

Description

Title of Invention: COMPOSITIONS AND METHODS FOR THE INDUCTION OF CD8+ T-CELLS

Technical Field

[0001] The disclosure relates to compositions and methods for the induction and/or proliferation of CD8+ T-cells. The disclosure also provides methods of treatment of diseases that can be treated by the induction and/or proliferation of CD8+ T-cells.

Background Art

[0002] Animals, including humans, harbor a multitude of microbes (collectively referred to as the microbiota) in anatomical locations including the mouth, esophagus, stomach, small intestine, large intestine, caecum, vagina, skin, nasal cavities, ear, and lungs. The human microbiota is responsible for a multitude of critical processes, including the development of the immune system, metabolism of carbohydrates, proteins and xenobiotics, formation and regeneration of the epithelium, fat storage, production of hormones, production of vitamins, and protection from pathogen infections, among others (See e.g., 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). Modification of the human microbiota, which can be caused by a number of factors such as antibiotic use, excessive hygiene, diet, genetic background or combinations of the above, has been associated with a number of unwanted effects including the occurrence of infectious diseases (e.g., *C. difficile* infections), inflammatory, autoimmune and allergic diseases (e.g., ulcerative colitis, Crohn's disease, Type I diabetes, food allergies, asthma, rheumatoid arthritis) and metabolic diseases (e.g., Type II diabetes, metabolic syndrome, obesity, malnutrition), and cancer, among others. For instance, modifications of the microbiota can lead to a loss of tolerance against harmless food antigens or commensal bacterial antigens, subsequent excessive inflammatory responses, metabolic dysregulation, and damage to the intestinal tissue, which compromises its ability to serve as a barrier between the gut lumen and the systemic circulation.

[0003] Manipulation of the immune response is of great importance in the treatment of cancer and in vaccination. Cancer therapies that target the immune system have attained improvements in survival rates. However, a large percentage of patients do not respond to cancer immunotherapies. Similarly, large population subsets (e.g., the elderly) cannot mount strong immune responses to vaccines.

[0004] Approaches for countering the harmful effects of microbiota modifications on health are limited, despite the role that such modifications play in promoting human

pathology. Interventions known to modulate the microbiota include antibiotics, prebiotics, probiotics and fecal transplants, each of which has limitations and potential adverse effects. Additional approaches to counter the detrimental effects of microbiome modification on human health are clearly needed. Furthermore, approaches for promoting stronger immune responses to cancer and to vaccines are also needed.

Summary of Invention

[0005] The inventors joined the Innovative Advanced Research and Development Support Project Incubation Type of Japan Agency for Medical Research and Development (AMED) in 2016, whose Research and Development Subject entitled “Creating New Drugs Using Intestinal Bacterial Strain Cocktail” (AMED-LEAP Research Program), and obtained the present invention as the result of the AMED-LEAP Research Program.

The disclosure relates to compositions of bacterial strains and methods for the induction and/or proliferation of CD8⁺ T-cells by administering these compositions. The disclosure also provides compositions and methods for the treatment of diseases that can be treated by the induction and/or proliferation of CD8⁺ T-cells. Diseases that can be treated by the induction and/or proliferation of CD8⁺ T-cells include infectious diseases and cancers.

[0006] As disclosed herein, for the first-time compositions of human-derived bacterial strains are provided which activate the immune system through the induction of interferon gamma producing CD8⁺ T cells (also referred to herein as IFN γ +CD8⁺ T cells, CD8⁺ IFN γ +T cells, CD8⁺ T cells or CD8 positive T-cells). While microbial-based compositions for inducing proliferation or accumulation of regulatory T-cells (WO2011/152566), and composition for inducing Th17 cells (WO2015/156419) were previously reported, this disclosure is the first report on microbial species which induce IFN γ +CD8⁺ T-cells. IFN γ +CD8⁺ T-cells play important roles in the immune system, in particular the surveillance of infections (e.g., viral infections) and cancer cell development. The compositions provided herein can therefore be used in, for instance, the treatment of infectious diseases and cancer immunotherapy.

[0007] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, Bac-

teroides sp., Lachnospiraceae bacterium HGA0140, Hungatella hathewayi, Clostridium lavalense, Ruminococcus sp., and Clostridium innocuum. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0008] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., Lachnospiraceae bacterium HGA0140, Hungatella hathewayi, Clostridium lavalense, Ruminococcus sp., and Clostridium innocuum. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0009] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0010] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides*

dorei, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0011] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0012] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

[0013] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture essentially consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides fluxus*, *Bacteroides uniformis*, *Bacteroides* sp. D20 *Subdoligranulum* sp., *Ruthenibacterium*

lactatiformans, *Ruminococcaceae* bacterium cv2, *Gemminger formicilis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Alistipes timonensis*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, *Parabacteroides* sp. CAG:2 and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0014] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

- 1) *Phascolarctobacterium faecium*, or *Phascolarctobacterium* sp. CAG:207,
- 2) *Fusobacterium ulcerans*, or *Fusobacterium varium*,
- 3) *Bacteroides dorei*, or *Bacteroides fluxus*,
- 4) *Bacteroides uniformis*, or *Bacteroides* sp. D20,
- 5) *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae* bacterium cv2, or *Gemminger formicilis*,
- 6) *Paraprevotella xylaniphila*,
- 7) *Parabacteroides johnsonii*,
- 8) *Alistipes* sp., *Alistipes timonensis*, or *Alistipes senegalesis*,
- 9) *Parabacteroides gordonii*, or *Parabacteroides* sp. HGS0025,
- 10) *Eubacterium limosum*, and
- 11) *Parabacteroides* sp. CAG:2 or *Parabacteroides distasonis*.

[0015] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:

- 1) *Phascolarctobacterium faecium*, or *Phascolarctobacterium* sp. CAG:207,
- 2) *Fusobacterium ulcerans*, or *Fusobacterium varium*,
- 3) *Bacteroides dorei*, or *Bacteroides fluxus*,
- 4) *Bacteroides uniformis*, or *Bacteroides* sp. D20,
- 5) *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae* bacterium cv2, or *Gemminger formicilis*,
- 6) *Paraprevotella xylaniphila*,
- 7) *Parabacteroides johnsonii*,
- 8) *Alistipes* sp., *Alistipes timonensis*, or *Alistipes senegalesis*,
- 9) *Parabacteroides gordonii*, or *Parabacteroides* sp. HGS0025,
- 10) *Eubacterium limosum*, and
- 11) *Parabacteroides* sp. CAG:2 or *Parabacteroides distasonis*.

[0016] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides*

dorei, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

[0017] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture essentially consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

[0018] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae* bacterium cv2, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae* bacterium cv2, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2.

[0019] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae* bacterium cv2, Para-

prevotella xylaniphila, Parabacteroides johnsonii, Alistipes senegalesis, Parabacteroides sp. HGS0025, Eubacterium limosum, and Parabacteroides sp. CAG:2.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture essentially consisting of Phascolarctobacterium sp. CAG:207, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides sp. D20, Ruminococcaceae bacterium cv2, Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes senegalesis, Parabacteroides sp. HGS0025, Eubacterium limosum, and Parabacteroides sp. CAG:2.

[0020] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of Phascolarctobacterium faecium, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides uniformis, Subdoligranulum sp., Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Parabacteroides gordonii, Eubacterium limosum, and Parabacteroides distasonis. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of Phascolarctobacterium faecium, Phascolarctobacterium sp. CAG:207, Fusobacterium ulcerans, Fusobacterium varium, Bacteroides dorei, Bacteroides fluxus, Bacteroides uniformis, Bacteroides sp. D20 Subdoligranulum sp., Ruthenibacterium lactatiformans, Ruminococcaceae bacterium cv2, Gemminger formicilis, Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Alistipes senegalesis, Parabacteroides gordonii, Parabacteroides sp. HGS0025, Eubacterium limosum, Parabacteroides sp. CAG:2 and Parabacteroides distasonis. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0021] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of Phascolarctobacterium faecium, Fusobacterium varium, Bacteroides dorei, Bacteroides uniformis, Ruthenibacterium lactatiformans, Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes senegalesis, Parabacteroides gordonii, Eubacterium limosum, and Parabacteroides distasonis. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group

consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae* bacterium cv2, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp.HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0022] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0023] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*,

Bacteroides salyersiae, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0024] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Subdoligranulum* sp., and *Eubacterium limosum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Subdoligranulum* sp., and *Eubacterium limosum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

[0025] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Bacteroides dorei*, *Bacteroides uniformis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides dorei*, *Bacteroides uniformis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0026] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID

NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0027] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0028] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

- [0029] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.
- [0030] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.
- [0031] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least

21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0032] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0033] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at

least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0034] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0035] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0036] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0037] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture

comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:64. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0038] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

[0039] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:1,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:2,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:3,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:4,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:5,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:6,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:7,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:8,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:9,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:10, and

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:11.

[0040] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

[0041] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:1,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:2,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:3,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:4,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:5,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:6,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:7,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:8,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:9,

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ ID NO:10, and

a bacterial strain comprising a 16S rDNA sequence of at least 97% homology to SEQ

ID NO:11.

[0042] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0043] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

[0044] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

[0045] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:1,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:2,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:3,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:4,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:5,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity

with SEQ ID NO:6,
a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:7,
a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:8,
a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:9,
a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:10, and
a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:11.

[0046] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:1,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:2,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:3,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:4,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:5,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:6,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:7,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:8,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:9,
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:10, and
a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:11.

[0047] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,

SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

[0048] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:1,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:2,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:3,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:4,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:5,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:6,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:7,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:8,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:9,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:10, and

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:11.

[0049] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:

- a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity

with SEQ ID NO:1,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:2,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:3,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:4,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:5,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:6,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:7,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:8,
 a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:9,
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:10, and
 a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:11.

[0050] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:64. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0051] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with 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, or SEQ ID NO:64. In some embodiments of the

compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0052] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:64.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with 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, or SEQ ID NO:64.

[0053] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:54,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:55,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:56,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:57,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:58,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:59,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:60,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:61,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:62,

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:63, and

- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:64.

[0054] In one aspect, the disclosure provides compositions comprising a purified bacterial

mixture comprising:

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:54,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:55,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:56,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:57,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:58,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:59,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:60,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:61,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:62,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:63, and

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:64.

[0055] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences with 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, or SEQ ID NO:64.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:64.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with 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, or SEQ ID NO:64.

- [0056] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:
- a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:54,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:55,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:56,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:57,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:58,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:59,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:60,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:61,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:62,
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:63, and
 - a bacterial strain comprising a 16S rDNA sequence of at least 97% sequence identity with SEQ ID NO:64.
- [0057] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:
- a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:54,
 - a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:55,
 - a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:56,
 - a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:57,
 - a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:58,
 - a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:59,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:60,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:61,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:62,

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:63, and

a bacterial strain comprising a 16S rDNA sequence of at least 99% sequence identity with SEQ ID NO:64.

[0058] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences with 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, or SEQ ID NO:64.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0059] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at

least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0060] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0061] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions

provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0062] In one aspect, the disclosure provides compositions comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0063] In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided

herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0064] In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

[0065] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions

provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

[0066] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with the SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

[0067] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0068] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0069] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0070] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions

provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0071] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0072] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0073] In one aspect, the disclosure provides compositions comprising a purified bacterial

mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0074] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26

bacterial strains.

[0075] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0076] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID

NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0077] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0078] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, and SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least

19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0079] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0080] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ

ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0081] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0082] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ

ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0083] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0084] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0085] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0086] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of

at least 95% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0087] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

[0088] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

[0089] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

[0090] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32,

SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the one or more bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0091] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% homology to the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 95% sequence identity with SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the bacterial strain comprises 16S rDNA sequences of at least 96%, at least 97%, at least 98%, or at least 99% sequence identity with the SEQ ID NOs. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0092] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In some embodiments of the compositions provided herein, at least 50% of the bacterial strains belong to the order of Bacteriodales. In some embodiments of the

compositions provided herein, one or more of the bacterial strains belong to the order of Bacteriodales and one or more of the bacterial strains belong to the order of Clostridiales. In some embodiments of the compositions provided herein, at least 25% of the bacterial strains belong to the family of Bacteroidaceae. In some embodiments of the compositions provided herein, one or more of the bacterial strains belongs to the genus Bacteroides. In some embodiments of the compositions provided herein, the composition does not include bacterial strains that belong to the order of Bacteriodales. In some embodiments of the compositions provided herein, one or more of the bacterial strains is a spore-former. In some embodiments of the compositions provided herein, one or more of the bacterial strains is in spore form. In some embodiments of the compositions provided herein, one or more of the bacterial strains is a non-spore former. In some embodiments of the compositions provided herein, the composition comprises only obligate anaerobic bacterial strains. In some embodiments of the compositions provided herein, one or more of the bacterial strains does not have an antibiotic resistance gene. In some embodiments of the compositions provided herein, the antibiotic resistance gene renders the bacterial strain resistant to vancomycin. In some embodiments of the compositions provided herein, the bacterial strains are human-derived bacteria. In some embodiments of the compositions provided herein, the bacterial strains are derived from more than one human donor. In some embodiments of the compositions provided herein, the composition induces proliferation and/or accumulation of CD8+T-cells.

[0093] In some embodiments of the compositions provided herein, the composition is a pharmaceutical composition. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition comprises a pharmaceutically acceptable excipient. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for oral administration. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for rectal administration. 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 some embodiments of the pharmaceutical compositions provided herein, one or more of the bacterial strains is lyophilized. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is in the form of a capsule. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition further comprises a pH sensitive composition comprising one or more enteric polymers.

In one aspect, the disclosure provides a food product comprising any of the com-

positions provided herein and a nutrient.

