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(73) Patenthaver: **Vedanta Biosciences, Inc., 19 Blackstone Street, Cambridge, MA 02139, USA**

(72) Opfinder: **KIM, Yun-Gi, 77 Waverley Avenue, Watertown, MA 02472, USA**
OLLE, Bernat, 68 Brookline Street, Apt. 104, Cambridge, MA 02139, USA
REDDY, Shilpa, 375 Mt Auburn Street, Apt. 2R, Watertown, MA 02472, USA
NORMAN, Jason, 179 Norton Street, North Weymouth, MA 02191, USA
PATARROYO, Juan, 1073 Massachusetts Avenue, Lexington, MA 02420, USA
SCHNEIDER, Jessica, 10 Rogers Street, Unit 506, Cambridge, MA 02142, USA

(74) Fuldmægtig i Danmark: **Plougmann Vingtoft A/S, Strandvejen 70, 2900 Hellerup, Danmark**

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DESCRIPTION

FIELD OF INVENTION

[0001] The disclosure relates to compositions of purified bacterial strains, and treatments of pathogenic infections, such as *Clostridium difficile* infections, by administering the compositions to a subject having a pathogenic infection.

BACKGROUND OF THE INVENTION

[0002] The collection of bacterial, viral, and fungal commensal microorganisms that reside within and on the human body are collectively known as the human microbiome. The bacterial subset of the human microbiome plays an important role in host nutrient acquisition, development, immunological homeostasis, neurological health, and protection against pathogens (LeBlanc et al. Curr. Opin. Biotechnol. (2013) 24(2): 160-168; Hooper et al. Science (2012) 336(6086): 1268-1273; Hughes et al. Am. J. Gastroenterol. (2013) 108(7): 1066-1074). As the largest reservoir of mammalian commensals, bacteria residing in the gastrointestinal (GI) tract influence nearly all of these aspects of human biology (Blaser J. Clin. Invest. (2014) 124(10): 4162-4165). Consequently, perturbation of the normal bacterial populations within the GI niche, a state known as dysbiosis, can predispose humans to a variety of diseases.

[0003] *Clostridium difficile* infection (CDI) arises after intestinal colonization by the anaerobic spore-forming Gram-positive pathogen *Clostridium difficile*. Upon colonization of the GI tract, *C. difficile* produces toxins which causes diarrhea and may ultimately lead to death. This illness is the most common identifiable cause of nosocomial diarrhea and is thought to arise as a direct result of dysbiosis (Calfee Geriatrics (2008) 63: 10-21; Shannon-Lowe et al BMJ (2010) 340: c1296). Not surprisingly, usage of nearly all classes of antibiotics has been associated with CDI, presumably by inducing dysbiosis in the GI tract and thereby enabling C. *difficile* outgrowth. The Center for Disease Control currently classifies CDI as a public health threat requiring immediate and aggressive action because of its natural resistance to many drugs and the emergence of a fluoroquinolone-resistant strain that is now prevalent throughout North America and Europe. *C. difficile* was responsible for almost half a million infections and was associated with approximately 29,000 deaths in 201 1 (Lessa et al. NEJM 2015, 372: 825-834).

[0004] The antibiotics metronidazole, vancomycin, and fidaxomicin are the current therapeutic options for treatment of CDI. However, metronidazole is inadequate because of decreased response rates and neither metronidazole nor vancomycin prevent disease recurrence, with up to 30% of patients initially responding experiencing a clinical recurrence after antibiotic cessation (Miller Expert Opin. Pharmacother. (2010) 11: 1569-1578). Fidaxomicin has been shown to be superior to vancomycin in preventing recurrent CDI (Mullane Ther. Adv. Chronic Dis. (2014) 5(2): 69-84). Because of its narrow spectrum of activity, fidaxomicin is thought to enable normal microbiome repopulation of the gut following dysbiosis and CDI, thereby lowering the likelihood of recurrent disease (Tannock et al. Microbiology (2010) 156 (Pt 11): 3354-3359; Louie et al. Clin. Infect. Dis. (2012) 55 Suppl. 2: S132-142). Nonetheless, 14% of fidaxomicin-treated patients experience CDI relapse and mutations conferring reduced sensitivity have already been reported (Eyre et al. J. Infect. Dis. (2014) 209(9): 1446-1451).

[0005] Because the risk of recurrent CDI is heightened by antibiotic use and C. *difficile* spores are inherently recalcitrant to the available chemotherapeutic arsenal, alternative therapeutic modalities are being pursued for the treatment of CDI. Fecal microbiota transplantation (FMT) is one such modality that has shown efficacy against CDI (Khoruts et al. Immunol. Lett. (2014) 162(2): 77-81; van Nood et al. N. Engl. J. Med. (2013) 368(5): 407-415). To date, results of FMT studies for the treatment of CDI, have reported cure rates up to 90% in three randomized controlled studies (Cammarota et al. Alimen. Pharmacol. Therap. (2015) 41(9): 835-843; Kassam et al. Am. J. Gastroenterol. (2013) 108(4): 500-508; van Nood et al. N. Engl. J. Med. (2013) 368(5): 407-415; Youngster et al. Infec. Dis. Soc. Am. (2014) 58(11): 1515-1522).

[0006] Despite the success of FMT, this therapeutic approach is not without risks and logistical concerns. Selection of FMT donors is critical and challenging. When FMT donor recruitment is performed with stringent screening and standardization protocols, most prospective donors fail this process. Only 6-10% of prospective FMT donors qualify, with the majority of failures arising from asymptomatic carriage of GI pathogens (Paramsothy et al. Inflamm. Bowel Dis. (2015) 21(7): 1600-1606; Borody et al. Curr. Opin. Gastroenterol. (2014) 30(10): 97-105; Burns et al. Gastroenterology (2015) 148: S96-S97; Surawicz Ann. Intern. Med. (2015) 162(9): 662-663). Furthermore, variation between donors may lead to variation in FMT efficacy. In addition, the risk of transmission of even non-infectious illnesses may be heightened by FMT. Indeed, significant weight gain has been reported in a patient who received an FMT from an overweight stool donor (Alang et al. Open Forum Infect. Dis. (Winter 2015) 2(1)).

[0007] Narushima et al., 2014. Gut Microbes. 5(3):333-9 discloses a composition of 17 strains which corresponds to "Composition E" of the present disclosure.

[0008] Bucci et al., 2016. Genome Biol. 17(1):121 states that it presents MDSINE, a suite of algorithms for inferring dynamical systems models from microbiome time-series data and predicting temporal behaviors.

SUMMARY OF THE INVENTION

[0009] The present invention provides a composition comprising eight purified bacterial strains of species *Flavonifractor plautii, Anaerotruncus colihominis, Drancourtella massiliensis, Clostridium symbiosum*, *Clostridium bolteae*, *Dorea longicatena*, *Blautia producta*, and *Clostridium innocuum*.

[0010] The present invention also provides a composition comprising eight purified bacterial strains comprising 16S rDNA sequences having at least 97% sequence identity to SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO:20, and SEQ ID NO:21.

[0011] In some embodiments of the compositions provided herein, the composition comprises at least one bacterial strain from Clostridium cluster XIVa and at least one bacterial strain from Clostridium cluster XVII. In some embodiments of the compositions provided herein, the composition comprises at least one bacterial strain from Clostridium cluster IV and at least one bacterial strain from Clostridium cluster XVII. In some embodiments of the compositions provided herein, the composition comprises at least one bacterial strain from Clostridium cluster XIVa, at least one strain from Clostridium cluster IV and at least one bacterial strain from Clostridium cluster XVII. In some embodiments of the compositions provided herein, the composition does not include *Clostridium scindens*.

[0012] In some embodiments of the compositions provided herein, one or more of the bacterial strains are spore formers. In some embodiments of the compositions provided herein, one or more of the bacterial strains are in spore form. In some embodiments of the compositions provided herein, each of the bacterial strains is in spore form.

[0013] In some embodiments of the compositions provided herein, one or more of the bacterial strains is in vegetative form. In some embodiments of the compositions provided herein, each of the bacterial strains is in vegetative form.

[0014] In some embodiments of the compositions provided herein, the composition comprises only obligate anaerobic bacterial strains. In some embodiments of the compositions provided herein, the composition comprises bacterial strains that originate from more than one human donor.

[0015] In some embodiments of the compositions provided herein, one or more of the bacterial strains are *baiCD*-. In some embodiments of the compositions provided herein, each of the bacterial strains is *baiCD*-. In some embodiments of the compositions provided herein, the composition does not mediate bile acid 7-alpha-

dehydroxylation. In some embodiments of the compositions provided herein, the composition inhibits *C. difficile* toxin production. In some embodiments of the compositions provided herein, the composition inhibits *C. difficile* replication and/or survival.

[0016] In some embodiments of the compositions provided herein, the bacterial strains are lyophilized.

[0017] In some embodiments of the compositions provided herein, the composition induces the proliferation and/or accumulation of regulatory T cells (Tregs).

[0018] In one aspect, the composition comprises at least one bacterial strain from Clostridium cluster XIVa and at least one bacterial strain from Clostridium cluster XVII. In one aspect, the composition comprises at least one bacterial strain from Clostridium cluster IV and at least one bacterial strain from Clostridium cluster XVII. In one aspect, the composition comprises at least one bacterial strain from Clostridium cluster IV, at least one bacterial strain from Clostridium cluster XIVa and at least one bacterial strain from Clostridium cluster XVII. In some embodiments of the compositions provided herein, the composition does not include *Clostridium scindens*.

[0019] In some embodiments of the compositions provided herein, one or more of the bacterial strains are spore formers. In some embodiments of the compositions provided herein, one or more of the bacterial strains are in spore form. In some embodiments of the compositions provided herein, each of the bacterial strains is in spore form.

[0020] In some embodiments of the compositions provided herein, one or more of the bacterial strains is in vegetative form. In some embodiments of the compositions provided herein, each of the bacterial strains is in vegetative form.

[0021] In some embodiments of the compositions provided herein, the composition comprises only obligate anaerobic bacterial strains.

[0022] In some embodiments of the compositions provided herein, the composition comprises bacterial strains that originate from more than one human donor.

[0023] In some embodiments of the compositions provided herein, one or more of the bacterial strains are *baiCD-*. In some embodiments of the compositions provided herein, each of the bacterial strains is *baiCD-*. In some embodiments of the compositions provided herein, the composition does not mediate bile acid 7-alpha-dehydroxylation. In some embodiments of the compositions provided herein, the composition inhibits C. *difficile* toxin production.. In some embodiments of the compositions provided herein, the composition inhibits C. *difficile* replication and/or survival.

[0024] In some embodiments of the compositions provided herein, the bacterial strains are lyophilized.

[0025] In some embodiments of the compositions provided herein, the composition induces the proliferation and/or accumulation of regulatory T cells (Tregs).

[0026] In one aspect, the disclosure provides a pharmaceutical composition comprising any of the compositions provided herein further comprising a pharmaceutically acceptable excipient. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for oral delivery. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for rectal delivery. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for delivery to the intestine. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for delivery to the colon. In one aspect, the disclosure provides a food product comprising any of the compositions provided herein further comprising a nutrient.

[0027] In one aspect, a pathogenic infection is treated by administering to the subject a therapeutically effective amount of any of the compositions or food products provided herein.

[0028] In some embodiments, the pathogenic infection is *C. difficile,* Vancomycin Resistant *Enterococci* (VRE), Carbapenem Resistant *Enterobacteriaceae* (CRE), *Neisseria gonorrheae,* Multidrug Resistant *Acinetobacter*, *Campylobacter*, Extended spectrum beta-lactamese (ESBL) producing Enterobacteriaceae, Multidrug Resistant *Pseudomonas aeruginosa*, *Salmonella*, Drug resistant non-typhoid *Salmonella*, Drug resistant *Salmonella Typhi*, Drug resistant *Shigella*, Methicillin Resistant *Staphylococcus aureus*, Drug resistant *Streptococcus pneumoniae*, Drug resistant Tuberculosis, Vancomycin resistant *Staphylococcus aureus*, Erythromycin Resistant Group A *Streptococcus*, Clindamycin resistant Group B *Streptococcus*, and combinations thereof. In some embodiments, the pathogenic infection is *C. difficile*. In some embodiments the pathogenic infection is Vancomycin-Resistant *Enterococci.*

[0029] In some embodiments, the subject is human. In some embodiments, the subject is an asymptotic carrier.

[0030] In some embodiments, the subject is administered a dose of an antibiotic prior to administration of the composition. In some embodiments, the subject is administered more than one dose of the antibiotic prior to administration of the composition. In some embodiments, herein, the subject has not been administered an antibiotic prior to administration of the composition.

[0031] In some embodiments, the composition is administered to the subject by oral administration. In some embodiments, the composition is administered to the subject by rectal administration. In some embodiments, the administering results in proliferation and/or accumulation of regulatory T cells (Tregs).

BRIEF DESCRIPTION OF THE DRAWINGS

[0032] The accompanying drawings are not intended to be drawn to scale. The figures are illustrative only and are not required for enablement of the disclosure. For purposes of clarity, not every component may be labeled in every drawing. In the drawings:

Figure 1 shows the strains of Compositions A-D. Each entry includes the SEQ ID NO of the 16S rDNA sequence of the strain, a strain identifier, and the species with the closest known homology (can be more than one species). The bracketed roman numeral indicates the *Clostridium* cluster classification of each strain based on the closest species homology. Strains that are not classified in Cluster XIVa are highlighted in bold. The two nonclostridial strains (SEQ ID NO:2, closest known species *Turicibacter sanguinis*, and SEQ ID NO:6, closest known species *Lactobacillus mucosae*) do not belong to the *Clostridium* genus.

Figure 2 shows various *Clostridium difficile* infection models. Timelines indicate antibiotic type, duration of treatment, as well as exposure to *C. difficile* spores. The top panel shows an antibiotic cocktail treatment model in which the antibiotic cocktail is provided in the drinking water from day -10 to day -3 followed by intraperitoneal clindamycin on day -1. The middle panel shows a clindamycin IP injection model, in which clindamycin is administered by intraperitoneal injection on day -1. The bottom panel shows the cefoperazone treatment model, in which cefoperazone is provided in the drinking water from day -12 to day -2, followed by administration of a live biotherapeutic product (LBP) on day - 1.

Figure 3 shows the experimental conditions described in Example 1. The groups of mice were divided based on the antibiotic regimen received prior to administration of the indicated amount of *C. difficile* spores. "Abx" refers to treatment with any of the antibiotic regimens.

Figures 4A-4L show data obtained in Example 1. Figures 4A-4D show survival of mice that received no treatment (Figure 4A), antibiotic cocktail (Figure 4B), clindamycin (Figure 4C), or cefoperazone (Figure 4D) prior to *C. difficile* infection. Figures 4E-4H show body weight of mice that received no treatment (Figure 4E), antibiotic cocktail (Figure 4F), clindamycin (Figure 4G), or cefoperazone (Figure 4H) prior to *C. difficile* infection. Figures 4I-4L show *C. difficile* burden (CFU) per gram of feces from mice that

received no treatment (Figure 4I), antibiotic cocktail (Figure 4J), clindamycin (Figure 4K), or cefoperazone (Figure 4L) prior to *C. difficile* infection. Open circles indicate infection with 10 *C. difficile* spores; closed squares indicate infection with 10,000 *C. difficile* spores. Black triangles in Figure 4J indicate an additional experimental arm in which mice were treated with vancomycin following C. *difficile* infection.

Figure 5 shows experimental conditions evaluated in Example 2, the results for which are presented in Figures 7-9. Composition E corresponds to a mixture of 17 bacterial strains (See *e.g.,* Narushima et al., Gut Microbes 5: 3, 333-339). Composition I corresponds to a mixture of *Clostridium scindens*, *Pseudoflavonifractor capillosus*, and *Blautia hansenii*. "Abx" refers to treatment with any of the antibiotic regimens.

Figure 6 shows survival of mice over time post infection with *C. difficile* spores, according to the experimental conditions shown in Figure 5. Mice losing >20% body weight of baseline were included in mortality numbers in survival curves.

Figures 7A-7I show weight of the mice at various times post infection with *C. difficile* spores. Groups of mice received cefoperazone (Abx) treatment followed by the indicated composition, or no cefoperazone (no Abx), then were administered *C. difficile* spores. Figure 7A shows weight of the mice that received no antibiotic treatment. Figure 7B shows weight of the mice that received cefoperazone treatment. Figure 7C shows weight of the mice that received cefoperazone treatment followed by vancomycin. Figure 7D shows weight of the mice that received cefoperazone treatment followed by Composition I. Figure 7E shows weight of the mice that received cefoperazone treatment followed by Composition E. Figure 7F shows weight of the mice that received cefoperazone treatment followed by composition A. Figure 7G shows weight of the mice that received cefoperazone treatment followed by composition B. Figure 7H shows weight of the mice that received cefoperazone treatment followed by composition C. Figure 7I shows weight of the mice that received cefoperazone treatment followed by composition D.

Figures 8A-8C show the load of *C. difficile* in colony forming units (CFUs) in fecal pellets at various times post infection with *C. difficile*. Figure 8A shows *C. difficile* CFU/g feces one-day post infection. Figure 8B shows *C. difficile* CFU/g feces 3 days post infection. Figure 8C shows *C. difficile* CFU/g feces 8 days post infection.

Figure 9 shows experimental conditions evaluated in Example 3, the results for which are presented in Figures 10-12.

Figure 10 shows survival of the mice over time post infection with C. *difficile* spores, according to the experimental conditions shown in Figure 9. Mice losing >20% body weight of baseline were included in mortality numbers in survival curves.

Figure 11 shows weight of the mice at various times post infection with *C. difficile* spores.

Figure 12 shows the *C. difficile* burden in colony forming units (CFUs) in fecal pellets collected from mice 1, 3, and 8 days post infection with *C. difficile*.

Figure 13 shows the strains of Composition F. The genus-species notation indicates the closest species based on the sequence of the isolated strain.

Figure 14 shows the classification by Clostridium cluster of the strains in Composition F and their short-chain fatty acid producing abilities.

Figure 15 shows experimental conditions evaluated in Example 4, the results for which are presented in Figures 16-18. The dosing days are relative to *C. difficile* infection. FMT refers to Fecal Matter Transplant with fecal matter isolated from mice or from humans.

Figures 16 shows survival of the mice over time post infection with *C. difficile* spores, according to the experimental conditions shown in Figure 15. Mice losing >20% body weight of baseline were included in mortality numbers in survival curves.

Figures 17A-17H show weight of the mice at various times post infection with C. *difficile* spores. Groups of mice received cefoperazone (Abx) treatment followed by the indicated composition, then were administered *C. difficile* spores. Figure 17A shows weight of the mice that received cefoperazone treatment. Figure 17B shows weight of the mice that received cefoperazone treatment followed by FMT with fecal matter from a human. Figure 17C shows weight of the mice that received cefoperazone treatment followed by FMT with fecal matter from a mouse. Figure 17D shows weight of the mice that received cefoperazone treatment followed by Composition B on day -1. Figure 17E shows weight of the mice that received cefoperazone treatment followed by Composition B on days -2 and -1. Figure 17F shows weight of the mice that received cefoperazone treatment followed by Composition B on days -2, -1, 1, 2, and 3. Figure 17G shows weight of the mice that received cefoperazone treatment followed by Composition F on day -1. Figure 17H shows weight of the mice that received cefoperazone treatment followed by Composition F on days -2, -1, 1, 2, and 3.

Figures 18A-18B show the load of *C. difficile* in colony forming units (CFUs) in fecal pellets at various times post infection with *C. difficile*. Figure 18A shows *C. difficile* CFU/g feces 8 days post infection. Figure 18B shows *C. difficile* CFU/g feces 17 days post infection.

Figure 19 shows the strains of Composition G. The genus-species notation indicates the closest species based on the sequence of the isolated strain.

Figure 20 shows experimental conditions evaluated in Example 5, the results for which are presented in Figures 21-23. Composition B1 = Composition B with *Bacteroides*; Composition B2 = Composition B with *Bacteroides* but without *Flavonifractor plautii*.

Figure 21 shows survival of the mice over time post infection with C. *difficile* spores, according to the experimental conditions shown in Figure 20. Mice losing >20% body weight of baseline were included in mortality numbers in survival curves.

Figures 22A-22J show weight of the mice at various times post infection with C. *difficile* spores. Figure 22A shows weight of the mice that received vehicle control. Figure 22B shows weight of the mice that received Composition F. Figure 22C shows weight of the mice that received Composition G. Figure 22D shows weight of the mice that received cefoperazone treatment followed by Composition B. Figure 22E shows weight of the mice that received cefoperazone treatment followed by Composition B2 (= Composition B without *Flavonifractor plautii* and with added *Bacteroides*). Figure 22F shows weight of the mice that received cefoperazone treatment followed by Composition B 1 (= Composition B with *Bacteroides* added). Figure 22G shows weight of the mice that received cefoperazone treatment followed by frozen Composition B. Figure 22H shows weight of the mice that received cefoperazone treatment followed by ethanol treated human fecal samples. Figure 22I shows weight of the mice that received cefoperazone treatment followed by ethanol treated Composition B. Figure 22J shows weight of the mice that received cefoperazone treatment followed by Composition J.

Figure 23 shows the load of *C. difficile* in colony forming units (CFUs) in fecal pellets at various times post infection with *C. difficile*.

Figure 24 shows weight of the indicated groups of mice at various times post infection with *C. difficile* spores.

Figure 25 shows experimental conditions evaluated in Example 6, the results of which are presented in Figures 27-29.

Figure 26 shows the strains in Composition H (SEQ ID NO:14 - VE202-13 - *Anaerotruncus colihominis* (Cluster IV); SEQ ID NO:16 - VE202-16 - *Clostridium symbiosum* (Cluster XIVa); SEQ ID NO:21 - 189 - *Clostridium innocuum* (Cluster XVII); SEQ ID NO:82 - PE9 - *Clostridium disporicum* (Cluster I); SEQ ID NO:81 - PE5 - *Clostridium bolteae* (Cluster XIVa); SEQ ID NO:80 - VE202-18 - *Erysipelatoclostridium ramosum* (Cluster XVIII).

Figures 27A and 27B shows survival and weight loss of the mice over time post infection with *C. difficile* spores, according to the experimental conditions shown in Figure 25. Mice losing >20% body weight of baseline were included in mortality numbers in survival curves. Figure 29A shows survival/mortality of mice that received the indicated treatment prior to *C. difficile* infection. Figure 29B shows the weight over time of mice that received the indicated treatment prior to *C. difficile* infection.

Figures 28A and 28B show results from the experimental conditions shown in Figure 25. Figure 28A shows survival/mortality of mice that received the indicated treatment prior to *C. difficile* infection. Figure 28B shows the weight over time of mice that received the indicated treatment prior to *C. difficile* infection.

Figures 29A and 29B show the *C. difficile* burden in CFU/gram feces collected from mice that received the indicated treatment prior to *C. difficile*. Figure 29A shows *C. difficile* burden at one-day post *C. difficile* infection. Figure 29B shows *C. difficile* burden at 4 days post *C. difficile* infection. Figure 29C shows *C. difficile* burden at 19 days post *C. difficile* infection.

Figure 30 shows that Composition B reduced the amount of *C. difficile* Toxin B compared to no treatment controls: "2-1 (Cdiff)" and "2-4 (Cdiff)" and FMT. In addition, Composition B reduced the amount of *C. difficile* Toxin B compared to Composition B with additional spores.

Figure 31 shows Composition B reduced *C. difficile* growth in *in vitro* competition experiments. Cultures of *C. difficile* were incubated in the presence of *B. thetaiotaomicron*, *C. bifermentans*, or Composition B, or in the absence of a competing strain(s) (C. diff only). The quantity of *C. difficile* is presented as the percentage of the control (C. diff only).

Figure 32 shows that inoculation with Composition B induced the percentage of FoxP3+ CD4+ cells (regulatory T cells) in the intestine of germ-free mice as compared to control mice ("GF").

DETAILED DESCRIPTION OF THE INVENTION

[0033] Disclosed herein are compositions comprising purified bacterial strains and pharmaceutical compositions and food products containing such compositions and bacterial strains. Also disclosed are the compositions for use in methods of treating a pathogenic infection, such as *Clostridium difficile (C. difficile)* infection, in a subject by administering said compositions to the subject.

[0034] Various factors including antibiotic usage can induce dysbiosis of the gastrointestinal tract, which may allow for colonization by pathogenic microorganisms, such as *C. difficile*. Such colonization or pathogenic infection can lead to a variety of adverse effects in the subject including diarrhea, which is one of the primary symptoms characteristic of *C. difficile* infection (CDI). In the case of CDI, diarrhea is thought to be a result of *C. difficile* production of Toxin B (also referred to as cytotoxin TcdB), which results in opening of the tight junctions between intestinal epithelial cells, increasing vascular permeability, hemorrhage, and inflammation.

[0035] The compositions described herein are effective in the treatment of *C. difficile* infection. As shown herein, the disclosed compositions are effective in suppressing the pathogenic effects of *C. difficile* infection. The compositions provided herein reduce the amount of *C. difficile* after infection and thereby provide an effective method for eliminating *C. difficile* from the body *(e.g.,* the gut). The compositions provided herein induce the proliferation and/or accumulation of regulatory T cells (Tregs), for example when administered to a subject. Remarkably, the compositions disclosed herein have been found to reduce or inhibit production or activity of *C. difficile* Toxin B and thereby represent effective compositions for the treatment or prevention of CDI. The compositions disclosed herein have also been found to inhibit the growth and/or survival of *C. difficile*.

[0036] The present disclosure provides compositions comprising purified bacterial strains that can be administered to subjects experiencing or having experienced a pathogenic infection to treat the infection. In some embodiments, the compositions may be administered to subjects who may be at risk for a pathogenic infection. Such subjects include subjects who previously had pathogenic infections, subjects who have been treated with antibiotics and subjects who will undergo a procedure that will put them at an increased risk for a pathogenic infection (*e.g.*, surgery and/or hospitalization). In some embodiments, the pathogenic infection, is infection by a pathogen that is present predominantly in the gut or the intestine. In some embodiments, the pathogen that is present predominantly in the gut or the intestine is *Clostridium difficile*.

[0037] In some embodiments, the one or more of the bacterial strains of the compositions provided herein colonize or recolonize the intestinal tract or parts of the intestinal tract (*e.g.*, the colon or the cecum) of the subject. Such colonization or recolonization may also be referred to as grafting. In some embodiments, one or more of the bacterial strains of the compositions recolonize the intestinal tract *(e.g.,* the colon or the cecum) of the subject after the naturally present microbiome has been partially or completely removed, *e.g.,* because of administration of antibiotics. In some embodiments, the one or more of the bacterial strains of the compositions colonize a dysbiotic gastrointestinal tract.

[0038] In some embodiments, the one or more of the bacterial strains of the compositions can "outgrow" a pathogen, such as *C. difficile*. Thus, in some embodiments, if a pathogen (*e.g., C. difficile*) and one or more bacteria of compositions provided herein are both present in the intestinal tract *(e.g.,* the colon or the cecum), the one or more bacteria of compositions provided herein grow faster *(e.g.,* have a shorter doubling time) than the pathogen, thereby preventing the pathogen from accumulating in the intestinal tract *(e.g.,* the colon or the cecum). In some embodiments, the faster growth results because the one or more bacteria of the compositions provided herein are better at grafting in the intestinal tract *(e.g.,* the colon or the cecum). In some embodiments, the faster growth results because the one or more bacteria of the compositions provided herein are better at metabolizing nutrients present in the intestinal tract *(e.g.,* the colon or the cecum). In some embodiments, the compositions of bacterial strains provided herein prevent or inhibit production of bacterial toxins by the pathogenic infection, or prevent or inhibit the cytopathic or cytotoxic effects of such bacterial toxins. In some embodiments, the bacterial strains of the compositions provided herein can treat pathogenic infections, because of the synergy between the bacterial strains. Thus, without being limiting, in some embodiments, the combination of the bacterial strains of the compositions provided herein act synergistically because the combination of the strains is particularly well-suited to use nutrients in the intestinal tract *(e.g.,* the colon or the cecum), or instance through metabolic interactions, and/or because the combination is superior in grafting *(e.g.,* by providing a favorable microenvironment).

[0039] In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein is superior in the use of nutrients when compared to the pathogen such as *C. difficile,* thereby suppressing the growth of the pathogen such as *C. difficile*. In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein is superior in grafting when compared to the pathogen such as *C. difficile,* thereby suppressing the growth of the pathogen such as *C. difficile*. In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein is superior in the use of nutrients and in grafting when compared to the pathogen such as *C. difficile,* thereby suppressing the growth of the pathogen such as *C. difficile*. In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein inhibits the growth and/or survival of the pathogen such as *C. difficile*. In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein induces regulatory T cells (Tregs) in the subject that results in reduction or elimination of the pathogen such as *C. difficile*. In some embodiments, a pathogenic infection such as *C. difficile* is treated because the combination of bacterial strains of the compositions provided herein inhibits the growth and/or survival of the pathogen and induces regulatory T cells (Tregs) in the subject that results in reduction or elimination of the pathogen such as *C. difficile*.

[0040] In some embodiments, the synergistic effect is provided by the capacity of the combination to colonize specific niches in the intestinal tract *(e.g.,* the colon or the cecum). In some embodiments, the synergistic effect is provided by the capacity of the combination to metabolize specific nutrients. In some embodiments, the synergistic effect is provided by the capacity of the combination to provide specific metabolites to the environment. Such specific metabolites may suppress growth of the pathogen and/or stimulate growth of non-pathogens. In some embodiments, the synergistic effect is provided by the capacity of the combination to provide short-chain fatty acids to the environment. In some embodiments, the synergistic effect is provided by the capacity of the combination to provide specific short-chain fatty acids to the environment. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce butyrate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce acetate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce lactate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce propionate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce succinate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce multiple metabolites. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce multiple short-chain fatty acids. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce both butyrate and acetate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce both butyrate and lactate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce both butyrate and propionate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce both butyrate and succinate. In some embodiments, the synergistic effect is provided by the capacity of the combination to produce butyrate, acetate and additional short-chain fatty acids.

[0041] The bacterial strains used in the compositions provided herein generally are isolated from the microbiome of healthy individuals. In some embodiments, the compositions include strains originating from a single individual. In some embodiments, the compositions include strains originating from multiple individuals. In some embodiments, the bacterial strains are obtained from multiple individuals, isolated and grown up individually. The bacterial compositions that are grown up individually may subsequently be combined to provide the compositions of the disclosure. It should be appreciated that the origin of the bacterial strains of the compositions provided herein is not limited to the human microbiome from a healthy individual. In some embodiments, the bacterial strains originate from a human with a microbiome in dysbiosis. In some embodiments, the bacterial strains originate from non-human animals or the environment (*e.g.*, soil or surface water). In some embodiments, the combinations of bacterial strains provided herein originate from multiple sources (*e.g.*, human and non-human animals).

[0042] In some embodiments, the bacteria of the compositions provided herein are anaerobic bacteria. In some embodiments, the bacteria of the compositions provided herein are obligate anaerobic bacteria. In some embodiments, the bacteria of the compositions provided herein are *clostridia*. *Clostridia* may be classified into phylogenetic clusters with other closely related strains and species. (See *e.g.,* Rajilic-Stojanovic, M., and de Vos, W.M. FEMS Microbiol Rev 38, (2014) 996-1047). In general, *clostridia* are classified as belonging to a specific cluster based on their 16S rRNA (or 16S rDNA) nucleic acid sequence. Methods for determining the identity of specific bacterial species based on their 16S rRNA (or 16S rDNA) nucleic acid sequence are well known in the art (See *e.g.*, Jumpstart Consortium Human Microbiome Project Data Generation Working, G. PLoS One (2012) 7, e39315).

[0043] Provided herein are compositions comprising bacterial strains belonging to specific Clostridium clusters that have been found to be effective in treating and/or preventing pathogenic infection (*e.g., C. difficile* infection). In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster IV. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster XIVa. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster XVII. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster I. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster IX. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster XIVa and at least one of the bacterial strains belongs to Clostridium cluster XVII. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster IV and at least one of the bacterial strains belongs to Clostridium cluster XVII. In some embodiments, at least one of the bacterial strains of the composition belongs to Clostridium cluster IV, at least one of the bacterial strains belongs to Clostridium cluster XIVa, and at least one of the bacterial strains belongs to Clostridium cluster XVII.

[0044] In some embodiments, the compositon has at least twice as many bacterial strains that belong to Clostridium cluster XIVa when compared to the bacterial strains that belong to Clostridium cluster IV. In some embodiments, at least two of the bacterial strains of the composition belong to Clostridium cluster IV and at least five of the bacterial strains belong to Clostridium cluster XIVa. In some embodiments, the compositon has at least twice as many bacterial strains that belong to Clostridium cluster XIVa when compared to the bacterial strains that belong to Clostridium cluster IV, and the composition has at least one strain that belongs to Clostridium cluster XVII. In some embodiments, at least two of the bacterial strains of the composition belong to Clostridium cluster IV, at least five of the bacterial strains belongs to Clostridium cluster XIVa, and at least one of the bacterial strains belongs to Clostridium cluster XVII.

[0045] In some embodiments, the compositions provided herein do not include bacterial strains belonging to Clostridium cluster XVIII. In some embodiments, the compositions provided herein do not include bacterial strains belonging to Clostridium cluster XVI. In some embodiments, the compositions provided herein do not include bacterial strains belonging to Clostridium cluster XI. In some embodiments, the compositions provided herein do not include bacterial strains belonging to Clostridium cluster I. It should be appreciated that SEQ ID NOs: 1-83 and 124-159 may include both full length and partial 16S rDNA sequences. It should be appreciated that for all compositions provided herein, in some embodiments, the bacterial strain or the bacterial strains are the active ingredient of the composition.

[0046] It should be appreciated that for all compositions provided herein, the bacterial strains are purified. The bacterial strains disclosed herein originally may have been obtained and purified from the microbiota of one or more human individuals or obtained from sources other than the human microbiota, including soil and non-human microbiota. As provided herein, in some embodiments, bacteria isolated from the human microbiota, non-human microbiota, soil, or any alternative source are purified prior to use in the compositions and methods provided herein.

[0047] As discussed above, in some embodiments, the bacterial strains are the active ingredient of the composition. The bacterial strains disclosed herein that have a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-83 and 124-159 have a high percent of homology (*e.g.*, greater than 90%) with 16S rDNA sequences of bacterial strains that have been described in various databases (See *e.g.,* the National Center for Biotechnology Information). Table 1 and Table 3 provides the closest known species by homology when the 16S rDNA sequences comprising SEQ ID NOs: 1-83 and 124-159 are compared to 16S rDNA sequences of bacterial species available in public databases. By way of example, the bacterial strain comprising a 16S rDNA sequence with SEQ ID NO:1 (also referred to herein as "Strain 71") disclosed herein has the highest homology with a bacterial strain of the species *Blautia wexlerae* as defined by Accession # NR_044054 (having 16S rDNA sequence SEQ ID NO:94). While the bacterial strain with SEQ ID NO:1 has homology with other published bacterial strains as well, the highest homology is with a bacterial strain of the species *Blautia wexlerae* as defined by Accession # NR_044054. In this particular example the homology of SEQ ID NO:1 is 96.6% with SEQ ID NO:94 (corresponding to *Blautia wexlerae*). It should be appreciated that multiple bacterial strains disclosed herein may have the highest homology with the same species. (*e.g.*, both SEQ ID NO:4 and SEQ ID NO:5 have the highest homology with a 16S rDNA sequence of a strain of the species *Blautia hansenii*).

[0048] It should further be appreciated that the bacterial strains disclosed herein that have a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-83 and 124-159, are also homologous to other strains based on their whole genome sequence, or subset of their whole genome sequence. Homologies based on whole genome analysis are provided in Table 2 and Table 3.

[0049] The invention also encompasses compositions comprising bacterial strains that are close in homology to and/or fall within, for example, the species *Blautia producta*, *Blautia producta ATCC 27340, Clostridia bacteria UC5.1-1D4*, *Eubacterium fissicatena*, *Sellimona intestinalis*, *Drancourtella massiliensis*, *Drancourtella massiliensis GD1*, *Ruminococcus torques*, *Flavonifractor plautii*, *Clostridium orbiscindens 1_3_50AFAA*, *Subdoligranulum*, *Anaerotruncus colihominis*, *Anaerotruncus colihominis DSM 17241*, *Clostridium symbiosum*, *Clostridium symbiosum WAL-14163*, *Clostridium bolteae*, *Clostrdium bolteae 90A9*, *Dorea longicatena*, *Dorea longicatena CAG:42*, *Clostridium innocuum*, and *Erysipelotrichaceae_bacterium_21-3*. Thus, the compositions of the disclosure include eight bacterial strains comprising 16S rDNA sequences having at least 97% homology SEQ ID NOs: 10, 14, 15, 16, 17, 19, 20 and 21.

[0050] The bacterial strains in Composition A are related to the following bacterial species: *Clostridium hathewayi*, *Blautia hansenii*, *Blautia producta*, *Blautia coccoides*, *Eubacterium contortum*, *Eubacterium fissicatena*, *Anaerostipes caccae*, *Clostridium scindens*, *Marvinbryanta formatexigens*, and *Eisenbergiella tayi* (See *e.g.,* Table 1). It should be appreciated that multiple bacterial strains of the compositions disclosed herein can have the same related bacterial species. For instance, the bacterial strains having 16S rDNA sequences with nucleic acid sequences SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:7 all have *Blautia hansenii* as related species.

