuperClass	SW480	enhancing	cells	Enterobacteriaceae	0,033695227
Cell Envelope	SuperClass	HCT15	enhancing	cells	Enterobacteriaceae	0,002765181
Glycerol fermentation to 1,3-propanediol	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,016986143
Phenylacetyl-CoA catabolic pathway (core)	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,000430919
Phenylacetyl-CoA catabolic pathway (core)	Subsystem	Caco2	enhancing	cells	Enterobacteriaceae	0,029933622
L-fucose dissimilation cluster	Subsystem	HEK293T	enhancing	secretomes	Clostridiaceae	0,015596175
Autoinducer 2 (AI-2) transport and processing (lsrACDBFGE operon)	Subsystem	Caco2	enhancing	secretomes	Enterobacteriaceae	1,37E-07
Cobalamin synthesis	Subsystem	HCT15	enhancing	secretomes	Bacteroidaceae	0,00327217
Cobalamin synthesis	Subsystem	HT29	enhancing	cells	Bacteroidaceae	0,024730743
Cobalamin synthesis	Subsystem	SW480	enhancing	cells	Bacteroidaceae	0,004290681
Cobalamin synthesis	Subsystem	HCT15	enhancing	cells	Bacteroidaceae	0,004322283
Cobalamin synthesis	Subsystem	HEK293T	enhancing	cells	Bacteroidaceae	0,006420869
Cobalamin synthesis	Subsystem	HCT116	enhancing	cells	Bacteroidaceae	0,000885398
Cobalamin synthesis	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,006127826
Cobalamin synthesis	Subsystem	Caco2	enhancing	cells	Enterobacteriaceae	0,029933622
Metabolism	SuperClass	SW480	inhibiting	secretomes	Enterobacteriaceae	0,039429132
Metabolism	SuperClass	Caco2	enhancing	cells	Enterobacteriaceae	0,00083275
Metabolism	SuperClass	SW480	inhibiting	cells	Enterobacteriaceae	0,036397619
Metabolism	SuperClass	HT29	inhibiting	cells	Enterobacteriaceae	0,02019638
Metabolism	SuperClass	SW480	enhancing	cells	Enterobacteriaceae	0,000130798
Metabolism	SuperClass	HCT15	enhancing	cells	Enterobacteriaceae	0,002765181
Ethanolamine utilization	Subsystem	HT29	inhibiting	secretomes	Clostridiaceae	5,04E-05
Ethanolamine utilization	Subsystem	HT29	inhibiting	cells	Fusobacteriaceae	0,024990067
Ethanolamine utilization	Subsystem	HCT15	inhibiting	cells	Fusobacteriaceae	0,022004459
Ethanolamine utilization	Subsystem	SW480	inhibiting	cells	Fusobacteriaceae	0,042265856
Ethanolamine utilization	Subsystem	HCT116	inhibiting	cells	Fusobacteriaceae	0,02504088
Histidine Degradation	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,045251785
Membrane Transport	SuperClass	Caco2	inhibiting	secretomes	Enterobacteriaceae	0,007575454
Membrane Transport	SuperClass	HEK293T	enhancing	secretomes	Enterobacteriaceae	0,03671857
Membrane Transport	SuperClass	HEK293T	inhibiting	secretomes	Enterobacteriaceae	0,03739392
Membrane Transport	SuperClass	HCT15	inhibiting	secretomes	Enterobacteriaceae	0,020242991
Membrane Transport	SuperClass	HCT116	inhibiting	secretomes	Enterobacteriaceae	0,027083664
Membrane Transport	SuperClass	SW480	inhibiting	secretomes	Enterobacteriaceae	6,35E-05
Membrane Transport	SuperClass	HT29	inhibiting	secretomes	Enterobacteriaceae	0,030080704
Membrane Transport	SuperClass	SW480	inhibiting	cells	Enterobacteriaceae	1,06E-05
Membrane Transport	SuperClass	HT29	inhibiting	cells	Enterobacteriaceae	2,27E-05
Membrane Transport	SuperClass	SW480	enhancing	cells	Enterobacteriaceae	0,001357179
Membrane Transport	SuperClass	HCT116	inhibiting	cells	Enterobacteriaceae	0,033516935
Membrane Transport	Products	HEK293T	enhancing	secretomes	Fusobacteriaceae	0,014422697
Membrane Transport	SuperClass	HEK293T	enhancing	secretomes	Fusobacteriaceae	0,017505156
Hyaluronate utilization	Subsystem	HCT15	enhancing	secretomes	Lachnospiraceae	0,033361224
D-threonate, L-threonate and D-erythronate utilization	Subsystem	HEK293T	inhibiting	secretomes	Enterobacteriaceae	0,010116446
Urea carboxylase and Allophanate hydrolase cluster	Subsystem	SW480	enhancing	secretomes	Enterobacteriaceae	0,000222083
Urea carboxylase and Allophanate hydrolase cluster	Subsystem	HT29	enhancing	cells	Enterobacteriaceae	2,43E-05
Urea carboxylase and Allophanate hydrolase cluster	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,016986143
Homoprotocatechuate degradative cluster	Subsystem	Caco2	enhancing	secretomes	Enterobacteriaceae	9,80E-08
Urease subunits	Subsystem	SW480	enhancing	cells	Enterobacteriaceae	0,003243115
Dpp dipeptide ABC transport system	Subsystem	SW480	enhancing	secretomes	Enterobacteriaceae	4,15E-05
Dpp dipeptide ABC transport system	Subsystem	HEK293T	enhancing	secretomes	Enterobacteriaceae	5,23E-06