[0094] In some embodiments of the compositions provided herein, the composition further comprises one or more anticancer agents. In some embodiments of the compositions provided herein, the anticancer agent is a chemotherapy agent. In some embodiments of the compositions provided herein, the anticancer agent is cancer immunotherapy agent. In some embodiments of the compositions provided herein, the cancer immunotherapy agent is an immune checkpoint inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a CTLA-4 inhibitor. In some embodiments of the compositions provided herein, the composition further comprises one or more cytokines. In some embodiments of the compositions provided herein, the cytokine is IL-2, IL-15, or IL-21. In some embodiments of the compositions provided herein, the composition further comprises one or more costimulatory agents. In some embodiments of the compositions provided herein, the costimulatory agent is a CD-28, OX-40, 4-1BB, or CD40 antibody.

In some embodiments of the compositions provided herein, the composition further comprises one or more vaccines. In some embodiments of the compositions provided herein, the vaccine is a dendritic cell vaccine. In some embodiments of the compositions provided herein, the composition is combined with adoptive cell transfer therapy. In some embodiments of the compositions provided herein, the adoptive cell transfer therapy is the use of engineered T-cell receptors or chimeric antigen receptors.

[0095] In one aspect, the disclosure provides a vaccine comprising any of the compositions provided herein and an antigen. In some embodiments of the vaccines provided herein, the antigen is an HIV antigen. In some embodiments of the vaccines provided herein, the antigen is a hepatitis antigen.

In some embodiments of the compositions provided herein, the composition further comprises one or more anti-inflammatory agents. In some embodiments of the compositions provided herein, the anti-inflammatory agent is an NSAID.

In some embodiments of the compositions provided herein, administration of the composition to a subject results in the induction of proliferation and/or accumulation of CD8⁺ T-cells in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in IFN γ -gamma production in the intestine of a subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in the presence of one or more bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein,

the one or more bacterial strains of the administered composition was not previously present in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in the engraftment of one or more bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, the one or more bacterial strains of the administered composition was not previously engrafted in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the number of the bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the number of the bacterial strains of the administered composition engrafted in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the amount of bacteria of the bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the amount of bacteria of the bacterial strains of the administered composition engrafted in the intestine of the subject.

[0096] In one aspect, the disclosure provides a method of treating a disease in a subject comprising administering any of the compositions provided herein to the subject in an effective amount to treat the disease. In some embodiments of the methods provided herein, the administration of the composition to the subject results in the induction of proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject. In some embodiments of the methods provided herein, the proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% when compared to the proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject before the administration of the composition. In some embodiments of the methods provided herein, the administration of the composition to the subject results in an increase of IFN γ -gamma production in the intestine of the subject when compared to the IFN γ -gamma production in the intestine of the subject before the administration of the composition. In some embodiments of the methods provided herein, the administration of the composition to the subject results in an increase of IFN γ -gamma production in the intestine of the subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% when compared to the IFN γ -gamma production in the intestine of the subject before the administration of the composition.

[0097] In some embodiments of the methods provided herein, the subject has cancer. In

some embodiments of the methods provided herein, the cancer is carcinoma, glioma, mesothelioma, melanoma, lymphoma, leukemia, adenocarcinoma, breast cancer, ovarian cancer, cervical cancer, glioblastoma, multiple myeloma, prostate cancer, Burkitt's lymphoma, head and neck cancer, colon cancer, colorectal cancer, non-small cell lung cancer, small cell lung cancer, cancer of the esophagus, stomach cancer, pancreatic cancer, hepatobiliary cancer, cancer of the gallbladder, cancer of the small intestine, rectal cancer, kidney cancer, bladder cancer, prostate cancer, penile cancer, urethral cancer, testicular cancer, vaginal cancer, uterine cancer, thyroid cancer, parathyroid cancer, adrenal cancer, pancreatic endocrine cancer, carcinoid cancer, bone cancer, skin cancer, retinoblastomas, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Kaposi's sarcoma, multicentric Castleman's disease, AIDS-associated primary effusion lymphoma, neuroectodermal tumors, or rhabdomyosarcoma. In some embodiments of the methods provided herein, the cancer is prostate cancer, bladder cancer, non-small cell lung cancer, urothelial carcinoma, melanoma, or renal cell carcinoma. In some embodiments of the methods provided herein, the subject is undergoing radiation treatment.

[0098] In some embodiments of the methods provided herein, the method further includes administering one or more anticancer agents. In some embodiments of the methods provided herein, the anticancer agent is a chemotherapy agent. In some embodiments of the methods provided herein, the anticancer agent is a cancer immunotherapy agent. In some embodiments of the methods provided herein, the cancer immunotherapy agent is an immune checkpoint inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a CTLA-4 inhibitor.

In some embodiments of the methods provided herein, the method further includes administering one or more cytokines. In some embodiments of the methods provided herein the cytokine is IL-2, IL-15, or IL-21.

In some embodiments of the methods provided herein, the method further includes administering one or more costimulatory agents. In some embodiments of the methods provided herein the costimulatory agent is a CD-28, OX-40, 4-1BB, or CD40 antibody.

[0099] In some embodiments of the methods provided herein, the method further includes administering one or more vaccines. In some embodiments of the methods provided herein, the vaccine is a dendritic cell vaccine.

In some embodiments of the methods provided herein, the method further includes administering adoptive cell transfer therapy. In some embodiments of the methods provided herein, the adoptive cell transfer therapy is the use of engineered T-cell

receptors or chimeric antigen receptors.

In some embodiments of the methods provided herein, the subject has an infectious disease. In some embodiments of the methods provided herein, the infectious disease is a bacterial infection, a viral infection, a parasitic infection, or a fungal infection. In some embodiments of the methods provided herein, the infectious disease is a viral infection. In some embodiments of the methods provided herein, the viral infection is HIV. In some embodiments of the methods provided herein, the infection is an infection by a hepatitis virus.

In some embodiments of the methods provided herein, the subject has an autoimmune disease or an allergic disease.

In some embodiments of the methods provided herein, the composition further includes one or more anti-inflammatory agents. In some embodiments of the methods provided herein, the anti-inflammatory is an NSAID. In some embodiments of the methods provided herein, the composition may be administered as one or more dose.

[0100] In one aspect, the disclosure provides a method that includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the composition is administered to the subject.

In some embodiments of the methods provided herein, the subject is undergoing, or will be undergoing, cancer treatment.

In one aspect, the disclosure provides a method for determining if a subject is expected to respond positively to cancer treatment, wherein the method includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the subject is not expected to respond positively to cancer treatment.

In some embodiments of the methods provided herein, the cancer treatment is cancer immunotherapy treatment.

In one aspect, the disclosure provides a method for reducing the risk of a viral infection in a subject, wherein the method includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the composition is administered to the subject, thereby reducing the risk of a viral infection in the subject.

[0101] In some embodiments of the methods provided herein, determining the presence of one or more of the bacterial species is done by sequencing fecal matter of the subject. In some embodiments of the methods provided herein, determining the presence of one or more of the bacterial species is done by sequencing the 16S rDNA sequences of fecal matter of the subject.

In one aspect, the disclosure provides compositions and methods to induce activation of CD8+ IFN γ -producing T-cells in the intestinal tract.

In one aspect, the disclosure provides a composition comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 95% homology to the sequences of the following NCBI accession numbers: LN998073, KR822463, CP011531, NR_112945, NZ-ACWW000000000, AB331897, AB261128, NZ-CAEG000000000, AB470343, AB595134, HE974920, NR_112933, AB490801, NZ-ACWB000000000, AY608696, CR626927, AB247141, NR_112935, AB249652, NR_113076 and AF139525. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains. In some embodiments of the compositions provided herein, the one or more bacterial strains comprises 16S rDNA sequences with at least 96%, at least 97%, at least 98%, or at least 99% homology with sequences provided herein.

[0102] In one aspect, the disclosure provides a composition that induces or activates CD8+IFN γ -producing T-cells, the composition comprising (i) one or more purified bacterial strains collected from human stool which possesses resistance to ampicillin, or (ii) a culture supernatant of (i). In some embodiments of the compositions provided herein, the composition comprises (a) a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of

Phascolarctobacterium faecium; LN998073,
Fusobacterium ulcerans; KR822463,
Bacteroides dorei; CP011531,
Bacteroides uniformis; NR_112945,
Subdoligranulum sp. 4_3_54A2FAA; NZ-ACWW000000000,
Paraprevotella xylaniphila; AB331897,
Parabacteroides johnsonii; AB261128,
Alistipes sp. JC136; NZ-CAEG000000000,
Parabacteroides gordonii; AB470343,
Eubacterium limosum; AB595134,
Parabacteroides distasonis; HE974920,

Bacteroides cellulosilyticus; NR_112933,
Bacteroides clarus; AB490801,
Anaerostipes sp. 3_2_56FAA; NZ-ACWB000000000,
Bacteroides salyersiae; AY608696,
Bacteroides fragilis; CR626927,
Bacteroides uniformis; AB247141,
Bacteroides eggerthii; NR_112935,
Clostridium sp. TM-40; AB249652,
Parabacteroides goldsteinii; NR_113076, and
Bacteroides sp. AR29; AF139525, or (b) one or more bacterial strains comprising a
 16S rRNA sequence having at least 97% homology to a 16S rRNA sequence of a
 species selected from the group consisting of
Phascolarctobacterium faecium; LN998073,
Fusobacterium ulcerans; KR822463,
Bacteroides dorei; CP011531,
Bacteroides uniformis; NR_112945,
Subdoligranulum sp. 4_3_54A2FAA; NZ-ACWW000000000,
Paraprevotella xylaniphila; AB331897,
Parabacteroides johnsonii; AB261128,
Alistipes sp. JC136; NZ-CAEG000000000,
Parabacteroides gordonii; AB470343,
Eubacterium limosum; AB595134,
Parabacteroides distasonis; HE974920,
Bacteroides cellulosilyticus; NR_112933,
Bacteroides clarus; AB490801,
Anaerostipes sp. 3_2_56FAA; NZ-ACWB000000000,
Bacteroides salyersiae; AY608696,
Bacteroides fragilis; CR626927,
Bacteroides uniformis; AB247141,
Bacteroides eggerthii; NR_112935,
Clostridium sp. TM-40; AB249652,
Parabacteroides goldsteinii; NR_113076, and
Bacteroides sp. AR29; AF139525

- [0103] In some embodiments of the compositions provided herein, the composition comprises a purified bacterial mixture comprising (a) one or more bacterial strains of species selected from the group consisting of
- Phascolarctobacterium faecium*; LN998073,
 - Fusobacterium ulcerans*; KR822463,

Bacteroides dorei; CP011531,
Bacteroides uniformis; NR_112945,
Subdoligranulum sp. 4_3_54A2FAA; NZ-ACWW000000000,
Paraprevotella xylaniphila; AB331897,
Parabacteroides johnsonii; AB261128,
Alistipes sp. JC136; NZ-CAEG000000000,
Parabacteroides gordonii; AB470343,
Eubacterium limosum; AB595134, and
Parabacteroides distasonis; HE974920; or (b) one or more bacterial strains comprising
a 16S rRNA sequence of a species belonging to the group consisting of
Phascolarctobacterium faecium; LN998073,
Fusobacterium ulcerans; KR822463,
Bacteroides dorei; CP011531,
Bacteroides uniformis; NR_112945,
Subdoligranulum sp. 4_3_54A2FAA; NZ-ACWW000000000,
Paraprevotella xylaniphila; AB331897,
Parabacteroides johnsonii; AB261128,
Alistipes sp. JC136; NZ-CAEG000000000,
Parabacteroides gordonii; AB470343,
Eubacterium limosum; AB595134, and
Parabacteroides distasonis; HE974920.

[0104] In some embodiments of the compositions provided herein, the CD8⁺ IFN γ -producing T-cells express CD103 or Granzyme B.

In some embodiments of the compositions provided herein, the composition activates the immune system.

In one aspect, the disclosure provides a method for activating the immune system, the method comprising administration of one or more of the compositions provided herein.

In one aspect, the disclosure provides a method for activating CD8⁺ IFN γ -producing T-cells, the method comprising administration of one or more of the compositions provided herein to a subject.

In one aspect, the disclosure provides a method for inducing the proliferation and/or accumulation of CD8⁺ T cells in the intestine, comprising administering to a subject any one or more of the compositions provided herein, wherein the administering results in the induction of proliferation and/or accumulation of CD8⁺ T cells in the intestine of the subject.

In one aspect, the disclosure provides a method for assisting in treatment, and/or preventing cancer or viral infection, comprising administering to a subject any one or

more of the compositions provided herein, wherein the administering prevents, treats, assists in treatment, and/or prevents cancer or viral infection.

In one aspect, the disclosure provides vaccine compositions which induce immune response against bacterial strains of any one of the compositions disclosed herein.

In one aspect, the disclosure provides a vaccine composition containing antigen derived from constituents and/or metabolites of bacterial species of any one of the compositions provided herein.

[0105] In one aspect, the disclosure provides a method for inducing an immune response in a subject, comprising administering to the subject any of the vaccines provided herein, wherein the administering results in the induction of immune response of the subject.

In one aspect, the disclosure provides immune suppressive compositions.

In one aspect, the disclosure provides a composition comprising a chemical substance that possesses antibacterial activity towards bacterial species of any one of the compositions provided herein, or a chemical substance which binds a physiologically active substance secreted from bacterial species of any one of the compositions provided herein.

In some embodiments of the compositions provided herein, administration of the composition to a subject results in suppression of activity of CD8+ and IFN γ -producing T-cells in the subject.

In one aspect, the disclosure provides a method for suppressing CD8+ and IFN γ -producing T-cells in the subject, the method comprising administration of one or more of the compositions provided herein to the subject.

In one aspect, the disclosure provides a method for prevention, treatment or improvement in a disease originated by over-activation of CD8+ and IFN γ -producing T-cells of the subject the method comprising administering to the subject any one or more of the compositions provided herein to the subject.