[0051] Each of the bacterial strains of Composition A are *BaiCD+,* meaning that the bacterial strains encode, or are predicted to encode, the bile inducible operon gene *BaiCD* and/or a protein with stereospecific NAD(H)-dependent 3-oxo-Δ^4-cholenoic acid oxidoreductase activity. The BaiCD status of a bacterial strain can be determined for instance by PCR (See *e.g.,* Wells et al. Clin Chim Acta (2003) May; 331(1-2):127-34). Furthermore, each of the strains of Composition A are classified as belonging to Clostridium cluster XIVa.

Table A

Composition A
SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*

SEQ_04 - 7 - Blautia_hansenii (XIVa)*
SEQ_05 - 10 - Blautia_hansenii (XIVa)*
SEQ_07 - 59 - Blautia_producta / Blautia_coccoides (XIVa)
SEQ_08 - 79 - Blautia_hansenii (XIVa)*
SEQ_09 - VE202-21 - Eubacterium_contortum / Eubacterium_fissicatena (XIVa)*
SEQ_11 - VE202-9 - Anaerostipes_caccae (XIVa)*
SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*
SEQ_13 - 136 - Marvinbryantia_formatexigens (XIVa)*
SEQ_23 - VE202-29 - Eisenbergiella_tayi (XIVa)*

*= BaiCD-

[0052] In one aspect, the disclosure provides Composition B (See *e.g.*, Figure 1, Table B). As shown in Figure 1, Composition B contains bacterial strains that comprise 16S rDNA sequences with nucleic acid sequences: SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO: 21. In some embodiments, the compositions include eight purified bacterial strains comprising 16S rDNA sequences with nucleic acid sequences SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO: 21. composition essentially consists of eight purified bacterial strains comprising 16S rDNA sequences with nucleic acid sequences SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID SEQ ID NO:20, and SEQ ID NO:21, respectively.

[0053] In some embodiments, the composition consists of eight purified bacterial strains comprising 16S rDNA sequences with nucleic acid sequences SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID SEQ ID NO:20, and SEQ ID NO:21, respectively.

[0054] In some embodiments, the composition essentially consists of eight purified bacterial strains comprising 16S rDNA sequences with nucleic acid sequences SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID SEQ ID NO:20, and SEQ ID NO:21, respectively.

[0055] The bacterial strains in Composition B are related to the following bacterial species: *Flavinofractor plautii, Lachnospiraceae bacterium 7_1_58FAA, Subdoligranulum Anaerotruncus colihominis, Eubacterium fissicatena, Ruminococcus torques, Clostridium symbiosum, Clostridium bolteae, Dorea longicatena, Blautia producta, Clostridium innocuum*, and *Erysipelotrichaceae_bacterium_21-3* (See *e.g.*, Table 2).

[0056] Selected strains were subjected to whole genome sequencing using a PacBio Biosciences platform (Menlo Park, CA) and sequences were assembled into whole genomes (Table 3). The 16S rDNA sequences were identified using Prokka and Barrnap. It was found that several strains contained more than one 16S sequence. All identified 16S rRNA gene nucleotide sequences for each strain were then clustered at 97% identity using the usearch (v 5.2.236) algorithm and the cluster seed sequence was selected as the representative sequence for each Composition B strain (The Consensus 16S sequence: column labeled "*Consensus SEQ ID # of 16S region as determined by WGS" in Table 3). Table 3 provides identification of the indicated strains included in Composition B based on Sanger sequencing of the 16S region as well as on whole genome sequencing (WGS). The closest species of the bacterial strains were identified both by comparison to a 16S database (column labeled: "Closest species based on Consensus SEQ ID # of 16S region as compared with 16S database") and to whole genome databases (column labeled: "Closest species based on WGS compared versus WG databases).

[0057] Based on identification of 16S sequences through whole genome sequencing, and by comparing these sequences with 16S databases, the bacterial strains in Composition B are related to the following bacterial species: *Clostridium bolteae*, *Anaerotruncus colihominis*, *Dracourtella massiliensis*, *Clostridium symbiosum Blautia producta*, *Dorea longicatena Clostridium innocuum and Flavinofractor plautii* (see, *e.g.*, Table 3).

[0058] Based on whole genome sequencing and comparing of the whole genome to whole genome databases, the bacterial strains in Composition B are most closely related to the following bacterial species: *Clostridium bolteae* 90A9, *Anaerotruncus colihominis* DSM 17241, *Dracourtella massiliensis GD1*, *Clostridium symbiosum* WAL-14163, *Clostridium bacterium* UC5.1-1D4, *Dorea longicatena* CAG:42, *Erysipelotrichaceae bacterium* 21_3, and *Clostridium orbiscindens* 1_3_50AFAA (see, *e.g.*, Table 3).

[0059] It should be appreciated that multiple strains of the compositions disclosed herein can have the same related bacterial species. For instance, the bacterial strains comprising 16S rDNA sequences with nucleic acid sequences SEQ ID NO 18, SEQ ID NO:20 and SEQ ID NO:22 all have *Dorea longicatena* as related bacterial species.

[0060] Each of the bacteria of Composition B are *BaiCD*- strains, meaning that the strains do not encode and/or are not predicted to encode the bile inducible operon gene *baiCD* and/or a protein with stereospecific NAD(H)-dependent 3-oxo-Δ^4-cholenoic acid oxidoreductase activity. In some embodiments, the bacteria are *BaiCD*- strains. The strains of Composition B are classified as belonging to Clostridium clusters IV, XIVa, and XVII. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters IV, XIVa, or XVII. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters IV or XVII. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters XIVa or XVII. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters IV or XIVa. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium cluster IV. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium cluster XIVa. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters XVII. In some embodiments, the bacteria are *BaiCD*- strains and belong to Clostridium clusters IV, XIVa, and XVII and do not belong to Clostridium clusters XVI or XVIII.

[0061] In some embodiments, the disclosure provides bacterial strains wherein the bacterial strains are spore forming bacterial strains.

[0062] In some embodiments, the disclosure provides bacterial strains wherein the bacteria include both spore formers and non-spore formers.

Table B:
Composition B
SEQ_10 - 211 - Flavonifractor_plautii (IV)
SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)
SEQ_15 - VE202-14 - Eubacterium_fissicatena (XIVa)
SEQ_16 - VE202-16 - Clostridium_symbiosum (XIVa)
SEQ_17 - VE202-7 - Clostridium_bolteae (XIVa)
SEQ_19 - 16 - Blautia_producta (XIVa)
SEQ_20 - 170 - Dorea_longicatena (XIVa)
SEQ_21 - 189 - Clostridium_innocuum (XVII)

[0063] While not being limited to a specific mechanism it is thought that the inclusion of a *Bacteroides* species in a bacterial compositions increases the ability to sense and adapt to nutrient availability or influence the host immune system so that it becomes more effective in fighting pathogens (*e.g.*, *C. difficile)*.

Table B1
Composition B1
SEQ_10 - 211 - Flavonifractor_plautii (IV)
SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)
SEQ_15 - VE202-14 - Eubacterium_fissicatena (XIVa)
SEQ_16 - VE202-16 - Clostridium_symbiosum (XIVa)
SEQ_17 - VE202-7 - Clostridium_bolteae (XIVa)
SEQ_20 - 170 - Dorea_longicatena (XIVa)
SEQ_19 - 16 - Blautia_producta (XIVa)
SEQ_21 - 189 - Clostridium_innocuum (XVII)
SEQ_83 *Bacteroides ovatus*

Table B2
Composition B2
SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)
SEQ_15 - VE202-14 - *Eubacterium_fissicatena* (XIVa)
SEQ_16 - VE202-16 - Clostridium_symbiosum (XIVa)
SEQ_17 - VE202-7 - Clostridium_bolteae (XIVa)
SEQ_20 - 170 - Dorea_longicatena (XIVa)
SEQ_19 - 16 - Blautia_producta (XIVa)
SEQ_21 - 189 - Clostridium_innocuum (XVII)
SEQ_83 Bacteroides ovatus

As shown in Figure 1, Composition C contains bacteria that have the following 16S rDNA sequences: SEQ ID NO:12, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:1, SEQ ID NO:7, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:10, SEQ ID NO:14, and SEQ ID NO:16.

[0064] The bacterial strains in Composition C are related to the following species: *Clostridium scindens*, *Clostridium hathewayi*, *Blautia hansenii*, *Blautia wexlerae*, *Blautia producta*, *Blautia coccoides*, *Dorea longicatena*, *Clostridium innocuum*, *Flavonifractor plautii*, *Lachnospiraceae bacterium 7_1_58FAA*, *Subdoligranulum*, *Anaerotruncus colihominis* and *Clostridium symbiosum*.

[0065] The strains of Composition C include both *BaiCD*$^+$ strains and *Bai CD*- strains.

[0066] The clostridial strains of Composition C are classified as belonging to Clostridium clusters IV, XIVa, and XVII.

Table C
Composition C
SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*
SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*
SEQ_05 - 10 - Blautia_hansenii (XIVa)*
SEQ_01 - 71 - Blautia_wexlerae (XIVa)*
SEQ_07 - 59 - Blautia_producta/Blautia_coccoides (XIVa)*
SEQ_18 - 148 - Dorea_longicatena (XIVa)
SEQ_21 - 189 - *Clostridium innocuum* (XVII)
SEQ_10 - 211 - Flavonifractor_plautii (IV)
SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)
SEQ_16 - VE202-16 - Clostridium_symbiosum) (XIVa)

*= BaiCD$^+$

[0067] As shown in Figure 1, Composition D contains bacteria that have the following 16S rDNA sequences: SEQ ID NO:12, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:1, SEQ ID NO:14, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:10, SEQ ID NO:2, and SEQ ID NO:6.

[0068] The strains of Composition D include both *BaiCD*$_+$ strains and *Bai CD*- strains.

[0069] Composition D includes the non-Clostridium strains *Turicibacter sanguinis* and *Lactobacillus mucosae*.

Table D
Composition D
SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*
SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*
SEQ_05 - 10 - Blautia_hansenii (XIVa)*
SEQ_01 - 71 - Blautia_wexlerae (XIVa)*
SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)
SEQ_18 - 148 - Dorea_longicatena (XIVa)
SEQ_21 - 189 - Clostridium_innocuum (XVII)
SEQ_10 - 211 - Flavonifractor_plautii (IV
SEQ_02 - 102 - Turicibacter_sanguinis (non-Clostridium)
SEQ_06 - 40 - Lactobacillus_mucosae (non-Clostridium)

*= BaiCD$^+$

[0070] As shown in Figure 13, Composition F contains bacteria that have the following 16S rDNA sequences: SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, and SEQ ID NO:79.

[0071] The bacterial strains in Composition F are related to the following bacteria: *Dorea longicatena*, *Ruminococcus obeum, Megasphaera elsdenii, Acidaminococcus fermentans, Acidaminococcus intestine, Megasphaera elsdenii, Ruminococcus faecis, Bacteroides cellulosilyticus, Anaerostipes hadrus, Ruminococcus obeum, Flavonifractor plautii, Eubacterium rectale, Flavonifractor plautii, Megasphaera elsdenii, Eubacterium rectale, Ruminococcus champanellensis, Ruminococcus albus, Ruminococcus champanellensis, Ruminococcus faecis, Bifidobacterium bifidum, Anaerostipes hadrus, Anaerostipes hadrus, Anaerostipes hadrus, Eubacterium rectale, Ruminococcus faecis, Blautia luti, Ruminococcus faecis, Anaerostipes hadrus, Anaerostipes hadrus, Ruminococcus faecis, Eubacterium rectale, Eubacterium rectale, Anaerostipes hadrus, Ruminococcus faecis, Ruminococcus faecis, Dorea longicatena, Roseburia faecis, Blautia luti, Fusicatenibacter saccharivorans, Fusicatenibacter saccharivorans, Roseburia faecis, Megasphaera elsdenii, Eubacterium rectale, Eubacterium rectale, Roseburia faecis, Blautia faecis, Fusicatenibacter saccharivorans*, and *Dorea formicigenerans.*

[0072] It should be appreciated that multiple strains of the compositions disclosed herein can have the same related bacterial species. For instance, Composition F includes 12 strains that have *Eubacterium rectale* as the closest related species.

[0073] Composition F includes non-clostridium bacterial strains.

Table F1

Composition F					
SEQ_NO	StrainID	Genus_species	SEQ_NO	StraindID	Genus_species
SEQ_24	YK96	Dorea_longicatena	SEQ_52	YK51	Eubacterium_rectale
SEQ_25	YK101	Ruminococcus_obeum	SEQ_53	YK52	Eubacterium_rectale
SEQ_26	YK110	Megasphaera_elsdenii	SEQ_54	YK54	Anaerostipes_hadrus
SEQ_27	YK149	Acidaminococcus_fermentans / Acidaminococcus_intestini	SEQ_55	YK56	Ruminococcus_faecis
SEQ_28	YK154	Megasphaera_elsdenii	SEQ_56	YK57	Ruminococcus_faecis
SEQ_29	YK36	Ruminococcus_faecis	SEQ_57	YK58	Dorea_longicatena
SEQ_30	YK95	Bacteroides_cellulosilyticus	SEQ_58	YK65	Roseburia_faecis
SEQ_31	YK32	Anaerostipes_hadrus	SEQ_59	YK67	Blautia_luti
SEQ_32	YK64	Ruminococcus_obeum	SEQ_60	YK69	Fusicatenibacter_saccharivorans
SEQ_33	YK73	Flavonifractor_plautii	SEQ_61	YK70	Fusicatenibacter_saccharivorans
SEQ_34	YK87	Eubacterium_rectale	SEQ_62	YK71	Roseburia_faecis
SEQ_35	YK105	Flavonifractor_plautii	SEQ_63	YK74	Megasphaera_elsdenii
SEQ_36	YK153	Megasphaera_elsdenii	SEQ_64	YK88	Eubacterium_rectale
SEQ_37	YK163	Eubacterium_rectale	SEQ_65	YK89	Eubacterium_rectale
SEQ_38	YK191	Ruminococcus_champanellensis / Ruminococcus_albus	SEQ_66	YK97	Roseburia_faecis
SEQ_39	YK99	Ruminococcus_champanellensis	SEQ_67	YK98	Blautia_faecis
SEQ_40	YK55	Ruminococcus_faecis	SEQ_68	YK139	Fusicatenibacter_saccharivorans
SEQ_41	YK75	Bifidobacterium_bifidum	SEQ_69	YK141	Dorea_formicigenerans
SEQ_42	YK90	Anaerostipes_hadrus	SEQ_70	YK142	Ruminococcus_faecis
SEQ_43	YK30	Anaerostipes_hadrus	SEQ_71	YK152	Blautia_hansenii
SEQ_44	YK31	Anaerostipes_hadrus	SEQ_72	YK155	Blautia_hansenii
SEQ_45	YK12	Eubacterium_rectale	SEQ_73	YK157	Eubacterium_rectale
SEQ_46	YK27	Ruminococcus_faecis	SEQ_74	YK160	Roseburia_faecis
SEQ_47	YK28	Blautia_luti	SEQ_75	YK166	Eubacterium_rectale
SEQ_48	YK29	Ruminococcus_faecis	SEQ_76	YK168	Eubacterium_rectale
SEQ_49	YK33	Anaerostipes_hadrus	SEQ_77	YK169	Eubacterium_rectale
SEQ_50	YK34	Anaerostipes_hadrus	SEQ_78	YK171	Eubacterium_rectale
SEQ_51	YK35	Ruminococcus_faecis	SEQ_79	YK192	Roseburia_faecis

Table F2

Composition F, strain groupings		
Cluster	**Composition F**	***SCFAs**
XIVa	*Eubacterium rectale* 12	A, B, L
	Ruminococcus faecis 8	A, L
	Ruminococcus obeum 2	A, L
	Blautia faecis 1	A, L
	Blautia hansenii 2	A, L
	Blautia luti 2	A, L
	Anaerostipes hadrus 7	B
	Roseburia faecis 5	A, B
	Fusicatenibacter saccharivorans 3	A, L
	Dorea formicigenerans 1	A
	Dorea longicatena 2	A
IV	*Flavonifractor_plautii* 2	A, B

Composition F, strain groupings		
Cluster	**Composition F**	***SCFAs**
	Ruminococcus champanellensis 2	A
IX	*Acidaminococcus fermentans* 1	A, B, P
	Megasphaera elsdeni 4	P
other	*Bacteroides cellulosilyticus* 1	A, S
	Bifiidobacterium Bifidum	L, A
A, acetate;	B, Butyrate;	L, lactate;
P, propionate;	S, succinate	
*Short chain fatty acid legend:		

[0074] As shown in Figure 19, Composition G contains bacteria that have the following 16S rDNA sequences: SEQ ID NO:27, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:70, SEQ ID NO:24, SEQ ID NO:34, SEQ ID NO:37, SEQ ID NO:46, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:35, SEQ ID NO:62, SEQ ID NO:26, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:40, SEQ ID NO:38, SEQ ID NO:47, SEQ ID NO:56, SEQ ID NO:25, and SEQ ID NO: 32.

[0075] The bacterial strains in Composition G are related to the following bacteria: *Acidaminococcus fermentans, Acidaminococcus intestine, Anaerostipes hadrus, Blautia faecis, Blautia hansenii, Dorea formicigenerans, Dorea longicatena, Eubacterium rectale, Flavonifractor plautii, Fusicatenibacter saccharivorans, Megasphaera elsdenii, Roseburia faecis*, *Ruminococcus champanellensis*, *Ruminococcus albus*, *Ruminococcus faecis*, and *Ruminococcus obeum*.

Table G

Composition G		
SEQ_27	YK149	Acidaminococcus_fermentans/Acidaminococcus_intesti
SEQ_43	YK90	Anaerostipes_hadrus
SEQ_44	YK30	Anaerostipes_hadrus
SEQ_51	YK34	Anaerostipes_hadrus
SEQ_55	YK54	Anaerostipes_hadrus
SEQ_68	YK98	Blautia_faecis
SEQ_72	YK152	Blautia_hansenii
SEQ_70	YK141	Dorea_formicigenerans
SEQ_24	YK96	Dorea_longicatena
SEQ_34	YK87	Eubacterium_rectale
SEQ_37	YK163	Eubacterium_rectale
SEQ_46	YK12	Eubacterium_rectale
SEQ_76	YK166	Eubacterium_rectale
SEQ_77	YK168	Eubacterium_rectale
SEQ_35	YK105	Flavonifractor_plautii
SEQ_62	YK70	Fusicatenibacter_saccharivorans
SEQ_26	YK110	Megasphaera_elsdenii
SEQ_63	YK71	Roseburia_faecis
SEQ_67	YK97	Roseburia_faecis
SEQ_40	YK99	Ruminococcus_champanellensis
SEQ_38	YK191	Ruminococcus_champanellensis/Ruminococcus_albus
SEQ_47	YK27	Ruminococcus_faecis
SEQ_56	YK56	Ruminococcus_faecis
SEQ_25	YK101	Ruminococcus_obeum
SEQ_32	YK64	Ruminococcus_obeum

[0076] As shown in Figure 26, Composition H contains bacteria that have the following 16S rDNA sequences: SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:21, SEQ ID NO:82, SEQ ID NO:81, and SEQ ID NO:80.

[0077] The bacterial strains in Composition H are related to the following bacteria: *Anaerotruncus colihominis, Clostridium symbiosum, Clostridium innocuum, Erysipelotrichaceae_bacterium_21-3, Clostridium disporicum, Clostridium bolteae,* and *Erysipelatoclostridium ramosum.*

[0078] Composition H includes bacteria from Clostridium cluster I, IV, XIVa, XVII and XVIII.

Table H

Composition H			
SEQ ID NO	**Strain**	**Closest species**	**Cluster**
SEQ ID NO: 14	VE202-13	*Anaerotruncus colihominis*	**Cluster IV**
SEQ ID NO: 16	VE202-16	Clostridium symbiosum WAL-14163	**Cluster XIVa**
SEQ ID NO: 21	189	*Clostridium innocuum*	**Cluster XVII**
SEQ ID NO: 82	PE9	*Clostridium disporicum*	**Cluster I**
SEQ ID NO: 81	PE5	*Clostridium bolteae*	**Cluster XIVa**
SEQ ID NO: 80	VE202-18	*Erysipelatoclostridium ramosum*	**Cluster XVIII**

[0079] In some embodiments, all the bacteria are anaerobic bacteria. In some embodiments, all the bacteria are obligate anaerobic bacteria.

[0080] In one aspect, the disclosure provides bacterial strains with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences of the

bacterial strains or species described herein. In some embodiments, the bacterial strain has at least 98%, 99%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% homology relative to any of the strains or bacterial species described herein over a specified region or over the entire sequence. It would be appreciated by one of skill in the art that the term "homology" or "percent homology," in the context of two or more nucleic acid sequences or amino acid sequences, refers to a measure of similarity between two or more sequences or portion(s) thereof. The homology may exist over a region of a sequence that is at least about 50 nucleotides in length, or more preferably over a region that is 100 to 500 or 1000 or more nucleotides in length. In some embodiments, the homology exists over the length the 16S rRNA or 16S rDNA sequence, or a portion thereof.

[0081] Additionally, or alternatively, two or more sequences may be assessed for the identity between the sequences. The terms "identical" or percent "identity" in the context of two or more nucleic acids or amino acid sequences, refer to two or more sequences or subsequences that are the same. Two sequences are "substantially identical" if two sequences have a specified percentage of amino acid residues or nucleotides that are the same *(e.g.*, at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% identical) over a specified region or over the entire sequence, when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual alignment and visual inspection. Optionally, the identity exists over a region that is at least about 50 nucleotides in length, or more preferably over a region that is 100 to 500 or 1000 or more nucleotides in length. In some embodiments, the identity exists over the length the 16S rRNA or 16S rDNA sequence.

[0082] Additionally, or alternatively, two or more sequences may be assessed for the alignment between the sequences. The terms " alignment" or percent" alignment " in the context of two or more nucleic acids or amino acid sequences, refer to two or more sequences or subsequences that are the same. Two sequences are "substantially aligned" if two sequences have a specified percentage of amino acid residues or nucleotides that are the same (*e.g.*, at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% identical) over a specified region or over the entire sequence, when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual alignment and visual inspection. Optionally, the alignment exists over a region that is at least about 50 nucleotides in length, or more preferably over a region that is 100 to 500 or 1000 or more nucleotides in length. In some embodiments, the identity exists over the length the 16S rRNA or 16S rDNA sequence.

[0083] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. Methods of alignment of sequences for comparison are well known in the art. See, *e.g.,* by the local homology algorithm of Smith and Waterman (1970) Adv. Appl. Math. 2:482c, by the homology alignment algorithm of Needleman and Wunsch, J. Mol. Biol. (1970) 48:443, by the search for similarity method of Pearson and Lipman. Proc. Natl. Acad. Sci. USA (1998) 85:2444 , by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group. Madison. WI), or by manual alignment and visual inspection (see. *e.g.,* Brent et al., Current Protocols in Molecular Biology, John Wiley & Sons, Inc. (Ringbou ed., 2003)). Two examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al., Nuc. Acids Res. (1977) 25:3389-3402, and Altschul et al., J. Mol. Biol. (1990) 215:403-410, respectively.

[0084] Disclosed herein are compositions comprising multiple purified bacterial strains (*e.g.*, Compositions A-J). For instance, Figures 1, 13, 19, and 26 present several example compositions comprising multiple bacterial strains. In one aspect, the 16S rDNA sequences of purified bacterial strains of the compositions were compared to 16S rDNA sequences of known bacterial species/strains in a bacterial genome database to identify the closest known related bacterial species to the bacterial strains disclosed herein (See *e.g.*, Table 1). It should be appreciated that multiple bacterial strains of the compositions disclosed herein may have the same closest related bacterial species.

[0085] It should be appreciated the compositions and treatments provided herein can be distinguished from compositions and treatments associated with the treatment of *C. difficile* infection that are available. For instance, it has been proposed that non-toxigenic *C. difficile* strains, *i.e.*, strains that do not produce *C. difficile* toxins, may be used to treat *C. difficile* infection (See, *e.g.,* US 6,635,260). The compositions disclosed herein can be distinguished at least because the compositions described herein do not comprise non-toxigenic strains of *C. difficile*.

[0086] It is also considered in the art that bacterial strains expressing a bile inducible 7α/β-dehydroxylation operon can be used in the treatment of *C. difficile (*see, *e.g.,* Buffie et al. Nature (2015) 517:205-208). The catalysis of bile acid 7α dihydroxylation is mediated by a stereo-specific NAD(H)-dependent 3-oxo-Δ^4-cholenoic acid oxidoreductase encoded by the gene *baiCD*. In some embodiments, the compositions provided herein do not mediate bile acid 7-alpha-dehydroxylation.

[0087] In contrast to the findings in the art, in some embodiments, as shown herein, combinations of bacterial strains that do not encode *baiCD* (or a homolog thereof), or encode a *baiCD* that comprises one or more mutations that result in a non-functional BaiCD protein ("baiCD-"), are more effective at treating *C. difficile* infection and/or reducing or inhibiting production of Toxin B by *C. difficile* than combinations of bacterial strains that have a functional BaiCD protein ("baiCD+"). Thus, in some embodiments, the compositions of bacterial strains provided herein are baiCD- (*i.e.,* the combination of the bacteria has no effective baiCD+ function). In some embodiments, all of bacterial strains in the compositions provided herein are baiCD-. In some embodiments, the majority (*i.e.,* 50% or greater) of the bacterial strains in the compositions are baiCD-. In some embodiments, the majority (*i.e.,* 50% or greater) of the bacterial strains in the compositions are baiCD- and the composition has no effective BaiCD function. In some embodiments, the minority (*i.e.,* 50% or less) of the bacterial strains in the compositions are baiCD- and the composition has no effective BaiCD function. In some embodiments, bacterial strains for the compositions are selected based on the absence (or presence) of a *baiCD* gene or a predicted *baiCD* gene. In some embodiments, bacterial strains may be modified (*e.g.*, genetically engineered) to prevent or reduce expression of a *baiCD* gene and/or to reduce or eliminate NAD(H)-dependent 3-oxo-Δ^4-cholenoic acid oxidoreductase activity of BaiCD protein. The NAD(H)-dependent 3-oxo-Δ^4-cholenoic acid oxidoreductase activity of a bacterial strain may be assessed by methods such as measuring the amount of 7α-dehydroxylated bile acid. In some embodiments, the compositions described herein comprise bacterial strains without the *baiCD* operon (*baiCD*$^-$) or *baiCD* function.

[0088] In some embodiments of the compositions provided herein, the compositions do not include bacterial strains that are resistant to one or more antibiotics. It should be appreciated that it may be desirable to have a mechanism to remove the bacterial compositions provided herein from the body of the subject after administration. One such mechanism is to remove the bacterial compositions by antibiotic treatment. Thus, in some embodiments, the compositions do not include bacterial strains that are resistant to one or more antibiotics. In some embodiments, the compositions do not include bacterial strains that are resistant to one or more antibiotics selected from the group consisting of penicillin, benzylpenicillin, ampicillin, sulbactam, amoxicillin, clavulanate, tazobactam, piperacillin, cefmetazole, vancomycin, imipenem, meropenem, metronidazole and clindamycin. In some embodiments, the compositions do not include bacterial strains that are resistant to vancomycin.

[0089] In some embodiments, the compositions include bacterial strains that are susceptible to at least four antibiotics that are efficacious in humans. In some embodiments, the compositions include bacterial strains that are susceptible to at least three antibiotics that are efficacious in humans. In some embodiments, the compositions include bacterial strains that are susceptible to at least two antibiotics that are efficacious in humans. In some embodiments, the compositions include bacterial strains that are susceptible to at least one antibiotic that is efficacious in humans. In some embodiments, the compositions include only bacterial strains that are susceptible to at least four antibiotics that are efficacious in humans. In some embodiments, the compositions include only bacterial strains that are susceptible to at least three antibiotics that are efficacious in humans. In some embodiments, the compositions include only bacterial strains that are susceptible to at least two antibiotics that are efficacious in humans. In some embodiments, the compositions include bacterial strains that are susceptible to at least one antibiotic that is efficacious in humans. As used herein, an "antibiotic that is efficacious in a human" refers to an antibiotic that has been used to successfully treat bacterial infections in a human.

[0090] In some embodiments, the compositions described herein comprise spore forming and non-spore forming bacterial strains. In some embodiments, the compositions described herein comprise spore forming bacterial strains. In some embodiments, the compositions described herein comprise only spore forming bacterial strains. In some embodiments, the compositions described herein comprise only non-spore forming bacterial strains. The spore-forming bacteria can be in spore form (*i.e.,* as spores) or in vegetative form (*i.e..,* as vegetative cells). In spore form, bacteria are generally more resistant to environmental conditions, such as heat, acid, radiation, oxygen, chemicals, and antibiotics. In contrast, in the vegetative state or actively growing state, bacteria are more susceptible to such environmental conditions, compared to in the spore form. In general, bacterial spores are able to germinate from the spore form into a vegetative/actively growing state, under appropriate conditions. For instance, bacteria in spore

format may germinate when thye are introduced in the intestine.

[0091] In some embodiments, at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is a spore former. In some embodiments, at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is in spore form. In some embodiments, at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is a non-spore former. In some embodiments, at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is in vegetative form (As discussed above, spore forming bacteria can also be in vegetative form). In some embodiments, at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is in spore form and at least one (*e.g.*, 1, 2, 3, 4, 5, or more) of the bacterial strains in the composition is in vegetative form. In some embodiments, at least one bacterial strain that is considered able to form spores (*i.e.*, a spore-former) but is present in the composition in vegetative form. In some embodiments, at least one bacterial strain that is considered able to form spores is present in the composition both in spore form and in vegetative form.

[0092] In some embodiments, the disclosure provides compositions wherein the compositions comprise bacterial strains that are spore forming bacterial strains. In some embodiments, the disclosure provides compositions wherein the compositions comprise bacterial strains that are non-spore forming bacterial strains. In some embodiments, the disclosure provides compositions wherein the compositions comprise bacterial strains that are spore forming bacterial strains and bacterial strains that are non-spore forming bacterial strains. In some embodiments, the disclosure provides compositions, wherein the compositions comprise a mixture of bacterial strains wherein at least 10% of the bacterial strains are spore forming bacterial strains, at least 20% of the bacterial strains are spore forming bacterial strains, at least 30% of the bacterial strains are spore forming bacterial strains, at least 40% of the bacterial strains are spore forming bacterial strains, at least 50% of the bacterial strains are spore forming bacterial strains, at least 60% of the bacterial strains are spore forming bacterial strains, at least 70% of the bacterial strains are spore forming bacterial strains, at least 80% of the bacterial strains are spore forming bacterial strains, at least 90% of the bacterial strains are spore forming bacterial strains bacteria up to 100% spore forming bacterial strains. Whether a bacterial strain is a spore forming strain can be determined for instance by evaluating the genome of the bacterial strain for the presence of sporulation genes. However, it should be appreciated that not all bacteria that are predicted to encode spore forming genes can be made to sporulate. In addition, whether a bacterial strain is a spore forming strain can be determined by exposing the bacterial strain to stress conditions, *e.g.,* heat or exposure to chemicals (*e.g.,* ethanol or chloroform), that are known to induce sporulation.

[0093] It should be appreciated that spore forming bacteria can be in spore form or in vegetative form. In some embodiments of the compositions provided herein, the spore forming bacteria are in spore form. In some embodiments of the compositions provided herein, the spore forming bacteria are in vegetative form. In some embodiments of the compositions provided herein, the spore forming bacteria are both present in spore form and in vegetative form. In some embodiments, the disclosure provides compositions, wherein the compositions comprise spore forming bacteria at least 10% of the spore forming bacteria are in spore format, at least 20% of the spore forming bacteria are in spore format, at least 30% of the spore forming bacteria are in spore format, at least 40% of the spore forming bacteria are in spore format, at least 50% of the spore forming bacteria are in spore format, at least 60% of the spore forming bacteria are in spore format, at least 70% of the spore forming bacteria are in spore format, at least 80% of the spore forming bacteria are in spore format, at least 90% of the spore forming bacteria are in spore format, up to 100% in spore format.

[0094] It is envisioned that the bacterial strains of the compositions provided herein are alive and will be alive when they reach the target area (*e.g.*, the intestines). Bacterial spores are considered to be alive in this regards. In some embodiments, bacteria that are administered as spores may germinate in the target area (*e.g.*, the intestines). It should further be appreciated that not all of the bacteria are alive and the compositions can include a percentage (*e.g.*, by weight) that is not alive. In addition, in some embodiments, the compositions include bacterial strains that are not alive when administered or at the time when the composition reaches the target area (*e.g.,* the intestines). It is envisioned that non-living bacteria may still be useful by providing some nutrients and metabolites for the other bacterial strains in the composition.

[0095] Methods of inducing sporulation of spore-forming bacterial strains are well known in the art (See *e.g.*, Paredes-Sabja et al., Trends Microbiol. (2011) 19(2):85-94). Generally, bacterial strains that are spore-formers can be made to go into spore form by stressing the bacterial strains. Non-limiting examples of stresses that can induce sporulation are an increase in temperature, change in the nutrients available and/or exposure to chemicals (*e.g.*, ethanol or chloroform). It should be noted that bacteria that are non-spore formers, for instance because they are missing sporulation genes, cannot be made to sporulate by stress. To prepare compositions in which all the bacterial strains are in the spore form, the composition or bacterial cultures used to prepare the composition may be subjected to treatment to kill any bacteria not in spore form (*e.g.,* in vegetative form), for example by exposing the composition to heat and are chemically breaking down the non-spore bacteria. The bacteria in spore format can subsequently be separated from the non-spore bacteria for instance by filtration.

[0096] The amount of spores can be quantified using techniques know in the art. These techniques include phase contrast microscopy for enumerating spores using a hemocytometer. In addition, the viability of spores can be determined by plating the spores and growing the spores. For instance, spores can be plated in appropriate media and incubated in the anaerobic chamber for a period of time (*e.g.*, 48-96 hrs.). Viability can subsequently be determined by quantifying the colony forming units which correspond to spores that germinated. For instance, spores can be plated on TCCFA plates (Taurocholate, cycloserine, cefoxintin, fructose agar plates), in which taurocholate helps the spores to germinate. In addition, spores can be quantified using the dipicolinic assay (DPA assay). DPA is an agent that allows for spore selection and is a clear indicator of endospores. When complexed with terbium, bright green luminescence is observed.

[0097] In any of the compositions provided herein, the bacterial strains are purified. In any of the compositions provided herein, in some embodiments, the bacterial strains are isolated. Any of the bacterial strains described herein may be isolated, for example, from a source such as a culture or a microbiota sample (*e.g.*, fecal matter). The bacterial strains used in the compositions provided herein generally are isolated from the microbiome of healthy individuals. However, bacterial strains can also be isolated from individuals that are considered not to be healthy. In some embodiments, the compositions include strains originating from multiple individuals.

[0098] As used herein, the term "isolated" bacteria that have been separated from one or more undesired component, such as another bacterium or bacterial strain, one or more component of a growth medium, and/or one or more component of a sample, such as a fecal sample. In some embodiments, the bacteria are substantially isolated from a source such that other components of the source are not detected.

[0099] As also used herein, the term "purified" refers to a bacterial strain or composition comprising such that has been separated from one or more components, such as contaminants. In some embodiments, the bacterial strain is substantially free of contaminants. In some embodiments, one or more bacterial strains of a composition may be independently purified from one or more other bacteria produced and/or present in a culture or a sample containing the bacterial strain. In some embodiments, a bacterial strain is isolated or purified from a sample and then cultured under the appropriate conditions for bacterial replication, *e.g.*, under anaerobic culture conditions. The bacteria that is grown under appropriate conditions for bacterial replication can subsequently be isolated/purified from the culture in which it is grown.

[0100] In some embodiments, the bacterial strains of the compositions provided herein are obligate anaerobes. In some embodiments, the bacterial strains of the compositions provided herein are facultative anaerobes. the treatment of

[0101] Aspects of the present disclosure are related to the treatment of a pathogenic infection in a subject by administering a therapeutically effective amount of any of the compositions described herein. In some embodiments, the subject is a mammalian subject, such as a human, non-human primate, rodent, rabbit, sheep, pig, dog, cat, horse, or cow. In some embodiments, the subject is a human subject. In some embodiments, the subject is a pig.

[0102] In some embodiments, the subject is a carrier of a pathogenic organism and is suffering from the effects of the infection (*e.g.*, diarrhea caused by *C. difficile* toxins). In some embodiments the subject is an asymptomatic carrier of a pathogen. In some embodiments, the subject is a carrier of *C. difficile*. In some embodiments the subject is an asymptomatic *C. difficile* carrier. In some embodiments, the subject has experienced recurrent or chronic pathogenic infections. In some embodiments, the subject is suffering from a first occurrence of a particular pathogenic infection. In some embodiments, the subject has been treated with antibiotics which resulted in the recurrence of the pathogenic infection. In some embodiments, the subject has been treated with antibiotics which resulted in a first occurrence of a pathogenic infection. In some embodiments, the subject is to undergo a procedure that puts the subject at a higher risk of infection. In some embodiments, the compositions provided herein are

administered to a subject to lower the risk of becoming infected by a pathogen.