Dpp dipeptide ABC transport system	Subsystem	HEK293T	enhancing	cells	Enterobacteriaceae	3,17E-06
Dpp dipeptide ABC transport system	Subsystem	HCT15	inhibiting	cells	Enterobacteriaceae	8,04E-06
Dpp dipeptide ABC transport system	Subsystem	HEK293T	enhancing	secretomes	Fusobacteriaceae	0,020180097
Riboflavin, FMN and FAD metabolism with fusion events	Subsystem	HT29	inhibiting	secretomes	Clostridiaceae	0,022400659
Riboflavin, FMN and FAD metabolism with fusion events	Subsystem	Caco2	inhibiting	cells	Erysipelotrichaceae	0,028588475
Arsenic resistance	Subsystem	HCT15	enhancing	secretomes	Bacteroidaceae	0,026841657
Cellular Processes	SuperClass	Caco2	enhancing	secretomes	Enterobacteriaceae	0,00481013
Cellular Processes	SuperClass	Caco2	enhancing	cells	Enterobacteriaceae	0,000932912
Cellular Processes	SuperClass	HEK293T	inhibiting	cells	Enterobacteriaceae	0,009543743
Cellular Processes	SuperClass	SW480	enhancing	cells	Enterobacteriaceae	0,008160047
Cellular Processes	SuperClass	HCT15	enhancing	cells	Enterobacteriaceae	0,016574654
Type 4 secretion and conjugative transfer	Subsystem	SW480	inhibiting	cells	Enterobacteriaceae	0
Type 4 secretion and conjugative transfer	Subsystem	HT29	inhibiting	cells	Enterobacteriaceae	0
Tricarballylate Utilization	Subsystem	SW480	enhancing	secretomes	Enterobacteriaceae	0,025496186
Tricarballylate Utilization	Subsystem	HT29	enhancing	cells	Enterobacteriaceae	0,012769654
Protein Processing	SuperClass	SW480	inhibiting	cells	Lachnospiraceae	0,008353249

Protein Processing	Products	HT29	enhancing	cells	Lachnospiraceae	0,047863977
Protein Processing	Products	SW480	inhibiting	cells	Lachnospiraceae	0,00672378
Energy	SuperClass	HCT15	enhancing	secretomes	Bacteroidaceae	0,042758192
Energy	SuperClass	HEK293T	enhancing	cells	Bacteroidaceae	0,044418417
Energy	SuperClass	HEK293T	inhibiting	cells	Enterobacteriaceae	0,016889509
Energy	SuperClass	HCT15	enhancing	cells	Enterobacteriaceae	0,032209953
Stress Response, Defense, Virulence	SuperClass	HCT15	enhancing	secretomes	Bacteroidaceae	0,023574463
Stress Response, Defense, Virulence	SuperClass	SW480	enhancing	secretomes	Bacteroidaceae	0,014792296
Listeria Pathogenicity Island LIPI-1 extended	Subsystem	SW480	enhancing	secretomes	Bacteroidaceae	0,045449008
Miscellaneous	SuperClass	HCT15	enhancing	secretomes	Bacteroidaceae	0,042758192
Miscellaneous	SuperClass	HEK293T	inhibiting	secretomes	Bacteroidaceae	0,013348729
Miscellaneous	SuperClass	HEK293T	enhancing	secretomes	Bacteroidaceae	0,043760887
Miscellaneous	SuperClass	SW480	enhancing	secretomes	Bacteroidaceae	0,02678131
Branched-Chain Amino Acid Biosynthesis	Subsystem	HEK293T	inhibiting	secretomes	Fusobacteriaceae	0,00125237
Branched-Chain Amino Acid Biosynthesis	Subsystem	SW480	inhibiting	secretomes	Fusobacteriaceae	0,001667137
Histidine Biosynthesis	Subsystem	HCT116	enhancing	secretomes	Clostridiaceae	0,007312145
Glutamate fermentation	Subsystem	SW480	enhancing	secretomes	Enterobacteriaceae	0,001367254
Glutamate fermentation	Subsystem	HEK293T	enhancing	secretomes	Enterobacteriaceae	0,000995688
Glutamate fermentation	Subsystem	HEK293T	enhancing	cells	Enterobacteriaceae	0,000664067
Glutamate fermentation	Subsystem	HCT15	inhibiting	cells	Enterobacteriaceae	0,000376733
Inositol catabolism	Subsystem	HEK293T	enhancing	secretomes	Clostridiaceae	0,002311461
Vir-like type 4 secretion system	Subsystem	Caco2	inhibiting	secretomes	Enterobacteriaceae	9,44E-05
Vir-like type 4 secretion system	Subsystem	HCT15	inhibiting	secretomes	Enterobacteriaceae	4,66E-06
Vir-like type 4 secretion system	Subsystem	SW480	inhibiting	secretomes	Enterobacteriaceae	0,006015428
Vir-like type 4 secretion system	Subsystem	HCT116	inhibiting	secretomes	Enterobacteriaceae	1,14E-05
Vir-like type 4 secretion system	Subsystem	HT29	inhibiting	secretomes	Enterobacteriaceae	3,86E-06
Vir-like type 4 secretion system	Subsystem	HCT116	inhibiting	cells	Enterobacteriaceae	1,03E-05
High affinity phosphate transporter and control of PHO regulon	Subsystem	SW480	enhancing	secretomes	Fusobacteriaceae	0,001624476
High affinity phosphate transporter and control of PHO regulon	Subsystem	Caco2	enhancing	secretomes	Fusobacteriaceae	0,000751743
Tryptophan synthesis	Subsystem	HCT15	inhibiting	cells	Lachnospiraceae	0,022298862
Na-driven 2-hydroxyglutarate pathway	Subsystem	Caco2	inhibiting	secretomes	Lachnospiraceae	0,037556695