In one aspect, the disclosure provides substances derived from the bacterial strains disclosed herein. In one aspect, the disclosure provides a physiologically active substance derived from a bacterial species of any one of the compositions provided herein. In one aspect, the disclosure provides a bacterial specific antigen of any one of the bacterial species of any one of the compositions provided herein.

[0106] In one aspect, the disclosure provides an antibody that specifically binds a bacterial species of any one of the compositions provided herein.

In one aspect, the disclosure provides a bacterial-specific nucleotide sequence contained in any one of the bacterial species of the compositions provided herein.

In one aspect, the disclosure provides animal models and test kits.

In one aspect, the disclosure provides an animal model comprising a non-human mammal, wherein the intestinal tract of the non-human mammal has been inoculated

with the bacterial species of any one of the compositions provided herein. In some embodiments of the animal model provided herein, the non-human mammal has a disease originated by irregularity of CD8⁺ IFN γ -producing T-cells.

In one aspect, the disclosure provides a kit for evaluating the activation of CD8⁺ IFN γ -producing T cells, the kit comprising: intestinal epithelial cells, peripheral blood mononuclear cells, and a bacterial species of any one of the compositions provided herein.

In one aspect, the disclosure provides methods of detection of CD8⁺ IFN γ -producing T cells in the human intestinal tract. In one aspect, the disclosure provides kits for evaluating activation of CD8⁺ IFN γ -producing T cells. In some embodiments, the kits comprise intestinal epithelial cells, peripheral mononuclear cells, and the bacterial species of any of the compositions described herein.

[0107] In one aspect, the disclosure provides a method for screening bacteria or a physiologically active substance derived from human intestinal bacteria, wherein the substance induces activation of CD8⁺ IFN γ producing T cells in the intestinal tract, comprising (i) allowing a non-human germ-free animal to ingest a physiologically active substance derived from human intestinal bacteria or bacteria, (ii) detecting the number, or activity of, CD8⁺ IFN γ -producing T cells in the intestinal tract of the non-human aseptic animal, wherein if activation of CD8⁺ IFN γ -producing T cells is detected, the physiologically active substance is identified as a substance that can activate CD8⁺ IFN γ -producing T cells.

In one aspect, the disclosure provides a method for screening bacteria or a physiologically active substance derived from human intestinal bacteria a, wherein the substance induces proliferation or activation of CD8⁺ IFN γ producing T cells in intestinal tract, comprising (i) adding a physiologically active substance derived from human intestinal bacteria or bacteria to the intestinal epithelial cells in a system comprising intestinal epithelial cells and peripheral blood mononuclear cells; (ii) detecting the number or activity of CD8⁺ IFN γ -producing T cells in said system, wherein if the activation of CD8⁺ IFN γ -producing T cells is detected, the physiologically active substance is identified as a substance that can activate CD8⁺ IFN γ -producing T cells.

[0108] In one aspect, the disclosure provides a method for screening for a substance that induces activation of CD8⁺ IFN γ -producing T cells in intestinal tract, comprising (i) adding a physiologically active substance derived from bacteria or bacteria contained in a composition provided herein to a system containing intestinal epithelial cells and peripheral blood mononuclear cells, (ii) adding a test substance, (iii) detecting the number or activity of CD8⁺ IFN γ -producing T cells in said system, wherein if the number or activity of CD8⁺ IFN γ producing T cells detected in the is increased, the

test substance is identified as a substance that induces activation of CD8+ IFN γ -producing T cells.

In one aspect, the disclosure provides a method for screening a substance that induces activation of CD8+ IFN γ -producing T cells in intestinal tract, comprising (i) the method for screening a non-human animal provided herein, (ii) detecting the number or activity of CD8+ IFN γ -producing T cells in the intestinal tract of the non-human animal, wherein if the number or activity of CD8+ IFN γ -producing T cells detected in the above step is increased, the test substance is identified as a substance that induces activation of CD8+ IFN γ -producing T cells.

In one aspect, the disclosure provides a composition for stimulating immunity, the composition comprising, as an active ingredient, a human intestinal bacterium or a physiologically active substance derived from a bacterium obtained by the screening methods provided herein. In some embodiments of the compositions provided herein, the composition induces the activation of CD8+ IFN γ -producing T cells.

[0109] In one aspect, the disclosure provides a vaccine composition comprising, as an active ingredient, human intestinal bacteria obtained by any of the screening methods provided herein, or an antigen specific to said bacterium.

In one aspect, the disclosure provides a method for screening a substance having an activity of inducing or exacerbating a disease caused by CD8+ IFN γ -producing T cells, comprising (i) allowing a test substance to be ingested by a non-human animal provided herein, (ii) detecting the degree of a disease-associated damage caused by CD8+ IFN γ -producing T cells in said non-human animal, wherein the test substance is identified as a substance that induces a disease caused by CD8+ IFN γ -producing T cells when the extent of the lesion detected in the above step is increased as compared to when no compound or placebo was added.

In one aspect, the disclosure provides a composition for inducing or exacerbating a disease caused by CD8+ IFN γ -producing T cells, wherein the composition comprises, as an active ingredient, the substance obtained by any one of the screening methods provided herein.

In one aspect, the disclosure provides a composition comprising a processed human fecal sample, wherein the processed human fecal sample is obtained by contacting a human fecal sample with ampicillin, and wherein the processed human fecal sample induces the proliferation and/or accumulation of CD8+ T-cells. In some embodiments, the disclosure provides a method of treatment of a disease in a subject, the method comprising administering to the subject any one of the compositions provided herein in an effective amount to treat the disease in the subject. In some embodiments of the methods provided herein, the disease is cancer or an infection (e.g., a viral infection).

[0110] In one aspect, the disclosure provides a method comprising inoculating a human

fecal sample in germ free mice, and determining if the human fecal sample induces the proliferation and/or accumulation of CD8+ T-cells.

In one aspect, the disclosure provides a method for determining if a human fecal sample induces proliferation and/or accumulation of CD8+ T cells, comprising inoculating germ-free mice with a human fecal sample, and determining if the human fecal sample induces the proliferation and/or accumulation of CD8+ T-cells. In one aspect, the disclosure provides a method for identifying a human fecal donor, comprising inoculating germ-free mice with a human fecal sample, and determining if the human fecal sample induces the proliferation and/or accumulation of CD8+ T-cells, wherein if the fecal sample induces the proliferation and/or accumulation of CD8+ T-cells, the human subject is identified as a human fecal donor.

In one aspect, the disclosure provides a method for analyzing expression levels of a marker in lymphocytes in a subject, comprising analyzing the expression levels of the marker, wherein the marker is induced by administering to the subject any of the compositions described herein, wherein the marker is CD44, gp70 MC38 peptide (KSPWFTTL; (SEQ ID NO: 53))-specific TCR β , tumor antigen derived ligand-specific TCR β , CD8, IFN γ , and/or GzmB.

[0111] In one aspect, the disclosure provides kits for analysis of expression levels of a marker in lymphocytes in a subject after induction, wherein the marker is induced by administering to the subject any of the compositions described herein, wherein the marker is CD44, gp70 MC38 peptide (KSPWFTTL; (SEQ ID NO: 53))-specific TCR β , tumor antigen derived ligand-specific TCR β , CD8, IFN γ , and/or GzmB.

In one aspect, the disclosure provides methods for screening a bacteria or a physiologically active substance derived from human intestinal bacteria, the method comprising, allowing a tumor-bearing non-human animal to ingest a physiologically active substance derived from human intestinal bacteria or bacteria, detecting the expression of a marker, in lymphocytes isolated from the tumor-bearing non-human animal, wherein if an increase in expression levels of the marker is detected, the physiologically active substance is identified as an immunostimulating agent for the tumor; and wherein the marker is CD44, gp70 MC38 peptide (KSPWFTTL; (SEQ ID NO: 53))-specific TCR β , tumor antigen derived ligand-specific TCR β , CD8, IFN γ , and/or GzmB.

[0112] In one aspect, the disclosure provides a companion diagnostic method for tumor therapy with an immune checkpoint inhibitor, the method comprising analyzing expression levels of a marker in lymphocytes before and after induction by administering to the subject any of the compositions described herein with or without co-administration of the immune checkpoint inhibitor, wherein if the expression levels of the marker in the lymphocytes of the subject are increased by at least 10%, at least

20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% as compared to the expression levels in the lymphocytes of the subject before the administration of the composition, co-administration of the inhibitor and any of the compositions described herein to the subject, the therapy is continued, wherein if the expression levels in the lymphocytes of the subject are not increased as compared to the expression levels in the lymphocytes of the subject, co-administration of the inhibitor and any of the compositions described herein is discontinued or reanalyzed after repeating the administration of any of the compositions described herein to the subject. In some embodiments, the methods further comprise analyzing expression levels of tumor antigen derived ligand-specific TCR β s in lymphocytes with specific antibodies that bind to the tumor antigen derived ligand-specific TCR β s or MHC multimers that bind to the tumor antigen derived ligand-specific TCR β s. In some embodiments, the methods are used in a tumor therapy with an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor. In some embodiments, the methods further comprise assessing PD-1 expression in T-cells in the subject. In some embodiments, the methods further comprise assessing PD-L1 expression in cancer cells in the subject. In some embodiments, the methods further comprise assessing CTLA-4 expression in T-cells in the subject.

[0113] In one aspect, the disclosure provides kits for carrying out companion diagnostic methods, wherein the kit comprises one or more molecules for monitoring of the expression levels of a marker in lymphocytes, wherein the marker is CD44, gp70 MC38 peptide (KSPWFTTL; (SEQ ID NO: 53))-specific TCR β , tumor antigen derived ligand-specific TCR β , CD8, IFN γ , and/or GzmB.

In one aspect, the disclosure provides methods for evaluating the immune activation with the degree of IFN γ production in splenocytes, the method comprising administering to a subject any of the compositions described herein.

In one aspect, the disclosure provides kits for evaluating the immune activation with the degree of IFN γ production in splenocytes, comprising one or more IFN γ marker molecules and one or more bacterial species of any of the compositions described herein.

In one aspect, the disclosure provides methods for identifying an immunostimulating agent for a tumor the method comprising screening a human intestinal bacteria or a physiologically active substance derived from human intestinal bacteria, the method comprising, (i) allowing a tumor-bearing non-human animal to ingest the human intestinal bacteria or the physiologically active substance derived from the human intestinal bacteria, and (ii) detecting IFN γ in splenocytes isolated from the tumor-bearing non-human animal, wherein if induction of IFN γ is detected, the human intestinal bacteria or physiologically active substance is identified as an immunos-

stimulating agent for the tumor.

- [0114] In one aspect, the disclosure provides a companion diagnostic method for tumor therapy with an immune checkpoint inhibitor, the method comprising evaluating the immune activation with the degree of IFN γ production in splenocytes before and after induction by administering to the subject any of the compositions described herein with or without co-administration of the inhibitor, wherein if the degree of IFN γ production in the splenocytes in the subject is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% as compared to the degree of IFN γ production in the splenocytes in the subject before the administration of the composition, co-administration of the inhibitor and any of the compositions described herein to the subject is continued, wherein if the degree of IFN γ production in the splenocytes of the subject is not increased, the co-administration of the inhibitor and any of the compositions described herein is discontinued or re-analyzed after repeat administration of any of the compositions described herein to the subject.

In some embodiments, the method further comprises analyzing expression levels of tumor antigens of the therapy target in splenocytes with the specific antibodies or the MHC multimers. In some embodiments, the method is for tumor therapy with an immune checkpoint inhibitor, wherein the tumor inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor. In some embodiments, the method further comprises assessing PD-1 expression in T-cells in the subject. In some embodiments, the method further comprises assessing PD-L1 expression in cancer cells in the subject. In some embodiments, the method further comprises assessing CTLA-4 expression in T-cells in the subject.

- [0115] In one aspect, the disclosure provides kits for carrying out the companion diagnostic methods described herein, comprising one or more IFN γ marker molecules.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium* sp., *Bacteroides dorei*, bacterium IARFR67, *Ruminococcaceae* bacterium, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Bacteroides* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least

11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium* sp., *Bacteroides dorei*, bacterium IARFR67, *Ruminococcaceae* bacterium, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Bacteroides* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp.. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0116] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium* sp., *Bacteroides dorei*, bacterium IARFR67, *Ruminococcaceae* bacterium, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Bacteroides* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium* sp., *Ruminococcaceae* bacterium, and *Eubacterium limosum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

[0117] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Bacteroides dorei*, bacterium IARFR67, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Bacteroides* sp., *Parabacteroides gordonii*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0118] Each of the limitations of the invention can encompass various embodiments of the invention. It is, therefore, anticipated that each of the limitations of the invention involving any one element or combinations of elements can be included in each aspect of the invention. This invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments and of being practiced or of being carried out in various ways.

Brief Description of Drawings

[0119] 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: [fig.1A-B] Figs. 1A and 1B show data of experiments with lymphocytes that were isolated from small intestine (SI) and colon mucosal lamina propria of SPF and germ-free (GF) mice and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 1A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 1B) Summarized data of the percentages of IFN γ positive cells within CD3, TCR β and CD8+ cells. Each plot represents individual mice. ** P < 0.01 (Student's t-test).

[fig.2A-B] Figs. 2A and 2B show data of experiments with lymphocytes that were isolated from the small intestinal mucosal lamina propria of SPF and germ-free mice and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8, CD103, IFN γ and GzmB were stained with antibodies and analyzed by flow cytometry. (Fig. 2A) The expression of IFN γ and CD103 (upper row) or GzmB (lower row) by the gated CD8 T cells of representative mice. (Fig. 2B) Summarized data of the percentages of each IFN γ positive cell fraction in CD3, TCR β and CD8+ cells. Each plot represents individual mice. * P < 0.05 (Student's t-test).