[0103] In some embodiments, the compositions provided herein are administered to a subject if the subject has a dysbiosis (*e.g.*, has as microbiome associated with a disease state). In some embodiments, treatment with the compositions provided herein results in the change in the microbiome of the subject. In some embodiments, treatment with the compositions provided herein removes the dysbiosis in the subject resulting in a healthy microbiome. In some embodiments, treatment with the compositions provided herein removes the dysbiosis in the subject resulting in microbiome refractory or less susceptible to infection by a pathogen.

[0104] As used herein, the term "pathogen" in regard to a pathogenic infection refers to a microorganism (*e.g.*, a bacterium) that causes a disease or a disease state in a subject. In some embodiments, the disease or disease state of the subject may include symptoms such as colitis, diarrhea, watery diarrhea, abdominal cramping, fever, blood or pus in the stool, nausea, dehydration, loss of appetite, chills, weight loss, and/or kidney failure. In some embodiments, the pathogenic infection may be diagnosed, for example, by detecting a pathogen (or protein or nucleic acid associated with a pathogen) in a fecal sample collected from the subject. In some embodiments, the pathogenic infection may be diagnosed, for example, by comparing the microbiota of a fecal sample of the subject with the microbiota in a fecal sample of a healthy subject.

[0105] In some embodiments, the pathogenic infection is *C. difficile; Clostridium perfringens; Clostridium botulinum; Clostridium tributtycum; Clostridium sporogenes; Escherichia coli; Pseudomonas aeruginosa*, such as Multidrug Resistant *Pseudomonas aeruginosa; Vancomycin* Resistant *Enterococci* (VRE)*;* Carbapenem Resistant *Enterobacteriaceae* (CRE)*; Neisseria gonorrheae; Acinetobacter*; Multidrug Resistant *Acinetobacter; Campylobacter;* Multi-drug resistant *Campylobacter; Candida*; Fluconazole-resistant *Candida*; Extended spectrum beta-lactamese (ESBL) producing Enterobacteriaceae; *Salmonella*, *Salmonella Typhimurium*, Drug resistant non-typhoid *Salmonella spp.*; Drug resistant *Salmonella Typhi*; Drug resistant *Shigella; Staphylococcus aureus*, such as *Methicillin* Resistant *S. aureus* or vancomycin resistant *S. aureus;* Drug resistant *Streptococcus pneumoniae;* Drug resistant Tuberculosis; Erythromycin Resistant Group A *Streptococcus;* Clindamycin resistant Group B *Streptococcus,* and any combinations thereof. In some embodiments, the pathogenic infection is *C. difficile*. In some embodiments, the *C. difficile* is an antibiotic-resistant *C. difficile*, *e.g.,* fluoroquinolone resistant *C. difficile*. In some embodiments, the pathogenic infection is vancomycin-resistant *Enterococci.*

[0106] Additional non-limiting examples of pathogens responsible for pathogenic infection that can be treated are *Leishmania*, *Staphylococcus epidermis, Staphylococcus saprophyticus, Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, Enterococcus faecalis, Corynebacterium diptheriae, Bacillus anthracis, Listeria monocytogenes, Clostridium perfringens, Clostridium tetanus, Clostridium botulinum, Clostridium difficile, Neisseria meningitidis, Neisseria gonorrhoeae, Escherichia coli, Salmonella typhimurium, Salmonella cholerasuis, Salmonella enterica, Salmonella enteriditis, Yersinia pestis, Yersinia pseudotuberculosis, Yersinia enterocolitica, Vibrio cholerae, Campylobacter jejuni, Campylobacter fetus, Helicobacter pylori, Pseudomonas aeruginosa, Pseudomonas mallei, Haemophilus influenzae, Bordetella pertussis, Mycoplasma pneumoniae, Ureaplasma urealyticum, Legionella pneumophila, Treponema pallidum, Leptospira interrogans, Borrelia burgdorferi, Mycobacterium tuberculosis, Mycobacterium leprae, Chlamydia psittaci, Chlamydia trachomatis, Chlamydia pneumoniae, Rickettsia ricketsii, Rickettsia akari, Rickettsia prowazekii, Brucella abortus, Brucella melitens, Brucella suis,* and *Francisella tularensis*. In general, any bacterium that is capable of inducing a disease in a subject and/or that is not present in healthy individual is considered a pathogen herein. It should be appreciated that a subject may carry multiple pathogens and/or have multiple pathogenic infections.

[0107] Any of the compositions described herein may be administered to a subject in a therapeutically effective amount or a dose of a therapeutically effective amount to treat or prevent a pathogenic infection (*e.g.*, one or more pathogenic infections). The terms "treat" or "treatment" refer to reducing or alleviating one or more of the symptoms associated with a pathogenic infection, reducing the amount of bacterial toxin produced by the pathogenic infection, and/or reducing the bacterial load of the pathogenic infection. The terms "prevent" or "prevention" encompass prophylactic administration and may reduce the incidence or likelihood of pathogenic infection or a recurrent or chronic pathogenic infection. For instance, in some embodiments, administration of the compositions provided herein result in a healthy microbiome that is refractory to pathogenic infection, thereby preventing the pathogenic infection.

[0108] As used herein, a "therapeutically effective amount" of composition, such as a pharmaceutical composition, is any amount that results in a desired response or outcome in a subject, such as those described herein, including but not limited to prevention of infection, an immune response or an enhanced immune response to the pathogenic infection, prevention or reduction of symptoms associated with pathogenic infection, and/or a reduction or inhibition of toxin production by the pathogenic infection. It should be appreciated that the term effective amount may be expressed in number of bacteria or bacterial spores to be administered. It should further be appreciated that the bacteria can multiply once administered. Thus, administration of even a relatively small amount of bacteria may have therapeutic effects.

[0109] In some embodiments, the therapeutically effective amount of any of the compositions described herein is an amount sufficient to enhance survival of the subject, reduce the bacterial burden of the pathogenic infection in the subject, and/or reduce or inhibit toxin production by the pathogenic infection. In some embodiments, the therapeutically effective amount is an amount sufficient to reduce the bacterial burden of the pathogenic infection in a fecal sample from the subject by at least 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 30-fold, 40-fold, 50-fold, 100-fold, 1000-fold, 10^4-fold, 10^5-fold or more, as compared to the bacterial burden in a subject with a pathogenic infection that has not received any of the compositions described herein, or as compared to a fecal sample from the same subject that was collected prior to administration of any of the compositions.

[0110] In some embodiments, the compositions provided herein inhibit the production of a bacterial toxin, *e.g., C. difficile* Toxin B. In some embodiments, the therapeutically effective amount is an amount sufficient to reduce or inhibit the amount of bacterial toxin (*e.g., C. difficile* Toxin B) produced by pathogenic infection in a fecal sample from the subject by at least 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 30-fold, 40-fold, 50-fold, 100-fold, 150-fold, 200-fold, 500-fold or more, as compared to the amount of the bacterial toxin in a subject with a pathogenic infection that has not received any of the compositions described herein or as compared to a fecal sample from the same subject that was collected prior to administration of any of the compositions.

[0111] In some embodiments, the compositions provided herein induce the proliferation and/or accumulation of regulatory T cells in the subject. As will be evident to one of ordinary skill in the art, regulatory T cells, also referred to as "Tregs," are a subset of T lymphocytes that are generally thought to suppress an abnormal or excessive immune response and play a role in immune tolerance. Regulatory T cells may be identified based expression of the markers Foxp3 and CD4 (Foxp3+ CD4+). The term regulatory T cells may also include Foxp3-negative regulatory T cells that are IL-10-producing CD4-positive T cells.

[0112] In some embodiments, the therapeutically effective amount is an amount sufficient to induce the proliferation and/or accumulation of Tregs in the subject (or in a sample obtained from a subject) by at least 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 30-fold, 40-fold, 50-fold, 100-fold, 150-fold, 200-fold, 500-fold or more, as compared to the amount of Tregs in a subject (*e.g.,* a subject with a pathogenic infection) that has not received any of the compositions described herein or as compared to a fecal sample from the same subject that was collected prior to administration of any of the compositions.

[0113] As used herein, the phrase "induces proliferation and/or accumulation of regulatory T cells" refers to an effect of inducing the differentiation of immature T cells into regulatory T cells, which differentiation leads to the proliferation and/or the accumulation of regulatory T cells. Further, the meaning of "induces proliferation and/or accumulation of regulatory T cells" includes *in vivo* effects, *in vitro* effects, and *ex vivo* effects. In some embodiments, the proliferation and/or accumulation of regulatory T cells may be assessed by detecting and/or quantifying the number of cells that express markers of regulatory T cells (*e.g.,* Foxp3 and CD4), for example by flow cytometry. In some embodiments, the proliferation and/or accumulation of regulatory T cells may be assessed by determining the activity of the regulatory T cells, such as the production of cytokines (*e.g.*, IL-10).

[0114] In some embodiments, the therapeutically effective amount is an amount sufficient to recolonize or repopulate the gastrointestinal tract of the subject with non-pathogenic bacteria. In some embodiments, the therapeutically effective amount is an amount sufficient to graft one or more of the bacterial strains of the composition in the gastrointestinal tract of the subject. In some embodiments, a fecal sample is obtained from the subject to assess the bacterial burden of the pathogenic infection and/or evaluate the efficacy of administration of the bacterial compositions described herein. In some embodiments, the microbiota of the subject (*e.g.,* the identity and abundance of strains and/or species of the microbiota) may be assessed to determine a disease state of the subject and/or assess progress of the treatment. In some embodiments, the

microbiota of the subject having a pathogenic infection is compared to the microbiota of a healthy subject, such as a subject that is not experiencing or has not experienced the pathogenic infection. In some embodiments, the microbiota of the subject having a pathogenic infection is compared to the microbiota of the same subject from a fecal sample obtained from the subject prior to the pathogenic infection.

[0115] Any of the compositions described herein, including the pharmaceutical compositions and food products comprising the compositions, may contain bacterial strains in any form, for example in an aqueous form, such as a solution or a suspension, embedded in a semi-solid form, in a powdered form or freeze dried form. In some embodiments, the composition or the bacterial strains of the composition are lyophilized. In some embodiments, a subset of the bacterial strains in a composition is lyophilized. Methods of lyophilizing compositions, specifically compositions comprising bacteria, are well known in the art. See, *e.g.,* US 3,261,761; US 4,205, 132; PCT Publications WO 2014/029578 and WO 2012/098358. The bacteria may be lyophilized as a combination and/or the bacteria may be lyophilized separately and combined prior to administration. A bacterial strain may be combined with a pharmaceutical excipient prior to combining it with the other bacterial strain or multiple lyophilized bacteria may be combined while in lyophilized form and the mixture of bacteria, once combined may be subsequently be combined with a pharmaceutical excipient. In some embodiments, the bacterial strain is a lyophilized cake. In some embodiments, the compositions comprising the one or more bacterial strains are a lyophilized cake.

[0116] The bacterial strains of the composition can be manufactured using fermentation techniques well known in the art. In some embodiments, the active ingredients are manufactured using anaerobic fermenters, which can support the rapid growth of anaerobic bacterial species. The anaerobic fermenters may be, for example, stirred tank reactors or disposable wave bioreactors. Culture media such as BL media and EG media, or similar versions of these media devoid of animal components, can be used to support the growth of the bacterial species. The bacterial product can be purified and concentrated from the fermentation broth by traditional techniques, such as centrifugation and filtration, and can optionally be dried and lyophilized by techniques well known in the art.

[0117] In some embodiments, the composition of bacterial strains may be formulated for administration as a pharmaceutical composition. The term "pharmaceutical composition" as used herein means a product that results from the mixing or combining of at least one active ingredient, such as any two or more purified bacterial strains described herein, and one or more inactive ingredients, which may include one or more pharmaceutically acceptable excipient.

[0118] An "acceptable" excipient refers to an excipient that must be compatible with the active ingredient and not deleterious to the subject to which it is administered. In some embodiments, the pharmaceutically acceptable excipient is selected based on the intended route of administration of the composition, for example a composition for oral or nasal administration may comprise a different pharmaceutically acceptable excipient than a composition for rectal administration. Examples of excipients include sterile water, physiological saline, solvent, a base material, an emulsifier, a suspending agent, a surfactant, a stabilizer, a flavoring agent, an aromatic, an excipient, a vehicle, a preservative, a binder, a diluent, a tonicity adjusting agent, a soothing agent, a bulking agent, a disintegrating agent, a buffer agent, a coating agent, a lubricant, a colorant, a sweetener, a thickening agent, and a solubilizer.

[0119] Pharmaceutical compositions of the invention can be prepared in accordance with methods well known and routinely practiced in the art (see *e.g.*, Remington: The Science and Practice of Pharmacy, Mack Publishing Co. 20th ed. 2000). The pharmaceutical compositions described herein may further comprise any carriers or stabilizers in the form of a lyophilized formulation or an aqueous solution. Acceptable excipients, carriers, or stabilizers may include, for example, buffers, antioxidants, preservatives, polymers, chelating reagents, and/or surfactants. Pharmaceutical compositions are preferably manufactured under GMP conditions. The pharmaceutical compositions can be used orally, nasally or parenterally, for instance, in the form of capsules, tablets, pills, sachets, liquids, powders, granules, fine granules, film-coated preparations, pellets, troches, sublingual preparations, chewables, buccal preparations, pastes, syrups, suspensions, elixirs, emulsions, liniments, ointments, plasters, cataplasms, transdermal absorption systems, lotions, inhalations, aerosols, injections, suppositories, and the like.

[0120] In some embodiments, the bacteria are formulated for delivery to the intestines (*e.g.*, the small intestine and/or the colon). In some embodiments, the bacteria are formulated with an enteric coating that increases the survival of the bacteria through the harsh environment in the stomach. The enteric coating is one which resists the action of gastric juices in the stomach so that the bacteria which are incorporated therein will pass through the stomach and into the intestines. The enteric coating may readily dissolve when in contact with intestinal fluids, so that the bacteria enclosed in the coating will be released in the intestinal tract. Enteric coatings may consist of polymer and copolymers well known in the art, such as commercially available EUDRAGIT (Evonik Industries). (See *e.g.,* Zhang, AAPS PharmSciTech, (2016) 17 (1), 56-67).

[0121] The bacteria may also be formulated for rectal delivery to the intestine (*e.g.*, the colon). Thus, in some embodiments, the bacterial compositions may be formulated for delivery by suppository, colonoscopy, endoscopy, sigmoidoscopy or enema. A pharmaceutical preparation or formulation and particularly a pharmaceutical preparation for oral administration, may include an additional component that enables efficient delivery of the compositions of the disclosure to the intestine (*e.g.*, the colon). A variety of pharmaceutical preparations that allow for the delivery of the compositions to the intestine (*e.g.,* the colon) can be used. Examples thereof include pH sensitive compositions, more specifically, buffered sachet formulations or enteric polymers that release their contents when the pH becomes alkaline after the enteric polymers pass through the stomach. When a pH sensitive composition is used for formulating the pharmaceutical preparation, the pH sensitive composition is preferably a polymer whose pH threshold of the decomposition of the composition is between about 6.8 and about 7.5. Such a numeric value range is a range in which the pH shifts toward the alkaline side at a distal portion of the stomach, and hence is a suitable range for use in the delivery to the colon. It should further be appreciated that each part of the intestine (*e.g.*, the duodenum, jejunum, ileum, cecum, colon and rectum), has different biochemical and chemical environment. For instance, parts of the intestines have different pHs, allowing for targeted delivery by compositions that have a specific pH sensitivity. Thus, the compositions provided herein may be formulated for delivery to the intestine or specific parts of the intestine (*e.g.*, the duodenum, jejunum, ileum, cecum, colon and rectum) by providing formulations with the appropriate pH sensitivity. (See *e.g.,* Villena et al., Int J Pharm 2015, 487 (1-2): 314-9).

[0122] Another embodiment of a pharmaceutical preparation useful for delivery of the compositions to the intestine (*e.g.,* the colon) is one that ensures the delivery to the colon by delaying the release of the contents (*e.g.,* the bacterial strains) by approximately 3 to 5 hours, which corresponds to the small intestinal transit time. In one embodiment of a pharmaceutical preparation for delayed release, a hydrogel is used as a shell. The hydrogel is hydrated and swells upon contact with gastrointestinal fluid, with the result that the contents are effectively released (released predominantly in the colon). Delayed release dosage units include drug-containing compositions having a material which coats or selectively coats a drug or active ingredient to be administered. Examples of such a selective coating material include in vivo degradable polymers, gradually hydrolyzable polymers, gradually watersoluble polymers, and/or enzyme degradable polymers. A wide variety of coating materials for efficiently delaying the release is available and includes, for example, cellulose-based polymers such as hydroxypropyl cellulose, acrylic acid polymers and copolymers such as methacrylic acid polymers and copolymers, and vinyl polymers and copolymers such as polyvinylpyrrolidone.

[0123] Additional examples of pharmaceutical compositions that allow for the delivery to the intestine (*e.g.*, the colon) include bioadhesive compositions which specifically adhere to the colonic mucosal membrane (for example, a polymer described in the specification of US Patent No. 6.368.586) and compositions into which a protease inhibitor is incorporated for protecting particularly a biopharmaceutical preparation in the gastrointestinal tracts from decomposition due to an activity of a protease.

[0124] Another example of a system enabling the delivery to the intestine (*e.g.*, the colon) is a system of delivering a composition to the colon by pressure change in such a way that the contents are released by utilizing pressure change caused by generation of gas in bacterial fermentation at a distal portion of the stomach. Such a system is not particularly limited, and a more specific example thereof is a capsule which has contents dispersed in a suppository base and which is coated with a hydrophobic polymer (for example, ethyl cellulose).

[0125] A further example of a system enabling the delivery of a composition to the intestine (*e.g.,* the colon), is a composition that includes a coating that can be removed by an enzyme present in the gut (*e.g.,* the colon), such as, for example, a carbohydrate hydrolase or a carbohydrate reductase. Such a system is not particularly limited, and more specific examples thereof include systems which use food components such as non-starch polysaccharides, amylose, xanthan gum, and azopolymers.

[0126] The compositions provided herein can also be delivered to specific target areas, such as the intestine, by delivery through an orifice (*e.g.,* a nasal tube) or through

surgery. In addition, the compositions provided herein that are formulated for delivery to a specific area (*e.g.*, the cecum or the colon), may be administered by a tube (*e.g.*, directly into the small intestine). Combining mechanical delivery methods such as tubes with chemical delivery methods such as pH specific coatings, allow for the delivery of the compositions provided herein to a desired target area (e.g., the cecum or the colon).

[0127] The compositions comprising bacterial strains are formulated into pharmaceutically acceptable dosage forms by conventional methods known to those of skill in the art. Dosage regimens are adjusted to provide the optimum desired response (*e.g.*, the prophylactic or therapeutic effect). In some embodiments, the dosage form of the composition is a tablet, pill, capsule, powder, granules, solution, or suppository. In some embodiments, the pharmaceutical composition is formulated for oral administration. In some embodiments, the pharmaceutical composition is formulated such that the bacteria of the composition, or a portion thereof, remain viable after passage through the stomach of the subject. In some embodiments, the pharmaceutical composition is formulated for rectal administration, *e.g.* as a suppository. In some embodiments, the pharmaceutical composition is formulated for delivery to the intestine or a specific area of the intestine (*e.g.*, the colon) by providing an appropriate coating (*e.g.*, a pH specific coating, a coating that can be degraded by target area specific enzymes, or a coating that can bind to receptors that are present in a target area).

[0128] Dosages of the active ingredients in the pharmaceutical compositions of the present invention can be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired pharmaceutical response for a particular subject, composition, and mode of administration, without being toxic or having an adverse effect on the subject. The selected dosage level depends upon a variety of factors including the activity of the particular compositions of the present invention employed, the route of administration, the time of administration, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compositions employed, the age, sex, weight, condition, general health and prior medical history of the subject being treated, and like factors.

[0129] A physician, veterinarian or other trained practitioner, can start doses of the pharmaceutical composition at levels lower than that required to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect (e.g., treatment of a pathogenic infection, reduction of bacterial burden of pathogenic infection, reduction or inhibition of toxin production) is achieved. In general, effective doses of the compositions of the present invention, for the prophylactic treatment of groups of people as described herein vary depending upon many different factors, including routes of administration, physiological state of the subject, whether the subject is human or an animal, other medications administered, and the therapeutic effect desired. Dosages need to be titrated to optimize safety and efficacy. In some embodiments, the dosing regimen entails oral administration of a dose of any of the compositions described herein. In some embodiments, the dosing regimen entails oral administration of multiple doses of any of the compositions described herein. In some embodiments, the composition is administered orally the subject once, twice, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, or at least 10 times.

[0130] The compositions, including the pharmaceutical compositions disclosed herein, include compositions with a range of active ingredients (*e.g.*, live bacteria, bacteria in spore format). The amount of bacteria in the compositions may be expressed in weight, number of bacteria and/or CFUs (colony forming units). In some embodiments, the pharmaceutical compositions disclosed herein contain about 10, about 10^2, about 10^3, about 10^4, about 10^5, about 10^6, about 10^7, about 10^8, about 10^9, about 10^{10}, about 10^{11}, about 10^{12}, about 10^{13} or more of each of the bacteria of the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain about 10, about 10^2, about 10^3, about 10^4, about 10^5, about 10^6, about 10^7, about 10^8, about 10^9, about 10^{10}, about 10^{11}, about 10^{12}, about 10^{13} or more total bacteria per dosage amount. It should further be appreciated that the bacteria of the compositions may be present in different amounts. Thus, for instance, as a non-limiting example, a composition may include 10^3 of bacteria A, 10^4 of bacteria B and 10^6 of bacteria C. In some embodiments, the pharmaceutical compositions disclosed herein contain about 10, about 10^2, about 10^3, about 10^4, about 10^5, about 10^6, about 10^7, about 10^8, about 10^9, about 10^{10}, about 10^{11}, about 10^{12}, about 10^{13} or more CFUs of each of the bacteria in the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain about 10^1, about 10^2, about 10^3, about 10^4, about 10^5, about 10^6, about 10^7, about 10^8, about 10^9, about 10^{10}, about 10^{11}, about 10^{12}, about 10^{13} or more CFUs in total for all of the bacteria combined per dosage amount. As discussed above, bacteria of the compositions may be present in different amounts. In some embodiments, the pharmaceutical compositions disclosed herein contain about 10^{-7}, about 10^{-6}, about 10^{-5}, about 10^{-4}, about 10^{-3}, about 10^{-2}, about 10^{-1} or more grams of each of the bacteria in the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain about 10^{-7}, about 10^{-6}, about 10^{-5}, about 10^{-4}, about 10^{-3}, about 10^{-2}, about 10^{-1} or more grams in total for all of the bacteria combined per dosage amount. In some embodiment, the dosage amount is one administration device (*e.g.*, one table, pill or capsule). In some embodiment, the dosage amount is the amount that is administered in a particular period (*e.g.*, one day or one week).

[0131] In some embodiments, the pharmaceutical compositions disclosed herein contain between 10 and 10^{13}, between 10^2 and 10^{13}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{13}, between 10^8 and 10^{13}, between 10^9 and 10^{13}, between 10^{10} and 10^{13}, between 10^{11} and 10^{13}, between 10^{12} and 10^{13}, between 10 and 10^{12}, between 10^2 and 10^{12}, between 10^3 and 10^{12}, between 10^4 and 10^{12}, between 10^5 and 10^{12}, between 10^6 and 10^{12}, between 10^7 and 10^{12}, between 10^8 and 10^{12}, between 10^9 and 10^{12}, between 10^{10} and 10^{12}, between 10^{11} and 10^{12}, between 10 and 10^{11}, between 10^2 and 10^{11}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{11}, between 10^8 and 10^{11}, between 10^9 and 10^{11}, between 10^{10} and 10^{11}, between 10 and 10^{10}, between 10^2 and 10^{10}, between 10^3 and 10^{10}, between 10^4 and 10^{10}, between 10^5 and 10^{10}, between 10^6 and 10^{10}, between 10^7 and 10^{10}, between 10^8 and 10^{10}, between 10^9 and 10^{10}, between 10 and 10^9, between 10^2 and 10^9, between 10^3 and 10^9, between 10^4 and 10^9, between 10^5 and 10^9, between 10^6 and 10^9, between 10^7 and 10^9, between 10^8 and 10^9, between 10 and 10^8, between 10^2 and 10^8, between 10^3 and 10^8, between 10^4 and 10^8, between 10^5 and 10^8, between 10^6 and 10^8, between 10^7 and 10^8, between 10 and 10^7, between 10^2 and 10^7, between 10^3 and 10^7, between 10^4 and 10^7, between 10^5 and 10^7, between 10^6 and 10^7, between 10 and 10^6, between 10^2 and 10^6, between 10^3 and 10^6, between 10^4 and 10^6, between 10^5 and 10^6, between 10 and 10^5, between 10^2 and 10^5, between 10^3 and 10^5, between 10^4 and 10^5, between 10 and 10^4, between 10^2 and 10^4, between 10^3 and 10^4, between 10 and 10^3, between 10^2 and 10^3, or between 10 and 10^2 of each of the bacteria of the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain between 10 and 10^{13}, between 10^2 and 10^{13}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{13}, between 10^8 and 10^{13}, between 10^9 and 10^{13}, between 10^{10} and 10^{13}, between 10^{11} and 10^{13} , between 10^{12} and 10^{13}, between 10 and 10^{12}, between 10^2 and 10^{12}, between 10^3 and 10^{12}, between 10^4 and 10^{12}, between 10^5 and 10^{12}, between 10^6 and 10^{12}, between 10^7 and 10^{12}, between 10^8 and 10^{12}, between 10^9 and 10^{12}, between 10^{10} and 10^{12}, between 10^{11} and 10^{12}, between 10 and 10^{11}, between 10^2 and 10^{11}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{11}, between 10^8 and 10^{11}, between 10^9 and 10^{11}, between 10^{10} and 10^{11}, between 10 and 10^{10}, between 10^2 and 10^{10}, between 10^3 and 10^{10}, between 10^4 and 10^{10}, between 10^5 and 10^{10}, between 10^6 and 10^{10}, between 10^7 and 10^{10}, between 10^8 and 10^{10}, between 10^9 and 10^{10}, between 10 and 10^9, between 10^2 and 10^9, between 10^3 and 10^9, between 10^4 and 10^9, between 10^5 and 10^9, between 10^6 and 10^9, between 10^7 and 10^9, between 10^8 and 10^9, between 10 and 10^8, between 10^2 and 10^8, between 10^3 and 10^8, between 10^4 and 10^8, between 10^5 and 10^8, between 10^6 and 10^8, between 10^7 and 10^8, between 10 and 10^7, between 10^2 and 10^7, between 10^3 and 10^7, between 10^4 and 10^7, between 10^5 and 10^7, between 10^6 and 10^7, between 10 and 10^6, between 10^2 and 10^6, between 10^3 and 10^6, between 10^4 and 10^6, between 10^5 and 10^6, between 10 and 10^5, between 10^2 and 10^5, between 10^3 and 10^5, between 10^4 and 10^5, between 10 and 10^4, between 10^2 and 10^4, between 10^3 and 10^4, between 10 and 10^3, between 10^2 and 10^3, or between 10 and 10^2 total bacteria per dosage amount.

[0132] In some embodiments, the pharmaceutical compositions disclosed herein contain between 10 and 10^{13}, between 10^2 and 10^{13}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{13}, between 10^8 and 10^{13}, between 10^9 and 10^{13}, between 10^{10} and 10^{13}, between 10^{11} and 10^{13} , between 10^{12} and 10^{13}, between 10 and 10^{12}, between 10^2 and 10^{12}, between 10^3 and 10^{12}, between 10^4 and 10^{12}, between 10^5 and 10^{12}, between 10^6 and 10^{12}, between 10^7 and 10^{12}, between 10^8 and 10^{12}, between 10^9 and 10^{12}, between 10^{10} and 10^{12}, between 10^{11} and 10^{12}, between 10 and 10^{11}, between 10^2 and 10^{11}, between

10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{11}, between 10^8 and 10^{11}, between 10^9 and 10^{11}, between 10^{10} and 10^{11}, between 10 and 10^{10}, between 10^2 and 10^{10}, between 10^3 and 10^{10}, between 10^4 and 10^{10}, between 10^5 and 10^{10}, between 10^6 and 10^{10}, between 10^7 and 10^{10}, between 10^8 and 10^{10}, between 10^9 and 10^{10}, between 10 and 10^9, between 10^2 and 10^9, between 10^3 and 10^9, between 10^4 and 10^9, between 10^5 and 10^9, between 10^6 and 10^9, between 10^7 and 10^9, between 10^8 and 10^9, between 10 and 10^8, between 10^2 and 10^8, between 10^3 and 10^8, between 10^4 and 10^8, between 10^5 and 10^8, between 10^6 and 10^8, between 10^7 and 10^8, between 10 and 10^7, between 10^2 and 10^7, between 10^3 and 10^7, between 10^4 and 10^7, between 10^5 and 10^7, between 10^6 and 10^7, between 10 and 10^6, between 10^2 and 10^6, between 10^3 and 10^6, between 10^4 and 10^6, between 10^5 and 10^6, between 10 and 10^5, between 10^2 and 10^5, between 10^3 and 10^5, between 10^4 and 10^5, between 10 and 10^4, between 10^2 and 10^4, between 10^3 and 10^4, between 10 and 10^3, between 10^2 and 10^3, or between 10 and 10^2 CFUs of each of the bacteria of the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain between 10 and 10^{13}, between 10^2 and 10^{13}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{13}, between 10^8 and 10^{13}, between 10^9 and 10^{13}, between 10^{10} and 10^{13}, between 10^{11} and 10^{13}, between 10^{12} and 10^{13}, between 10 and 10^{12}, between 10^2 and 10^{12}, between 10^3 and 10^{12}, between 10^4 and 10^{12}, between 10^5 and 10^{12}, between 10^6 and 10^{12}, between 10^7 and 10^{12}, between 10^8 and 10^{12}, between 10^9 and 10^{12}, between 10^{10} and 10^{12}, between 10^{11} and 10^{12}, between 10 and 10^{11}, between 10^2 and 10^{11}, between 10^3 and 10^{13}, between 10^4 and 10^{13}, between 10^5 and 10^{13}, between 10^6 and 10^{13}, between 10^7 and 10^{11}, between 10^8 and 10^{11}, between 10^9 and 10^{11}, between 10^{10} and 10^{11}, between 10 and 10^{10}, between 10^2 and 10^{10}, between 10^3 and 10^{10}, between 10^4 and 10^{10}, between 10^5 and 10^{10}, between 10^6 and 10^{10}, between 10^7 and 10^{10}, between 10^8 and 10^{10}, between 10^9 and 10^{10}, between 10 and 10^9, between 10^2 and 10^9, between 10^3 and 10^9, between 10^4 and 10^9, between 10^5 and 10^9, between 10^6 and 10^9, between 10^7 and 10^9, between 10^8 and 10^9, between 10 and 10^8, between 10^2 and 10^8, between 10^3 and 10^8, between 10^4 and 10^8, between 10^5 and 10^8, between 10^6 and 10^8, between 10^7 and 10^8, between 10 and 10^7, between 10^2 and 10^7, between 10^3 and 10^7, between 10^4 and 10^7, between 10^5 and 10^7, between 10^6 and 10^7, between 10 and 10^6, between 10^2 and 10^6, between 10^3 and 10^6, between 10^4 and 10^6, between 10^5 and 10^6, between 10 and 10^5, between 10^2 and 10^5, between 10^3 and 10^5, between 10^4 and 10^5, between 10 and 10^4, between 10^2 and 10^4, between 10^3 and 10^4, between 10 and 10^3, between 10^2 and 10^3, or between 10 and 10^2 total CFUs per dosage amount.

[0133] In some embodiments, the pharmaceutical compositions disclosed herein contain between 10^{-7} and 10^{-1}, between 10^{-6} and 10^{-1}, between 10^{-5} and 10^{-1}, between 10^{-4} and 10^{-1}, between 10^{-3} and 10^{-1}, between 10^{-2} and 10^{-1}, between 10^{-7} and 10^{-2}, between 10^{-6} and 10^{-2}, between 10^{-5} and 10^{-2}, between 10^{-4} and 10^{-2}, between 10^{-3} and 10^{-2}, between 10^{-7} and 10^{-3}, between 10^{-6} and 10^{-3}, between 10^{-5} and 10^{-3}, between 10^{-4} and 10^{-3}, between 10^{-7} and 10^{-4}, between 10^{-6} and 10^{-4}, between 10^{-5} and 10^{-4}, between 10^{-7} and 10^{-5}, between 10^{-6} and 10^{-5}, or between 10^{-7} and 10^{-6} grams of each of the bacteria in the composition per dosage amount. In some embodiments, the pharmaceutical compositions disclosed herein contain between 10^{-7} and 10^{-1}, between 10^{-6} and 10^{-1}, between 10^{-5} and 10^{-1}, between 10^{-4} and 10^{-1}, between 10^{-3} and 10^{-1}, between 10^{-2} and 10^{-1}, between 10^{-7} and 10^{-2}, between 10^{-6} and 10^{-2}, between 10^{-5} and 10^{-2}, between 10^{-4} and 10^{-2}, between 10^{-3} and 10^{-2}, between 10^{-7} and 10^{-3}, between 10^{-6} and 10^{-3}, between 10^{-5} and 10^{-3}, between 10^{-4} and 10^{-3}, between 10^{-7} and 10^{-4}, between 10^{-6} and 10^{-4}, between 10^{-5} and 10^{-4}, between 10^{-7} and 10^{-5}, between 10^{-6} and 10^{-5}, or between 10^{-7} and 10^{-6} grams of all of the bacteria combined per dosage amount.

[0134] Also with the scope of the present disclosure are food products comprising any of the bacterial strains described herein and a nutrient. Food products are, in general, intended for the consumption of a human or an animal. Any of the bacterial strains described herein may be formulated as a food product. In some embodiments, the bacterial strains are formulated as a food product in spore form. In some embodiments, the bacterial strains are formulated as a food product in vegetative form. In some embodiments, the food product comprises both vegetative bacteria and bacteria in spore form. The compositions disclosed herein can be used in a food or beverage, such as a health food or beverage, a food or beverage for infants, a food or beverage for pregnant women, athletes, senior citizens or other specified group, a functional food, a beverage, a food or beverage for specified health use, a dietary supplement, a food or beverage for patients, or an animal feed. Non-limiting examples of the foods and beverages include various beverages such as juices, refreshing beverages, tea beverages, drink preparations, jelly beverages, and functional beverages; alcoholic beverages such as beers; carbohydrate-containing foods such as rice food products, noodles, breads, and pastas; paste products such as fish hams, sausages, paste products of seafood; retort pouch products such as curries, food dressed with a thick starchy sauces, soups; dairy products such as milk, dairy beverages, ice creams, cheeses, and yogurts; fermented products such as fermented soybean pastes, yogurts, fermented beverages, and pickles; bean products; various confectionery products such as Western confectionery products including biscuits, cookies, and the like, Japanese confectionery products including steamed bean-jam buns, soft adzuki-bean jellies, and the like, candies, chewing gums, gummies, cold desserts including jellies, cream caramels, and frozen desserts; instant foods such as instant soups and instant soy-bean soups; microwavable foods; and the like. Further, the examples also include health foods and beverages prepared in the forms of powders, granules, tablets, capsules, liquids, pastes, and jellies.

[0135] Food products containing bacterial strains described herein may be produced using methods known in the art and may contain the same amount of bacteria (*e.g.,* by weight, amount or CFU) as the pharmaceutical compositions provided herein. Selection of an appropriate amount of bacteria in the food product may depend on various factors, including for example, the serving size of the food product, the frequency of consumption of the food product, the specific bacterial strains contained in the food product, the amount of water in the food product, and/or additional conditions for survival of the bacteria in the food product.

[0136] Examples of food products which may be formulated to contain any of the bacterial strains described herein include, without limitation, a beverage, a drink, a bar, a snack, a dairy product, a confectionery product, a cereal product, a ready-to-eat product, a nutritional formula, such as a nutritional supplementary formulation, a food or beverage additive.

[0137] In some embodiments, the subject has not received a dose of an antibiotic prior to administration of the bacterial composition. In some embodiments, the subject has not been administered an antibiotic at least 1, at least 2, at least 3, at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 60, at least 90, at least 120, at least 180 or at least 360 days prior to administration of the compositions provided herein. In some embodiments, the person has not been administered and antibiotic to treat the pathogenic infection. In some embodiments, the compositions provided herein comprise the first treatment of the pathogenic infection.

[0138] In some embodiments, the subject may be administered one or more doses of an antibiotic prior to or concurrently with a bacterial composition. Generally, the first line of defense in the treatment of a pathogenic infection is the administration of an antibiotic.

[0139] In some embodiments, the subject is administered a single dose of an antibiotic prior to the bacterial composition. In some embodiments, the subject is administered multiple doses of an antibiotic prior to the bacterial composition. In some embodiments, the subject is administered at least 2, 3, 4, 5 or more doses of an antibiotic prior to the bacterial composition. In some embodiments, the subject is administered a dose of an antibiotic at substantially the same time as the bacterial composition. Examples of antibiotics that can be administered include, without limitation, kanamycin, gentamicin, colistin, metronidazole, vancomycin, clindamycin, fidaxomicin, and cefoperazone.

[0140] Table 1 below provides sequence identifier numbers (SEQ ID NOs) used in the compositions of the experiments disclosed herein, along with the accompanying strain identification number (Strain ID). The closest bacterial species to the indicated strain is presented by genus-species. The 16S rDNA sequence associated with each genus species identified as the closest related genus species is also provided. The percent alignment presents the percent identity between the sequence of the indicated strain with the sequence from the closest genus species and the length of the alignment. The GenBank Accession Number of the closest related species is provided in the last column.

Table 1: Closest bacterial species to the strains described herein

SEQ ID	Strain ID	Closest Genus_species	SEQ ID NO. of closest species	Percent alignment	Alignment lenght	Accession # of closest species
SEQ ID NO: 01	71	Blautia wexlerae	SEQ_94	96.62	207	NR_044054
SEQ ID NO: 02	102	Turicibacter_sanguinis	SEQ_91	97.81	183	NR_028816
SEQ ID NO: 03	5	Clostridium_hathewayi	SEQ_105	92.42	198	NR_036928
SEQ ID NO: 04	7	Blautia_hansenii	SEQ_99	96.62	207	NR_104687
SEQ ID NO: 05	10	Blautia_hansenii	SEQ_99	98.06	206	NR_104687
SEQ ID NO: 06	40	Lactobacillus_mucosae	SEQ_90	87.57	185	NR_024994
SEQ ID NO: 07	59	Blautia_producta	SEQ_106	98.54	206	NR_113270
SEQ ID NO: 07	59	Blautia_coccoides	SEQ_103	98.54	206	NR_104700
SEQ ID NO: 08	79	Blautia_hansenii	SEQ_99	100	194	NR_104687
SEQ ID NO: 09	VE202-21	Eubacterium_contortum	SEQ_109	94.59	296	NR_117147
SEQ ID NO: 09	VE202-21	Eubacterium_fissicatena	SEQ_108	94.59	296	NR_117142
SEQ ID NO: 10	211	Flavonifractor_plautii	SEQ_93	98.49	199	NR_043142
SEQ ID NO: 11	VE202-9	Anaerostipes_caccae	SEQ_88	99.5	399	NR_028915
SEQ ID NO: 12	VE202-26	Clostridium_scindens	SEQ_87	95.76	354	NR_028785
SEQ ID NO: 13	136	Marvinbryantia_formatexigens	SEQ_89	94.66	131	NR_042152
SEQ ID NO: 14	VE202-13	Anaerotruncus_colihominis	SEQ_95	99.34	1365	NR_027558
SEQ ID NO: 15	VE202-14	Eubacterium_fissicatena	SEQ_102	93.33	1530	NR_117563
SEQ ID NO: 16	VE202-16	Clostridium_symbiosum	SEQ_122	98.43	1469	NR_118730
SEQ ID NO: 17	VE202-7	Clostridium_bolteae	SEQ_110	99.86	1390	NR_113410
SEQ ID NO: 18	148	Dorea_longicatena	SEQ_97	99.7	1318	NR_028883
SEQ ID NO: 19	16	Blautia_producta	SEQ_106	98.33	1493	NR_113270
SEQ ID NO: 20	170	Dorea_longicatena	SEQ_97	99.7	1318	NR_028883
SEQ ID NO:21	189	Clostridium_innocuum	SEQ_98	98.64	1476	NR_029164
SEQ ID NO: 22	169	Dorea_longicatena	SEQ_97	99.58	475	NR_028883
SEQ ID NO: 23	VE202-29	Eisenbergiella_tayi	SEQ_121	100	354	NR_118643
SEQ ID NO: 24	YK96	Dorea_longicatena	SEQ_97	99.48	191	NR_028883
SEQ ID NO: 25	YK101	Ruminococcus_obeum	SEQ_85	96.81	188	NR_118692
SEQ ID NO: 26	YK110	Megasphaera_elsdenii	SEQ_119	96.62	207	NR_102980
SEQ ID NO: 27	YK149	Acidaminococcus_fermentans	SEQ_115	99.48	192	NR_074928
SEQ ID NO: 27	YK149	Acidaminococcus_intestini	SEQ_112	99.48	192	NR_074306
SEQ ID NO: 28	YK154	Megasphaera_elsdenii	SEQ_119	96.12	206	NR_102980
SEQ ID NO: 29	YK36	Ruminococcus_faecis	SEQ_96	99.29	425	NR_116747
SEQ ID NO: 30	YK95	Bacteroides_cellulosilyticus	SEQ_100	99.54	437	NR_112933
SEQ ID NO: 31	YK32	Anaerostipes_hadrus	SEQ_107	98.8	415	NR_104799
SEQ ID NO: 32	YK64	Ruminococcus_obeum	SEQ_84	99.04	415	NR_119185
SEQ ID NO: 33	YK73	Flavonifractor_plautii	SEQ_93	98.56	418	NR_043142
SEQ ID NO: 34	YK87	Eubacterium_rectale	SEQ_114	99.52	416	NR_074634

SEQ ID	Strain ID	Closest Genus_species	SEQ ID NO. of closest species	Percent alignment	Alignment lenght	Accession # of closest species
SEQ ID NO: 35	YK105	Flavonifractor_plautii	SEQ_93	99.26	407	NR_043142
SEQ ID NO: 36	YK153	Megasphaera_elsdenii	SEQ_119	96.04	429	NR_102980
SEQ ID NO: 37	YK163	Eubacterium_rectale	SEQ_114	99.76	415	NR_074634
SEQ ID NO: 38	YK191	Ruminococcus_champanellensis	SEQ_117	94.47	416	NR_102884
SEQ ID NO: 38	YK191	Ruminococcus_albus	SEQ_113	94.47	416	NR_074399
SEQ ID NO: 39	YK99	Ruminococcus_champanellensis	SEQ_117	97.28	184	NR_102884
SEQ ID NO: 40	YK55	Ruminococcus_faecis	SEQ_96	99.02	408	NR_116747
SEQ ID NO: 41	YK75	Bifidobacterium_bifidum	SEQ_118	99.45	183	NR_102971
SEQ ID NO: 42	YK90	Anaerostipes_hadrus	SEQ_107	98.97	194	NR_104799
SEQ ID NO: 43	YK30	Anaerostipes_hadrus	SEQ_107	99.48	191	NR_104799
SEQ ID NO: 44	YK31	Anaerostipes_hadrus	SEQ_107	98.97	194	NR_104799
SEQ ID NO: 45	YK12	Eubacterium_rectale	SEQ_114	99.27	412	NR_074634
SEQ ID NO: 46	YK27	Ruminococcus_faecis	SEQ_96	99.51	412	NR_116747
SEQ ID NO: 47	YK28	Blautia_luti	SEQ_111	99.5	400	NR_041960
SEQ ID NO: 48	YK29	Ruminococcus_faecis	SEQ_96	99.03	413	NR_116747
SEQ ID NO: 49	YK33	Anaerostipes_hadrus	SEQ_107	99.27	413	NR_104799
SEQ ID NO: 50	YK34	Anaerostipes_hadrus	SEQ_107	99.51	410	NR_104799
SEQ ID NO: 51	YK35	Ruminococcus_faecis	SEQ_96	99.51	409	NR_116747
SEQ ID NO: 52	YK51	Eubacterium_rectale	SEQ_114	99.27	413	NR_074634
SEQ ID NO: 53	YK52	Eubacterium_rectale	SEQ_114	99.03	413	NR_074634
SEQ ID NO: 54	YK54	Anaerostipes_hadrus	SEQ_107	85.82	409	NR_104799
SEQ ID NO: 55	YK56	Ruminococcus_faecis	SEQ_96	99.03	413	NR_116747
SEQ ID NO: 56	YK57	Ruminococcus_faecis	SEQ_96	98.79	413	NR_116747
SEQ ID NO: 57	YK58	Dorea_longicatena	SEQ_97	98.8	417	NR_028883
SEQ ID NO: 58	YK65	Roseburia_faecis	SEQ_92	99.27	413	NR_042832
SEQ ID NO: 59	YK67	Blautia_luti	SEQ_111	98.57	419	NR_041960
SEQ ID NO: 60	YK69	Fusicatenibacter_saccharivorans	SEQ_116	99.27	413	NR_114326
SEQ ID NO: 61	YK70	Fusicatenibacter_saccharivorans	SEQ_116	98.79	414	NR_114326
SEQ ID NO: 62	YK71	Roseburia_faecis	SEQ_92	99.28	414	NR_042832
SEQ ID NO: 63	YK74	Megasphaera_elsdenii	SEQ_119	96.06	431	NR_102980
SEQ ID NO: 64	YK88	Eubacterium_rectale	SEQ_114	99.28	415	NR_074634
SEQ ID NO: 65	YK89	Eubacterium_rectale	SEQ_114	99.27	413	NR_074634
SEQ ID NO: 66	YK97	Roseburia_faecis	SEQ_92	99.28	414	NR_042832
SEQ ID NO: 67	YK98	Blautia_faecis	SEQ_104	98.02	405	NR_109014
SEQ ID NO: 68	YK139	Fusicatenibacter_saccharivorans	SEQ_116	99.03	412	NR_114326
SEQ ID NO: 69	YK141	Dorea_formicigenerans	SEQ_120	98.51	402	NR_044645
SEQ ID NO: 70	YK142	Ruminococcus_faecis	SEQ_96	98.79	413	NR_116747
SEQ ID	YK152	Blautia_hansenii	SEQ_99	99.5	401	NR_104687

SEQ ID	Strain ID	Closest Genus_species	SEQ ID NO. of closest species	Percent alignment	Alignment lenght	Accession # of closest species
NO: 71						
SEQ ID NO: 72	YK155	Blautia_hansenii	SEQ_99	98.79	413	NR_104687
SEQ ID NO: 73	YK157	Eubacterium_rectale	SEQ_114	99.27	413	NR_074634
SEQ ID NO: 74	YK160	Roseburia_faecis	SEQ_92	99.03	414	NR_042832
SEQ ID NO: 75	YK166	Eubacterium_rectale	SEQ_114	99.27	409	NR_074634
SEQ ID NO: 76	YK168	Eubacterium_rectale	SEQ_114	99.27	413	NR_074634
SEQ ID NO: 77	YK169	Eubacterium_rectale	SEQ_114	99.28	416	NR_074634
SEQ ID NO: 78	YK171	Eubacterium_rectale	SEQ_114	97.87	188	NR_074634
SEQ ID NO: 79	YK192	Roseburia_faecis	SEQ_92	99.03	414	NR_042832
SEQ ID NO:80	VE202-18	Erysipelatoclostridium_ramosum	SEQ_123	100	1485	NR_113243
SEQ ID NO: 81	PE5	Clostridium_bolteae	SEQ_110	100	1385	NR_113410
SEQ ID NO: 82	PE9	Clostridium_disporicum	SEQ_86	99.21	382	NR_026491
SEQ ID NO: 83	211-B	Bacteroides_ovatus	SEQ_101	95.64	436	NR_112940

Table 2: Bacterial species with a high degree of homology based on whole genome analysis:

Strain	Whole genome homology
	Lachnospiraceae bacterium 7_1_58FAA
	Subdoligranulum
SEQ_10 - 211	*Flavinofractor plautii*
SEQ_14 - VE202-13	*Anaerotruncus_colihominis*
	Eubacterium_fissicatena
SEQ_15 - VE202-14	*Ruminococcus torques*
SEQ_16 - VE202-16	*Clostridium_symbiosun*
SEQ_17 - VE202-7	*Clostridium_bolteae*
SEQ_22 - 169 / SEQ_20 - 170	*Dorea_longicatena*
SEQ_19 - 16	*Blautia_producta*
	Clostridium_innocuum
SEQ_21 - 189	*Erysipelotrichaceae_bacterium_21_3*

Table 3: Bacterial species with highest degree of homology based on whole genome analysis

Composition B strain number	Strain identifier	SEQ ID # of 16S region as determined by Sanger sequencing	Closest species based on Sanger sequencing of 16S region	SEQ ID # of 16S regions as determined by WGS^	*Consensus SEQ ID # of 16S region as determined by WGS	Closest species based on Concensus SEQ ID # of 16S region as compared with 16S database	Closest species based on WGS compared versus WG databases	Additional closely related sequences	Clostridium cluster
1	VE202-7	17	Clostridium bolteae	124, 125, 126, 127, 128	124	Clostridium bolteae	Clostridium bolteae 90A9		XIVa
2	VE202-13	14	Anaerotruncus colihominis	129,130, 131	129	Anaerotruncus colihominis	Anaerotruncus colihominis DSM 17241		IV
3	VE202-14	15	Eubacterium fissicatena	132, 133, 134, 135, 136	132	Dracourtella massiliensis	Dracourtella massiliensis GD1	Ruminococcus torques; Sellimonas intestinalis	XIVa
4	VE202-16	16	Clostridium symbiosum	137, 138, 139, 140	137	Clostridium symbiosum	Clostridium symbiosum WAL-14163		XIVa
5	strain #16	19	Blautia producta	141, 142, 143, 144, 145	141	Blautia producta	Clostridium bacterium UC5.1-1D4	Blautia product ATCC 27340	XIVa
6	strain #170	20	Dorea longicatena	146, 147, 148, 149, 150, 151	146	Dorea longicatena	Dorea longicatena CAG:42		XIVa
7	strain #189	21	Clostridium innocuum	152, 153, 154, 155, 156	152	Clostridium innocuum	Erysipelotrichaceae bacterium 21_3		XVII
							Clostridium	Subdolinogranulum	

Composition B strain number	Strain identifier	SEQ ID # of 16S region as determined by Sanger sequencing	Closest species based on Sanger sequencing of 16S region	SEQ ID # of 16S regions as determined by WGS^	*Consensus SEQ ID # of 16S region as determined by WGS	Closest species based on Concensus SEQ ID # of 16S region as compared with 16S database	Closest species based on WGS compared versus WG databases	Additional closely related sequences	Clostridium cluster
8	strain #211	10	Flavinofractor plautii	157, 158, 159	157	Flavinofractor plautii	orbiscindens 1_3_50AFAA		IV
^WGS refers to Whole Genome Sequencing performed on a PacBio Biosciences platform (Menlo Park, CA). *Consensus sequence is defined as the 16S sequence that has the most overlap with all other identified 16S sequences.									

[0141] In some embodiments, in any of the compositions described herein, *Clostridum bolteae* can be replaced with *Clostridium bolteae* 90A9 . In some embodiments, in any of the compositions described herein, *Anaerotruncus colihominis* can be replaced with *Anaerotruncus colihominis* DSM 17241. In some embodiments, in any of the compositions described herein, *Eubacterium fissicatena* can be replaced with *Sellimonas instestinalis, Drancourtella massiliensis* or *Drancourtella massiliensis GP1*. In some embodiments, in any of the compositions described herein, *Clostridium symbiosum* can be replaced with *Clostridium symbiosum* WAL-14163. In some embodiments, in any of the compositions described herein, *Blautia producta* can be replaced with *Clostridium bacterium* CD5.1-1D4 or *Blautia product ATCC27340*. In some embodiments, in any of the compositions described herein, *Dorea longicatena* can be replaced with *Dorea longicatena* CAG:42. In some embodiments, in any of the compositions described herein, *Clostridium innocuum* can be replaced with *Erysipelotrichaceae bacterium* 21_3. In some embodiments, in any of the compositions described herein, *Flavonifractor plautii* can be replaced with *Clostridium orbiscindens* 1_3_50AFAA.

[0142] Aspects described herein provide pharmaceutical composition comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some aspects, the bacterial strains have at least 98% homology to SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some aspects, the bacterial strains have at least 99% homology to SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21.

[0143] In some aspects, at least a portion of the bacteria of the pharmaceutical composition are in spore-form. In some aspects, the pharmaceutical composition further comprises a pharmaceutically acceptable excipient.

[0144] In some aspects, the pharmaceutical composition is formulated for oral administration. In some aspects, the pharmaceutical composition is in the form of a capsule. In some aspects, the pharmaceutical composition is formulated for delivery to the colon. In some aspects, the pharmaceutical composition further comprises a pH sensitive composition comprising one or more enteric polymers.

[0145] Aspects described herein provide pharmaceutical compositions comprising a purified bacterial mixture consisting of the following bacterial strains: *Clostridium bolteae, Anaerostruncus colihominis, Sellimonas intestinalis, Clostridium symbiosum, Blautia producta, Dorea Longicatena, Erysipelotrichaceae bacterium,* and *Clostridium orbiscindens.*

[0146] In some aspects, at least a portion of the bacterial strains are in spore-form. In some aspects, the pharmaceutical composition further comprises a pharmaceutically acceptable excipient.

[0147] In some aspects, the pharmaceutical composition is formulated for oral administration. In some aspects, the pharmaceutical composition is in the form of a capsule. In some aspects, the pharmaceutical composition is formulated for delivery to the colon. In some aspects, the pharmaceutical composition further comprises a pH sensitive composition comprising one or more enteric polymers.

[0148] Aspects described herein provide administering the pharmaceutical composition of any of the an aspects described herein to the subject in an amount sufficient to treat an infectious disease. In some aspects, the infectious disease is *Clostridium difficile* infection.

[0149] The nucleic acid sequences of the 16S rDNA, or portion thereof, for the bacterial strains described herein are provided below:

> SEQ ID NO: 011711

GCGCGGAGCACTTGATGTGAAGCATCGGTCACCTGTGCAGTGCATTGGAACTGTGATACTTGAGTGCGGAGCGT
AAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGTGGCGAAGCCGGCTTACTGA
CGGTAACTGAGGTTGAGGCTCGAAACCGTGCGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 0211021

CTAACCGTCGAGGTCATTCGAAACTCGTCAACTTGAGTGCAGAAGAGGGAAGTGGAATTCCATCTGTAGCGGTGA
AATGCGTAGACATATGGAGGAACACCAGTGGCGAAGGCGGCTTCCTGGTCTGTAACTGACACTGAGGCGCGAAAG
CGTGGGGAGCAAACAGGATTAGATACCCCGGTAA

> SEQ ID NO: 03151

ATGAAAGCCGGGGCTCAACCCCGGTACTGCTTTGGAAACTGTTTGACTTGAGTGCTTGAGAGGTAAGTGGAATTC
CTAGTGTAGCGGGAAATGTTTAGATATTAGGAGGACACCAGTGGCGAAGGCGGCTTACTGGACTGTAACTGACGT
TGTGGCTCGATTTGTGGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 04171

CGGAAGGCCGATGTGAAGGTCGGGGCTTACCCCGGACTGCATTGGAAACTGTTTTCCTAGAGTGCCGAGAGGC
AAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTTAGATATTAGGAGGAACACCAGTGGCGAAGGCGGCTTACTGG
ACGGTAACTGACGTTGAGGCTCGAAAGCGTCGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 051101

CGATGTCGAGTGAAGGCTGGGGCTTACCCCAGGACTGCATTGGAAACTGTTCTTGAGAGTGCCGGAGAGGTAAG
CGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGTGGCGAAGGCGGCTTACTGGACGG
TAACTGACGTTGAGGCTCGAAAGCGTCGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 061401

TTAACCAAGAAGTGCATTGGAAACTGTCAGACTTGGAGGAAAAAAGACAGTGCAACTCCATGTGTAGCGGTGAAA
TGCTCCATATATAGGAAGAACACCAGTGGCGAAGGCGGCTGTCTGGTCCTGCAACTGACGCTGAGGCTCGAAACC
ATGGGTAGAAAGCATTAGTCCCTTGCAA

> SEQ ID NO: 071591

ACCGGCTTGGTCTGAGGTGAGGCTGGGGCTTAACCCCAGGACTGCATTGGAAACTGTTGTTCTAGAGTGCCGGAG
AGGTAAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGTGGCGAAGGCGGCTTAC
TGGACGGTAACTGACGTTGAGGCTCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 081791

TAGGCTGGCGCTTAACCCCAGGACTGCATTCGAAACTGTTTTTCTAGAGTGCCCGAGAGGTAACCGGAATTCCTA
GTGTAGCGCTGAAATGCGTAGATATTAGGAGGAACACCAGTCGCCGAAGGCGGCTTACTCGACGGTAACTGACGT
GAGGCTCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 09|VE202-21|

TTGCATTGGACACTATGTCAGCTGAGTGTCGGAGAGGTAAGTGGAATTCCTAGTGTAGCGGTGAAATGCGTAGAT

ATTAGGAGGAACACCAGTGGCGAAGGCGGCTTACTGCACGTTTTCTGACGTTGAGGCTCGAAATCGTGGGGAGCA
AACAAAAATACATACCCTGGTAGTCCACGCCGTAAACGATGCATACTAGGTGTCGGGTGGCAAAGCCATTCGGTG
CCGCAGCAAACGCAATAAGTATGCCACCTGGGGAGTACGTTCGCAAGAATGAAACTCAAATAAATTGACGGA

> SEQ ID NO: 1012111

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AGTAACTGACGCTGAGGCGCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCTCATAA

> SEQ ID NO: 11|VE202-9|

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CGGTACCTGACTAAGAAGCCCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGGGCAAGCGTTATCCG
GAATTACTGGGTGTAAAGGGTGCGTAGGTGGCATGGTAAGTCAGAAGTGAAAGCCCGGGGCTTAACCCCGGGACT
GCTTTTGAAACTGTCATGCTGGAGTCCAGGAGAGGTAAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATAT

TAGGAGGAACACCAGTGGCGAAGGCGGCTTACTGGACTGTCACTGACACTGATGCACGAAAGCGTGGGGAGCAAA
CAGGATTAGATACCCTGGAAGTCCAT

> SEQ ID NO: 12|VE202-26|

ATGGAGCGTAGATGGCGACTGGGCCATATGTGACAGCCCTGGTCTCAACCCCTTAACTGCATTTGGAACTGAGT
GGCTGGAGTGTCGGAGAGGCAGGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGT
GGCGAAGGCGGCCTGCTGGACGATGACTGACGTTGAGGCTCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCT
GGTAGTCCACGCCGTAAACGATGACTACTAGGTGTCGGGTGGCAAGGACATTCGGTGCCGCAGCAAACGCAATAA
GTAGTCCACCTGGGGAGTACGTTCGCAAGAATGAAACTCAAAGGAAATTGACGGA

> SEQ ID NO: 1311361

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TGAGGCTCCAAAGTGTGGGGAGCAAACAGGATTAGATACCCTGGTAA

> SEQ ID NO: 14|VE202-13|

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GGTGAAATGCGTAGATATTAGGAGGAACACCAGTGGCGAAGGCGGCCTGCTGGGCTTTAACTCACGCTGAGGCTC
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TAACGTCTCAGTTCGGATTGTAGTCTGCAACTCGACTACATGAAGCTGGAATCGCTAGTAATCGCGGATCAGCAT
GCCGCGGTCAATACGTTCCCGGGTCTTGTACACACCGCCCGTCACACCATGGGAGTCAGTAACGCCCGAAGCCAG
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CGGTGGTACAAGATGGACCCGCGTCTGATTAGCTAGTTGGTAAGGTAACGGCTTACCAAGGCCACGATCAGTAGC
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> SEQ ID NO: 17|VE202-7|

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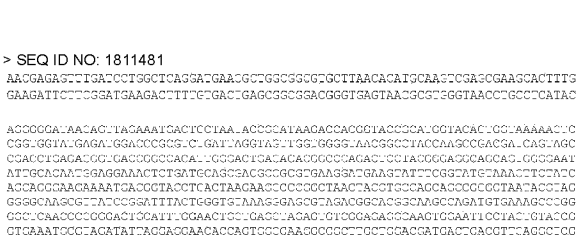

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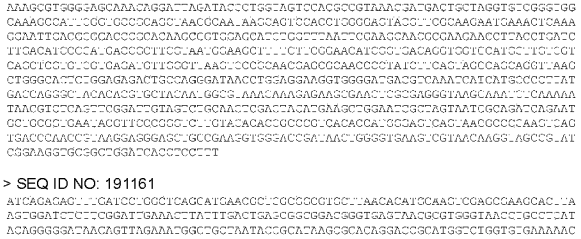

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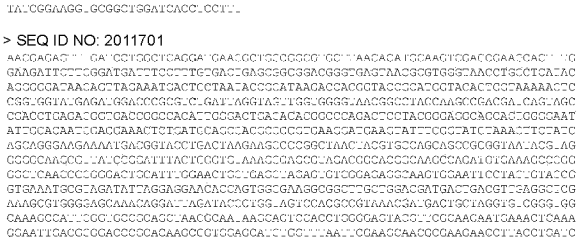

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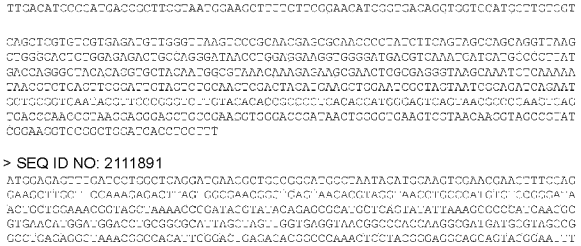

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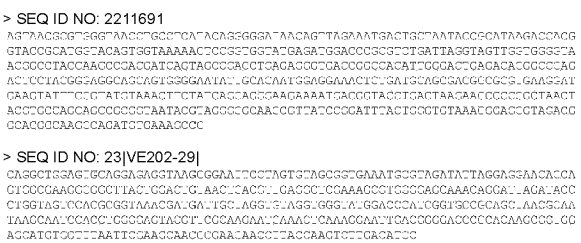
> SEQ ID NO: 24|YK96|



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> SEQ ID NO: 26|YK110|

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> SEQ ID NO: 27|YK149|

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> SEQ ID NO: 28|YK154|

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> SEQ ID NO: 29|YK36|

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> SEQ ID NO: 30|YK95|

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> SEQ ID NO: 32|YK64|

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> SEQ ID NO: 34|YK87|

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> SEQ ID NO: 35|YK105|

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> SEQ ID NO: 37|YK163|

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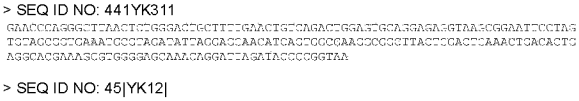

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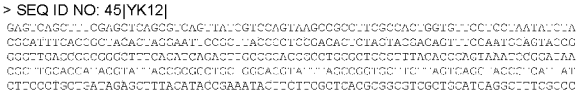

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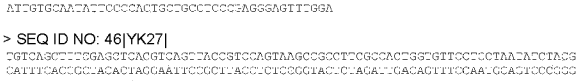

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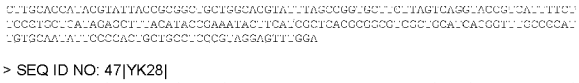

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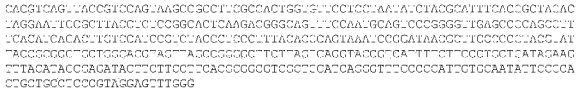

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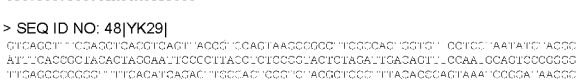

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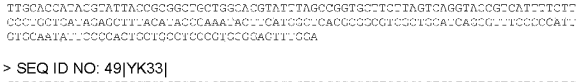

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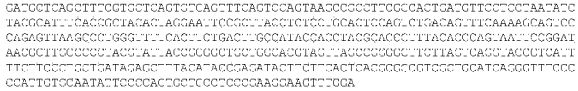

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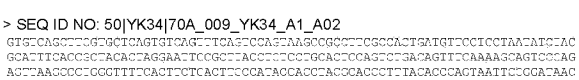

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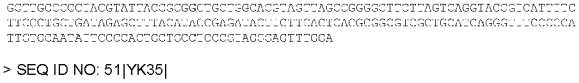

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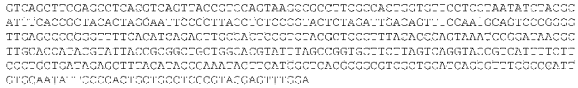

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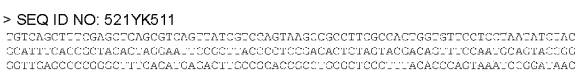

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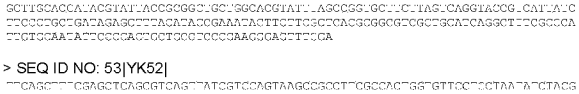

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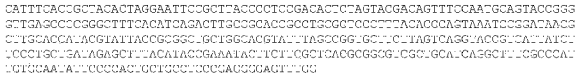

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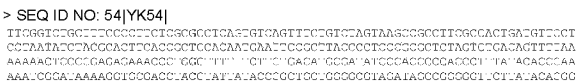

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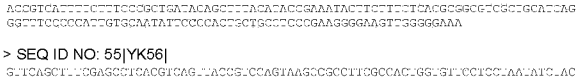

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> SEQ ID NO: 68|YK139|

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GGGTTGACCCCCGGGCTTCACATCAGACTTGCCCCACCGCCTGCGCTCCCTTTACACCCAGTAAATCCCGGATAA
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> SEQ ID NO: 781YK1711
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> SEQ ID NO: 79|YK192|
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> SEQ ID NO: 80|VE202-18|
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TACGG
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CAAAT
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CAAGCGTTATCCGGAATTATTGGGCGTAAAGAGGGAGCAGGCGGCAGCAAGGGTCTGTGGTGAAAGCCTGAAGCT
TAACTTCAGTAAGCCATAGAAACCACCGAGCTAGAGTCGAGCAGACGAGGATCGTTCGAATTCGATCCTACCGGTCAA
ATGCG
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GCCCG
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CTCCAGAGATGGAGAGTAGTACATGAGATACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCGTGAGATGTTG
GGTTAAGTCCCGCAACGAGCGCAACCCTTACGTTAGTTACCATCATTAAGTTGGGGACTCTAGCGAGACTGCCA
CTGAC
AAGCTGGAGGAAGGCGGGGATGACGTCAAAATCATCATGCCCCTTATGACCTGGGCTACACACGTGCTACAATGCA
TGGTGCAGAGGGAAGCGAAGGCGGAGGTGAAGCAAAACCCATAAAACCATTCTCAGTTCGGATTGTAGTCTGCA
ACTCGACTACATGAAGTTGGAATCGCTAGTAATCGCGAATCAGCATGTCGCGGTGAATACGTTCTCGGGCCTTGT
ACACA
CCGCCCGTCACACCACGAGAGTTGATAACACCCGAAGCCGGTGGCCTAACCCGCAAGGAGGAGCTGTCCTAAGTG
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> SEQ ID NO: 811PE51
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CAGGG
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> SEQ ID NO: 82|PE9|
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AGCGTGGGGAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAATACTAGGTGTAGGGGTTGT
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> SEQ ID NO: 831211-BI
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CCGTAAAATTGCAGTTGAAACTGGCAGTCTTGAGTACAGTAGAGGTGGGCGGAATTCGTGGTGTAGCGGTGAAAT
GCTTAGATATCACGAAGAACTCCGATTGCGAAGGCAGCTCACTAGACTGTCACTGACACTGATGCTGCAAAGGTG
GGGTATCAAACAGGATTAGATACCCTGGTAGTCCACACAGTAAACGATGAATCACTCGCTGTTGCGATATACAGT
AAGCGGCCAAACGAAAGCATTAAGTATTCCACCTGGGGAGTACGCCGGCAACGGTGAAACTCAAAGAAATTGACG
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> SEQ ID NO: 84|NR_119185.1|Ruminococcus obeum 16S ribosomal RNA gene, complete sequence
GGCGGCGTGCTTAACACATGCAAGTCGAACGGAAACCTTCTCATTGAAGCTTCGGCAGATTTGGNNCGTTTCTAG
TGGCGGACGGGTGAGTAACGCGTGGCTAACCTGCCTTATACAGGGGGATAACAACCAGAAATGGTTGCTAATACC
GCATAAGGGCACAGGACCGCATGGTCTGGTGTGAAAAACTCCGGTGGTATAAGATGGACCCGCGTTGGATTAGCT
AGTTGGCAGGCTAACGGCCTACCAACCGACGATCCATAGCCGGCCTGAGAGGGTGAACGGCCACATTGGGACTG
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CCGCGTGAAGGAAGAAGTATCTCGGTATGTAAACTTCTATCAGCAGGGAAGAAAGTGACGGTACCTGACTAAGAA
GCCCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGGCAAGCGTTATCCGGAATTATTGGGCGTAAAG
GGGAGCGTAGACGGACTGGCAAGTCTGATGTGAAAGGCGGGGGCTCAACCCCTGGGACTGCATTGGAAACTGTTAG
TCTTGAGTCCCGGAGAGGTAAGCGGAATTCCTAGTTAGCGGTGAAATCCCTAGATATTACGAGGAACACCATTG
GCGAAGGCGGCTTACTGGACGGTAACTGACGTTGAGGCTCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCTG

GTAGTCCACGCCGTAAACGATGATTACTAGGTGTTGGGGAGCAAAGCTCTTCGGTGCCGCCGCAAACGCATTAAG
TATTCCACCTCGGGAGTACGTTCGCAAGAATGAAACTCAAAGGAATTGACGGGGACCCGCACAAGCGGTGGAGCA
TGTGGTTTAATTCGAAGCAACGCGAAGAACCTTACCAAGTCTTGACATCCCTCTGACCGNCCCTTAACCGGATCT
TTCCTTCGGGACAGGGGAGACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCGTGAGATGTTGGGTTAAGTCCCG
CAACGAGCGCAACCCCTATCCCCAGTAGCCAGCAGTCCGGCTGGGCACTCTGAGGAGACTGCCAGGGATAACCTG
GAGGAAGGCGGGGATGACGTCAAATCATCATGCCCCTTATGATTTGGGCTACACACGTGCTACAATGGCGTAAAC
AAAGGGAAGCAAGCCTGCGAAGGTAAGCAAATCCCAAAAATAACGTCCCAGTTCGGACTGCAGTCTGCAACTCGA
CTGCACGAAGCTGGAATCGCTAGTAATCGCGGATCAGAATGCCGCGGTGAATACGTTCCCGGGTCTTGTACACAC
CGCCCGTCACACCATGGGAGTCAGTAACGCCCGAAGTCAGTGACCTAACTGCAAAGAAGGAGCTGCCGAAGGCGG
GACCGATGACTGGGGTGAAGTCGTAACAAGGT

> SEQ ID NO: 85|NR_118692.1|Ruminococcus obeum strain ATCC 29174 16S ribosomal RNA gene, complete sequence
GGCGTGCTTAACACATGCAAGTCGAACGGGAAACTTTTCATTGAAGCTTCGGCAGATTTGGTCTGTTTCTAGTGG
CGGACGGGTGAGTAACGCGTGGGTAACCTGCCTTATACAGGGGGATAACAACCAGAAATGGTTGCTAATACCGCA
TAAGCGCACAGGACCGCATGGTCTGGTGTGAAAAACTCCGGTGGTATAAGATGGACCCGCGTTGGATTAGCTAGT

TGGCAGGGTAACGGCCTACCAAGGCGACGATCCATAGCCGGCCTGAGAGGGTGAACGGCCACATTGGGACTGAGA
CACGGCCCAGACTCCTCGGGAGGCACCAGTGGGAATATTGCACAATGGGGGAAACCCTGATCCAGCCACGCCGC
GTGAAGGAAGAAGTATCTCGGTATGTAAACTTCTATCAGCAGGGAAGATAGTGACGGTACCTGACTAAGAAGCCC
CGKCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGGGCAAGCGTTATCCGGATTTACTGGGTGTAAAGGGA
GCGTAGACGGACTGGCAAGTCTGATGTGAAAGGCGGGGGCTCAACCCCTGGACTGCATTGGAAACTGTTAGTCTT
GAGTGCCGGAGAGGTAAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGTGGCGA
AGGCGGCTTACTGGACGGTAACTGACGTTGAGGCTCGAAAGCGTGGGGAGCAAACAGGATTACATACCCTGGTAG
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CCACCTGGGGAGTACGTTCGCAAGAATGAAACTCAAAGGAATTGACGGGGACCCGCACAAGCCGTGGAGCATGTG
GTTTAATTCGAAGCAACGCGAAGAACCTTACCAAGTCTTGACATCCCTCTGACCGTCCCTTAACCGGATCTTTCC
TTCGGGACAGGGGAGACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCGTGAGATGTTGGGTTAAGTCCCGCAAC
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AAGGCGGGGATGACGTCAAATCATCATGCCCCTTATGATTTGGGCTACACACGTGCTACAATGGCGTAAACAAAG
GGAAGCNAGCCTKCGRAGGTAAGCAAATCCCANAAATAACGTCCCAGTTCGGACTGCAGTCTCCAACTCGACTGC
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> SEQ ID NO: 86INR_026491.1IClostridium disporicum strain DS1 16S ribosomal RNA gene, partial sequence
GCTCAGGACGAACGCTGGCGGCGTGCCTAACACATGCAAGTCGAGCGAGTTGATTCTCTTCGGAGATGAAGCTAG
CGGCGGACGGGTGAGTAACACGTGGGCAACCTGCCTCATAGAGGGGAATAGCCTCCCGAAAGGGAGATTAATACC
GCATAAGATTCTAGCTTCGCATGAACTAGCAATTAAAGGAGCAATCCGCTATGAGATGGGCCCGCGGCGCATTAG
CTAGTTGGTGAGGTAACGGCTCACCAAGGCGACGATGCGTAGCCGACCTGAGAGGGTGATCGGCCACATTGGGAC
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CGCCGCGTGAGTGATGACGGCCTTCGGGTTGTAAAGCTCTGTCTTCAGGGACGATAATGACGGTACCTGAGGAGG
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AGTATTCCGCCTGGGGAGTACGGTCGCAAGATTAAAACTCAAAGGAATTGACGGGGGCCCGCACAAGCAGCGGAG
CATGTGGTTTAATTCGAAGCAACGCGAAGAACCTTACCTAGACTTGACATCTCCTGAATTACCGTAACTGGGGA
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CGCAACGAGCGCAACCCTTATTGTTAGTTGCTACCATTTAGTTGAGCACTCTAGCGAGACTGCCCGGGTTAACCG
GGAGGAAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGTCTAGGGCTACACACGTGCTACAATGGCAACTA
CAAAGAGAAGCAAGACCGCGAGGTGGAGCAAAACTCAAAAACTTGTCTCAGTTCGGATTGTAGGCTGAAACTCGC
CTACATGAAGCTGGAGTTGCTAGTAATCGCGAATCAGCATGTCGCGGTGAATACGTTCCCGGGCCTTGTACACAC
CGCCCGTCACACCATGAGAGTTGGCAATACCCAACCTACGTGATCTAACCCGCAAGGGAGGAAGCCTCCTAACGT
AGGGTCAGCGATTGGGGTGAAGTCGTAACAAGGTAGCCGTAGGAGAA