[fig.3A-B] Figs. 3A and 3B show data of experiments with lymphocytes that were isolated from small intestine (SI) and large intestine (Colon) mucosal lamina propria of SPF mice delivered from different laboratory animal facilities and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 3A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 3B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. * P < 0.05, ** P < 0.01 (one-way ANOVA).

[fig.4A-B] Figs. 4A and 4B show data of experiments in which after co-housing of SPF mice from Charles River Laboratories with CLEA Japan for 2 or 6 weeks, lymphocytes

were isolated from intestinal (SI) and colon mucosal lamina propria and stimulated with PMA / ionomycin for 3.5 h. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 4A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 4B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. * P < 0.05, ** P < 0.01 (one-way ANOVA).

[fig.5A-B] Figs. 5A and 5B show data of experiments with stools from healthy volunteers (A~F) which were orally administered into germ free mice individually in sterile vinyl isolators. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 5A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 5B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. ** P < 0.01 (one-way ANOVA).

[fig.6A-B] Figs. 6A and 6B show data of experiments with the cecal contents of B#5 mouse, which was orally administered to germ free mice. One day later, their drinking waters were switched to ampicillin (AMP), metronidazole (MNZ), streptomycin (STM) or tylosin (Tylo.) until the end of experiment. The contents of the cecum of B#5 treated with 3% of chloroform were administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8, IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 6A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 6B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. * P < 0.05 (one-way ANOVA).

[fig.7A-B] Figs. 7A and 7B show 16S rRNA gene sequence data of the cecal microbiota of the mice prepared in Figs. 6A and 6B, which were comprehensively analyzed using the next generation sequencer. (Fig. 7A) Figure of the proportion of operational taxonomic unit (OTU). On the right end, the OTU corresponding to the isolated strains of the B#5-AMP-2 mouse is shown in green. (Fig. 7B) Identification of isolated strains and the homologous bacterial name (Closest sequence) and similarity (S - ab score) are shown.

[fig.8A-B] Figs. 8A and 8B show data on the mixture of 21 isolated strains which was orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by

flow cytometry. (Fig. 8A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 8B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. ** P < 0.01 (Student's t-test).

[fig.9A-B]Figs. 9A and 9B show data on the mixture of 21 isolated strains which was orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8, CD103, IFN γ and GzmB were stained with antibodies and analyzed by flow cytometry. (Fig. 9A) The expression of IFN γ and CD103 (upper row) or GzmB (lower row) by the gated CD8 T cells of representative mice. (Fig. 9B) Summarized data of the percentages of each IFN γ positive cell fraction in CD3, TCR β and CD8+ cells. Each plot represents individual mice. * P < 0.05, ** P < 0.01 (Student's t-test).

[fig.10A-B]Figs. 10A and 10B show data on the mixture of the 21 strains or 11 strains (11 strain mixture corresponds to strains # 1-11; See Table 1), which were orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 10A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 10B) Summarized data of the percentages of IFN γ positive cells in CD3, TCR β and CD8+ cells. Each plot represents individual mice. *** P < 0.001, ****P < 0.0001 (one-way ANOVA).

[fig.11]Fig. 11 shows the compositions of the 10-mix and 11-mix bacterial strains that were inoculated into GF mice (See Figs. 12A and 12B).

[fig.12A-B]Figs. 12A and 12B show data obtained from mixtures of 11 or 10 strains (see Fig. 11), or a mixture of 17 strains that are known Treg-inducers, which were orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 12A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 12B) Summarized data of the percentages of CD8+ IFN γ + cells in CD3+ TCR β + cells (left), IFN γ + cells in CD8T cells (middle) and the numbers of CD8+ IFN γ + cells (right). Each plot represents individual mice. ** P < 0.01, *** P < 0.001, ****P < 0.0001 (one-way ANOVA).

[fig.13]Fig. 13 shows a phylogenetic tree which was constructed from the 16S rRNA gene sequences of the 11 strains (See Fig. 11), their closest sequences and some type strains using the MEGA v5.0 package and the neighbor-joining method. The strains which were inoculated into GF mice as a 7 mix or 4 mix are shown as well (The results

of the inoculation experiments are shown in Figs. 14A and 14B).

[fig.14A-B] Figs. 14A and 14B show data of the mixtures of the 11 strains, 7 or 4 strains mixtures listed in Fig. 13, which were orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 14A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 14B) Summarized data of the percentages of CD8⁺IFN γ ⁺ cells in CD3⁺ TCR β ⁺ cells (left), IFN γ ⁺ cells in CD8T cells (middle) and the numbers of CD8⁺IFN γ ⁺ cells (right). Each plot represents individual mice. * P <0.05, ** P <0.01, *** P <0.001 (one-way ANOVA).

[fig.15] Fig. 15 shows data on experiments with six weeks-old SPF C57BL/6 mice, which were purchased from Japan SLC and treated with antibiotics (1 g/L Ampicillin, 0.5 g/L Vancomycin, 1g/L Metronidazole and 1 g/L Neomycin; “AVMN”) in their drinking water. Then, mice were subcutaneously injected into the right flank with 3x10⁵ MC38 tumor cells line at day 0. When tumors appeared and were palpable, antibiotics treatment was stopped (day 2). Mice were injected intraperitoneally with 200 μ g of anti-PD1 antibody (clone J43) at day 3, 5 and 9 (“+anti-PD1Ab”). Mice were gavaged with the 11 mix 2 or 3 times a week including day 3, 5 and 9 (“+11 mix”). Tumor size was measured using a caliper and tumor volume was determined as length $\times$ width² $\times$ 0.5. ** P <0.01, *** P <0.001, **** P <0.0001 (two-way ANOVA).

[fig.16A-B] Figs. 16A and 16B show data on lymphocytes isolated from tumor cells. At day 23 or 27, lymphocytes were isolated from tumors and stimulated with PMA / ionomycin for 4 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry. (Fig. 16A) The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice. (Fig. 16B) Summarized data of the percentages of CD8⁺IFN γ ⁺ cells in CD3⁺ TCR β ⁺ cells (left), IFN γ ⁺ cells in CD8T cells (middle) and the numbers of CD8⁺IFN γ ⁺ cells (right). Each plot represents individual mice. * P <0.05, ** P <0.01, *** P <0.001 (one-way ANOVA).

[fig.17A-B] Figs. 17A, 17B show data on lymphocytes isolated from tumor cells. At day 23 or 27, lymphocytes were isolated from tumors and stimulated with PMA / ionomycin for 4 hours. CD3, TCR β , CD8, gp70 MC38 peptide (KSPWFTTL (SEQ ID NO: 53))-specific TCR β , CD44, GzmB and IFN γ were stained with antibodies and peptide-H2K^b tetramer, and analyzed by flow cytometry. (Fig. 17A) The expression of gp70-specific TCR β , CD44, GzmB and IFN γ by the gated CD3, TCR β and CD8⁺ cells of representative mice. (Fig. 17B). Summarized data of the percentages of each IFN γ positive cell fraction in CD8T cells. Each plot represents individual mice. ** P <0.01,

*** P <0.001, **** P <0.0001 (one-way ANOVA).

[fig.18]Fig. 18 shows data on lymphocytes isolated from tumor cells. The effect on IFN γ +CD4 T cells is shown in Figure 18.

[fig.19]Fig. 19 shows data on lymphocytes isolated from tumor cells. At day 23 or 27, whole splenocytes were isolated and plated at 10^6 cells per well and stimulated with 0.5 μ g/mL gp70 MC38 peptide (KSPWFTTL (SEQ ID NO: 53)) for 36 hours at 37 $^{\circ}$ C. Spots were developed using the Mouse IFN γ ELISPOT Ready-SET Go![®] kit (eBioscience), and the number of spots was measured using an Immunospot Series 4 Analyzer and analyzed using ImmunoSpot software (Cellular Technology). Each plot represents individual mice. “Naive” is a mouse which was not treated with antibiotics, not injected with MC38 cells and not treated with 11mix and anti-PD1 antibody. * P <0.05, ** P <0.01, *** P <0.001 (one-way ANOVA).

[fig.20]Fig. 20 shows data on 26 isolated strains, including 11 selected strains.

[fig.21]Fig. 21 shows data on induction of GzmB⁺ IFN γ ⁺ CD8 T cells by 11-mix bacterial strains.

[fig.22]Fig. 22 shows that slower tumor growth was accompanied by increased infiltration of IFN γ ⁺ CD8 T cells into the tumor.

[fig.23]Fig. 23 shows that the combination of α PD1 Ab and 11-mix bacterial strains boosted infiltration of GzmB⁺ IFN γ ⁺ CD8 cytotoxic T cells into the tumor.

[fig.24]Fig. 24 shows a schematic of the experimental plan described in Example 4 relating to treatment with the 11-mix and/or an anti-CTLA-4 antibody.

[fig.25]Fig. 25 shows body weight of mice that received the combination of α CTLA-4 Ab and the 11-mix of bacterial strains (left panel). Mice that received the combination of α CTLA-4 Ab and the 11-mix of bacterial strains had a significant reduction in tumor growth (right panel) in the experiment presented in Fig. 24 (Example 4).

[fig.26]Fig. 26 shows that the combination of α CTLA-4 Ab and the 11-mix of bacterial strains had a significant effect on the survival of the mice in the experiment presented in Fig. 24 (Example 4).

[fig.27]Fig. 27 shows tumor volume plots of individual mice treated in the experiments described in Example 4 (control, 11-mix; α CTLA-4 Ab; 11-mix + α CTLA-4 Ab).

[fig.28]Fig. 28 shows a schematic of the experimental plan described in Example 5 relating to treatment with the 11-mix or 4-mix and/or an anti-PD-1 antibody.

[fig.29]Fig. 29 shows body weight (left panel) and tumor volume (right panel) of mice that received the combination of α PD1 Ab and the 4-mix of bacterial strains or α PD1 Ab and the 11-mix of bacterial strains, and the various control groups.

[fig.30]Fig. 30 shows tumor volume plots of individual mice treated in experiments of Example 5 (11-mix; α PD-1 Ab; 11-mix + α PD-1 Ab). The tumor volume did not increase in multiple animals in the 11-mix + α PD-1 Ab treatment group (bottom right

panel).

[fig.31]Fig. 31 shows survival plots of mice treated in experiments of Example 5 (11-mix; α PD-1 Ab; 11-mix + α PD-1 Ab).

[fig.32]Fig. 32 shows tumor volume plots of individual mice treated in experiments of Example 5 (4-mix; α PD-1 Ab; 4-mix + α PD-1 Ab). The tumor volume did not increase in multiple animals in the 4-mix + α PD-1 Ab treatment (bottom right panel).

[fig.33]Fig. 33 shows plots of mice treated in experiments of Example 5. Highlighted are treatment with α PD-1 Ab, 11-mix + α PD-1 Ab, and 4-mix + α PD-1 Ab.

[fig.34]Fig. 34 shows data of experiments with the Braf Pten melanoma model (Example 6). Briefly, mice were administered antibiotics ("AVMN") from day -3 to day 2 and engrafted with 7×10^5 Braf Pten cells on day 0. On days 3, 6, and 9 the indicated groups of mice were administered an anti-PD1 antibody (arrows on the timeline) and SLC SPF feces from specific-pathogen free (SPF) mice obtained from Japan SLC (SLC SPF feces), with or without the 11-mix (arrows with asterisk on the timeline). The groups of mice indicated as having received the 11-mix were administered the 11-mix 2 or 3 times per week. The plot shows the average tumor volume at each of the timepoints for the groups of mice**** P<0.0001, *** P<0.001 (two-way ANOVA).

[fig.35]Fig. 35 shows data of experiments with the Braf Pten melanoma model (Example 6). Briefly, mice were administered antibiotics ("AVMN") from day -3 to day 2 and engrafted with 7×10^5 Braf Pten cells on day 0. On days 3, 6, and 9 the indicated groups of mice were administered an anti-PD1 antibody (arrows on the timeline) and SLC SPF feces from specific-pathogen free (SPF) mice obtained from Japan SLC (SLC SPF feces), with or without the 11-mix (arrows with asterisk on the timeline). The groups of mice indicated as having received the 11-mix were administered the 11-mix 2 or 3 times per week. The plot shows the average tumor area at each of the timepoints for the groups of mice. **** P<0.0001, *** P<0.001 (two-way ANOVA).

[fig.36]Fig. 36 shows data on the weight of tumors obtained on days 22 and 24 from the indicated groups of mice. * P<0.05 (one-way ANOVA).

[fig.37A-C]Figs. 37A-37C show data on lymphocytes isolated from tumor cells. On days 22 and 24, lymphocytes were isolated from tumors. CD3, TCR β , CD8, and IFN γ were stained with antibodies. Fig. 37A shows the percentage of CD8+ IFN γ + cells in the CD3+ TCR β + CD8 α + population of cells isolated from the tumors. Fig. 37B shows the number of CD8+ IFN γ + cells isolated from the tumors. Fig. 37C shows the number of CD8+ IFN γ + cells per gram of tumors. ** P<0.01, * P<0.05 (one-way ANOVA).

[fig.38]Fig. 38 shows the percentage of IFN γ + cells in the population of CD8T cells

isolated from the tumors. *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$ (one-way ANOVA).

[fig.39A-D] Figs. 39A-39D show data on lymphocytes isolated from tumor cells. On days 22 and 24, lymphocytes were isolated from tumors. CD3, TCR β , CD8, IFN γ , GzmB, IL-17, and CD4 were stained with antibodies. Fig. 39A shows the percentage of IFN γ + GzmB+ cells in the CD3+ TCR β + CD8 α + population of cells isolated from the tumors. Fig. 39B shows the percentage of Th1 cells in the CD3+ TCR β + CD4+ population of cells isolated from the tumors. Fig. 39C shows the percentage of Th17 cells in the CD3+ TCR β + CD4+ population of cells isolated from the tumors. Fig. 39D shows the percentage of Treg cells in the CD3+ TCR β + CD4+ population of cells isolated from the tumors.

[fig.40] Fig. 40 shows a schematic of the experimental plan described in Example 7 (the dosing study).

[fig.41A-C] Figs. 41A-41C show data on lymphocytes isolated from mice in the experiment shown in Fig. 40 (Example 7). CD3, TCR β , CD8, and IFN γ were stained with antibodies. Fig. 41A shows the percentage of CD8+ IFN γ + cells in the CD3+ TCR β + CD8 α + population of cells isolated from the indicated mice. Fig. 41B shows the number of CD8+ IFN γ + cells isolated from the indicated mice. Fig. 41C shows the percentage of IFN γ + cells in the population of CD8T cells isolated from the indicated mice.

[fig.42A-C] Figs. 42A-42C show data on lymphocytes isolated from mice from the experiment shown in Fig. 40 (Example 7). CD3, TCR β , CD8, IFN γ , CD103, IL-17, and CD4 were stained with antibodies. Fig. 42A shows the percentage of IFN γ + CD103+ cells in the CD3+ TCR β + CD8 α + population of cells isolated from the indicated mice. Fig. 42B shows the percentage of Th17 cells in the CD3+ TCR β + CD4+ population of cells isolated from the indicated mice. Fig. 42C shows the percentage of Th1 cells in the CD3+ TCR β + CD4+ population of cells isolated from the indicated mice.

[fig.43A-C] Figs. 43A-43C and 44 show the results from the experiments of Example 8. The experiments show that BATF3 is required for the 11-mix to induce CD8-T cells. BATF3 is not required to induce Th17. Fig. 43A shows the percentage of IFN γ + in the CD3+ TCR β + CD8 α + (CD8 T cell) population of cells isolated from the indicated mice. Fig. 43B shows the number of CD8+ IFN γ + cells. Fig. 43C shows the percentage of Th17 cells in the CD3+ TCR β + CD4+ population of cells isolated from the indicated mice. **** $P < 0.0001$, *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$ (one-way ANOVA).

[fig.44A-B] Fig. 44 shows that BATF3 is required for the 11-mix to induce CD8-T cells, as evidenced by the flow cytometry (Fig. 44A), and the percentage of IFN γ + in the CD3+ TCR β + CD8 α + (CD8 T cells) population of cells isolated from the indicated

mice (Fig. 44B).

[fig.45]Figs. 45-46 show the results from the experiments of Example 9. The experiments show that the 11-mix is effective in treating *Listeria* infections. Fig. 45 shows that feces + 11-mix is effective in clearing *Listeria* from infected mice, as evidenced in a decrease in the amount of *Listeria* CFUs in the feces.

[fig.46]Fig. 46 shows that the body weight of *Listeria* infected mice treated with feces and the 11-mix is higher than treatment with feces only.

[fig.47A-B]Figs. 47A and 47B shows data relating to Example 2. The mixtures of the 11 strains, 7 or 4 strains mixtures listed in Fig. 13, were orally administered to germ free mice. Four weeks later, lymphocytes were isolated from the lamina propria of the large intestine and stimulated with PMA / ionomycin for 3.5 hours. CD3, TCR β , CD8 and IFN γ were stained with antibodies and analyzed by flow cytometry (Fig. 47A). The expression of CD8 and IFN γ by the gated CD3 and TCR β positive cells of representative mice is shown in Fig. 47B, as indicated by the percentage of IFN γ ⁺ cells in CD8T cells. Each plot represents individual mice. * P < 0.05, ** P < 0.01, *** P < 0.001 (one-way ANOVA).

[fig.48]Fig. 48 relates to Example 10 and shows that the CD8 induction effect of the 11-mix in mice that are not otherwise challenged is limited to the intestine / gut compartment. (SI = short intestine, CIEL = colonic intraepithelial lymphocytes, LN = lymph nodes)

[fig.49]Fig. 49 shows that the frequencies of DC subsets in colonic LP were only slightly changed by the colonization with 11-mix.

[fig.50]Figs. 50-52 show that MHC CLP class cells are activated by the administration of the 11-mix, and that the activation is strongest within the first week of activation. There is no activation of the MHC MLN class cells. The individual measurements are shown in Figs. 50 and 51, while the accumulated data are depicted in Fig. 52.

[fig.51]Figs. 50-52 show that MHC CLP class cells are activated by the administration of the 11-mix, and that the activation is strongest within the first week of activation. There is no activation of the MHC MLN class cells. The individual measurements are shown in Figs. 50 and 51, while the accumulated data are depicted in Fig. 52.

[fig.52]Figs. 50-52 show that MHC CLP class cells are activated by the administration of the 11-mix, and that the activation is strongest within the first week of activation. There is no activation of the MHC MLN class cells. The individual measurements are shown in Figs. 50 and 51, while the accumulated data are depicted in Fig. 52.

[fig.53]Figs. 53 and 54 show that MHC CLP class cells are activated by the admin-

istration of the 11-mix, while there is no activation of the MHC MLN class cells. The individual measurements are shown in Fig. 53, while the accumulated data are depicted in Fig. 54 expressed as percentage of CD3⁺ TCDRbeta⁺ CD8alpha⁺ cells.

[fig.54]Figs. 53 and 54 show that MHC CLP class cells are activated by the administration of the 11-mix, while there is no activation of the MHC MLN class cells. The individual measurements are shown in Fig. 53, while the accumulated data are depicted in Fig. 54 expressed as percentage of CD3⁺ TCDRbeta⁺ CD8alpha⁺ cells.

[fig.55]Fig. 55 shows that MHC CLP class cells are activated by the administration of the 11-mix, as evidenced by Ki67 status, while there is no activation of the MHC MLN class cells.

[fig.56]Figs. 56 and 57 show that MHC CLP class cells are activated by the administration of the 11-mix, as evidenced by CD103⁺ status, while there is no activation of the MHC MLN class cells. The individual measurements are shown in Fig. 56, while the accumulated data are depicted in Fig. 57 expressed as percentage of CD3⁺ TCRbeta⁺ + CD8alpha⁺ IFNgamma⁺ cells.

[fig.57]Figs. 56 and 57 show that MHC CLP class cells are activated by the administration of the 11-mix, as evidenced by CD103⁺ status, while there is no activation of the MHC MLN class cells. The individual measurements are shown in Fig. 56, while the accumulated data are depicted in Fig. 57 expressed as percentage of CD3⁺ TCRbeta⁺ + CD8alpha⁺ IFNgamma⁺ cells.

Description of Embodiments

[0120] DETAILED DESCRIPTION

Provided herein are compositions and methods for the induction and/or proliferation of CD8⁺ T-cells, and methods for the treatment of diseases and conditions that can be treated through the induction and/or proliferation of CD8⁺ T-cells, including infectious diseases and cancers.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains with unique biological properties. In one aspect, the compositions of the bacterial strains disclosed herein, also referred to as bacterial compositions, can induce the proliferation and/or accumulation of CD8⁺ T-cells. In one aspect, the compositions of the bacterial strains disclosed herein can induce the proliferation and/or accumulation of CD8⁺ T-cells.

[0121] In one aspect, the bacteria of the compositions disclosed herein can be identified by their 16S rRNA (or 16S rDNA) nucleic acid sequence. In general, bacteria are classified as belonging to a specific species and/or genus based on their 16S rRNA nucleic acid sequence. Bacteria, such as bacteria derived from the microbiome, may also be classified into phylogenetic clusters with other closely related strains and

species. (See e.g., Rajilic-Stojanovic, M., and de Vos, W.M. (2014). The first 1000 cultured species of the human gastrointestinal microbiota. *FEMS Microbiol Rev* 38, 996-1047). 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. (2012). Evaluation of 16S rDNA-based community profiling for human microbiome research. *PLoS One* 7, e39315).

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0122] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID

NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0123] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0124] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at

least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0125] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0126] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial

strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:64. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0127] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:64. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at

least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0128] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, or SEQ ID NO:26. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0129] In one aspect, the disclosure provides compositions comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ

ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0130] In one aspect, the disclosure provides compositions comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, or SEQ ID NO:21. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

[0131] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:10. In some embodiments of the compositions provided herein, the

purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0132] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:11. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0133] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0134] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0135] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0136] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains.

[0137] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0138] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial

mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

[0139] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:52. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0140] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0141] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, or SEQ ID NO:47. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, or at least 4 bacterial strains.

[0142] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID

NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31 or SEQ ID NO:36. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0143] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:37. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

[0144] In one aspect, the disclosure provides compositions comprising a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26. In one aspect, the disclosure provides compositions comprising as an active ingredient a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26. 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.

In one aspect, the disclosure provides compositions comprising a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-21. In one aspect, the disclosure provides compositions comprising as an active ingredient a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-21.

In one aspect, the disclosure provides compositions comprising a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-11. In one aspect, the disclosure provides compositions comprising as an active ingredient a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-11.

[0145] In one aspect, the disclosure provides compositions comprising a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:54-64. In one aspect, the disclosure provides compositions comprising as an active ingredient a bacterial strain comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:54-64.

It should be appreciated that for all compositions provided herein, in some embodiments, the bacterial strains are purified. Thus, for example the disclosure provides purified bacterial strains comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26. In addition, for example, the disclosure provides compositions comprising purified bacterial strains comprising a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26. 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.

[0146] In one aspect, the disclosure provides compositions comprising one or more bacterial strains, wherein the one or more bacterial strains comprise a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26. In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains comprise 16S rDNA sequences having

at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. As discussed previously, in some embodiments, the bacterial strains are purified. Thus, in one aspect, the disclosure provides compositions comprising one or more purified bacterial strains wherein the one or more purified bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. As discussed previously, in some embodiments, the bacterial strains are purified. Thus, in one aspect, the disclosure provides compositions comprising one or more purified bacterial strains wherein the one or more purified bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26.

[0147] In one aspect, the disclosure provides compositions comprising two or more purified bacterial strains wherein the two or more purified bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. As discussed above, in some embodiments, the bacterial strains are the active ingredient of the composition. Thus, in some embodiments, the disclosure provides compositions comprising as an active ingredient two or more purified bacterial strains wherein the two or more purified bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26.

In one aspect, the disclosure provides compositions comprising two or more purified bacterial strains wherein the two or more purified bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. As discussed above, in some embodiments, the bacterial strains are the active ingredient of the composition. Thus, in some embodiments, the disclosure provides compositions comprising as an active ingredient two or more purified bacterial strains wherein the two or more purified bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26.

[0148] In one aspect, the disclosure provides bacterial strains and combinations of bacterial strains that are homologous or have a high percent of homology with bacterial strains comprising 16S rDNA sequences selected from the group consisting of SEQ ID NOs:1-26. As discussed previously, in some embodiments, the bacterial strains are purified. 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:1-26 have a

high percent of homology (e.g., greater than 90%) or sequence identity, 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 provides the closest known species by homology when the 16S rDNA sequences comprising SEQ ID NOs:1-26 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 disclosed herein has the highest homology with a bacterial strain of the species *Phascolarctobacterium faecium* as defined by NCBI Accession # LN998073 (having 16S rDNA sequence SEQ ID NO:27). 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 *Phascolarctobacterium faecium* as defined by NCBI Accession # LN998073. It should be appreciated that multiple bacterial strains disclosed herein may have the highest homology with the same species.

[0149] 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:1-26, are also homologous to other strains based on their whole genome sequence, or subset of their whole genome sequence.

Thus, it should be appreciated that, in one aspect, the disclosure also provides compositions and methods comprising bacterial species with close homology to the bacterial strains that have a 16S rDNA sequence with a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-26.

[0150] In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains are of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains are of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium*

limosum, Parabacteroides distasonis, Bacteroides cellulosilyticus, Bacteroides clarus, Anaerostipes caccae, Bacteroides salyersiae, Bacteroides fragilis; Bacteroides uniformis, Bacteroides eggerthii, Clostridium sp., Parabacteroides goldsteinii, and Bacteroides sp.

[0151] In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains are of species selected from the group consisting of Phascolarctobacterium faecium, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides uniformis, Subdoligranulum sp., Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Parabacteroides gordonii, Eubacterium limosum, and Parabacteroides distasonis.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains are of species selected from the group consisting of Bacteroides cellulosilyticus, Bacteroides clarus, Anaerostipes caccae, Bacteroides salyersiae, Bacteroides fragilis, Bacteroides uniformis, Bacteroides eggerthii, Clostridium sp., Parabacteroides goldsteinii, Bacteroides sp., Lachnospiraceae bacterium HGA0140, Hungatella hathewayi, Clostridium lavalense, Ruminococcus sp., and Clostridium innocuum.

In one aspect, the disclosure provides compositions comprising one or more bacterial strains wherein the one or more bacterial strains are of species selected from the group consisting of Bacteroides cellulosilyticus, Bacteroides clarus, Anaerostipes caccae, Bacteroides salyersiae, Bacteroides fragilis, Bacteroides uniformis, Bacteroides eggerthii, Clostridium sp., Parabacteroides goldsteinii, and Bacteroides sp.

[0152] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of Phascolarctobacterium faecium, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides uniformis, Subdoligranulum sp., Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Parabacteroides gordonii, Eubacterium limosum, Parabacteroides distasonis, Bacteroides cellulosilyticus, Bacteroides clarus, Anaerostipes caccae, Bacteroides salyersiae, Bacteroides fragilis, Bacteroides uniformis, Bacteroides eggerthii, Clostridium sp., Parabacteroides goldsteinii, Bacteroides sp., Lachnospiraceae bacterium HGA0140, Hungatella hathewayi, Clostridium lavalense, Ruminococcus sp., and Clostridium innocuum. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, or at least 26 bacterial strains.