> SEQ ID NO: 87INR_028785.1 IClostridium scindens strain ATCC 35704 16S ribosomal RNA gene, complete sequence
GAGAGTTTGATCCTGGCTCAGGATGAACGCTGGCGGCGTGCCTAACACATGCAAGTCGAACGAAGCGCCTGGCCC
CGACTTCTTCGGAACGAGGAGCCTTCCGACTGAGTGGCGGACGGGTGAGTAACGCGTGGGCAACCTGCCTTGCAC
TGGGGGATAACACCCAGAAATGGCTCCTAATACCGCATAAGACCGAAGCGCCGCATGGCGCGCCCGCCAAAGCCC
CGGCGGTGCAAGATGGGCCCGCGTCTGATTAGGTAGTTGGCGGGGTAACGGCCCACCAAGCCGACGATCAGTAGC
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> SEQ ID NO: 88|NR_028915.1|Anaerostipes caccae strain L1-92 16S ribosomal RNA gene, partial sequence
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GACCGATAACTGGGGTGAAGTCGTAACAAGG

> SEQ ID NO: 89|NR_042152.1|Marvinbryantia formatexigens strain I-52 16S ribosomal RNA gene, partial sequence >gi|636558750|ref|NR_114807.1|Marvinbryantia formatexigens strain I-52 16S ribosomal RNA gene, complete sequence
TGGCGGCGTGCTTAACACATGCAAGTCGAGCGAAGCATTTTAAATGAAGTTTTCGGACGGAATTTAAAATGACTG
AGCGGCGGACTGGTGAGTAACGCGTCGATAACCTGCCTTATACAGGGGGATAACAGCCAGAAATGGCTGCTAATA
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GGCTACATGAAGCTGGAATCGCTAGTAATCCCGGATCAGCATGCCGCGGTGAATACGTTCCCGGGTCTTGTACAC
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GGGGCCGGTAACTGGGGTGAAGTCGTAACAA

> SEQ ID NO: 90|NR_024994.1|Lactobacillus mucosae strain S32 16S ribosomal RNA gene, complete sequence

> SEQ ID NO: 91|NR_028816.1|Turicibacter sanguinis strain MOL361 16S ribosomal RNA gene, complete sequence

> SEQ ID NO: 92|NR_042832.1|Roseburia faecis strain M72/1 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 931NR_043142.11Flavonifractor plautii strain Prevot S1 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 94|NR_044054.1|Blautia wexlerae strain DSM 19850 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 95|NR_027558.1|Anaerotruncus colihominis strain WAL 14565 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 961NR_116747.11Ruminococcus faecis strain Eg2 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 97|NR_028883.1|Dorea longicatena strain 111-35 16S ribosomal RNA gene, partial sequence

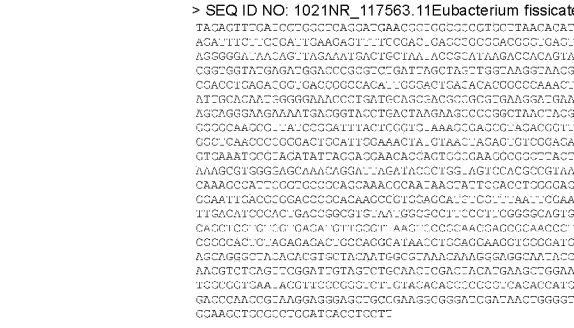
> SEQ ID NO: 98INR_029164.1IClostridium innocuum strain B-3 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 99INR_104687.1IBlautia hansenii strain JCM 14655 16S ribosomal RNA gene, partial sequence

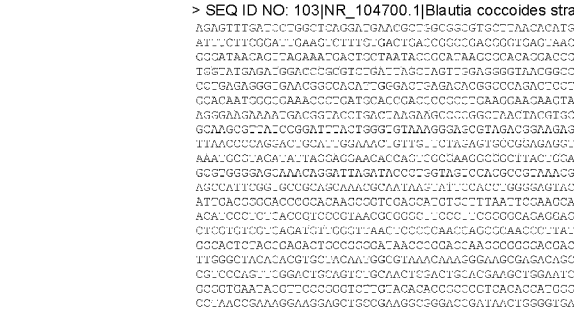
> SEQ ID NO: 100|NR_112933.1|Bacteroides cellulosilyticus strain JCM 15632 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 10|NR_112940.1|Bacteroides ovatus strain JCM 5824 16S ribosomal RNA gene, partial sequence

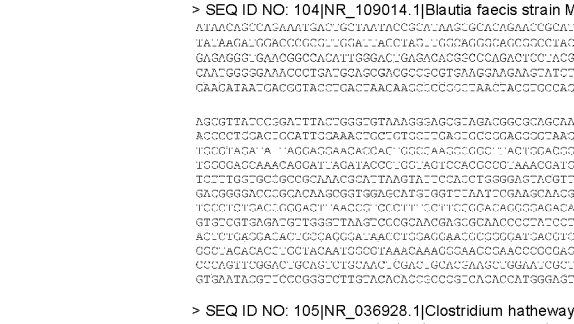
> SEQ ID NO: 1021NR_117563.11Eubacterium fissicatena 16S ribosomal RNA gene, partial sequence



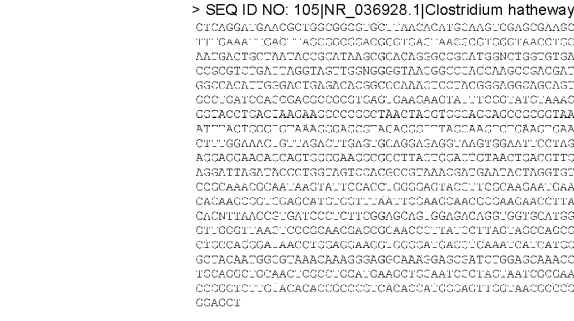
> SEQ ID NO: 103|NR_104700.1|Blautia coccoides strain JCM 1395 16S ribosomal RNA gene, partial sequence



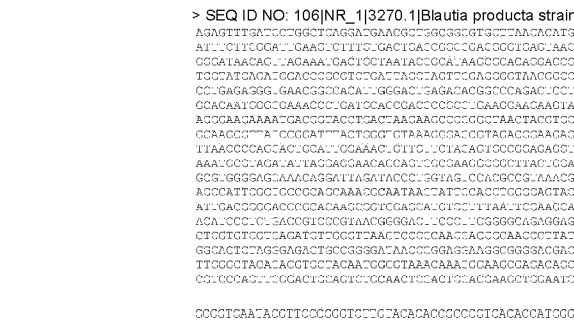
> SEQ ID NO: 104|NR_109014.1|Blautia faecis strain M25 16S ribosomal RNA gene, partial sequence



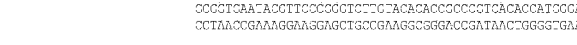
> SEQ ID NO: 105|NR_036928.1|Clostridium hathewayi strain 1313 16S ribosomal RNA gene, partial sequence



> SEQ ID NO: 106|NR_1|3270.1|Blautia producta strain JCM 1471 16S ribosomal RNA gene, partial sequence



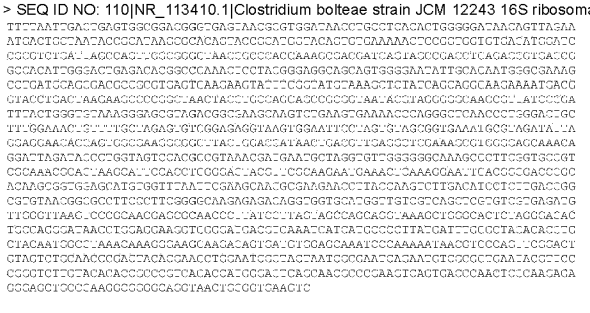
> SEQ ID NO: 107|NR_104799.1|Anaerostipes hadrus strain DSM 3319 16S ribosomal RNA gene, partial sequence



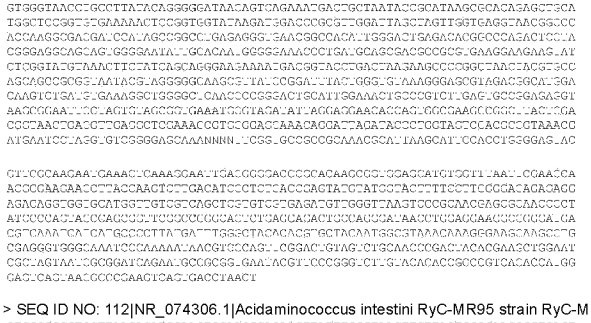
> SEQ ID NO: 108|NR_117142.1|Eubacterium fissicatena strain DSM 3598 16S ribosomal RNA gene, partial sequence

> SEQ ID NO: 109|NR_117147.1|Eubacterium contortum strain DSM 3982 16S ribosomal RNA gene, partial sequence

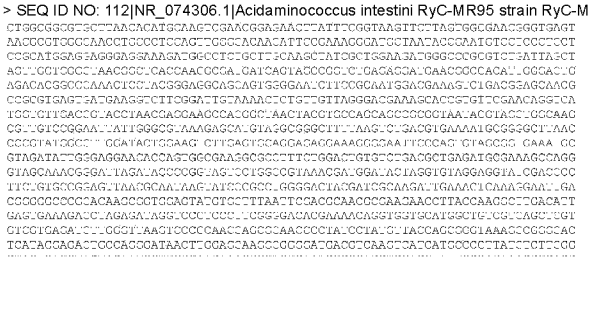
> SEQ ID NO: 110|NR_113410.1|Clostridium bolteae strain JCM 12243 16S ribosomal RNA gene, partial sequence



> SEQ ID NO: 111|NR_041960.1|Blautia luti strain BlnIX 16S ribosomal RNA gene, complete sequence



> SEQ ID NO: 112|NR_074306.1|Acidaminococcus intestini RyC-MR95 strain RyC-MR95 16S ribosomal RNA, complete sequence



CTACACACGTACTACAATGGTCGGCAACAAAGGGCAGCGAAACCGCGAGGTGGAGCAAATCCCAGAAACCCGACC
CCAGTTCGGATCGTAGGCTGCAACCCGCCTACGTGAAGTTGGAATCGCTAGTAATCGCAGGTCAGCATACTGCGG
TGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCACACCACGAAAGTTGGTAACACCCGAAGCCGGTGAGATA
ACCTTTTAGGAGTCAGCTGTCTAAGCTGGGGCCGATGATTGGGGTGAAGTCGTAACAAGGTACC

> SEQ ID NO: 113|NR_074399.1|Ruminococcus albus strain 7 16S ribosomal RNA gene, complete sequence
AGAGTTTGATCCTGGCTCAGGACGAACGCTGGCGGCACGCTTAACACATGCAAGTCGAACGAGCGAAAGAGTGCT
TGCACTCTCTAGCTAGTGGCGGACGCGTGACTAACACCTGAGCAATCTGCCTTTCGGAGAGGCATACCAATTCGA
AACGATTGTTAATACCTCATAACATAACGAAGCCGCATGACTTTGTTATCAAATGAATTTCGCCGAAAGATGAGC
TCGCGTCTGATTAGGTAGTTGGTGAGGTAACGGCCCACCAAGCCGACGATCAGTAGCCGGACTGAGAGGTTGAAC
GGCCACATTGCGACTGAGACACGGCCCAGACTCCTACGGGAGGCAGCAGTGGGGAATATTGCACAATCGGCGAAA
GCCTGATGCAGCGATGCCGCGTGAGGGAAGAAGGTTTTAGGATTGTAAACCTCTGTCTTTGGGGACGATAATGAC
GGTACCCAAGGAGGAAGCTCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGAGCGAGCGTTGTCCGG
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CACAAGCAGTGGAGTATGTGGTTTAATTCGAAGCAACGCGAAGAACCTTACCAGGTCTTGACATCGTACGCATAG
CATAGAGATATGTGAAATCCCTTCGCGGACCTATAGACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCGTGAGA
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GTTGACAAAACGGAGGAAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGACCTGGGCTACACACGTACTAC
AATGGCTGTTAACAGAGGGAAGCAAAACAGTGATGTGGAGCAAAACCCTAAAAGCAGTCTTAGTTCGGATTGTAG
GCTGCAACCCGCCTACATGAAGTCGGAATTGCTAGTAATCGCGGATCAGCATGCCGCGGTGAATACGTTCCCGGG
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AGTCGAAGGTGGGATTGATGACTGGGGTGAAGTCGTAACAAGGTAGCCGTATCGGAAGGTGCGGCTGGATCACCT

> SEQ ID NO: 114|NR_074634.1|Eubacterium rectale strain ATCC 33656 16S ribosomal RNA gene, complete sequence
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ATTTCCTTCGGGACTGATTATTTTGTGACTGAGTGGCGGACGGGTGAGTAACGCGTGGGTAACCTGCCTTGTACA
GGGGGATAACAGTTGGAAACGGCTGCTAATACCGCATAAGCGCACGGCATCGCATGATGCAGTGTGAAAAACTCC
GGTGGTATAAGATGGACCCGCGTTGGATTAGCTAGTTGGTGAGGTAACGGCCCACCAAGGCGACGATCCATAGCC
GACCTGAGAGGGTGACCGGCCACATTGGGACTGAGACACGGCCCAAACTCCTACGGGAGGCAGCAGTGGGGAATA
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AGCTCGTGTCGTGAGATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTATCTTTAGTAGCCAGCGGTTCGGCC
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GAAGGTGCGGCTGGATCACCT

> SEQ ID NO: 115|NR_074928.1|Acidaminococcus fermentans strain DSM 20731 16S ribosomal RNA gene, complete sequence
AGAGTTTGATCCTGGCTCAGGACGAACGCTGGCGGCGTGCTTAACACATGCAAGTCGAACGGAGAACTTTCTTCG
GAATGTTCTTAGTGGCGAACGGGTGAGTAACGCGTAGGCAACCTGCCCTCTGGTTGGGGACAACATTCCGAAAGG
GATGCTAATTACCGAATGAGATCCTCTTTTCCCCATGGAGAGAGGATTGAAAGATTGGCCTCTACTTGTAACCTATTGGC
CAGAAGATGGCCCTGCGTCTGATTACCTAGTAGGTCAGGTAACGGCTCACCTAGGCGATGATCAGTAGCCGGTCT
CAGACGATGAACGGCCACATTGGGACTGAGACACGGCCCAAACTCCTACGGGAGGCAGCAGTCGGGAATCTTCCG
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TCGCAAGATTGAAACTCAAAGGAATTGACGGGGGCCCGCACAAGCGGTGGAGTATGTGGTTTAATTCGACGCAAC
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AGGTGGTGCATGGCTGTCGTCAGCTCGTGTCGTGAGATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTATCC
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CTAGTAATCGCAGGTCAGCATACTGCGGTGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCACACCACGAAA
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AGTCGTAACAAGGTAGCCGTTCGAGAACGACGGCTGGATCACCT

> SEQ ID NO: 116|NR_114326.1|Fusicatenibacter saccharivorans strain HT03-11 16S ribosomal RNA gene, partial sequence
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ATTCTTGACTGACTGAGCGGCGGACGGGTGAGTAACGCGTGGGTGACCTGCCCCATACCGGGGGATAACAGCTGG
AAACGGCTGCTAATACCGCATAAGCGCACAGAGCTGCATGGCTCGGTGTGAAAAACTCCGGTGGTATGGGATGGG
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CGGCCACATTGGGACTGAGACACGGCCCAAACTCCTACGGGAGGCAGCAGTGGGGAATATTGCACAATGGGGGAA
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CGGTACCTGACTAAGAAGCCCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGGCAAGCGTTATCCG
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TGCTACAATGGCGTAAACAAAGGGAGGCAAAGCCGCGAGGTGGAGCAAATCCCAAAAATAACGTCTCAGTTCGGA
CTGCAGTCTGCAACTCGACTGCACGAAGCTGGAATCGCTAGTAATCGCGAATCAGAATGTCGCGGTGAATACGTT
CCCGGGTCTTGTACACACCGCCCGTCACACCATGGCACTTGGTAACGCCCGAAGTCAGTGACCCAACCTTTTA

> SEQ ID NO: 117|NR_102884.1|Ruminococcus champanellensis strain 18P13 16S ribosomal RNA gene, complete sequence
AGAGTTTGATCCTGGCTCAGGACGAACGCTGGCGGCACGCCTAACACATGCAAGTCGAACGGAGATAAAGACTTC
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GCGTCTGATTAGCTAGATGGTGAGGTAACGGCTCACCATGGCGACGATCAGTAGCCGGACTGAGAGGTTGAACGG
CCACATTGGGACTGAGACACGGCCCAGACTCCTACGGGAGGCAGCAGTGGGGAATATTGCACAATGGGCGCAAGC
CTGATGCAGCGATGCCGCGTGGAGGAAGAAGGTTTTCGGATTGTAAACTCCTGTCTTAAGGGACGATAATGACGG
TACCTTAGGAGGAAGCTCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGGAGCGAGCGTTGTCCGGAA
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AAAACGGAGGAAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGACCTGGGCTACACACGTACTACAATGGC
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ACTCGCCTACATGAAGTCGGAATTGCTAGTAATCGCAGATCAGCATGCTGCGGTGAATACGTTCCCGGGCCTTGT
ACACACCGCCCGTCACACCATGGGAGTCGGTAACACCCGAAGCCAGTAGCCTAACCGCAAGGAGGGCGCTGTCGA
AGGTGGGATTCATGACTGGGGTGAACTCGTAACAACGTAGCCGTATCGGAAGGTGCGGCTCGATCACCT

> SEQ ID NO: 118|NR_102971.1|Bifidobacterium bifidum S17 strain S17 16S ribosomal RNA, complete sequence
TTTTTGTGGACGGTTCGATTCTGGCTCAGGATGAACGCTGGCGGCGTGCTTAACACATGCAACTCGAACGGGATC
CATCGGGCTTTGCTTGGTGGTGAGAGTGGCCAACGGCTGAGTAATGCGTGACCGACCTGCCCCATGCTCCGGAAT
AGCTCCTGGAAACGGGTGGTAATGCCGGATGTTCCACATGATCGCATGTGATTGTGGGAAAGATTCTATCGGCGT
GGGATGGGGTCGCGTCCTATCAGCTTGTTGGTGAGGTAACGGCTCACCAAGGCTTCGACGGGTAGCCGGCCTGAG
AGGGCGACCGGCCACATTGGGACTGAGATACGGCCCAGACTCCTACGGGAGGCAGCAGTGGGGAATATTGCACAA
TGGGCGCAAGCCTGATGCAGCGACGCCGCGTGAGGGATGGAGGCCTTCGGGTTGTAAACCTCTTTTGTTTGGGAG
CAAGCCTTCGGGTGAGTGTACCTTTCGAATAAGCGCCGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAGGG
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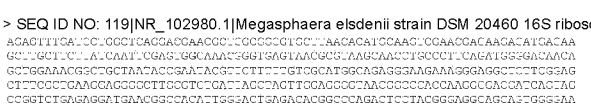
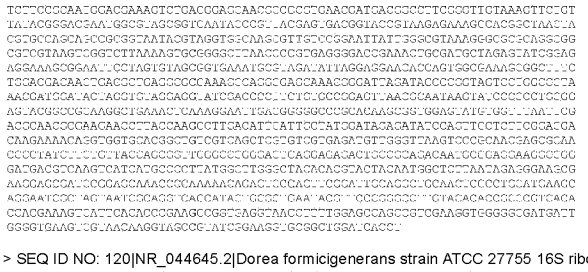
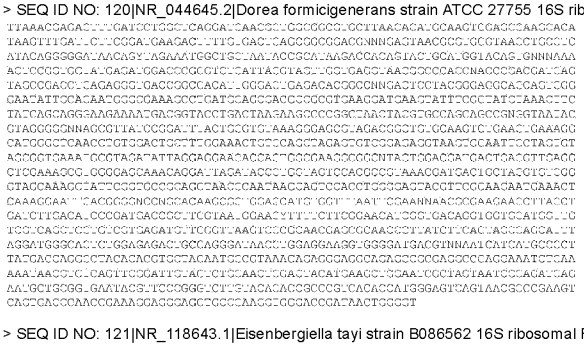


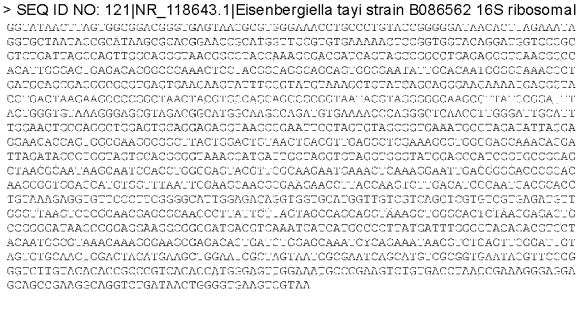
> SEQ ID NO: 119|NR_102980.1|Megasphaera elsdenii strain DSM 20460 16S ribosomal RNA gene, complete sequence



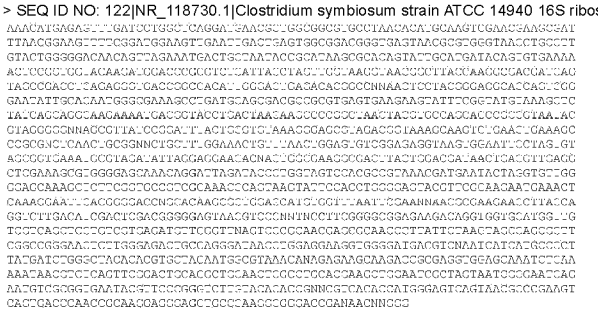
> SEQ ID NO: 120|NR_044645.2|Dorea formicigenerans strain ATCC 27755 16S ribosomal RNA gene, complete sequence



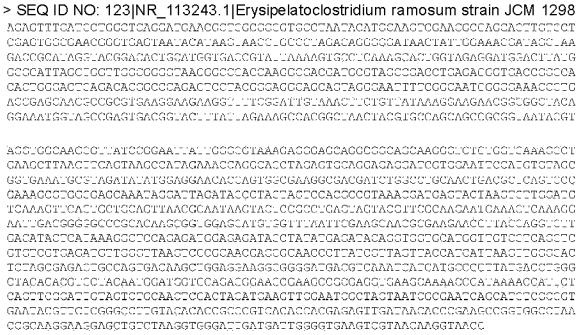
> SEQ ID NO: 121|NR_118643.1|Eisenbergiella tayi strain B086562 16S ribosomal RNA gene, partial sequence



> SEQ ID NO: 122|NR_118730.1|Clostridium symbiosum strain ATCC 14940 16S ribosomal RNA gene, partial sequence



> SEQ ID NO: 123|NR_113243.1|Erysipelatoclostridium ramosum strain JCM 1298 16S ribosomal RNA gene, partial sequence



>SEQ ID NO: 124 |PROKKA_00507 16S ribosomal RNA gene ! VE202-7

>SEQ ID NO: 125 |PROKKA_00709 16S ribosomal RNA gene ! VE202-7

>SEQ ID NO: 126 |PROKKA_01766 16S ribosomal RNA gene ! VE202-7

>SEQ ID NO: 127 |PROKKA_01779 16S ribosomal RNA gene ! VE202-7

>SEQ ID NO: 128 |PROKKA_05926 16S ribosomal RNA gene ! VE202-7

>SEQ ID NO: 129 | PROKKA_01784 16S ribosomal RNA gene

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ACTGACCCCTTCCGTGCCGCAGTTAACACAATAAGTAATCCACCTGGGGAGTACGGCCGCAAGGTTGAAACTCAA
AGGAATTGACGGGGGCCCGCACAAGCAGTGGAGTATGTGGTTTAATTCGAAGCAACGCGAAGAACCTTACCAGGT
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CAGCTCGTGTCGTGAGATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTATTATTAGTTGCTACGCAAGACCA
CTCTAATGAGACTGCCGTTGACAAAACGGACGAAGCTGGGGATGACGTCAAATCATCATGCCCCTTATGACCTGG
GCTACACACGTACTACAATGGCACTAAAACAGAGGGCGGCGACACCGCGAGGTGAAGCGAATCCCGAAAAAGTGT
CTCAGTTCAGATTGCAGGCTGCAACCCGCCTGCATGAAGTCGGAATTGCTAGTAATCGCGGATCAGCATGCCGCG
GTGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCACACCATGGGAGTCGGTAACACCCGAAGCCAGTAGCCT
AACCGCAAGGCGGGCGCTGTCGAAGCTGGGATTGATGACTGGGGTGAAGTCGTAACAAGGTACCCGTATCGGAAG
GTGCGGCTGGATCACCTCCTTT

>SEQ ID NO: 130 | PROKKA_01864 16S ribosomal RNA gene
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TCTAATGAGACTGCCGTTGACAAAACGGAGGAAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGACCTGGG
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TCAGTTCAGATTGCAGGCTGCAACCCGCCTGCATGAAGTCGGAATTGCTAGTAATCGCGGATCAGCATGCCGCGG
TGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCACACCATGGGAGTCGGTAACACCCGAAGCCAGTAGCCTA

ACCGCAAGGGGGGCGCTGTCGAAGGTGGGATTGATGACTGGGGTGAAGTCGTAACAAGGTAGCCGTATCGGAAGG
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>SEQ ID NO: 131 | PROKKA_02671 16S ribosomal RNA gene
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CAATCCGCTGAAAGATGGGCTCGCGTCCGATTAGCCAGTTGGCGGGGTAACGGCCCACCAAAGCGACGATCGGTA
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>SEQ ID NO: 133 | PROKKA_00991 16S ribosomal RNA gene
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>SEQ ID NO: 135 | PROKKA_02310 16S ribosomal RNA gene
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>SEQ ID NO: 136 | PROKKA_02993 16S ribosomal RNA gene
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>SEQ ID NO: 137 | PROKKA_00436 16S ribosomal RNA gene
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>SEQ ID NO: 138 | PROKKA_00685 16S ribosomal RNA gene
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>SEQ ID NO: 139 | PROKKA_01171 16S ribosomal RNA gene
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>SEQ ID NO: 140 | PROKKA_05969 16S ribosomal RNA gene
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TGGGGGACAACAGTTAGAAATGACTCCTAATACCGCATAAGCGCACAGTATCGCATGATACACTGTGAAAAACTC
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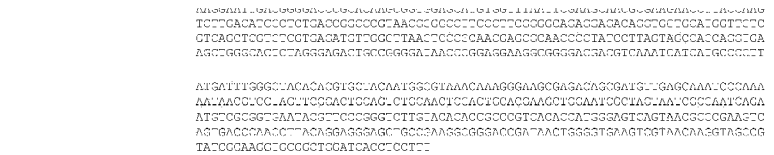
>SEQ ID NO: 141 | PROKKA_00279 16S ribosomal RNA gene

>SEQ ID NO: 142 | PROKKA_01221 16S ribosomal RNA gene

>SEQ ID NO: 143 | PROKKA_02318 16S ribosomal RNA gene

>SEQ ID NO: 144 | PROKKA_02336 16S ribosomal RNA gene

>SEQ ID NO: 145 | PROKKA_04947 16S ribosomal RNA gene



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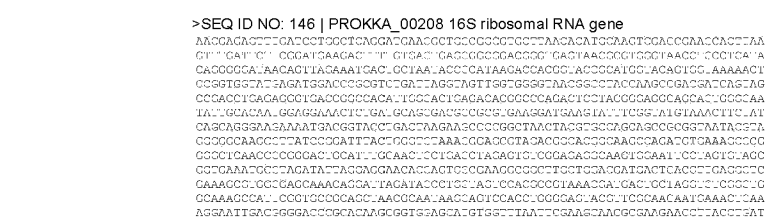

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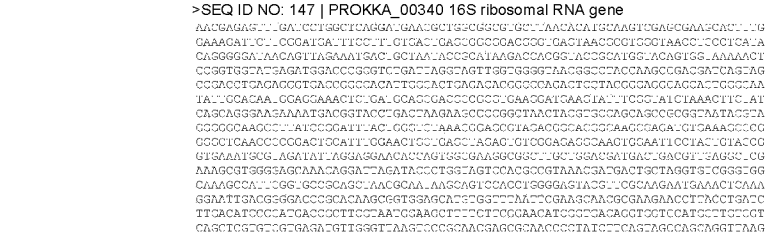

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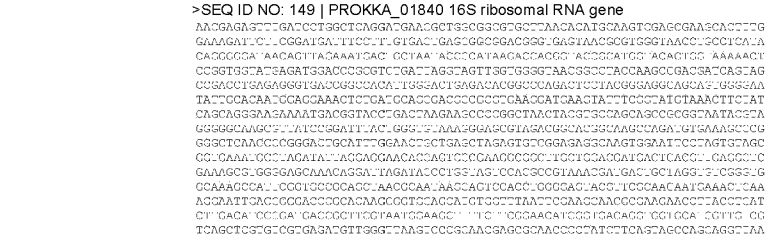

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>SEQ ID NO: 151 | PROKKA_04036 16S ribosomal RNA gene

>SEQ ID NO: 152 | PROKKA_00437 16S ribosomal RNA gene

>SEQ ID NO: 153 | PROKKA_00896 16S ribosomal RNA gene

>SEQ ID NO: 154 | PROKKA_02845 16S ribosomal RNA gene

>SEQ ID NO: 155 | PROKKA_04164 16S ribosomal RNA gene

>SEQ ID NO: 156 | PROKKA_04921 16S ribosomal RNA gene

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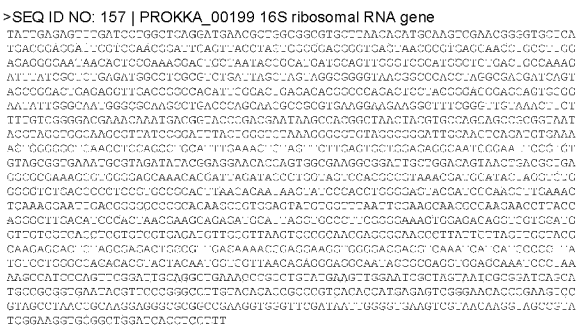

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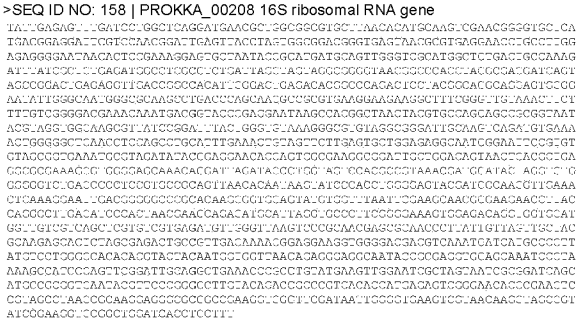

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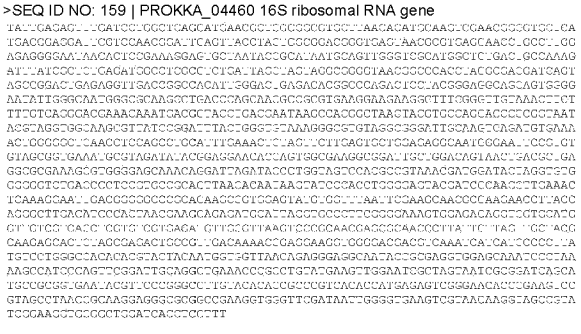

The use of "including," "comprising," or "having," "containing," "involving," and variations thereof herein, is meant to encompass the items listed thereafter and equivalents thereof as well as additional items.

[0150] Unless otherwise defined herein, scientific and technical terms used in connection with the present disclosure shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms hall include the singular. The methods and techniques of the present disclosure are generally performed according to conventional methods well-known in the art. Generally, nomenclatures used in connection with, and techniques of biochemistry, enzymology, molecular and cellular biology, microbiology, virology, cell or tissue culture, genetics and protein and nucleic chemistry described herein are those well-known and commonly used in the art. The methods and techniques of the present disclosure are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated.

EXAMPLES

Example 1: Mouse model of *C. difficile* infection

Mouse husbandry

[0151] Experiments were performed using C57BL/6J female mice purchased from Jackson Laboratories (Bar Harbor, ME) and housed in ventilated sterile cages. All animals were maintained in a specific-pathogen-free facility. Animals were acclimated to the vivarium for at least 3 days prior to study (*i.e.,* commencing antibiotic courses). For experiments involving *C. difficile* infection, mice were administered 10-10^4 *C. difficile* VPI 10463 spores in 200 µl PBS by oral gavage. Experiments were performed in compliance with institutional guidelines and approved by the institution's Institutional Animal Care and Use Committee. Sterile food and drinking water were provided to the animals

Live Biotherapeutic Product (LBP) Preparation

[0152] Individual bacterial strains were isolated from fecal material obtained from healthy donors. The individual strains were struck out from 15% glycerol freezer stocks onto EG (Eggerth Gagnon) agar plates containing 5% horse blood in an anaerobic chamber and incubated for 24-48 hours at 37°C. Colonies were inoculated into pre-reduced liquid Peptone Yeast Glucose (PYG) media and grown for 24-48 hours until dense (static in the anaerobic chamber). Optical density (OD_{600}) of the cultures was assessed and live biotherapeutic product (LBP) cocktails were prepared inside an anaerobic chamber adjusting inputs based upon OD_{600} for equal CFU ratio cocktails in PBS (sterile, pre-treated).

***C. difficile* colony forming unit (CFU) determination**

[0153] Fecal pellets were collected, transported to an anaerobic chamber (<2 hours), and manually homogenized in 500 µL of pre-reduced PBS using a pipette tip and through repeated pipetting. Serial dilutions of fecal homogenates were prepared in pre-reduced PBS, 100 µL of which was spread onto cycloserine-cefoxitin-fructose agar with sodium taurocholate (TCCFA) plates, and incubated anaerobically at 37°C. *C. difficile* CFUs were enumerated at 48 hours.

Murine susceptibility to *C. difficile* infection

[0154] Groups of mice were evaluated for susceptibility to C. *difficile* using three antibiotic regimen protocols: (1) an antibiotic cocktail, (2) clindamycin administration, or (3) cefoperazone administration (Figures 2 and 3). The antibiotic cocktail consisted of kanamycin (0.4 mg/ml), gentamicin (0.035 mg/ml), colistin (0.056 mg/ml), metronidazole (0.215 mg/ml), vancomycin (0.045 mg/ml) in the drinking water from day -10 to day -3, followed by a single intraperitoneal clindamycin injection (200 µg/mouse). The clindamycin administration involved a single intraperitoneal injection of clindamycin (200 µg/mouse) on day -1. The notation of days is relative to day 0, the day of *C. difficile* infection.

[0155] Mice were treated with the indicated antibiotic regimen as described above and then infected with either 10 or 10^4 *C. difficile* spores by oral gavage on day 0 (Figures 2 and 3). An additional experimental arm was added to the antibiotic treatment model in which mice were treated with vancomycin after *C. difficile* infection (Figure 4J; black triangles).

[0156] Mice were monitored daily following infection for mortality/survival (Figures 4A-4D) and weight (Figures 4E-4H). Fecal pellets were also collected daily and used for *C. difficile* CFU enumeration, presented as CFU/gram feces (Figures 4I-4L).

[0157] The groups of mice that received cefoperazone treatment had a significant change in weight (Figure 4H) and substantial *C. difficile* bacterial load in the fecal pellets (Figure 4L), even following administration with 10 *C. difficile* spores. These results indicated that the cefoperazone pre-treatment regimen provided a good model for *C. difficile* infection and for evaluating protection and/or treatment of *C. difficile* infection. In the absence of antibiotic treatment prior to infection, *C. difficile* infection was not established (Figure 4I) and all mice survived (Figure 4A) without significant change in body weight (Figure 4E).

Example 2: Live Biotherapeutic Product (LBP) preparations protect against C. *difficile* infection.

[0158] The following LBP compositions were evaluated for their capacity to protect and/or treat C. *difficile* infection:

Composition A,

Composition B,

Composition C,

Composition D,

Composition E (See *e.g.,* Narushima et al., Gut Microbes (2014) 5(3) 333-339), and

Composition I: a mixture of *Clostridium scindens*, *Pseudoflavonifractor capillosus* and *Blautia hansenii* (Figure 5).

[0159] In general, LBP cocktails were mixed in PYG media, and each mouse was administered a dose by oral gavage in 250 µL pre-reduced PBS (media-free). For composition E, bacteria were mixed in equal volumes (not equal ratios/CFUs) and administered in a 250 µL dose. Each LBP of Compositions A-D contained 10^8 CFUs total in a 250 µL dose, comprised of 10^7 CFU of each of the bacterial strains (Figure 1), for a total of 10^8 CFU administered to each animal. Composition I contained a total of 10^6 CFUs in a 250 µL dose (approximately 333,000 of each of the 3 bacteria mixed).