[0153] In one aspect, the disclosure provides compositions comprising a purified bacterial

mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21 bacterial strains. In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0154] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides fluxus*, *Bacteroides uniformis*, *Bacteroides* sp. D20 *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae bacterium* cv2, *Gemminger formicilis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Alistipes senegalensis*, *Parabacteroides gordonii*, *Parabacteroides* sp.HGS0025, *Eubacterium limosum*, *Parabacteroides* sp. CAG:2 and *Parabacteroides distasonis*. In some embodiments of

the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0155] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising:

- 1) *Phascolarctobacterium faecium*, or *Phascolarctobacterium* sp. CAG:207;
- 2) *Fusobacterium ulcerans*, or *Fusobacterium varium*;
- 3) *Bacteroides dorei*, or *Bacteroides fluxus*,
- 4) *Bacteroides uniformis*, or *Bacteroides* sp. D20,
- 5) *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae* bacterium cv2, or *Gemminger formicilis*,
- 6) *Paraprevotella xylaniphila*,
- 7) *Parabacteroides johnsonii*,
- 8) *Alistipes* sp., *Alistipes timonensis*, or *Alistipes senegalesis*,
- 9) *Parabacteroides gordonii*, or *Parabacteroides* sp. HGS0025,
- 10) *Eubacterium limosum*, and
- 11) *Parabacteroides* sp. CAG:2 or *Parabacteroides distasonis*.

[0156] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of:

- 1) *Phascolarctobacterium faecium*, or *Phascolarctobacterium* sp. CAG:207;
- 2) *Fusobacterium ulcerans*, or *Fusobacterium varium*;
- 3) *Bacteroides dorei*, or *Bacteroides fluxus*,
- 4) *Bacteroides uniformis*, or *Bacteroides* sp. D20,
- 5) *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae* bacterium cv2, or *Gemminger formicilis*,
- 6) *Paraprevotella xylaniphila*,
- 7) *Parabacteroides johnsonii*,
- 8) *Alistipes* sp., *Alistipes timonensis*, or *Alistipes senegalesis*,
- 9) *Parabacteroides gordonii*, or *Parabacteroides* sp. HGS0025,
- 10) *Eubacterium limosum*, and
- 11) *Parabacteroides* sp. CAG:2 or *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at

least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0157] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising one or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae bacterium* cv2, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0158] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae bacterium* cv2, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae bacterium* cv2, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp. HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides fluxus*, *Bacteroides uniformis*, *Bacteroides* sp. D20 *Subdoligranulum* sp., *Ruthenibacterium lactatiformans*, *Ruminococcaceae bacterium* cv2, *Gemminger formicilis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Alistipes timonensis*,

Alistipes senegalesis, *Parabacteroides gordonii*, *Parabacteroides* sp.HGS0025, *Eubacterium limosum*, *Parabacteroides* sp. CAG:2 and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0159] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium varium*, *Bacteroides dorei*, *Bacteroides uniformis*, *Ruthenibacterium lactatiformans*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium* sp. CAG:207, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides* sp. D20, *Ruminococcaceae bacterium cv2*, *Paraprevotella xyliniphila*, *Parabacteroides johnsonii*, *Alistipes senegalesis*, *Parabacteroides* sp.HGS0025, *Eubacterium limosum*, and *Parabacteroides* sp. CAG:2. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or at least 11 bacterial strains.

[0160] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae bacterium HGA0140*, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, or at least 15 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, and *Bacteroides* sp. In some

embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 bacterial strains.

[0161] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Subdoligranulum* sp., and *Eubacterium limosum*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises at least 3, or at least 4 bacterial strains.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising two or more bacterial strains of species selected from the group consisting of *Bacteroides dorei*, *Bacteroides uniformis*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, and *Parabacteroides distasonis*. In some embodiments of the compositions provided herein, the purified bacterial mixture comprises, at least 3, at least 4, at least 5, at least 6, or at least 7 bacterial strains.

It should be appreciated that the compositions may include multiple strains of a particular species. Thus, for illustration, a non-limiting example of the compositions disclosed herein, comprises one strain of *Bacteroides salyersiae* and two strains of *Bacteroides uniformis*.

The disclosure provides also encompasses compositions comprising bacterial strains that are close in homology to and/or fall within the species *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*.

[0162] Thus, in one embodiment, the compositions of the disclosure include one or more bacterial strains comprising 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:27-52. In some embodiments, the compositions of the disclosure include two or more bacterial strains comprising 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:27-52.

Thus, in one embodiment, the compositions of the disclosure include one or more bacterial strains comprising 16S rDNA sequences having at least 97% sequence

identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:27-52. In some embodiments, the compositions of the disclosure include two or more bacterial strains comprising 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:27-52.

[0163] In one aspect, the compositions of the disclosure include two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. In some embodiments, the compositions of the disclosure include two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. In some embodiments, the compositions of the disclosure include two or more bacterial strains of species selected from the group consisting of *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum*. In some embodiments, the compositions of the disclosure include two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NO:27-52. In some embodiments, the compositions of the disclosure include two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NO:27-52.

[0164] In some embodiments, the disclosure provides compositions with two or more purified bacterial strains that comprise 16S rDNA sequences with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. In some embodiments, the disclosure provides compositions with five or more purified bacterial strains that comprise 16S rDNA sequences with nucleic acid sequences selected from the group consisting of SEQ ID NOs:1-26. In some embodiments, the disclosure provides compositions with at least ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences with nucleic acid sequences SEQ ID NOs:1-26, respectively. In some embodiments, the disclosure provides a composition consisting of ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences with nucleic acid sequences SEQ ID NOs:1-26, respectively. In some em-

bodiments, the disclosure provides a composition essentially consisting of eleven purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences with nucleic acid sequences SEQ ID NOS:1-26, respectively. As used herein, essentially consisting of refers to a composition that includes no additional bacterial strains.

[0165] In some embodiments, the disclosure provides compositions with bacterial strains that comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of: SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with two or more purified bacterial strains that comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with five or more purified bacterial strains that comprise 16S rDNA having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with at least ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences SEQ ID NOS:1-26, respectively. In some embodiments, the disclosure provides a composition consisting of ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences SEQ ID NOS:1-26, respectively. In some embodiments, the disclosure provides a composition essentially consisting of ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences having at least 97% homology with nucleic acid sequences SEQ ID NOS:1-26, respectively.

[0166] In some embodiments, the disclosure provides compositions with bacterial strains that comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of: SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with two or more purified bacterial strains that comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with five or more purified bacterial strains that comprise 16S rDNA having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NOS:1-26. In some embodiments, the disclosure provides compositions with at least ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences SEQ ID NOS:1-26, respectively. In some embodiments, the disclosure provides a composition consisting of ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA

sequences having at least 97% sequence identity with nucleic acid sequences SEQ ID NOs:1-26, respectively. In some embodiments, the disclosure provides a composition essentially consisting of ten purified bacterial strains, wherein the bacterial strains comprise 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences SEQ ID NOs:1-26, respectively.

[0167] In one aspect, the disclosure provides a composition comprising bacterial strains that are related to the following bacterial species: *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium limosum*, *Parabacteroides distasonis*, *Bacteroides cellulosilyticus*, *Bacteroides clarus*, *Anaerostipes caccae*, *Bacteroides salyersiae*, *Bacteroides fragilis*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Clostridium* sp., *Parabacteroides goldsteinii*, *Bacteroides* sp., *Lachnospiraceae* bacterium HGA0140, *Hungatella hathewayi*, *Clostridium lavalense*, *Ruminococcus* sp., and *Clostridium innocuum* (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. In some embodiments, the disclosure provides compositions with two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% homology with nucleic acid sequences selected from the group consisting of SEQ ID NO:27-52. In some embodiments, the disclosure provides compositions with two or more purified bacterial strains comprising 16S rDNA sequences having at least 97% sequence identity with nucleic acid sequences selected from the group consisting of SEQ ID NO:27-52.

[0168] 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 60%, at least 70%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.6%, at least 99.7%, at least 99.8%, at least 99.9%, or up to 100% 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.

- [0169] 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.
- [0170] 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.
- [0171] 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.* 48:443, 1970, by the search for similarity method of Pearson and Lipman. *Proc. Natl. Acad. Sci. USA* 85:2444, 1988, 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.* 25:3389-3402, 1977; and Altschul et al., *J. Mol. Biol.* 215:403-410, 1990, respectively.

[0172] In one aspect, the disclosure provides compositions comprising multiple purified 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 and Table 3). It should be appreciated that multiple bacterial strains of the compositions disclosed herein may have the same closest related bacterial species. In one aspect, the disclosure provides compositions comprising one or more bacterial strains or species with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences provided by SEQ ID NOs:1-26. In some embodiments, the species with 16S rDNA sequences with homology to a nucleic acid sequence of any one of the closest related species to any of the strains described herein, correspond to bacterial strains with 16S rDNA sequences provided by SEQ ID NOs:27-52. In one aspect, the disclosure provides compositions comprising one or more bacterial strains or species with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences provided by SEQ ID NOs:1-21. In some embodiments, the species with 16S rDNA sequences with homology to a nucleic acid sequence of any one of the closest related species to any of the strains described herein, correspond to bacterial strains with 16S rDNA sequences provided by SEQ ID NOs:27-47. In one aspect, the disclosure provides compositions comprising one or more bacterial strains or species with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences provided by SEQ ID NOs:1-11. In some embodiments, the species with 16S rDNA sequences with homology to a nucleic acid sequence of any one of the closest related species to any of the strains described herein, correspond to bacterial strains with 16S rDNA sequences provided by SEQ ID NOs:27-37. In one aspect, the disclosure provides compositions comprising one or more bacterial strains or species with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences provided by SEQ ID NOs:12-26. In some embodiments, the species with 16S rDNA sequences with homology to a nucleic acid sequence of any one of the closest related species to any of the strains described herein, correspond to bacterial strains with 16S rDNA sequences provided by SEQ ID NOs:38-52. In one aspect, the disclosure provides compositions comprising one or more bacterial strains or species with 16S rDNA sequences that have homology to a nucleic acid sequence of any one of the sequences provided by SEQ ID NOs:12-21. In some embodiments, the species

with 16S rDNA sequences with homology to a nucleic acid sequence of any one of the closest related species to any of the strains described herein, correspond to bacterial strains with 16S rDNA sequences provided by SEQ ID NOs:38-47.

[0173] In some embodiments, the compositions disclosed herein provide at least one of the bacterial strains (e.g., purified bacterial strains) described herein. In some embodiments, the compositions that comprise at least one bacterial strain, comprise at least one bacterial strain with a 16S rDNA sequence selected from any one of SEQ ID NOs:1-26. In some embodiments, the compositions that comprise at least one bacterial strain, comprise at least one bacterial strain with a 97% homology to 16S rDNA sequence selected from any one of SEQ ID NOs:1-26. In some embodiments, the compositions that comprise at least one bacterial strain, comprise at least one bacterial strain with a 97% sequence identity with a 16S rDNA sequence selected from any one of SEQ ID NOs:1-26.

In some embodiments, the compositions disclosed herein comprise two or more bacterial strains. In some embodiments, the compositions described herein comprise at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 or more bacterial strains (e.g., purified bacterial strains).

[0174] In some embodiments of the compositions provided herein, at least 50% of the bacterial strains belong to the order of Bacteriodales. In some embodiments of the compositions provided herein, at least 50% of the bacterial strains belong to the genus Bacteroides or Parabacteroides. In some embodiments of the compositions provided herein, one or more strains belongs to the genus Bacteroides and one or more strains belongs to the genus Parabacteroides. In some embodiments of the compositions provided herein, at least 25% of the bacterial strains belong to the family of Bacteroidaceae. In some embodiments of the compositions provided herein, one or more of the bacterial strains belongs to the genus Bacteroides. In some embodiments of the compositions provided herein, one or more of the bacterial strains belongs to the genus Parabacteroides.

In some embodiments of the compositions provided herein, the composition does not include bacterial strains that belong to the order of Bacteriodales.

[0175] In some embodiments of the compositions provided herein, one or more of the bacterial strains belong to the order of Bacteriodales and one or more of the bacterial strains belong to the order of Clostridiales. In some embodiments of the compositions provided herein, at least 50% of the bacterial strains belong to the order of Bacteriodales and one or more of the bacterial strains belong to the order of Clostridiales. In some embodiments of the compositions provided herein, at least 75% of the bacterial

strains belong to the order of Bacteriodales and one or more of the bacterial strains belong to the order of Clostridiales. In some embodiments of the compositions provided herein, at least 90% of the bacterial strains belong to the order of Bacteriodales and one or more of the bacterial strains belong to the order of Clostridiales. In some embodiments, the compositions provided herein do not include *E. coli*. In some embodiments, the compositions provided herein do not include *Bifidobacterium*. In some embodiments, the compositions provided herein do not include *Bacillus*. In some embodiments, the compositions provided herein do not include *Enterococcus*. In some embodiments, the compositions provided herein do not include *Barnesiella*. In some embodiments, the compositions provided herein do not include *B. fragilis*. In some embodiments, the compositions provided herein do not include *B. thetaiotaomicron*. In some embodiments, the compositions provided herein do not include *Akkermansia*. In some embodiments, the compositions provided herein do not include *Proteobacteria*. In some embodiments, the compositions provided herein do not include *Burkholderia*. In some embodiments, the compositions provided herein do not include clostridium species belonging to Cluster IV. In some embodiments, the compositions provided herein do not include *Faecalibacterium*. In some embodiments, the compositions provided herein do not include clostridium species belonging to Cluster XIVa. In some embodiments, the compositions do not comprise fungi, such as *Monilla* species.

[0176] In one aspect, the disclosure provides purified fractions of human stool sample that can induce CD8 T cells.

In some embodiments of the compositions provided herein, one or more of the bacterial strains are human-derived bacteria. In some embodiments of the compositions provided herein, all of the bacterial strains are human-derived bacteria. In some embodiments of the compositions provided herein, the bacterial strains are derived from more than one human donor.

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).

[0177] In some embodiments of the compositions provided herein, the composition includes one or more anaerobic bacteria. In some embodiments of the compositions provided herein, the composition includes only anaerobic bacteria. In some embodiments of the compositions provided herein, the composition includes one or more facultative anaerobic bacteria. In some embodiments of the compositions provided herein, the composition includes only facultative anaerobic bacteria. In some embodiments of the compositions provided herein, the composition includes one or more obligate anaerobic bacteria. In some embodiments of the compositions provided herein, the composition includes only obligate anaerobic bacteria.

In some embodiments of the compositions provided herein, one or more of the bacterial strains does not have an antibiotic resistance gene. In some embodiments of the compositions provided herein, the bacterial strains do not have an antibiotic resistance gene that renders the bacterial strain resistant to vancomycin.

[0178] 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 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.

[0179] 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 ef-

ficacious 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. (An “antibiotic that is efficacious in a human” as used herein is an antibiotic that has been used to successfully treat bacterial infections in a human).

[0180] In some embodiments of the compositions provided herein, one or more of the bacterial strains is a spore-former. In some embodiments of the compositions provided herein, one or more of the bacterial strains is in spore form. In some embodiments of the compositions provided herein, one or more of the bacterial strains is a non-spore former.

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 they are introduced in the intestine.

[0181] 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.

[0182] 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.

[0183] In any of the compositions provided herein, in some embodiments, 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 and/or purified, 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. 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. 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.

[0184] In one aspect, the disclosure provides bacterial strains and mixtures of bacterial strains with unique biological properties. In some embodiments of the compositions provided herein, the composition induces proliferation and/or accumulation of CD8+ T-cells. In some embodiments, the bacterial strains of the compositions provided herein can induce proliferation and/or accumulation of CD8+ T-cells, because of the

synergy between the bacterial strains. Thus, without being limiting to a specific mechanism, in some embodiments, the combination of the bacterial strains of the compositions provided herein act synergistically in the induction of proliferation and/or accumulation of CD8+ T-cells because the combination of the strains is particularly well-suited to generate metabolites and/or cellular signals that stimulate the induction of proliferation and/or accumulation of CD8+ T-cells. The bacterial compositions may do so, for instance through the use of nutrients in the intestinal tract (e.g., the colon or the cecum), and/or metabolic interactions that result in metabolites and/or cellular signals that stimulate the induction of proliferation and/or accumulation of CD8+ T-cells. In addition, without being limiting to a specific mechanism, in some embodiments, the combination of the bacterial strains of the compositions provided herein act synergistically in the induction of proliferation and/or accumulation of CD8+ T-cells because the combination of the strains is superior in engrafting specific niches in the intestinal tract (e.g., the colon or the cecum) that will result in the induction of proliferation and/or accumulation of CD8+ T-cells (e.g., by providing a favorable microenvironment). In some embodiments, the combination of the bacterial strains of the compositions provided herein act synergistically in the induction of proliferation and/or accumulation of CD8+ T-cells because the combination of the strains is particularly well-suited to generate metabolites and/or cellular signals that stimulate the induction of proliferation and/or accumulation of CD8+ T-cells, and the combination is well suited to engraft in specific niches, that result in localization of the metabolites and/or cellular signals to a target for the induction of proliferation and/or accumulation of CD8+ T-cells

[0185] Treatment of diseases
Cancer

In one aspect, the disclosure includes compositions and methods for the treatment of diseases in a subject. In some embodiments of the methods provided herein, the subject has cancer. In one aspect, the cancers that can be treated according to the compositions and methods provided herein, include without limitation, carcinoma, glioma, mesothelioma, melanoma, lymphoma, leukemia, adenocarcinoma, breast cancer, ovarian cancer, cervical cancer, glioblastoma, multiple myeloma, prostate cancer, Burkitt's lymphoma, head and neck cancer, colon cancer, colorectal cancer, non-small cell lung cancer, small cell lung cancer, cancer of the esophagus, stomach cancer, pancreatic cancer, hepatobiliary cancer, cancer of the gallbladder, cancer of the small intestine, rectal cancer, kidney cancer, bladder cancer, prostate cancer, penile cancer, urethral cancer, testicular cancer, vaginal cancer, uterine cancer, thyroid cancer, parathyroid cancer, adrenal cancer, pancreatic endocrine cancer, carcinoid cancer, bone cancer, skin cancer, retinoblastomas, Hodgkin's lymphoma, non-Hodgkin's lymphoma,

Kaposi's sarcoma, multicentric Castleman's disease, AIDS-associated primary effusion lymphoma, neuroectodermal tumors, or rhabdomyosarcoma. In some embodiments of the methods provided herein, the cancer is prostate cancer, bladder cancer, non-small cell lung cancer, urothelial carcinoma, melanoma, or renal cell carcinoma. In some embodiments of the methods provided herein, the subject is undergoing radiation treatment.

[0186] In some embodiments of the methods provided herein, the method further includes administering one or more anticancer agents. In some embodiments of the methods provided herein, the anticancer agent is a chemotherapy agent. In some embodiments of the methods provided herein, the anticancer agent is a cancer immunotherapy agent.

In some embodiments of the methods provided herein, the cancer immunotherapy agent is an immune checkpoint inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L-1 inhibitor, or CTLA-4 inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a CTLA-4 inhibitor.

[0187] In some embodiments of the methods provided herein, the cancer immunotherapy agent is a cancer vaccine that acts to increase the response of a subject's immune system to cancer cells. For example, cancer vaccines include cancer antigen(s) that act to induce or stimulate an immune response against cells bearing the cancer antigen(s). The immune response induced or stimulated can include an antibody (humoral) immune response and/or a T-cell (cell-mediated) immune response. CD8+ T-cells can differentiate into cytotoxic T-cells that kill target cells bearing the antigen recognized by CD8+ T-cells. Induction of CD8+ T-cells can, therefore, enhance the immune response to cancer antigens provided in a cancer vaccine.

In some embodiments of the methods provided herein, the cancer immunotherapy agent is a CAR-T therapeutic. CAR-T cells include T-cells taken from a patient that are genetically engineered to produce chimeric antigen receptors (CARs) on their surface. The CARs are engineered to recognize a specific antigen on cancer cells. After the CAR-T cells are infused into the patient, they recognize and kill cancer cells that express the specific antigen on their surfaces. Induction of CD8+ T-cells is useful to provide cells for conversion into CAR-T cells.

[0188] In some embodiments of the methods provided herein, the method further includes administering one or more cytokines. In some embodiments of the methods provided herein the cytokine is IL-2, IL-15, or IL-21.

In some embodiments of the methods provided herein, the method further includes administering one or more costimulatory agents. In some embodiments of the methods provided herein the costimulatory agent is a CD-28, OX-40, 4-1BB, or CD40 antibody.

In some embodiments of the methods provided herein, the method further includes administering one or more vaccines. In some embodiments of the methods provided herein, the vaccine is a dendritic cell vaccine.

In some embodiments of the methods provided herein, the method further includes administering adoptive cell transfer therapy. In some embodiments of the methods provided herein, the adoptive cell transfer therapy is the use of engineered T-cell receptors or chimeric antigen receptors.

[0189] In some embodiments of the compositions provided herein, the composition further comprises one or more anticancer agents. In some embodiments of the compositions provided herein, the anticancer agent is a chemotherapy agent. In some embodiments of the compositions provided herein, the anticancer agent is cancer immunotherapy agent. In some embodiments of the compositions provided herein, the cancer immunotherapy agent is an immune checkpoint inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, CTLA-4 inhibitor, IDO1 inhibitor, LAG3 inhibitor or TIM3 inhibitor. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is nivolumab. In some embodiments, the PD-1 inhibitor is pembrolizumab. In some embodiments, the PD-1 inhibitor is pidilizumab. In some embodiments of the compositions provided herein, the immune checkpoint inhibitor is a PD-L1 inhibitor. In some embodiments, the PD-L1 inhibitor is atezolizumab. In some embodiments, the PD-L1 inhibitor is avelumab. In some embodiments, the PD-L1 inhibitor is durvalumab. In some embodiments of the methods provided herein, the immune checkpoint inhibitor is a CTLA-4 inhibitor. In some embodiments, the CTLA-4 inhibitor is an anti-CTLA-4 antibody. Examples of anti-CTLA-4 antibodies include, without limitation, ipilimumab, tremelimumab (CP-675,206), 9H10, 4F10, and 9D9. In some embodiments, the CTLA-4 inhibitor is ipilimumab. In some embodiments, the CTLA-4 inhibitor is tremelimumab. It should further be appreciated that multiple anticancer agents (e.g., immune checkpoint inhibitors) may be included in the compositions and methods disclosed herein. For instance, in a non-limiting example, the compositions and methods disclosed include both a PD-1 inhibitor and a CTLA-4 inhibitor.

[0190] In one aspect, the disclosure provides a composition comprising a purified bacterial mixture comprising *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum* sp., *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes* sp., *Parabacteroides gordonii*, *Eubacterium*

limosum, and Parabacteroides distasonis, and a PD-1 inhibitor.

In one aspect, the disclosure provides a composition comprising a purified bacterial mixture comprising Phascolarctobacterium faecium, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides uniformis, Subdoligranulum sp., Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Parabacteroides gordonii, Eubacterium limosum, and Parabacteroides distasonis, and a PD-L-1 inhibitor.

In one aspect, the disclosure provides a composition comprising a purified bacterial mixture comprising Phascolarctobacterium faecium, Fusobacterium ulcerans, Bacteroides dorei, Bacteroides uniformis, Subdoligranulum sp., Paraprevotella xylaniphila, Parabacteroides johnsonii, Alistipes sp., Parabacteroides gordonii, Eubacterium limosum, and Parabacteroides distasonis, and a CTLA-4 inhibitor.

[0191] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a PD-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a PD-L-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% homology to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a CTLA-4 inhibitor.

[0192] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a PD-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a PD-L-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97%

sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, and a CTLA-4 inhibitor.

[0193] In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, and SEQ ID NO:64, and a PD-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, and SEQ ID NO:64, and a PD-L-1 inhibitor.

In one aspect, the disclosure provides compositions comprising a purified bacterial mixture comprising bacterial strains comprising 16S rDNA sequences of at least 97% sequence identity with 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, and SEQ ID NO:64, and a CTLA-4 inhibitor.

[0194] In some embodiments of the compositions provided herein, the composition further includes one or more cytokines. In some embodiments of the compositions provided herein, the cytokine is IL-2, IL-15, or IL-21. In some embodiments of the compositions provided herein, the composition further comprises one or more costimulatory agents. In some embodiments of the compositions provided herein, the costimulatory agent is a CD-28, OX-40, 4-1BB, or CD40 antibody.

In some embodiments of the compositions provided herein, the composition further comprises one or more vaccines. In some embodiments of the compositions provided herein, the vaccine is a dendritic cell vaccine. In some embodiments of the compositions provided herein, the composition is combined with adoptive cell transfer therapy. In some embodiments of the compositions provided herein, the adoptive cell transfer therapy is the use of engineered T-cell receptors or chimeric antigen receptors.

[0195] Infectious disease

In one aspect, the disclosure includes compositions and methods for the treatment of diseases in a subject. In some embodiments of the methods provided herein, the subject has an infectious disease. In some embodiments of the methods provided herein, the infectious disease is a bacterial infection, a viral infection, a parasitic infection, or a fungal infection. In some embodiments of the methods provided herein, the infectious disease is a viral infection. In some embodiments of the methods provided herein, the viral infection is HIV. In some embodiments of the methods

provided herein, the infection is an infection by a hepatitis virus.

In some embodiments, the compositions provided herein can be used as a pharmaceutical composition for preventing or treating (reducing, partially or completely the adverse effects of) an infectious disease, such as a bacterial infection, a viral infection, a parasitic infection, and a fungal infection.

[0196] Bacterial infections that can be treated according to the methods provided herein include, but are not limited to *P. aeruginosa*, *E. coli*, *C. tetani*, *N. gonorrhoeae*, *C. botulinum*, *Klebsiella* sp., *Serratia* sp., *Pseudomonas* sp., *P. cepacia*, *Acinetobacter* sp., *S. epidermis*, *E. faecalis*, *S. pneumoniae*, *S. aureus*; *S. mutans*, *Haemophilus* sp., *Neisseria* Sp., *N. meningitidis*, *Bacteroides* sp., *Citrobacter* sp., *Branhamella* sp., *Salmonella* sp., *Shigella* sp., *S. pyogenes*, *Proteus* sp., *Clostridium* sp., *Erysipelothrix* sp., *Listeria* sp., *Pasteurella multocida*, *Streptobacillus* sp., *Spirillum* sp., *Fusospirocheta* sp., *Treponema pallidum*, *Borrelia* sp., *Actinomycetes*, *Mycoplasma* sp., *Chlamydia* sp., *Rickettsia* sp., *Spirochaeta*, *Borrelia burgdorferi*, *Legionella* sp., *Mycobacteria* sp, *Ureaplasma* sp, *Streptomyces* sp., *Trichomonas* sp., *P. mirabilis*; *Vibrio cholera*, enterotoxigenic *Escherichia coli*, *Clostridium difficile*, *Salmonella typhi*, *C. diphtheria*, *Mycobacterium leprae*, *Mycobacterium lepromatosis*. Bacterial infections caused by drug resistant bacteria that can be treated according to the methods provided herein include, but are not limited to *Clostridium perfringens*; *Clostridium botulinum*; *Clostridium tributicum*; *Clostridium sporogenes*; *Escherichia coli*; *Pseudomonas aeruginosa*, such as Multidrug Resistant *Pseudomonas aeruginosa*; Vancomycin Resistant Enterococci (VRE); Carbapenem Resistant Enterobacteriaceae (CRE); *Neisseria gonorrhoeae*; *Acinetobacter*, Multidrug Resistant *Acinetobacter*; *Campylobacter*; Multidrug-resistant *Campylobacter*; *Candida*, Fluconazole-Resistant *Candida*, Extended spectrum beta-lactamase (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.