[0160] Groups of mice were subjected to cefoperazone treatment, as described in Example 1, and were administered the indicated composition by oral gavage 2 days after the cessation of cefoperazone treatment. Twenty-four hours later, the mice were subjected to infection with 10^4 *C. difficile* spores (Figure 5). Mice evaluated for survival/mortality (Figure 6), weight (Figures 7A-7I, and C. *difficile* CFUs (Figures 8A-8C). The results show that administration of Composition B prior to *C. difficile* infection is an effective protection and/or treatment against *C. difficile* infection.

Example 3: Composition B protects against and/or treats C. *difficile* infection.

[0161] Groups of 10-12 week old mice were used in the C. *difficile* mouse model (Figure 9). Mice were subjected to cefoperazone treatment as described in Example 1. One group of mice was then administered Composition B (10^8 CFU per mouse) administered by oral gavage, as described in Examples 1 and 2, 2 days after the cessation of cefoperazone treatment. The other group of mice did not receive a live biotherapeutic product after cefoperazone treatment (control). Twenty-four hours later, the mice were subjected to C. *difficile* infection (10^4 C. *difficile* spores) and then evaluated for survival/mortality (Figure 10), weight (Figure 11), and *C. difficile* burden (CFUs per gram feces; Figure 12). These results confirm the results of Example 2 that demonstrate treatment with Composition B prior to *C. difficile* infection is an effective protection and/or treatment against *C. difficile* infection.

Example 4: LBP Composition F protects against and/or treat C. *difficile* infection.

[0162] Figure 13 shows the strains of live biotherapeutic product (LBP) Composition F. The genus-species classification indicates the closest species based on the sequence of the isolated strain. Figure 14 shows the classification by *Clostridium* cluster of the strains in Composition F.

[0163] Groups of mice were administered cefoperazone, as described in the Examples above, then administered LBPs or fecal matter transplant (FMT) from mice or human (Figure 15). Composition B was administered to the indicated groups on day -1; days -2 and -1; or on days -2, -1, 1, 2, and 3, relative to infection with 10^4 *C. difficile* spores. Composition F was administered to the indicated groups on day -1 or on days -2, -1, 1, 2, and 3, relative to administration of *C. difficile* spores. Additional groups received FMT from mice or from humans (200µL of a 10% fecal sample s per mouse). Mice were then evaluated for survival/mortality (Figure 16), weight (Figures 17A-17H), and C. *difficile* burden (CFU/gram feces) on days 1, 3, 8 and 17 after infection (Figures 18A and 18B). The data demonstrate that Composition B, Composition F, and FMT protect against and/or treat C. *difficile* infection.

Example 5: LBP compositions protect against and/or treat C. *difficile* infection.

[0164] Figure 19 shows the strains of LBP Composition G. The genus-species notation indicates the closest species based on the sequence of the isolated strain. Composition G includes a subset of the strains of Composition F. Groups of mice were administered cefoperazone, as described in the Examples above, then administered the LBP:

Composition B;

Composition B-1 (Composition B with *Bacteroides* added);

Composition B-2 (Composition B from which *Flavonifractor plautii* was removed and *Bacteroides* added);

Composition F;

Composition G;

Human fecal samples subjected to ethanol treatment;

Composition B subjected to ethanol treatment;

Composition B that had been frozen; or

Composition J: *Clostridium innocuum*, *Clostridium bolteae* and *Clostridium symbiosum* subjected to ethanol treatment;

(See also Figure 20).

[0165] The *Bacteroides* strain used in Composition B-1 and B-2 was *Bacteroides ovatus* (strain identifier 211-B; SEQ ID NO: 83).

[0166] Mice were challenged with *C. difficile* VPI 10463 spores (10^4) and monitored daily (Day 0 to Day 7 post *C. difficile* infection) for survival/mortality (Figures 21 and 23) and change in weight (Figures 22A-22J and 24). These data show that the compositions protect against and/or treat *C. difficile* infection.

Example 6: LBP compositions protect against and/or treat C. *difficile* infection.

[0167] Groups of mice were subjected to cefoperazone treatment, as described above, then administered human fecal matter transplant, Composition B, Composition B + 4 spores, or Composition H (Figure 25). "Composition B + 4 spores" refers to Composition B plus the following four strains in spore form: *Clostridium bolteae, Anaerotruncus colihominis, Clostridium symbiosum* and *Clostridium innocuum*. Composition H contains the following six strains in spore form: *Clostridium bolteae, Anaerotruncus colihominis, Clostridium symbiosum, Clostridium innocuum, Clostridium disporicum and Erysipelatoclostridium ramosum* (Figure 26).

[0168] Mice were then challenged with C. *difficile* infection with 10^4 *C. difficile* VPI 10463 spores and monitored for survival/mortality (Figures 27A and 28A), weight (Figures 27B and 28B). Mice that lost more than 20% body weight relative to baseline were included in mortality numbers in survival curves. The *C. difficile* burden was assessed by CFU in fecal pellets on days 1, 4 and 19 after infection (Figures 29A-29C).

[0169] These data indicate that Composition B as well as other compositions can improve survival in the cefoperazone-induced C. *difficile* mouse model and protect against and/or treat *C. difficile* infection.

Example 7: *C. difficile* toxin experiment

[0170] Vero cells, epithelial cells derived from African Green Monkey kidney epithelium, are sensitive to a variety of bacterial toxins, including *C. difficile* Toxin B. Exposure of cells to *C. difficile* Toxin B results in inhibition of the function of Rho, Rac, and Cdc42 leading to a decline in F-actin, a change in cell morphology (*e.g.*, cell rounding), and eventually apoptosis.

[0171] To determine whether administration of bacterial compositions described herein has an effect on the production or activity of *C. difficile* Toxin B, a cellular assay was performed. Briefly, groups of mice were treated with cefoperazone, as described above, and administered human fecal matter transplant (FMT) ("4-3"); Composition B ("5-3"); Composition B plus four strains in spore form: *Clostridium bolteae, Anaerotruncus colihominis, Clostridium symbiosum* and *Clostridium innocuum* ("7-4"), or no treatment. Each of the groups of mice were then exposed to *C. difficile* infection with 10^4 *C. difficile* spores. The groups of mice that did not receive a treatment after cefoperazone administration and prior to *C. difficile* infection are referred to as "2-1 (Cdiff)" and "2-4 (Cdiff)." An additional group of mice was not exposed to *C. difficile* as indicated by "N3 (Healthy)".

[0172] Fecal pellets were collected from each of the groups of mice, weighed, and homogenized in PBS and normalized to a fixed concentration (-25 mg/mL). The samples were centrifuged to prepare a clarified supernatant, which was then diluted in 10-fold serial dilutions to produce a range from 1:10 to $1:10^{-6}$ dilutions of clarified pellet supernatant. Vero cell cultures were exposed to the diluted samples for approximately 18 hours, then visualized by phase contract microscopy to assess morphological changes (*i.e.*, cell rounding) associated with *C. difficile* toxin exposure. The cells were scored based on the highest concentration of supernatant that did not yield a change in morphology (Figure 30). The samples from mice that had been treated with Composition B prior to *C. difficile* infection had reduced amounts of *C. difficile* Toxin B, as compared to samples from control mice that did not receive a treatment after cefoperazone administration and prior to *C. difficile* infection ("2-1 (Cdiff)" and "2-4 (Cdiff)") as well as compared to samples from mice that received FMT. Notably, the samples from mice that had been treated with Composition B also had reduced amounts of *C. difficile* Toxin B, as compared to samples from mice that had been treated with Composition B with additional spores.

Example 8: *In vitro* Competition Between Compositions B and C. *difficile*

[0173] Composition B was assessed for its ability to suppress *Clostridium difficile* growth by an *in vitro* mixed culture competition assay. From glycerol freezer stocks, individual strains of Composition B, *C. difficile* (Cdiff), *Clostridium bifermentans*, and *Bacteroides thetaiotaomicron* were struck out onto Eggerth-Gagnon agar plates with horse blood (EG+HB). Single colonies of each of the strains were subsequently inoculated into brain heart infusion (BHI) liquid media and allowed to grow in pure culture for 24-48 hours. Turbid cultures were sub-cultured then grown to exponential phase and finally diluted and combined to prepare a mixed culture with an optical density (OD_{600}) of 0.1. Exponential phase Cdiff culture was added to the mixed culture at a final concentration with an OD of 0.1. After the cultures were combined and incubated for 2-3 hours, samples were collected, serially diluted, and plated on Taurocholate-Cycloserine-Cefoxitin-Fructose Agar (TCCFA) plates to select for Cdiff growth. After 48-72 hours, the colony forming units (CFUs) of Cdiff in each competition experiment were determined by manual colony counting.

[0174] EG+HB agar plates were prepared according to standard procedures and reduced in an anaerobic environment for at least 6-8 hours prior to use. Liquid BHI medium was obtained from BD Biosciences (Catalog # 211059, San Jose, CA), prepared according to the manufacturer's instructions, and reduced in an anaerobic environment for at least 18-24 hours prior to use. TCCFA plates were prepared according to standard procedures and reduced in an anaerobic environment for at least 6-8 hours prior to use. *Clostridium difficile* strain used in the experiments: American Type Culture Collection (ATCC) 43255.

Table 4: Composition B strains

Composition B	
VE202-7	
VE202-13	
VE202-14	
VE202-16	
Strain #16	
Strain #170	
Strain #189	
Strain #211	

[0175] Strains were struck out onto EG+HB agar plates from frozen glycerol stocks inside an anaerobic chamber for 48-72 hours. Single colonies were inoculated into 10 mL of BHI media and grown 24-48 hours at 37°C in the anaerobic chamber. Turbid cultures were then diluted to an OD of 0.1 and grown for 2-3 hours at 37°C in the anaerobic chamber. Exponential phase cultures were diluted and combined at equivalent ODs. For the competition assay, each of the strains of Combination B (Table 4) were combined in equal parts, based on OD_{600}, to reach a final consortium OD_{600} of 0.1. *C. bifermentans* and *B. thetaiotaomicron* were setup to compete with Cdiff individually at an OD of 0.1. The OD600 for Cdiff in each of the mixed culture competition experiments was 0.1. After combination, the cultures were incubated for 2-3 hours at 37°C in the anaerobic chamber, then prepared for enumerations on Cdiff selective plates.

[0176] TCCFA plates are selective for Cdiff growth, and none of the Combination B strains, nor either of the control strains (*C. bifermentans* and *B. thetaiotaomicron*), grow on these plates. Inside an anaerobic chamber, a 100 µL sample of each competition culture was collected and serially diluted 1:10 to reach a final dilution of $1x10^{-6}$. Plates for CFU enumeration were prepared by spreading 100 µL of each of the $1×10^{4}$ through $1×10^{-6}$ dilutions on TCCFA plates using sterile spreading loops. CFU plates were incubated for 48-72 hours at 37°C in the anaerobic chamber. CFU enumeration was completed by manually counting colonies.

[0177] To determine the effect of competition, the ratio of CFUs determined for the competition samples and Cdiff alone was calculated and expressed as a percentage. Inhibition of Cdiff growth by the Composition B cocktail was compared to the responses of *B. thetaiotaomicron* (negative control) and *C. bifermentans* (positive control). The results are shown in Table 5 and Figure 31.

Table 5: Summary Results for *In Vitro* Competition

Experiment Number	No Competing Strain(s)	Competition with *B. thetaiotaomicron*	Competition with *C. bifermentans*	Competition with Composition B
n=1	100			33.8
n=2	100	9.90	0.1	0.5
n=3	100	115	39.5	33.1
n=4	100	41.3	0.7	0.7
n=5	100	105	14.1	20.9
n=6	100	57.4	4.1	1.6
Mean	100	65.6	11.7	15.1
Std. Dev.	0	43.8	16.5	16.2
Total N	6	5	5	6

[0178] Data is expressed as Cdiff CFU as a percentage of control. Each n is representative of a single biological replicate, independent of other measurements.

[0179] In *in vitro* competition, Composition B inhibited Cdiff growth to 15.1 ± 16.2 % of control (absence of competing strain(s)). This result is consistent with the inhibition observed by the positive control, *C. bifermentans*, of 11.7 ± 16.5 % of control. *B. thetaiotaomicron*, a negative control, yielded a negligible effect on Cdiff growth at 65.6 ± 43.8 % of control. Given the variability inherent in the assessment of CFU, inhibition of growth to < 25 % of control is considered to be significant inhibition and both the positive control and Composition B cocktail meet this threshold of activity. The Composition B consortium attenuated Cdiff growth *in vitro* comparable to the direct competition observed by *C. bifermentans*. Direct competition with *B. thetaiotaomicron* did not significantly inhibit Cdiff growth.

Example 9: Determination of *In Vitro* Short-Chain Fatty Acid Production

[0180] Each strain of Composition B was assessed for individual short-chain fatty acid (SCFA) production *in vitro*. Composition B strains were grown in pure cultures inside an anaerobic chamber. Spent supernatant from liquid media cultures was harvested by centrifugation, filter sterilized, and then stored at < -70°C. Frozen clarified supernatant specimens were analyzed for short-chain fatty acids (SCFAs).

[0181] EG+HB agar plates (Eggerth-Gagnon agar plates with horse blood) were prepared according to standard methods and reduced in an anaerobic environment for at least 6-8 hours prior to use. Liquid PYG medium (pre-formulated, pre-reduced) was obtained from Anaerobe Systems (Catalog#AS-822; Morgan Hill, CA).

[0182] Strains were struck out onto EG+HB agar plates from frozen 15% glycerol stocks inside an anaerobic chamber for 48 - 72 hours. Single colonies were inoculated into 7 mL PYG media and grown 24-48 hours at 37°C in the anaerobic chamber. Unless otherwise noted, when the optical density (OD) was ≥ 0.2, samples were collected for

CFU enumeration and filtration. Inside an anaerobic chamber, a 100 µL sample of turbid culture was collected and serially diluted 1:10 to reach a final dilution of $1x10^{-6}$. Plates for CFU enumeration were prepared by spreading 100 µL/dilution for the 1×10^{-4} through 1×10^{-6} dilutions on EG+HB agar plates using sterile glass beads. CFU plates were incubated for 48-72 hours in the anaerobic chamber. CFU enumeration was completed using the EasyCount 2 (bioMérieux SA, Marcy-l'Etoile, France). Immediately after samples of turbid cultures were collected for CFU enumeration, the remaining turbid cultures were centrifuged at approximately 1000 RCF for 10 minutes to pellet cellular debris. The clarified supernatants were transferred to a 0.2 µm plate filter and vacuum filtered to remove any remaining particulates prior to bioanalysis. In the event of blockage in the filter plate, clarified supernatants were manually filtered using 0.2 µm syringe filters. Filtered supernatants were aliquoted and stored at < - 70°C prior to bioanalysis of SCFAs.

[0183] To facilitate easier comparisons between samples, raw SCFA data (µg/mL) was normalized by the $\log_{10}$ of corresponding determined/estimated CFU for the culture. The results are depicted in Table 6 and Table 7 below.

Table 6: Enumerated CFUs for Composition B Strains

Sample ID	OD600	Enumerated CFU (CFU/mL)
VE202-7	> 2	6.11E+08
VE202-13	0.8	4.00E+08
VE202-14	> 2	1.60E+09
VE202-16	1.92	1.28E+09
#16	1.97	1.69E+08
# 170	1.8	1.08E+08
# 189	1.03	1.74E+09
# 211	0.35	3.71E+08

Table 7: SFCAs produced by individual Composition B strains

Sample ID	Normalized (µg/Log(CFU/mL)*mL)							
	Acetate	Propionate	Isobutyrate	Butyrate	2-Methylbutyrate	Iso-valerate	Valerate	Hexanoate
VE202-7	123.7	0.077	0.102	0.208	0.015	0.056	BLOQ	0.031
VE202-13	30.1	0.545	0.116	34.452	0.288	0.188	0.097	0.034
VE202-14	110.5	0.054	0.022	0.248	0.011	0.014	BLOQ	0.009
VE202-16	313.2	0.000	0.000	0.280	0.004	0.000	BLOQ	0.009
# 16	104.0	0.005	0.000	50.988	0.014	0.033	BLOQ	0.009
# 170	87.1	0.055	0.025	0.215	0.011	0.039	BLOQ	0.016
# 189	0.0	BLOQ	0.000	35.751	0.005	0.019	0.359	0.587
# 211	57.6	5.289	0.000	78.227	0.028	0.050	0.053	0.095

[0184] Seven strains of Composition B were found to produce significant quantities (> 1 µg/Log(CFU/mL)*mL) of the 2-carbon SCFA, acetate. One strain, (#211), produced substantial quantities of the 3-carbon SCFA, propionate. Four strains of Composition B produced substantial quantities of the 4-carbon SCFA, butyrate. Trace quantities (< 1 µg/Log(CFU/mL)*mL) of other SCFAs were also produced by the Composition B strains.

Example 10: Composition B induces regulatory T cells (Tregs)

[0185] Each of the bacterial strains of Composition B were grown to log phase, combined to a total dose of ~10^8 cfu per mouse. Germ-free mice were inoculated with Composition B or a negative control by oral gavage and sacrificed following four weeks of colonization. Lamina propria leukocytes were isolated from colonic tissue of individual mice by standard procedures and assessed by flow cytometry. The regulatory T cell content was evaluated as the percentage of Foxp3-positive cells among CD4+ T cells.

[0186] As shown in Figure 32, mice that were inoculated with Composition B were found to have significantly more regulatory T cells as compared to mice that were inoculated with the control.

REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Sammensætning omfattende 8 oprensede bakteriestammer af species *Flavonifractor plautii, Anaerotruncus colihominis, Drancourtella massiliensis, Clostridium symbiosum, Clostridium bolteae, Dorea longicatena, Blautia producta* og *Clostridium innocuum.*

2. Sammensætning omfattende 8 oprensede bakteriestammer omfattende 16S rDNA-sekvenser med mindst 97% sekvensidentitet med SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO:20 og SEQ ID NO:21.

3. Sammensætningen ifølge et hvilket som helst af de foregående krav, hvor en eller flere af bakteriestammerne er i vegetativ form.

4. Sammensætningen ifølge et hvilket som helst af de foregående krav, hvor en eller flere af bakteriestammerne er i sporeform.

5. Sammensætningen ifølge et hvilket som helst af de foregående krav, hvor bakteriestammerne er frysetørret.

6. Sammensætningen ifølge et hvilket som helst af de foregående krav, hvor sammensætningen yderligere omfatter en eller flere enteriske polymerer.

7. Farmaceutisk sammensætning omfattende sammensætningen ifølge et hvilket som helst af kravene 1-6, yderligere omfattende en farmaceutisk acceptabel excipiens.

8. Den farmaceutiske sammensætning ifølge krav 7, hvor den farmaceutiske sammensætning er formuleret til oral levering.

9. Den farmaceutiske sammensætning ifølge krav 7 eller 8, hvor den farmaceutiske sammensætning er formuleret til levering til tarmen.

10. Fødevareprodukt omfattende sammensætningen ifølge et hvilket som helst af kravene 1-5 og et næringsstof.

11. Sammensætningen ifølge et hvilket som helst af kravene 1-9 eller fødevareproduktet ifølge krav 10 til anvendelse i en fremgangsmåde til behandling af en *Clostridium difficile* infektion hos et individ.

12. Sammensætningen eller fødevareproduktet til anvendelse ifølge krav 11, hvor *C. difficile* infektionen er en første forekomst af *C. difficile* infektionen.

13. Sammensætningen eller fødevareproduktet til anvendelse ifølge krav 11, hvor *C. difficile* infektionen er en tilbagevendende *C. difficile* infektion.

14. Sammensætningen eller fødevareproduktet til anvendelse ifølge et hvilket som helst af kravene 11-13, hvor individet indgives en dosis af et antibiotikum forud for indgivelse af den farmaceutiske sammensætning.

15. Sammensætningen eller fødevareproduktet til anvendelse ifølge krav 14, hvor antibiotikummet er vancomycin, kanamycin, gentamicin, colistin, metronidazol, clindamycin, fidaxomicin eller cefoperazon.

Figure 1

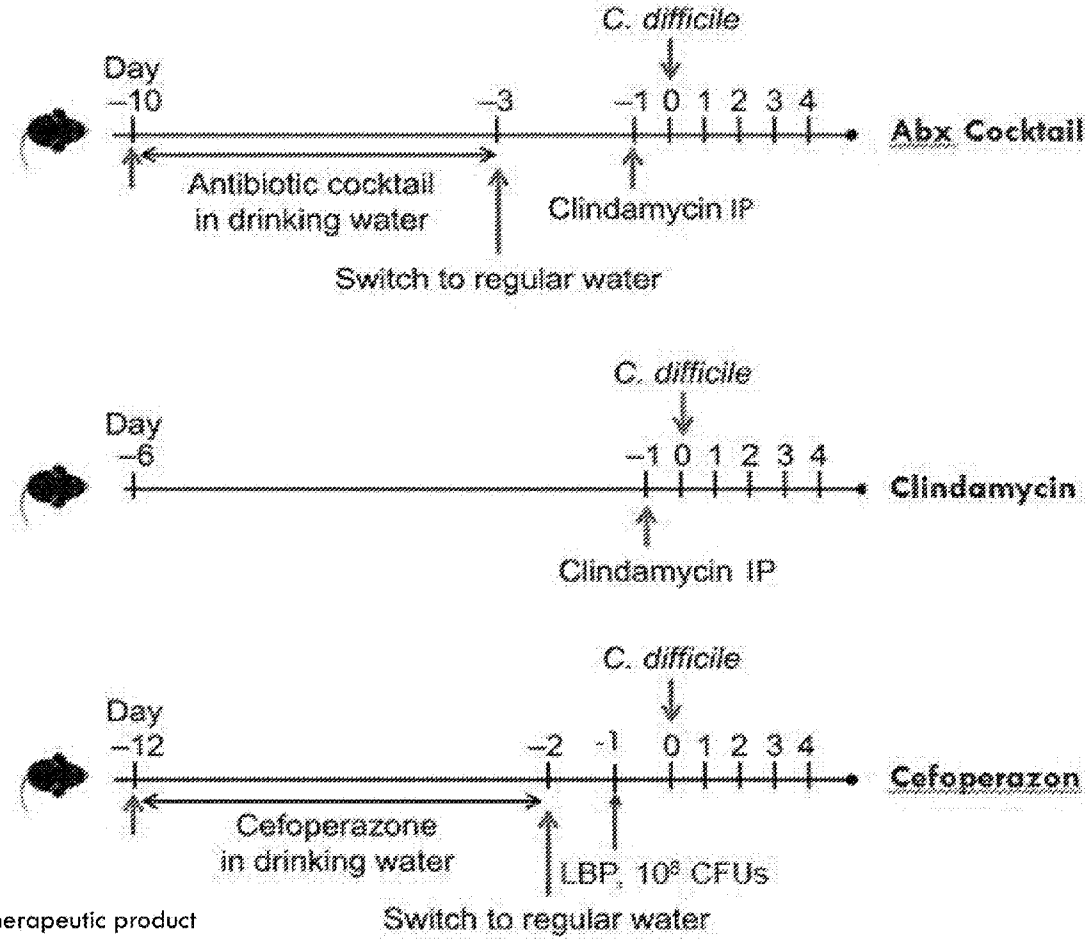
Composition A	Composition B	Composition C	Composition D
SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*	**SEQ_10 - 211 - Flavonifractor_plautii (IV)**	SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*	SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*
SEQ_04 - 7 - Blautia_hansenii (XIVa)*	**SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)**	SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*	SEQ_03 - 5 - Clostridium_hathewayi (XIVa)*
SEQ_05 - 10 - Blautia_hansenii (XIVa)*	SEQ_15 - VE202-14 - Eubacterium_fissicatena (XIVa)	SEQ_05 - 10 - Blautia_hansenii (XIVa)*	SEQ_05 - 10 - Blautia_hansenii (XIVa)*
SEQ_07 - 59 - Blautia_producta / Blautia_coccoides (XIVa)	SEQ_16 - VE202-16 - Clostridium_symbiosum (XIVa)	SEQ_01 - 71 - Blautia_wexlerae (XIVa)*	SEQ_01 - 71 - Blautia_wexlerae (XIVa)*
SEQ_08 - 79 - Blautia_hansenii (XIVa)*	SEQ_17 - VE202-7 - Clostridium_bolteae (XIVa)	SEQ_07 - 59 - Blautia_producta/Blautia_coccoides (XIVa)*	**SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)**
SEQ_09 - VE202-21 - Eubacterium_contortum / Eubacterium_fissicatena (XIVa)*	SEQ_20 – 170 – Dorea longicatena (XIVa)	SEQ_18 - 148 - Dorea_longicatena (XIVa)	SEQ_18 - 148 - Dorea_longicatena (XIVa)
SEQ_11 - VE202-9 - Anaerostipes_caccae (XIVa)*	SEQ_19 - 16 - Blautia_producta (XIVa)	**SEQ_21 - 189 - Clostridium_innocuum (XVII)**	**SEQ_21 - 189 - Clostridium_innocuum (XVII)**
SEQ_12 - VE202-26 - Clostridium_scindens (XIVa)*	**SEQ_21 - 189 - Clostridium_innocuum (XVII)**	**SEQ_10 - 211 - Flavonifractor_plautii (IV) /**	**SEQ_10 - 211 - Flavonifractor_plautii (IV) /**
SEQ_13 - 136 - Marvinbryantia_formatexigens (XIVa)*		**SEQ_14 - VE202-13 - Anaerotruncus_colihominis (IV)**	**SEQ_02 - 102 - Turicibacter_sanguinis (non-Clostridium)**
SEQ_23 - VE202-29 - Eisenbergiella_tayi (XIVa)*		SEQ_16 - VE202-16 - Clostridium_symbiosum (XIVa)	**SEQ_06 - 40 - Lactobacillus_mucosae (non-Clostridium)**

*= BaiCD$^+$

bolding indicates strains other than Clostridium cluster XIVa

Figure 2

Clostridium difficile Infection Mouse Models



LBP, live biotherapeutic product

Figure 3

Groups	# of animals	Abx	*C. difficile* Spores
(1) Control	5	-	10^1
(2) Control	5	-	10^4
(3) Abx cocktail	5	+	10^1
(4) Abx cocktail	5	+	10^4
(5) Clindamycin	5	+	10^1
(6) Clindamycin	5	+	10^4
(7) Cefoperazone	5	+	10^1
(8) Cefoperazone	5	+	10^4

Figure 4A

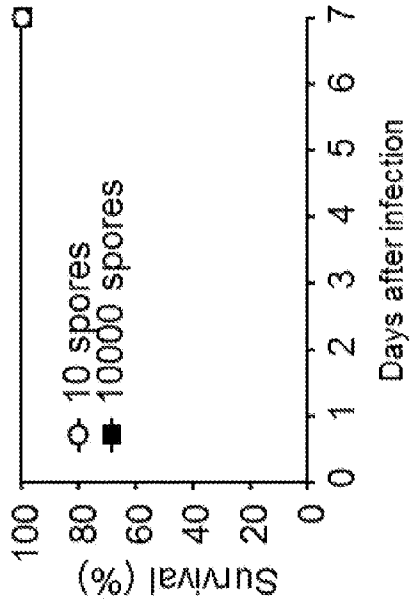


Figure 4B

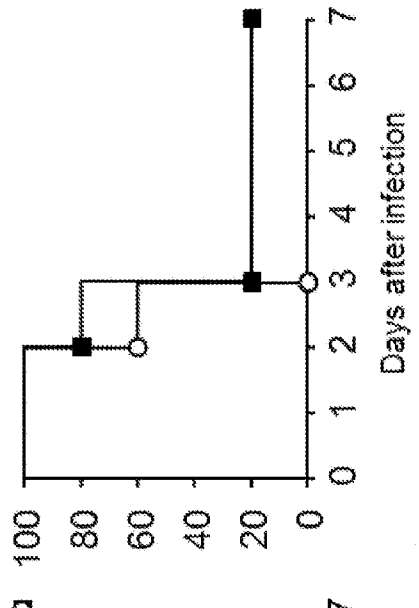


Figure 4C

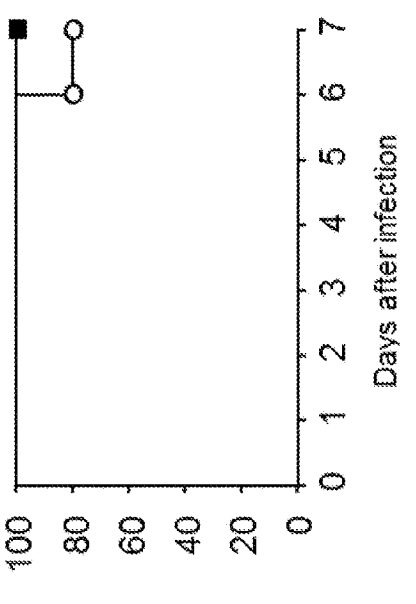


Figure 4D

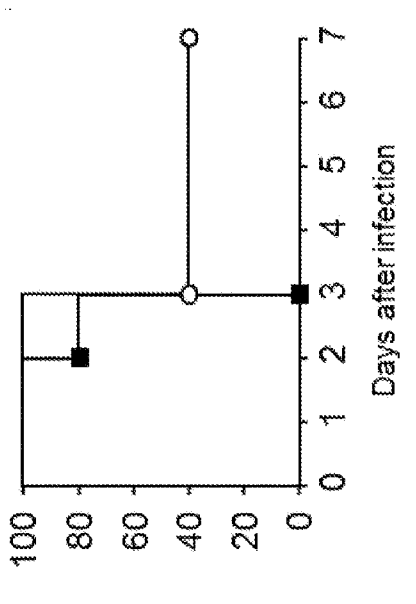


Figure 4E

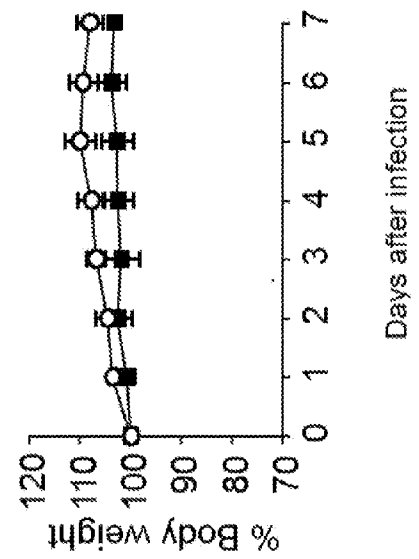


Figure 4F

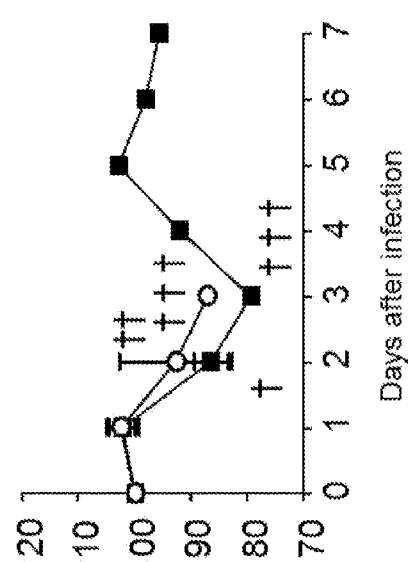


Figure 4G

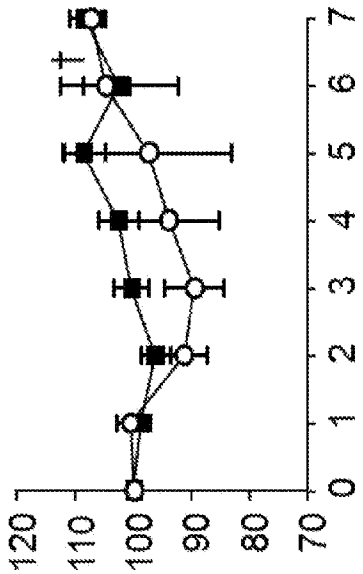


Figure 4H

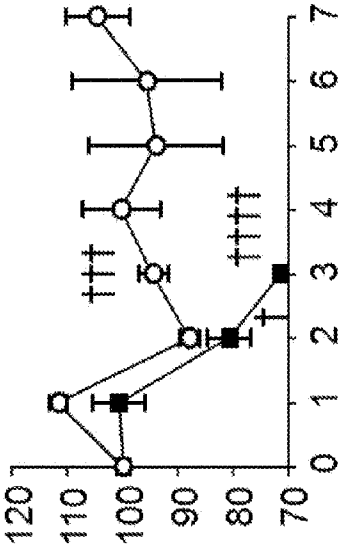


Figure 4I

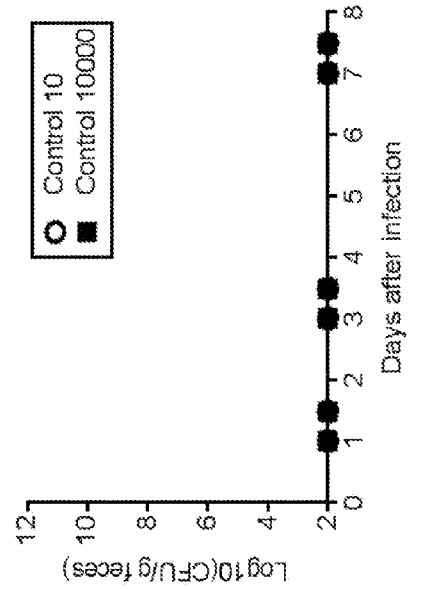


Figure 4J

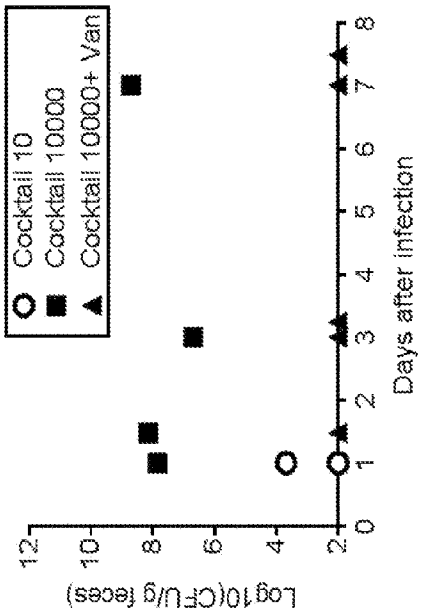


Figure 4K

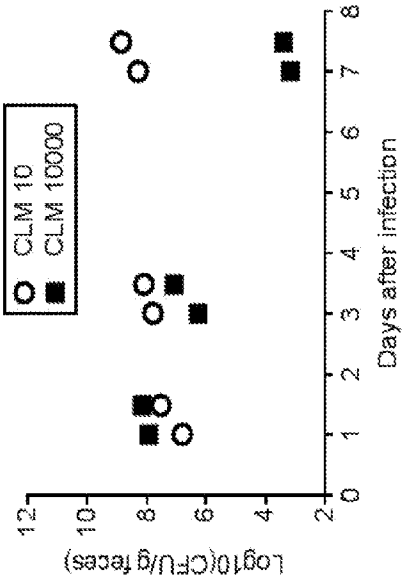


Figure 4L

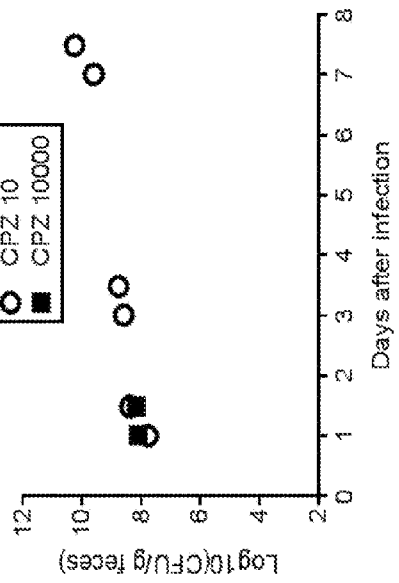


Figure 5

Groups	# of animals	Abx	CFUs (Spores)
(1) Control-	5	-	10^4
(2) Control+	5	+	10^4
(3) Van	5	+	10^4
(4) Composition E	5	+	10^4
(5) Composition I	5	+	10^4
(6) Composition A	5	+	10^4
(7) Composition B	5	+	10^4
(8) Composition C	5	+	10^4
(9) Composition D	5	+	10^4

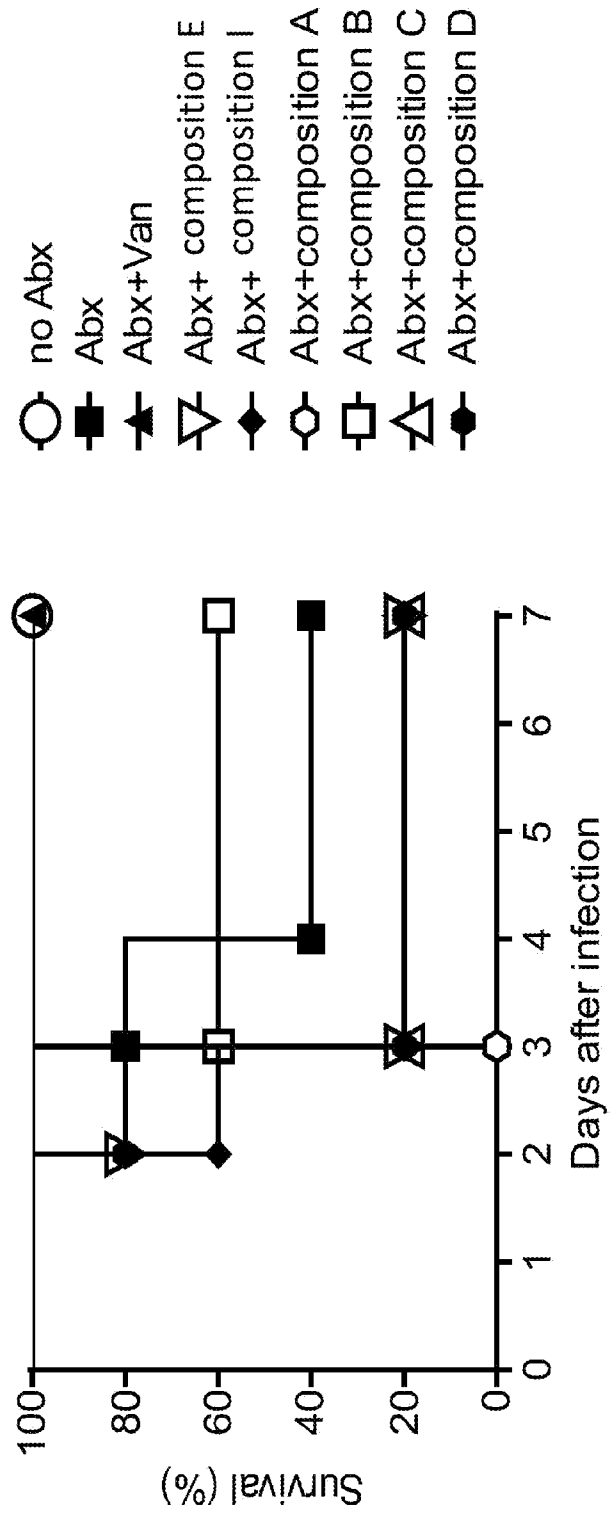

no Abx
Abx
Abx+Van
Abx+ composition E
Abx+ composition I
Abx+composition A
Abx+composition B
Abx+composition C
Abx+composition D
Survival (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Days after infection

Figure 6

Figure 7A

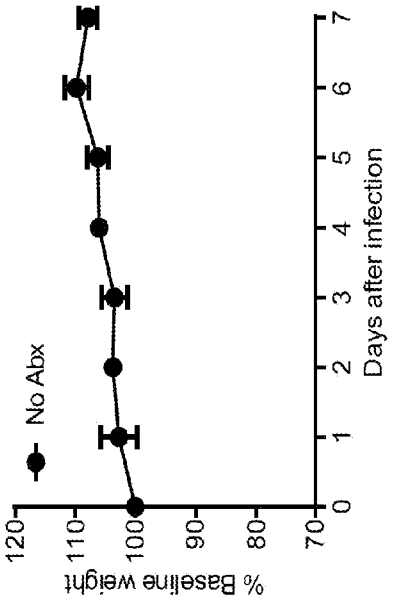


Figure 7B

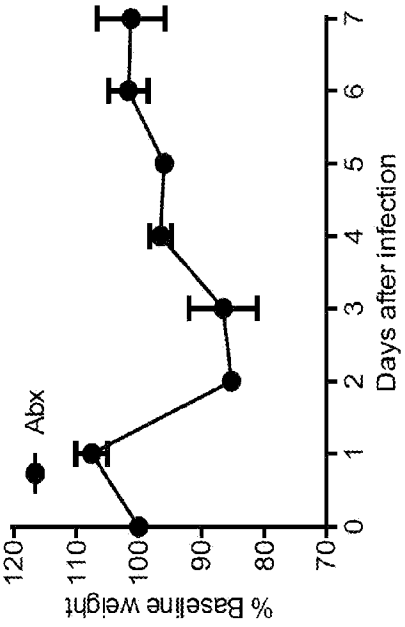


Figure 7C

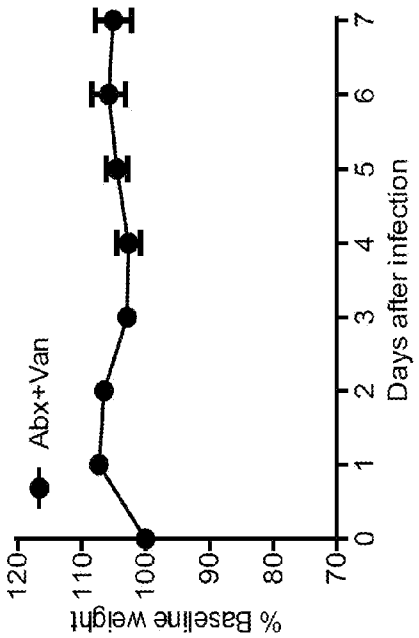


Figure 7D

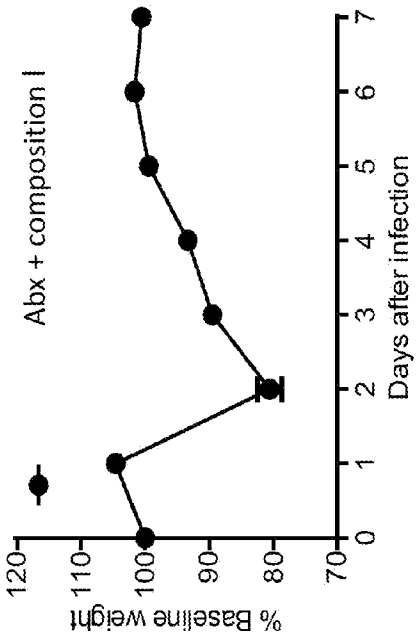


Figure 7E

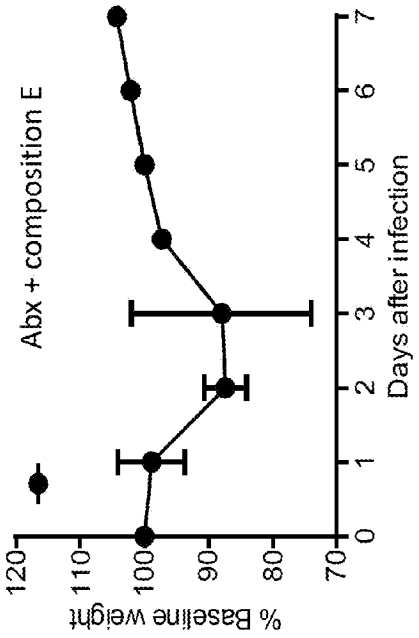


Figure 7F

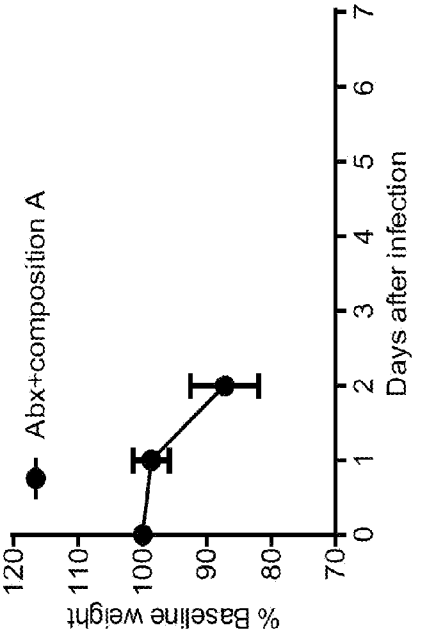


Figure 7G

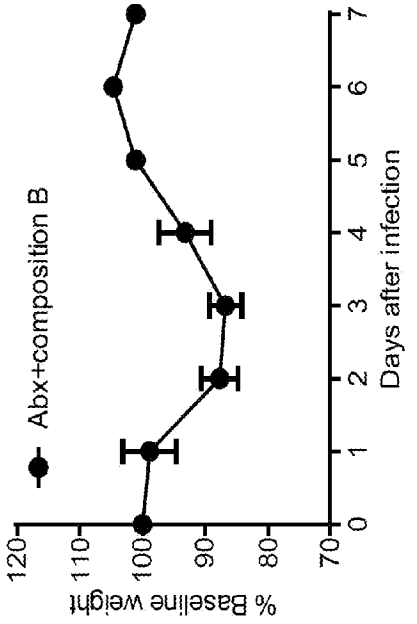


Figure 7H

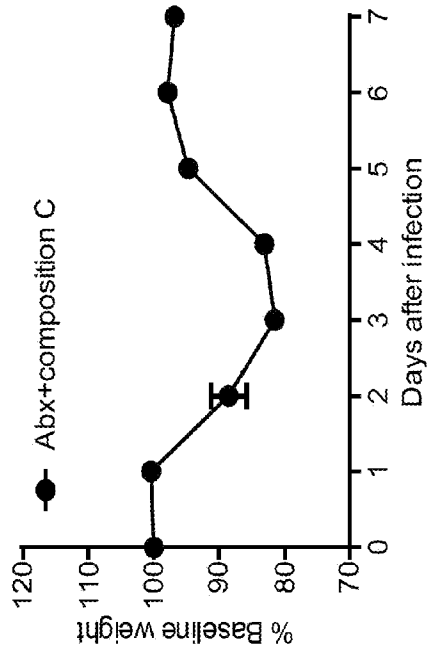
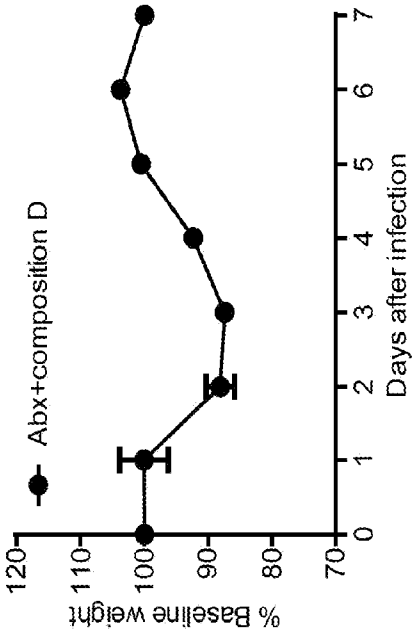


Figure 7I



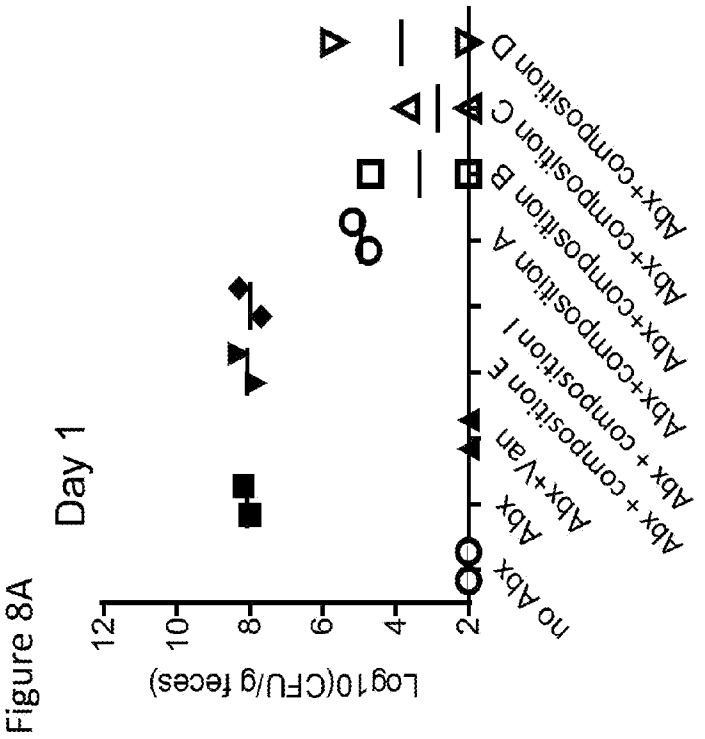


Figure 8A

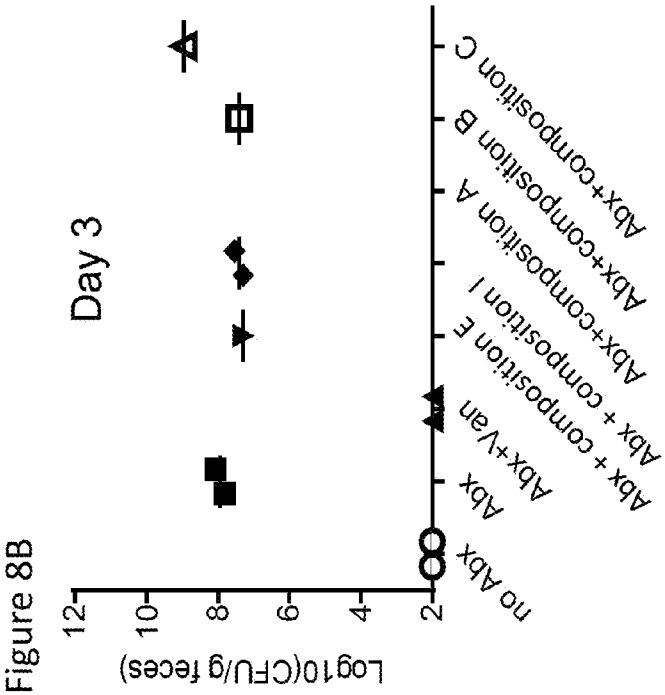


Figure 8B

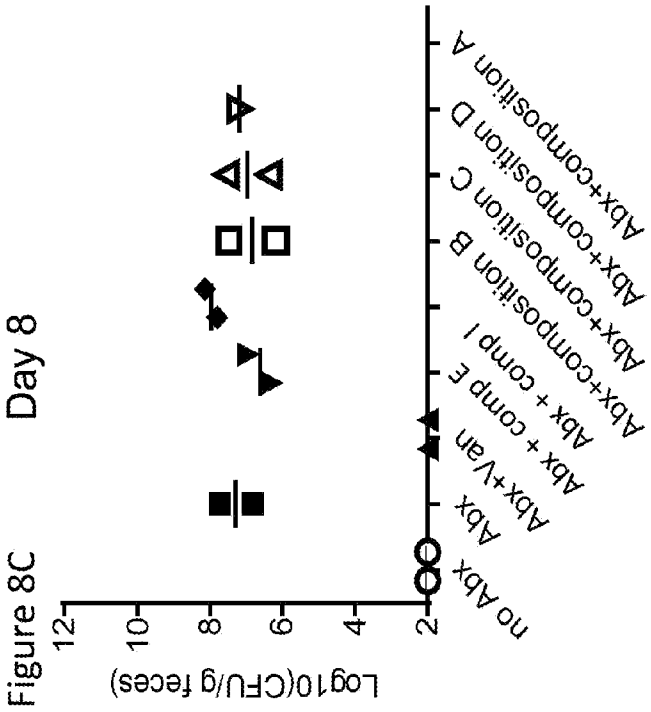
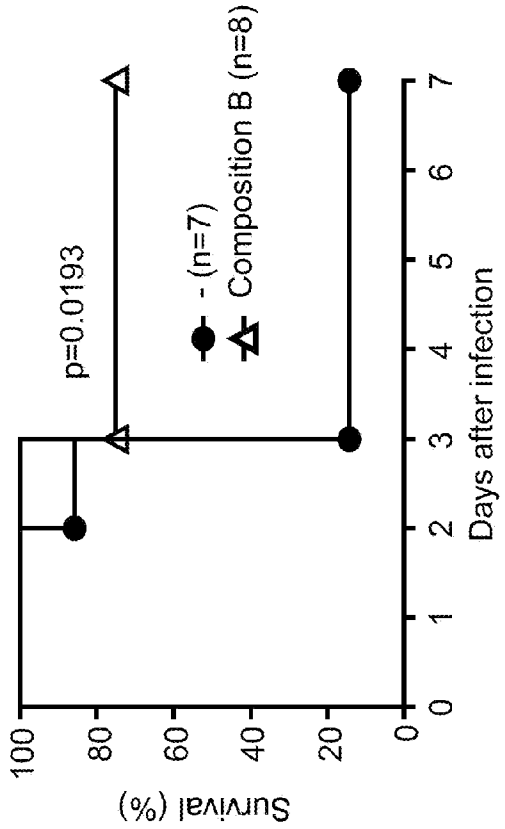

Day 8
Log10(CFU/g feces)
12
10
8
6
4
2
no Abx
Abx
Abx+Van
Abx + comp E
Abx + comp I
Abx+composition B
Abx+composition C
Abx+composition D
Abx+composition A

Figure 8C

Figure 9

Groups	# of animals	Abx	*C. difficile* spore	CFUs LBPs
(1) Control	7	+	10^4	-
(2) Composition B	8	+	10^4	10^8/mouse

Figure 10



(Natural death + >20% weight loss)

Figure 11

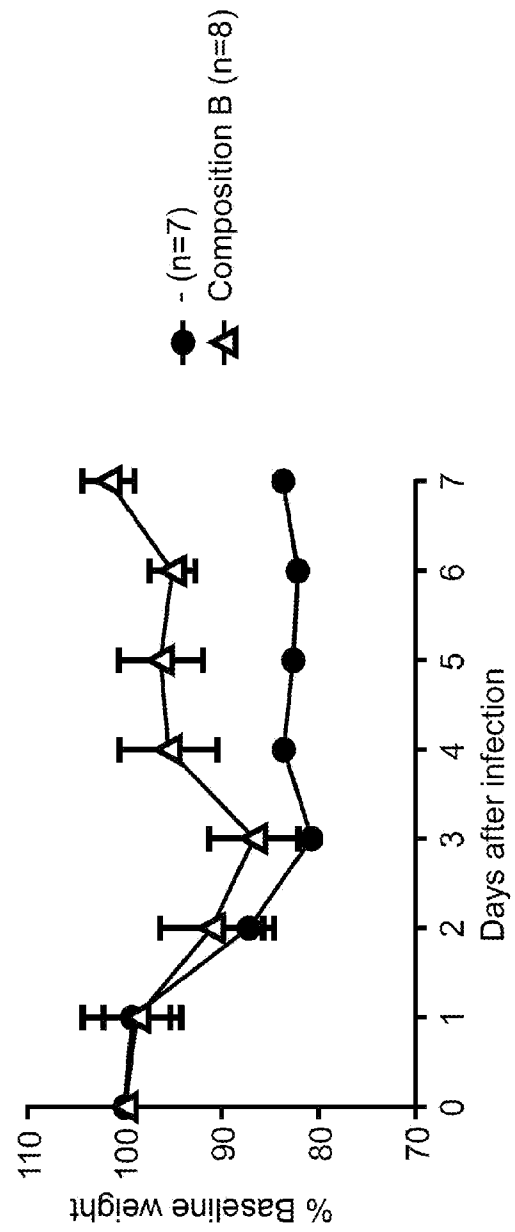

- (n=7)
Composition B (n=8)
% Baseline weight
110
100
90
80
70
0
1
2
3
4
5
6
7
Days after infection

Figure 12

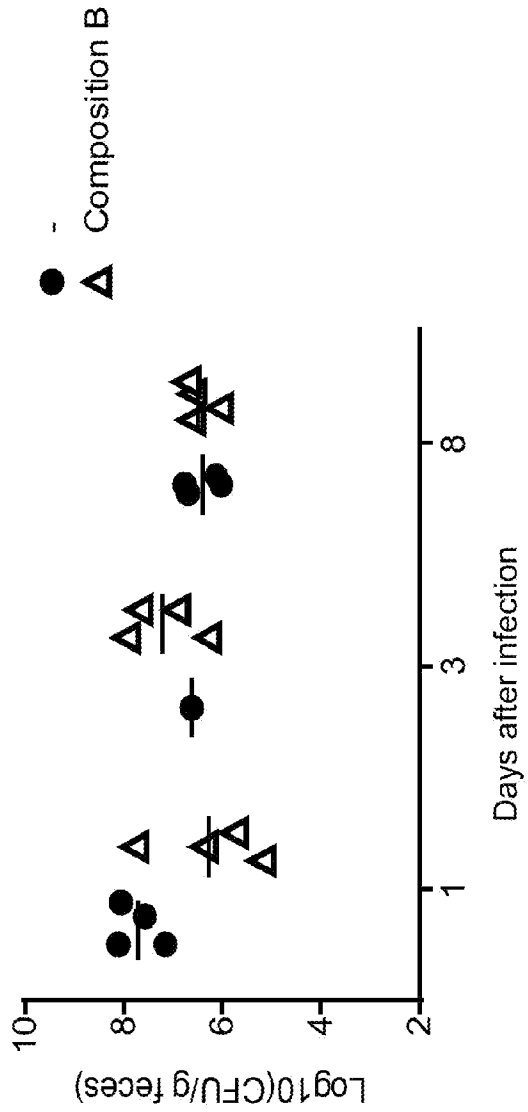

-
Composition B
Log10(CFU/g feces)
10
8
6
4
2
1
3
8
Days after infection

Figure 13

Composition F

SEQ_NO	StrainID	Genus_species	SEQ_NO	StrainID	Genus_species
SEQ_24	YK96	Dorea_longicatena	SEQ_52	YK51	Eubacterium_rectale
SEQ_25	YK101	Ruminococcus_obeum	SEQ_53	YK52	Eubacterium_rectale
SEQ_26	YK110	Megasphaera_elsdenii	SEQ_54	YK54	Anaerostipes_hadrus
SEQ_27	YK149	Acidaminococcus_fermentans / Acidaminococcus_intestini	SEQ_55	YK56	Ruminococcus_faecis
SEQ_28	YK154	Megasphaera_elsdenii	SEQ_56	YK57	Ruminococcus_faecis
SEQ_29	YK36	Ruminococcus_faecis	SEQ_57	YK58	Dorea_longicatena
SEQ_30	YK95	Bacteroides_cellulosilyticus	SEQ_58	YK65	Roseburia_faecis
SEQ_31	YK32	Anaerostipes_hadrus	SEQ_59	YK67	Blautia_luti
SEQ_32	YK64	Ruminococcus_obeum	SEQ_60	YK69	Fusicatenibacter_saccharivorans
SEQ_33	YK73	Flavonifractor_plautii	SEQ_61	YK70	Fusicatenibacter_saccharivorans
SEQ_34	YK87	Eubacterium_rectale	SEQ_62	YK71	Roseburia_faecis
SEQ_35	YK105	Flavonifractor_plautii	SEQ_63	YK74	Megasphaera_elsdenii
SEQ_36	YK153	Megasphaera_elsdenii	SEQ_64	YK88	Eubacterium_rectale
SEQ_37	YK163	Eubacterium_rectale	SEQ_65	YK89	Eubacterium_rectale
SEQ_38	YK191	Ruminococcus_champanellensis / Ruminococcus_albus	SEQ_66	YK97	Roseburia_faecis
SEQ_39	YK99	Ruminococcus_champanellensis	SEQ_67	YK98	Blautia_faecis
SEQ_40	YK55	Ruminococcus_faecis	SEQ_68	YK139	Fusicatenibacter_saccharivorans
SEQ_41	YK75	Bifidobacterium_bifidum	SEQ_69	YK141	Dorea_formicigenerans
SEQ_42	YK90	Anaerostipes_hadrus	SEQ_70	YK142	Ruminococcus_faecis
SEQ_43	YK30	Anaerostipes_hadrus	SEQ_71	YK152	Blautia_hansenii
SEQ_44	YK31	Anaerostipes_hadrus	SEQ_72	YK155	Blautia_hansenii
SEQ_45	YK12	Eubacterium_rectale	SEQ_73	YK157	Eubacterium_rectale
SEQ_46	YK27	Ruminococcus_faecis	SEQ_74	YK160	Roseburia_faecis
SEQ_47	YK28	Blautia_luti	SEQ_75	YK166	Eubacterium_rectale
SEQ_48	YK29	Ruminococcus_faecis	SEQ_76	YK168	Eubacterium_rectale
SEQ_49	YK33	Anaerostipes_hadrus	SEQ_77	YK169	Eubacterium_rectale
SEQ_50	YK34	Anaerostipes_hadrus	SEQ_78	YK171	Eubacterium_rectale
SEQ_51	YK35	Ruminococcus_faecis	SEQ_79	YK192	Roseburia_faecis

Figure 14

Cluster	Composition F	SCFAs
XIVa	*Eubacterium rectale* 12	A, B, L
	Ruminococcus faecis 8	A, L
	Ruminococcus obeum 2	A, L
	Blautia faecis 1	A, L
	Blautia hansenii 2	A, L
	Blautia luti 2	A, L
	Anaerostipes hadrus 7	B
	Roseburia faecis 5	A, B
	Fusicatenibacter saccharivorans 3	A, L
	Dorea formicigenerans 1	A
	Dorea longicatena 2	A
IV	*Flavonifractor_plautii* 2	A, B
	Ruminococcus champanellensis 2	A
IX	*Acidaminococcus fermentans* 1	A, B, P
	Megasphaera elsdeni 4	P
other	*Bacteroides cellulosilyticus* 1	A, S
	Bifiidobacterium Bifidum	L, A

A, acetate;
B, Butyrate;
L, lactate;
P, propionate;
S, succinate

Figure 15

Groups	# of animals	Abx	*C. difficile* spore	CFUs LBPs
(1) Control	10	+	10^4	-
(2) Composition B dosed at day -1	10	+	10^4	10^8/mouse
(3) Composition B dosed at day -2 and -1	10	+	10^4	10^8/mouse
(4) Composition B dosed at day -2, -1, 1, 2, and 3	10	+	10^4	10^8/mouse
(5) Composition F dosed at day -1	5	+	10^4	OD Normalized
(6) Composition F dosed at day -2, -1, 1, 2, and 3	5	+	10^4	OD Normalized
(7) FMT mouse	5	+	10^4	200ul of 10% fecal samples/mouse
(8) FMT human	5	+	10^4	200ul of 10% fecal samples/mouse

Figure 16

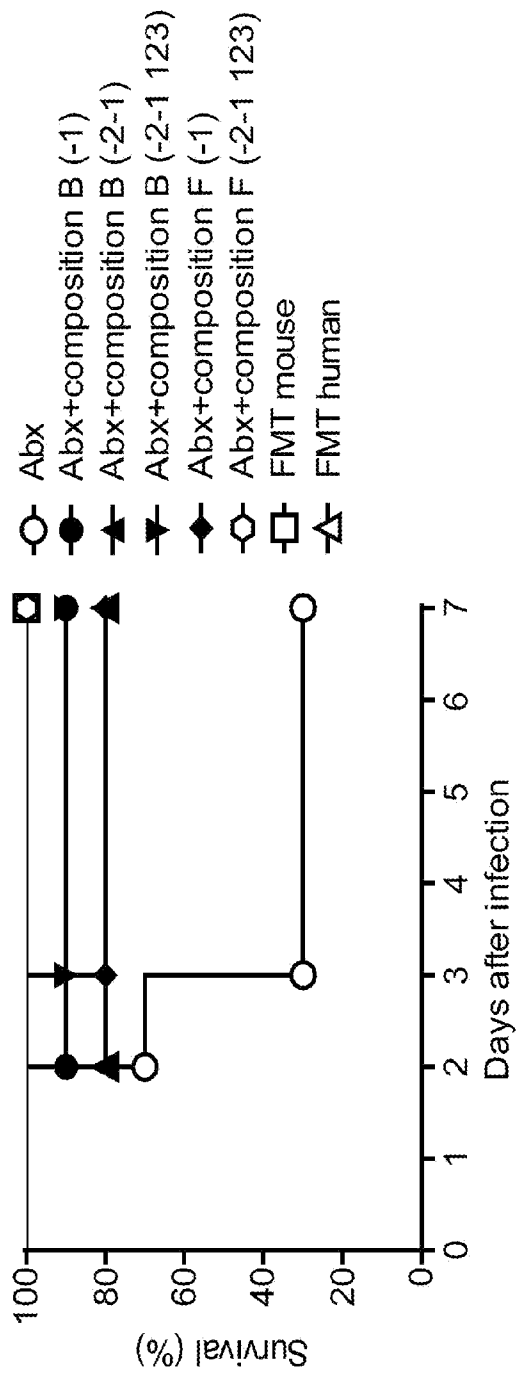

Abx
Abx+composition B (-1)
Abx+composition B (-2-1)
Abx+composition B (-2-1 123)
Abx+composition F (-1)
Abx+composition F (-2-1 123)
FMT mouse
FMT human
Survival (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Days after infection

Figure 17A

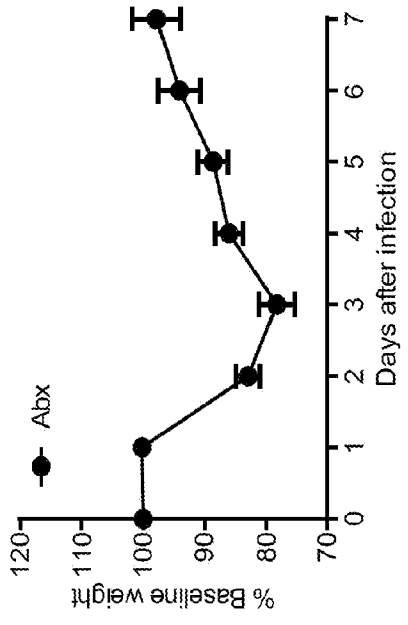


Figure 17B

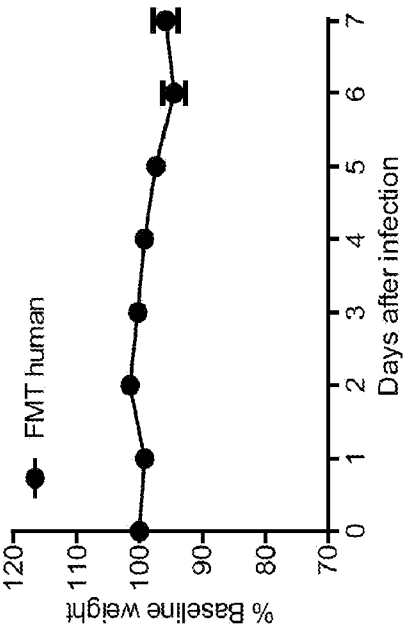


Figure 17C

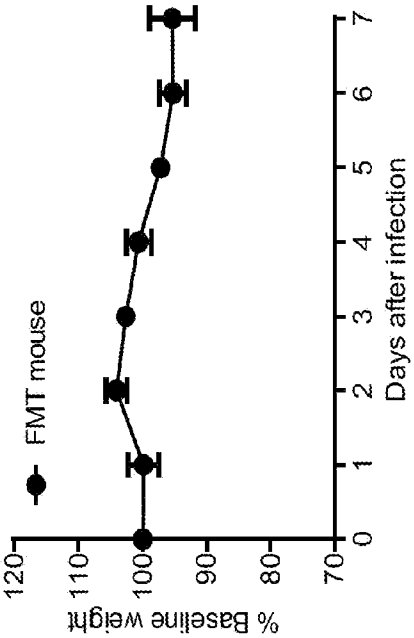


Figure 17D

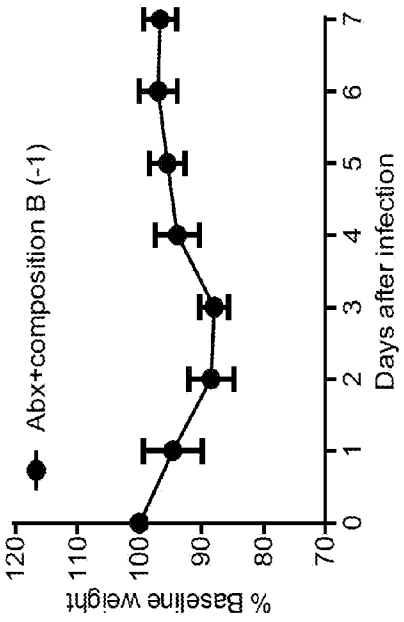


Figure 17E

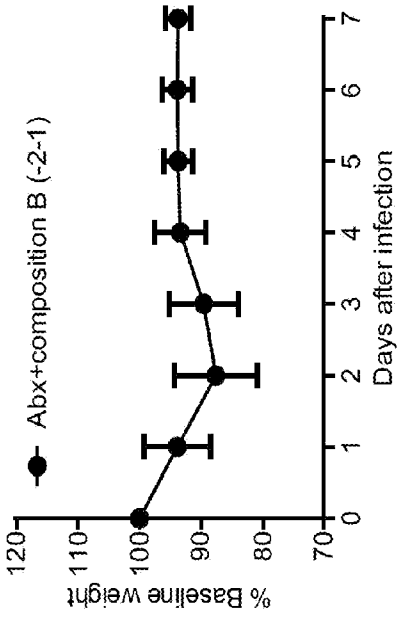


Figure 17F

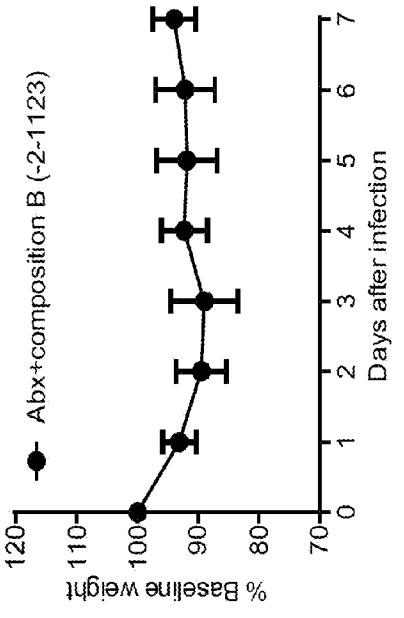


Figure 17G

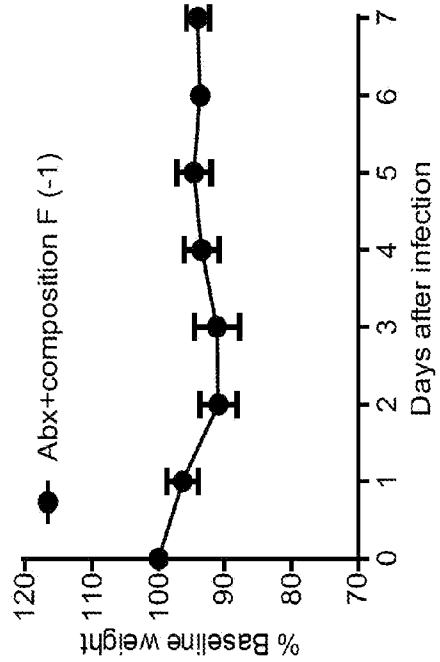
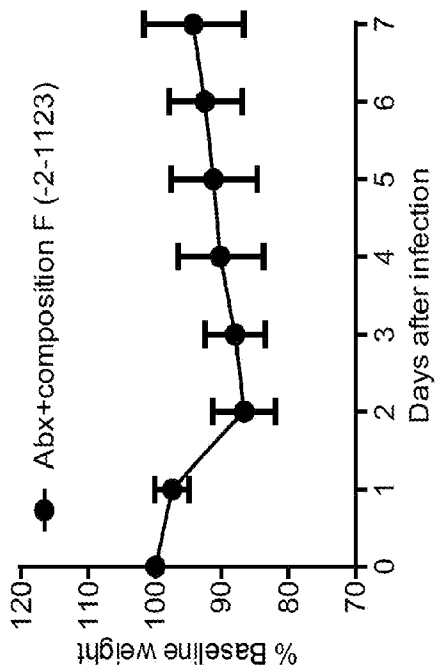


Figure 17H



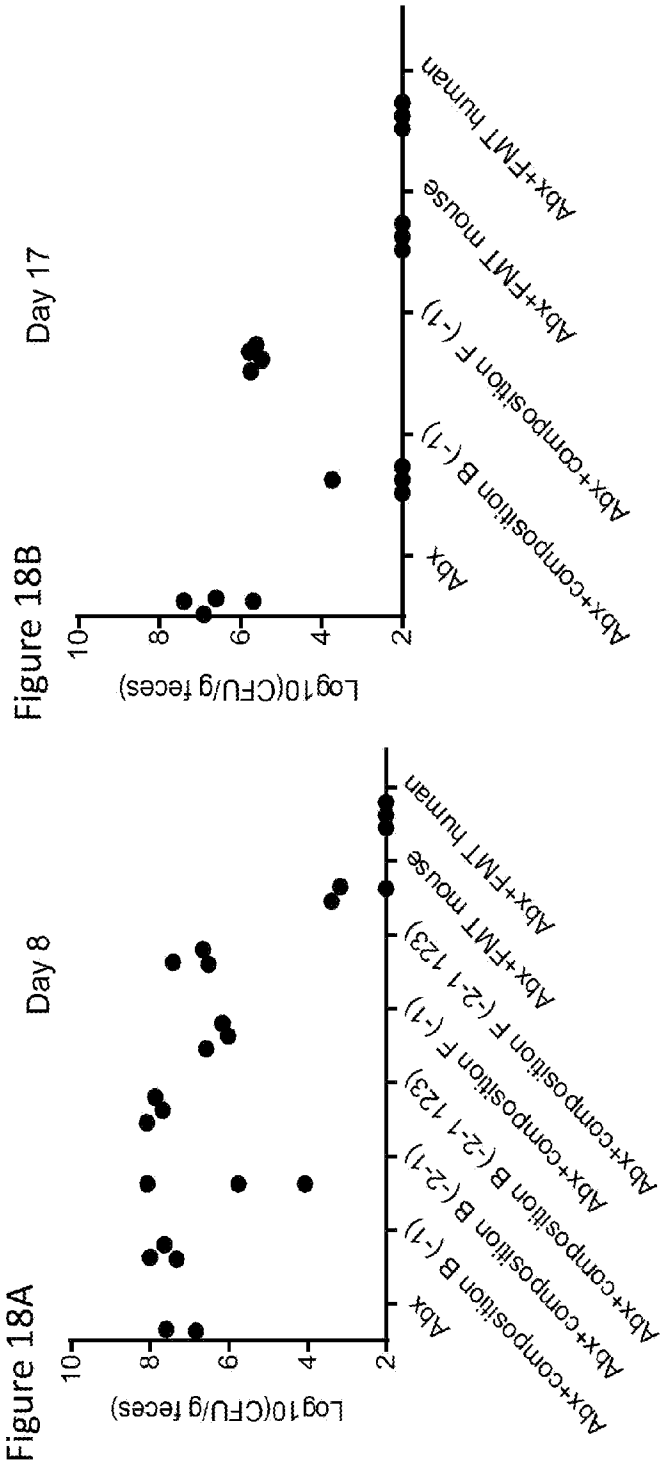


Figure 18A
Day 8
Log10(CFU/g feces)
10
8
6
4
2
Abx
Abx+composition B (-1)
Abx+composition B (-2-1)
Abx+composition B (-2-1 123)
Abx+composition F (-1)
Abx+composition F (-2-1 123)
Abx+FMT mouse
Abx+FMT human
Figure 18B
Day 17
Log10(CFU/g feces)
10
8
6
4
2
Abx
Abx+composition B (-1)
Abx+composition F (-1)
Abx+FMT mouse
Abx+FMT human

Figure 19

Composition G

SEQ_27	YK149	Acidaminococcus_fermentans/Acidaminococcus_intesti
SEQ_43	YK90	Anaerostipes_hadrus
SEQ_44	YK30	Anaerostipes_hadrus
SEQ_51	YK34	Anaerostipes_hadrus
SEQ_55	YK54	Anaerostipes_hadrus
SEQ_68	YK98	Blautia_faecis
SEQ_72	YK152	Blautia_hansenii
SEQ_70	YK141	Dorea_formicigenerans
SEQ_24	YK96	Dorea_longicatena
SEQ_34	YK87	Eubacterium_rectale
SEQ_37	YK163	Eubacterium_rectale
SEQ_46	YK12	Eubacterium_rectale
SEQ_76	YK166	Eubacterium_rectale
SEQ_77	YK168	Eubacterium_rectale
SEQ_35	YK105	Flavonifractor_plautii
SEQ_62	YK70	Fusicatenibacter_saccharivorans
SEQ_26	YK110	Megasphaera_elsdenii
SEQ_63	YK71	Roseburia_faecis
SEQ_67	YK97	Roseburia_faecis
SEQ_40	YK99	Ruminococcus_champanellensis
SEQ_38	YK191	Ruminococcus_champanellensis/Ruminococcus_albus
SEQ_47	YK27	Ruminococcus_faecis
SEQ_56	YK56	Ruminococcus_faecis
SEQ_25	YK101	Ruminococcus_obeum
SEQ_32	YK64	Ruminococcus_obeum

Figure 20

Groups	N	Abx	CFUs *C. difficile*	CFUs LBPs
(1) Vehicle	7	+	10^4	200ul of PBS
(2) Composition B	8	+	10^4	10^8/mouse
(3) Composition B1	8	+	10^4	10^8/mouse
(4) Composition B2	8	+	10^4	10^8/mouse
(5) Composition F	7	+	10^4	OD Normalized
(6) Composition G	7	+	10^4	OD Normalized
(7) EtOH treated Human fecal samples	5	+	10^4	200ul of 10% fecal samples/mouse
(8) EtOH treated Composition B	5	+	10^4	10^8/mouse
(9) Frozen Composition B	5	+	10^4	10^8/mouse
(10) EtOH treated Composition J	5	+	10^4	colony scrapes

Figure 21

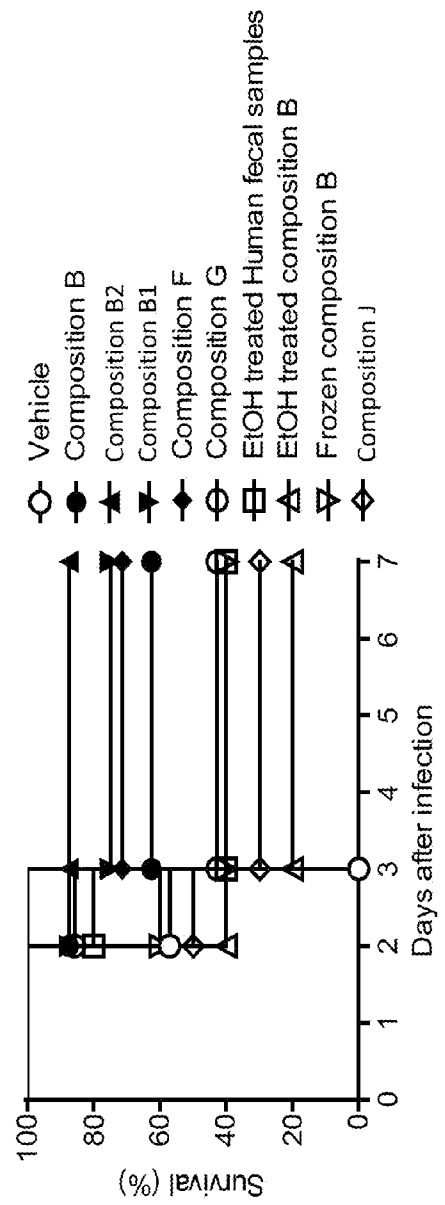

Vehicle
Composition B
Composition B2
Composition B1
Composition F
Composition G
EtOH treated Human fecal samples
EtOH treated composition B
Frozen composition B
Composition J
Survival (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Days after infection

Figure 22A

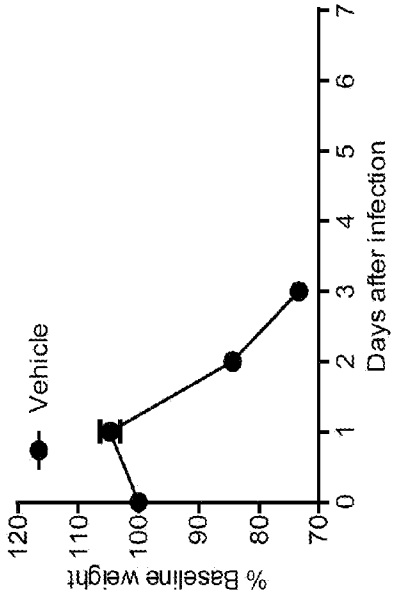


Figure 22B

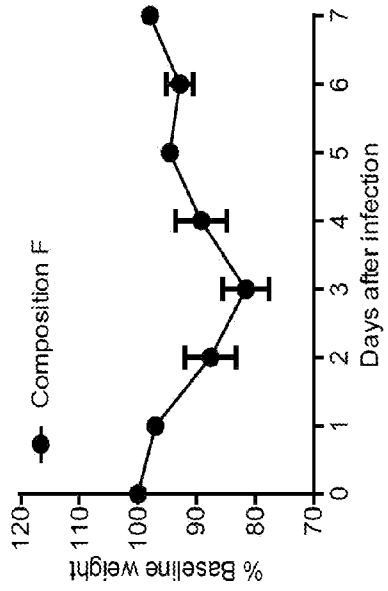


Figure 22C

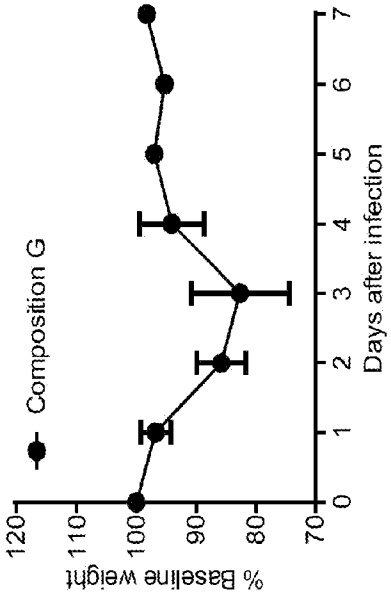


Figure 22D

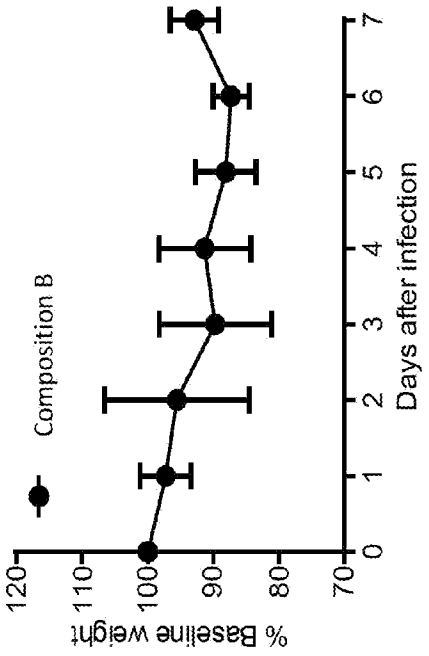


Figure 22E

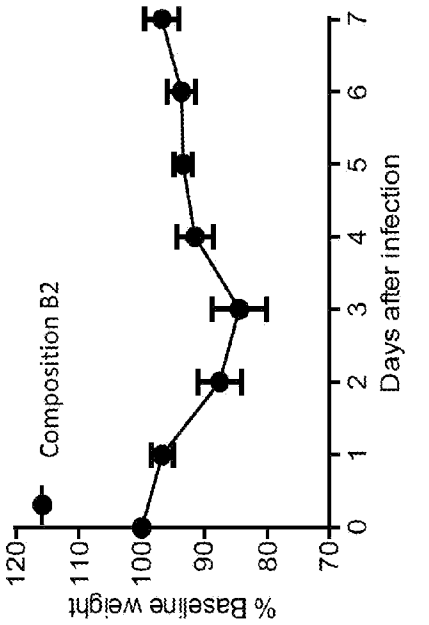


Figure 22F

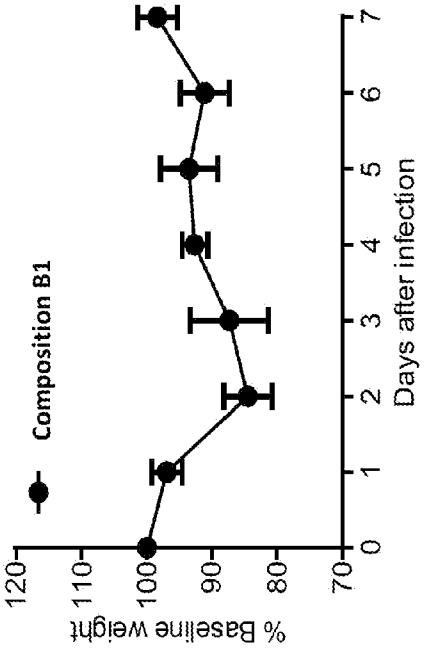


Figure 22G

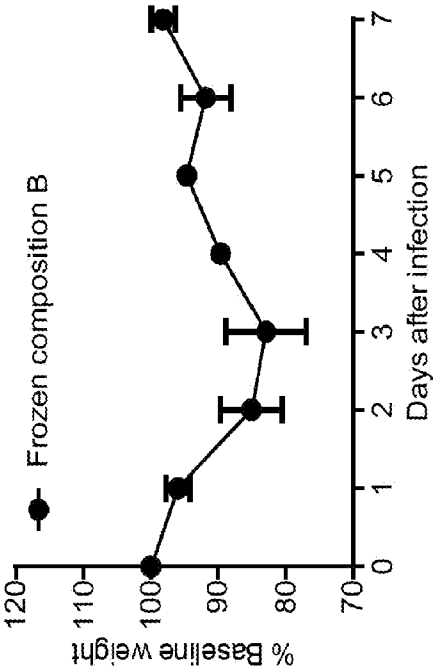


Figure 22I

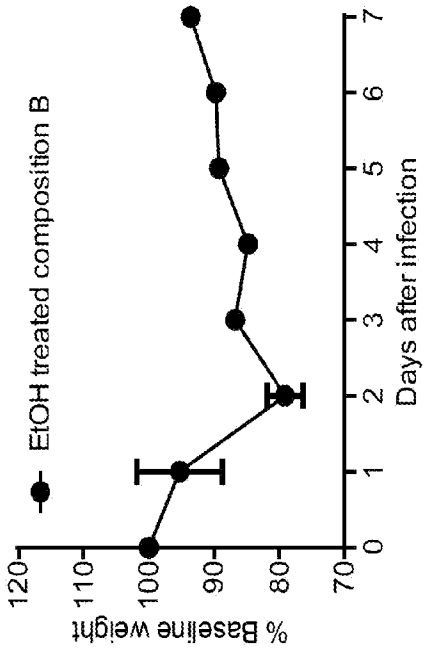


Figure 22H

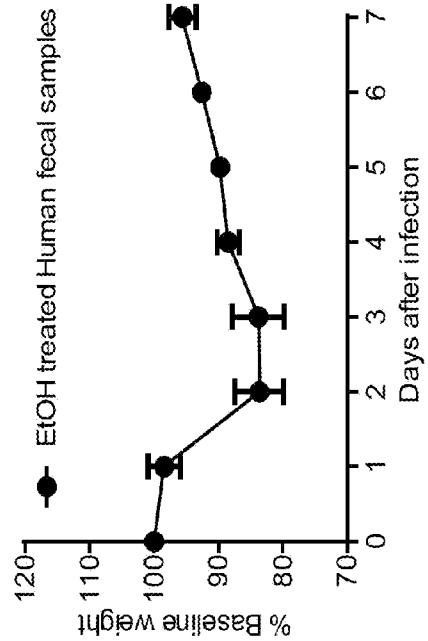


Figure 22J

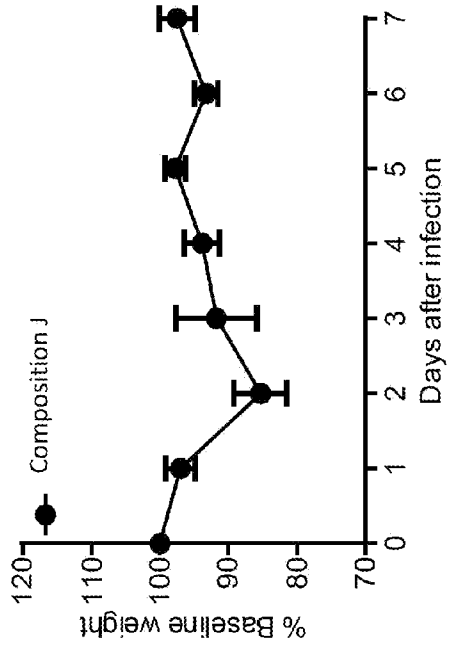


Figure 23

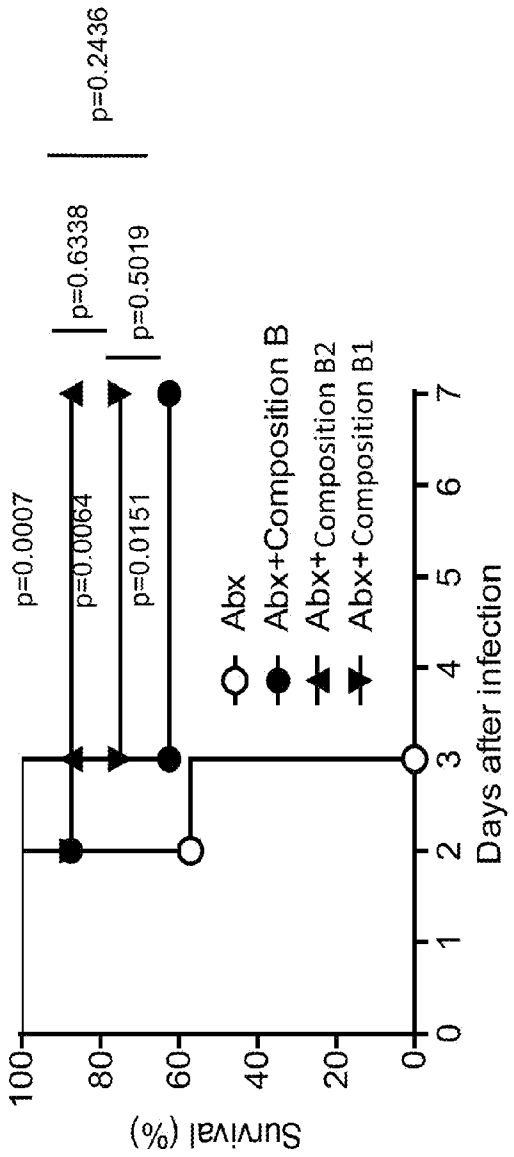

p=0.0007
p=0.0064
p=0.0151
p=0.6338
p=0.5019
p=0.2436
Abx
Abx+Composition B
Abx+Composition B2
Abx+Composition B1
Survival (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Days after infection

Figure 24

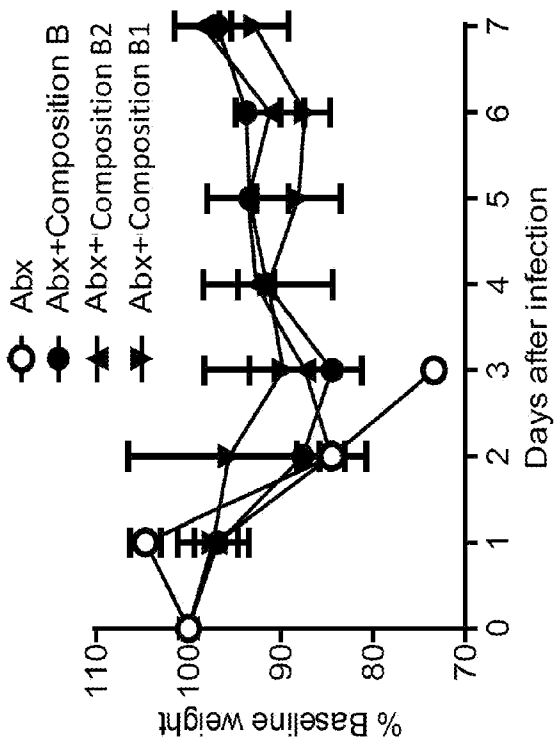

Abx
Abx+Composition B
Abx+Composition B2
Abx+Composition B1
% Baseline weight
110
100
90
80
70
0
1
2
3
4
5
6
7
Days after infection

Figure 25

Groups	N	Abx	CFUs *C. difficile*	CFUs LBPs
(1) Vehicle	10	+	10^4	200ul of PBS
(2) human FMT	10	+	10^4	200ul of 10% fecal samples/mouse
(3) Composition B	10	+	10^4	10^8/mouse
(4) Composition B + 4 spores*	10	+	10^4	10^8 live bacteria+spores/mouse
(5) Composition H**	10	+	10^4	10^8/mouse

*Composition B + 4 spores = The strains of Composition B plus the following four strains in spore form: *Clostrodium bolteae*, *Anaerotruncus colihominis*, *Clostridium symbiosum*, and *Clostridium innocuum*

**Composition H contains the following six strains in spore form: *Clostrodium bolteae*, *Anaerotruncus colihominis*, *Clostridium symbiosum*, *Clostridium innocuum*, *Clostridium disporicum*, and *Erysipelatoclostridium ramosum*

Figure 26

Composition H

**Composition H = The following six strains in spore form *Clostrodium bolteae, Anaerotruncus colihominis, Clostridium symbiosum, Clostridium innocuum, Clostridium disporicum and Erysipelatoclostridium ramosum*

Composition H sequence info:

SEQ ID NO: 14 - VE202-13 – *Anaerotruncus colihominis*	**Cluster IV**
SEQ ID NO: 16 - VE202-16 – *Clostridium symbiosum*	**Cluster XIVa**
SEQ ID NO: 21 - 189 – *Clostridium innocuum*	**Cluster XVII**
SEQ ID NO: 82 - PE9 – *Clostridium disporicum*	**Cluster I**
SEQ ID NO: 81 – PE5 – *Clostridium bolteae*	**Cluster XIVa**
SEQ ID NO: 80 – VE202-18 – *Erysipelatoclostridium ramosum*	**Cluster XVIII**

Figure 27A

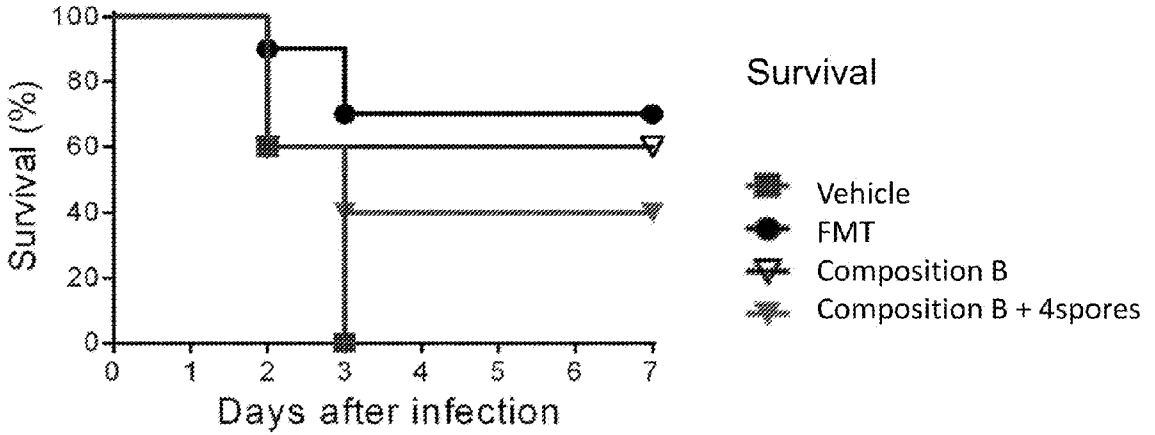


Figure 27B

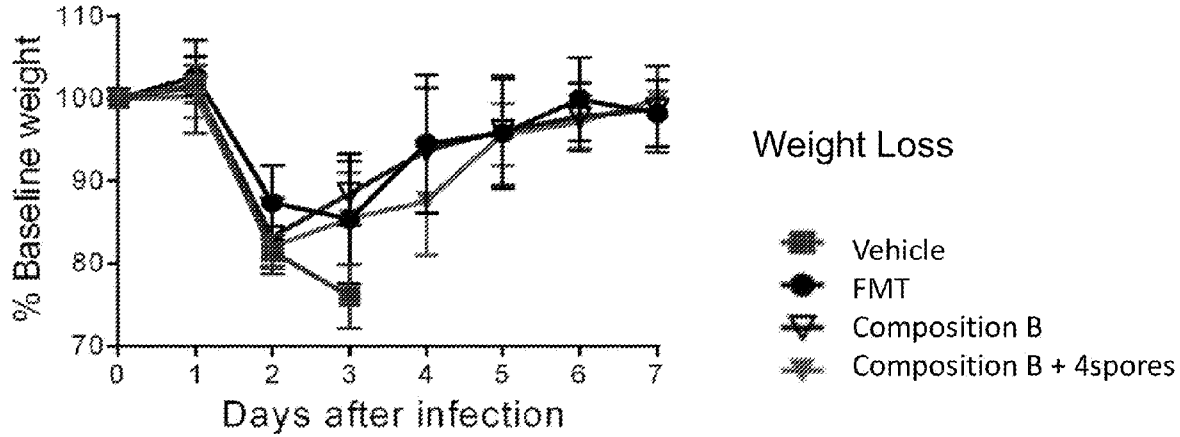


Figure 28A

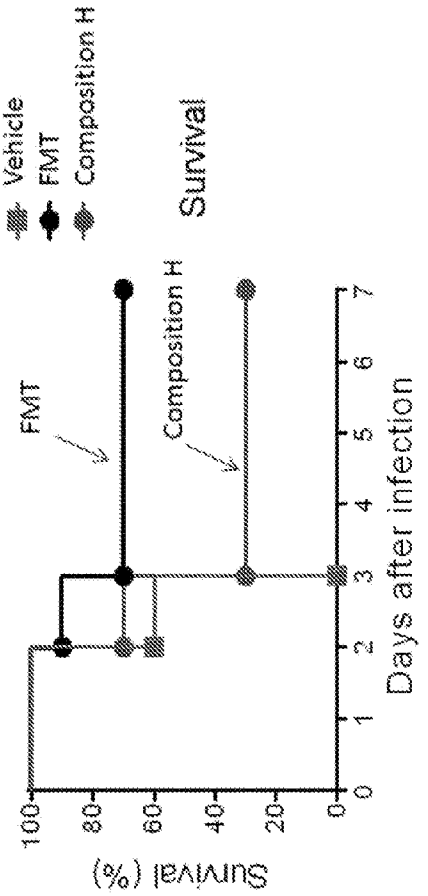


Figure 28B

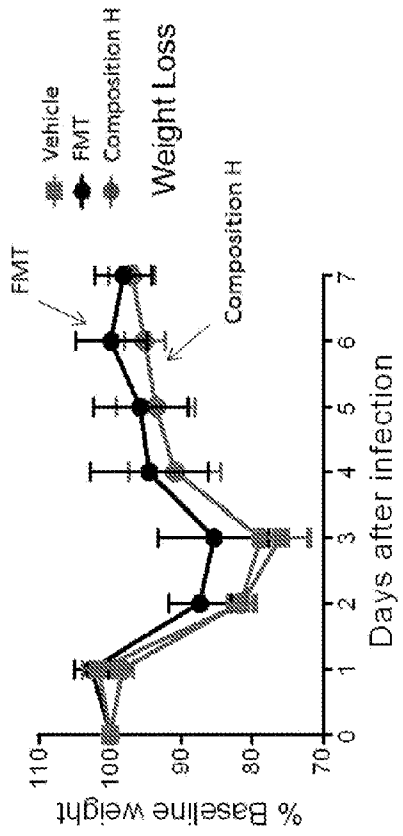


Figure 29A

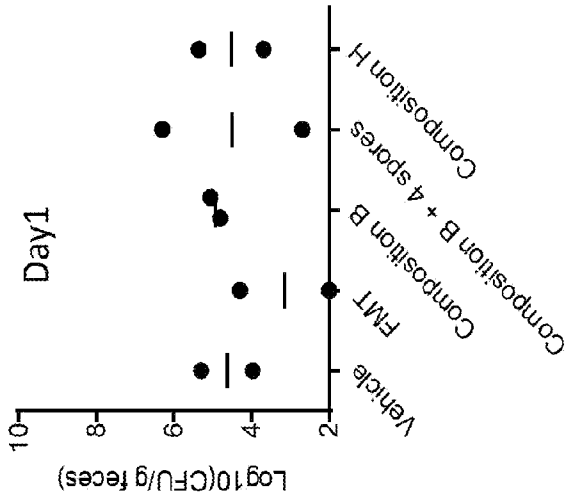


Figure 29B

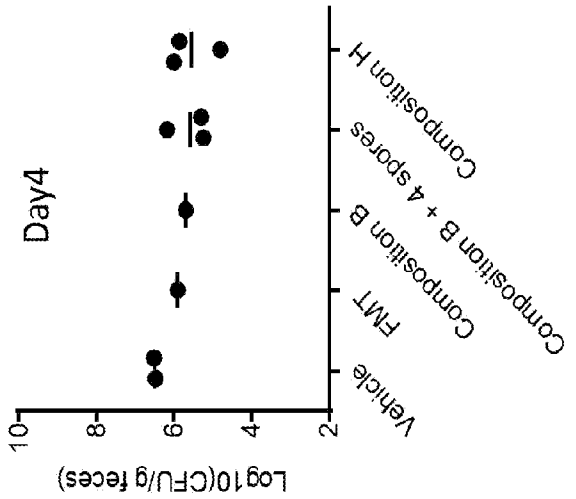


Figure 29C

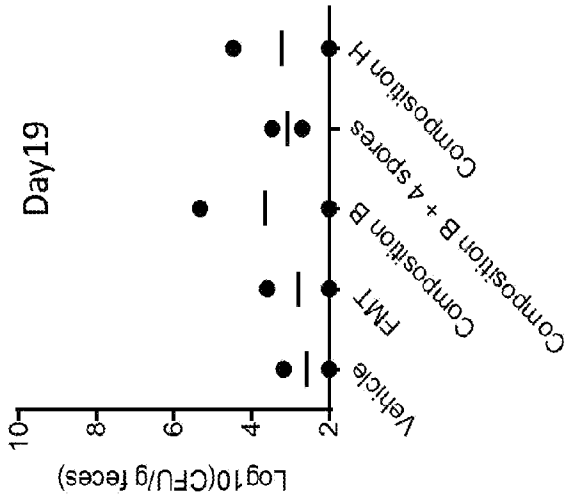


Figure 30

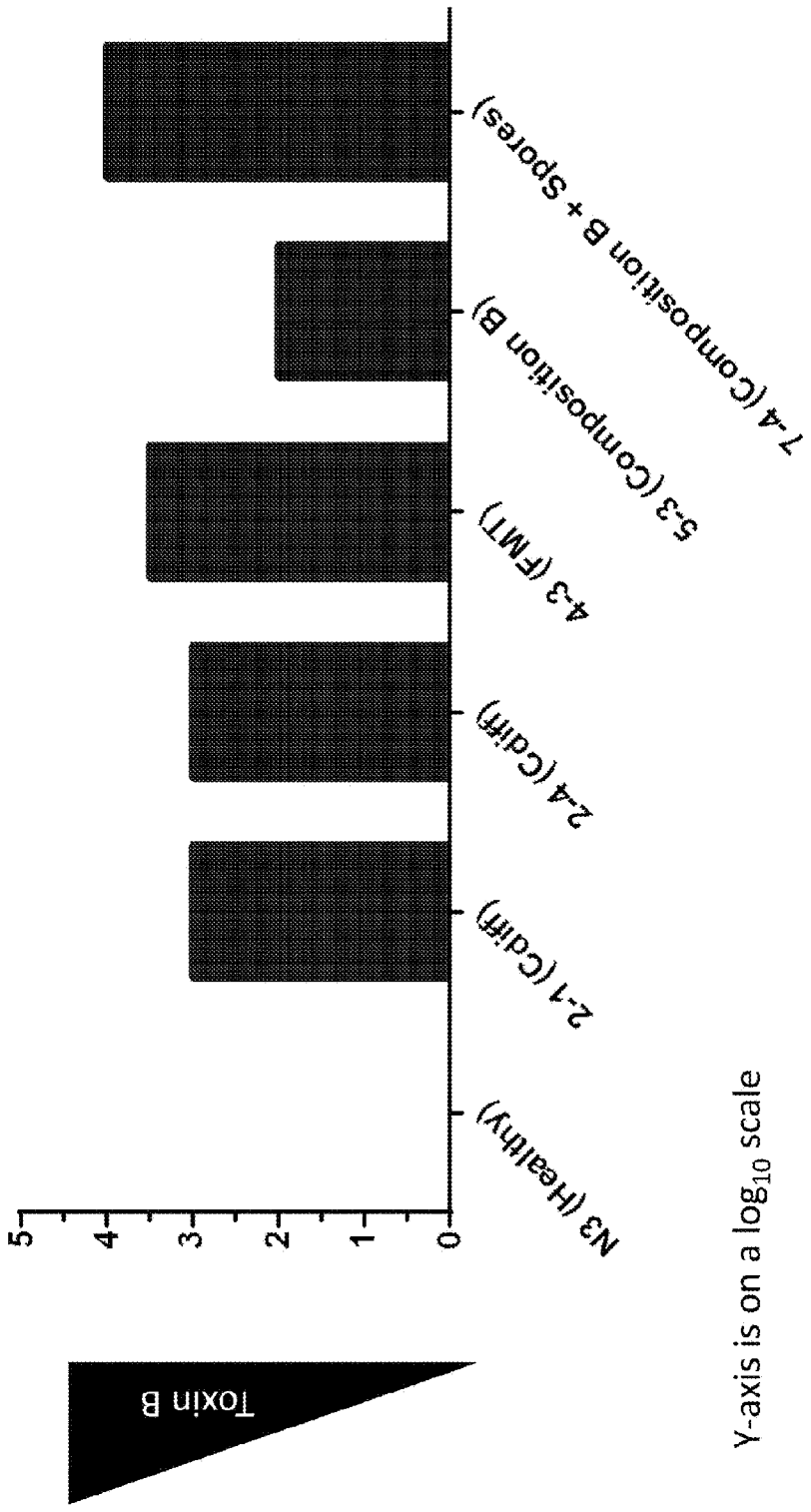

Toxin B
5
4
3
2
1
0
N3 (Healthy)
2-1 (Cdiff)
2-4 (Cdiff)
4-3 (FMT)
5-3 (Composition B)
7-4 (Composition B + Spores)
Y-axis is on a log10 scale

Figure 31

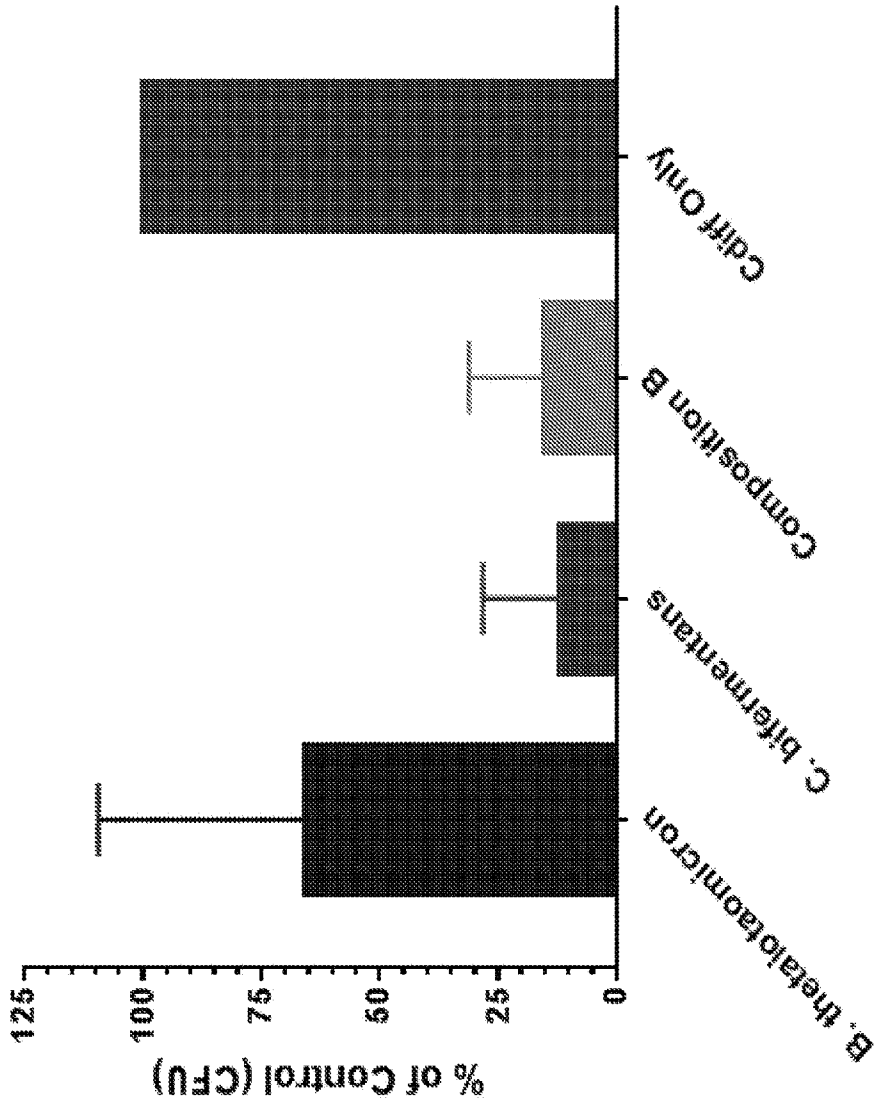
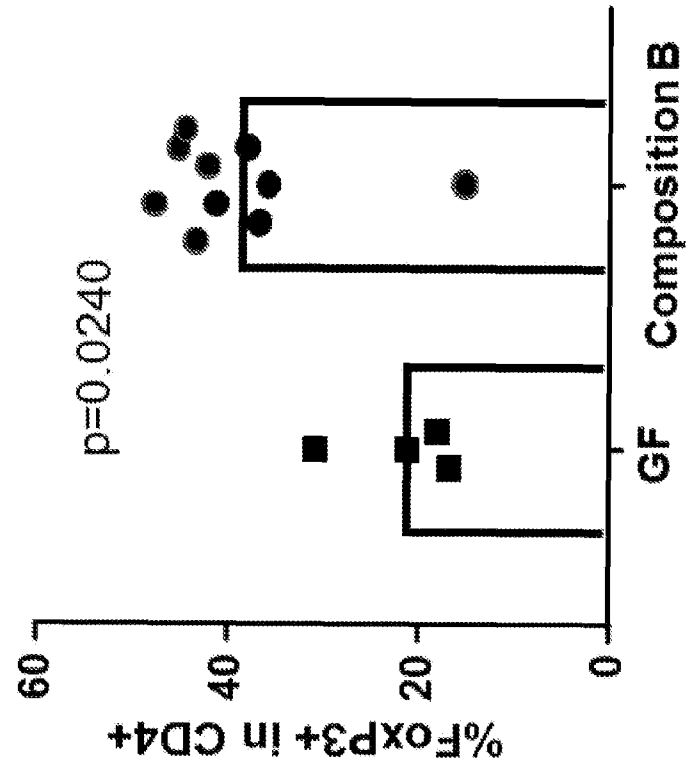

% of Control (CFU)
125
100
75
50
25
0
B. thetaiotaomicron
C. bifermentans
Composition B
Cdiff Only

Figure 32



SEKVENSLISTE

Sekvenslisten er udeladt af skriftet og kan hentes fra det Europæiske Patent Register.

The Sequence Listing was omitted from the document and can be downloaded from the European Patent Register.