Viral infections that can be treated according to the methods provided herein include, but are not limited to, picornaviridae, caliciviridae, togaviridae, flaviviridae, coronaviridae, rhabdoviridae, filoviridae, paramyxoviridae, orthomyxoviridae, bunyaviridae, arenaviridae, reoviridae, retroviridae, hepadnaviridae, parvoviridae, papovaviridae, adenoviridae, herpesviridae, poxviridae, rotavirus, parainfluenza virus, influenza virus A and B, hepatitis virus, syphilis, HIV, rabies virus, Epstein-Barr virus, and herpes simplex virus.

- [0197] Viral infections that can be treated according to the methods provided herein include, but are not limited to *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malaria*, *Toxoplasma gondii*, *Leishmania mexicana*, *L. tropica*, *L. major*, *L. aethiopica*, *L. donovani*, *Trypanosoma cruzi*, *T. brucei*, *Schistosoma mansoni*, *S. haematobium*, *S. japonicum*, *Trichinella spiralis*, *Wuchereria bancrofti*, *Brugia malayi*, *Entamoeba histolytica*, *Enterobius vermicularis*, *Taenia solium*, *T. saginata*, *Trichomonas vaginalis*, *T. hominis*, *T. tenax*; *Giardia lamblia*, *Cryptosporidium parvum*, *Pneumocystis carinii*, *Babesia bovis*, *B. divergens*, *B. microti*, *Isospora belli*, *L. hominis*, *Dientamoeba fragilis*, *Onchocerca volvulus*, *Ascaris lumbricoides*, *Necator americanus*, *Ancylostoma duodenale*, *Strongyloides stercoralis*, *Capillaria philippinensis*, *Angiostrongylus cantonensis*, *Hymenolepis nana*, *Diphyllobothrium latum*, *Echinococcus granulosus*, *E. multilocularis*, *Paragonimus westermani*, *P. caliensis*, *Chlonorchis sinensis*, *Opisthorchis felinae*, *G. Viverini*, *Fasciola hepatica*, *Sarcoptes scabiei*, *Pediculus humanus*, *Phthirus pubis*, and *Dermatobia hominis*.
- [0198] Fungal infections that can be treated according to the methods provided herein include, but are not limited to *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Aiellomyces dermatitidis*, *Histoplasma capsulatum*, *Coccidioides immitis*, *Candida* species, including *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. guilliermondii* and *C. krusei*, *Aspergillus* species, including *A. fumigatus*, *A. flavus*, *A. niger*, *Rhizopus* species, *Rhizomucor* species, *Cunninghamella* species, *Apophysomyces* species, including *A. saksenaea*, *A. mucor* and *A. absidia*, *Sporothrix schenckii*, *Paracoccidioides brasiliensis*, *Pseudallescheria boydii*, *Torulopsis glabrata*; and *Dermatophytes* species.
- [0199] In one aspect, the disclosure provides a vaccine comprising any of the compositions provided herein and an antigen. In some embodiments of the vaccines provided herein, the antigen is an HIV antigen. In some embodiments of the vaccines provided herein, the antigen
- is a hepatitis antigen. In some embodiments, the bacterial compositions are administered as an adjuvant in combination with antigenic material. The antigenic material can include one or more portions of the protein coat, protein core, or functional proteins and peptides of a pathogen, or a full pathogen (live, killed, inactivated, or attenuated), or may comprise one or a plurality of cancer epitopes or cancer antigens. The antigenic material can be co-administered, administered before, or after the bacterial composition. The bacterial composition may also be administered with existing mucosal vaccines such as influenza vaccines, (e.g. FluMist from MedImmune or NASOVAC from Serum Institute of India), rotavirus vaccines (e.g. RotaTaq from Merck or Rotarix from GlaxoSmithKline), typhoid vaccines (e.g. Vivotif from Crucell, Ty21A), cholera vaccines (e.g. Orochol from Crucell, Shanchol

from Shantha Biotechnics), traveller's diarrhea vaccines (e.g. Dukoral from Crucell), and with antigens of live attenuated Influenza A virus HI strain, live attenuated Influenza A virus H3 strain, Influenza B virus, live attenuated H1N1 influenza virus (swine flu), live attenuated rotavirus, mono- and multi-valent poliovirus, live attenuated Salmonella Typhi, live recombinant Vibrio cholerae lacking cholera toxin subunit A, whole killed Vibrio cholerae 01 classical and El Tor biotypes with or without cholera toxin subunit B, cancer antigens, cancer epitopes, and combinations thereof.

[0200] Autoimmune disease or allergic disease

In one aspect, the disclosure includes compositions and methods for the treatment of diseases in a subject. In some embodiments of the methods provided herein, the subject has an autoimmune disease or an allergic disease.

The compositions and methods of the current disclosure can be used for preventing or treating autoimmune disease and allergic disease. Autoimmune disease that can be treated include, but are not limited to, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, or Hashimoto's disease. Allergic diseases that can be treated include, but are not limited to, food allergy, pollenosis, or asthma.

[0201] Additional examples of autoimmune and allergic disease that can be treated according to the methods and compositions provided herein include, without limitation, rejection in organ transplantations, such as inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, sprue, autoimmune arthritis, rheumatoid arthritis, Type I diabetes, multiple sclerosis, graft vs. host disease following bone marrow transplantation, osteoarthritis, juvenile chronic arthritis, Lyme arthritis, psoriatic arthritis, reactive arthritis, spondyloarthritis, systemic lupus erythematosus, insulin dependent diabetes mellitus, thyroiditis, asthma, psoriasis, dermatitis scleroderma, atopic dermatitis, graft versus host disease, acute or chronic immune disease associated with organ transplantation, sarcoidosis, atherosclerosis, disseminated intravascular coagulation, Kawasaki's disease, Grave's disease, nephrotic syndrome, chronic fatigue syndrome, Wegener's granulomatosis, Henoch-Schoenlein purpura, microscopic vasculitis of the kidneys, chronic active hepatitis, uveitis, septic shock, toxic shock syndrome, sepsis syndrome, cachexia, acquired immunodeficiency syndrome, acute transverse myelitis, Huntington's chorea, Parkinson's disease, Alzheimer's disease, stroke, primary biliary cirrhosis, hemolytic anemia, polyglandular deficiency type I syndrome and polyglandular deficiency type II syndrome, Schmidt's syndrome, adult (acute) respiratory distress syndrome, alopecia, alopecia areata, seronegative arthropathy, arthropathy, Reiter's disease, psoriatic arthropathy, chlamydia, yersinia and salmonella associated arthropathy, spondyloarthritis,

atheromatous disease/arteriosclerosis, allergic colitis, atopic allergy, food allergies such as peanut allergy, tree nut allergy, egg allergy, milk allergy, soy allergy, wheat allergy, seafood allergy, shellfish allergy, or sesame seed allergy, autoimmune bullous disease, pemphigus vulgaris, pemphigus foliaceus, pemphigoid, linear IgA disease, autoimmune haemolytic anaemia, Coombs positive haemolytic anaemia, acquired pernicious anaemia, juvenile pernicious anaemia, myalgic encephalitis/Royal Free Disease, chronic mucocutaneous candidiasis, giant cell arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, Acquired Immunodeficiency Disease Syndrome, Acquired Immunodeficiency Related Diseases, Hepatitis C, common varied immunodeficiency (common variable hypogammaglobulinaemia), dilated cardiomyopathy, fibrotic lung disease, cryptogenic fibrosing alveolitis, postinflammatory interstitial lung disease, interstitial pneumonitis, connective tissue disease associated interstitial lung disease, mixed connective tissue disease associated lung disease, systemic sclerosis associated interstitial lung disease, rheumatoid arthritis associated interstitial lung disease, systemic lupus erythematosus associated lung disease, dermatomyositis/polymyositis associated lung disease, Sjogren's disease associated lung disease, ankylosing spondylitis associated lung disease, vasculitic diffuse lung disease, haemosiderosis associated lung disease, drug-induced interstitial lung disease, radiation fibrosis, bronchiolitis obliterans, chronic eosinophilic pneumonia, lymphocytic infiltrative lung disease, postinfectious interstitial lung disease, gouty arthritis, autoimmune hepatitis, type-1 autoimmune hepatitis (classical autoimmune or lupoid hepatitis), type-2 autoimmune hepatitis (anti-LKM antibody hepatitis), autoimmune mediated hypoglycemia, type B insulin resistance with acanthosis nigricans, hypoparathyroidism, acute immune disease associated with organ transplantation, chronic immune disease associated with organ transplantation, osteoarthritis, primary sclerosing cholangitis, idiopathic leucopenia, autoimmune neutropenia, renal disease NOS, glomerulonephritides, microscopic vasculitis of the kidneys, discoid lupus, erythematosus, male infertility idiopathic or NOS, sperm autoimmunity, multiple sclerosis (all subtypes), insulin dependent diabetes mellitus, sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture's syndrome, pulmonary manifestation of polyarteritis nodosa, acute rheumatoid fever, rheumatoid spondylitis, Still's disease, systemic sclerosis, Takayasu's disease/arteritis, autoimmune thrombocytopenia, idiopathic thrombocytopenia, autoimmune thyroid disease, hyperthyroidism, goitrous autoimmune hypothyroidism (Hashimoto's disease), atrophic autoimmune hypothyroidism, primary myxoedema, phacogenic uveitis, primary vasculitis, vitiligo, allergic rhinitis (pollen allergies), anaphylaxis, pet allergies, latex allergies, drug allergies, allergic rhinoconjunctivitis, eosinophilic esophagitis, hypereosinophilic syndrome, eosinophilic gastroenteritis cutaneous lupus erythematosus,

eosinophilic esophagitis, hypereosinophilic syndrome, eosinophilic gastroenteritis, and diarrhea.

[0202] In some embodiments of the methods and compositions provided herein, the composition further comprises one or more anti-inflammatory agents. In some embodiments of the methods and compositions provided herein, the anti-inflammatory agent is a non-steroidal anti-inflammatory drug (NSAID). Exemplary NSAIDs include, but are not limited to, aspirin, ibuprofen, naproxen, celecoxib, rofecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ketoprofen, ketorolac, mefenamic acid, meloxicam, nabumetone, oxaprozin, piroxicam, sulindac, tolmetin and combinations thereof. In some embodiments, the NSAID is an immune selective anti-inflammatory derivative (ImSAID).

[0203] Treatment of disease

In one aspect, the disclosure provides compositions and methods of treatment for disease in a subject. In one aspect, and without being limiting, the compositions disclosed herein can treat disease because their administration results in the induction of proliferation and/or accumulation of CD8+ T-cells. In some embodiments, the disclosure provides compositions and methods of treatment for disease in a subject for diseases that can be treated by the induction of proliferation and/or accumulation of CD8+ T-cells. In some embodiments, the diseases that can be treated by the induction of proliferation and/or accumulation of CD8+ T-cell is cancer, an infectious disease, an autoimmune disease or allergic disease.

[0204] In one aspect, the disclosure provides a method of treating a disease in a subject comprising administering any of the compositions provided herein to the subject in an effective amount to treat the disease. In some embodiments of the methods provided herein, the administration of the composition to the subject results in the induction of proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject. In some embodiments of the methods provided herein, the proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% when compared to the proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject before the administration of the composition. In some embodiments of the methods provided herein, the administration of the composition to the subject results in an increase of IFN γ -gamma production in the intestine of the subject when compared to the IFN γ -gamma production in the intestine of the subject before the administration of the composition. In some embodiments of the methods provided herein, the administration of the composition to the subject results in an increase of IFN γ -gamma production in the intestine of the subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, or at least 200% when compared

to the IFN γ -gamma production in the intestine of the subject before the administration of the composition.

[0205] 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 disease (e.g., cancer or infectious disease). The terms “treat” or “treatment” refer to reducing or alleviating one or more of the symptoms associated with a disease (e.g., cancer or infectious disease). The terms “prevent” or “prevention” encompass prophylactic administration and may reduce the incidence or likelihood of the occurrence of the disease (e.g., cancer or infectious disease). For instance, in some embodiments, administration of the compositions provided herein result in a healthy microbiome that induces proliferation and/or accumulation of CD8+ T-cells thereby protecting a subject against cancer and/or infectious disease.

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 and/or augmentation of cancer treatment. It should be appreciated that the term effective amount may be expressed in number of bacteria or CFUs 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.

[0206] In some embodiments, the therapeutically effective amount of any of the compositions described herein is an amount sufficient to treat the disease, e.g., enhance survival of the subject, suppress an infection and/or treat the cancer.

Any of the methods described herein may be for the treatment of cancer in a subject. As used herein, methods of treating cancer involve relieving or alleviating at least one symptom associated with the cancer, or slowing or reversing the cancer progression. A method of treating cancer may, for example, eliminate or reduce a subject's tumor burden, reduce the number or replication of cancer cells, and/or prevent, delay or inhibit metastasis.

Also provided herein are methods for the treatment or prevention of an infectious disease in a subject. As used herein, methods of treating an infectious disease may involve relieving or alleviating at least one symptom associated with infection, or slowing or reversing the progression of the infection. A method of treating an infectious disease may, for example, eliminate or reduce the load of an infectious organism (e.g., bacteria, virus, fungus, or parasite), or inhibit or reduce one or more symptoms of the infection. As also used herein, the terms “prevent,” “prevention,” and “preventing,” include the administration of a composition to a subject to reduce, or delay the onset of the manifestation of clinical or subclinical symptoms, complications,

pathologies or biochemical indicia of the infection, or to reduce or inhibit the spread/transmission of the infectious organism (e.g., bacteria, virus, fungus, or parasite).

[0207] Aspects of the present disclosure are related to methods for treating a disease or condition 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.

The compositions and methods described herein may be utilized in conjunction with other types of therapy (i.e., combination treatment), such as additional therapeutic agents. Examples of additional combination therapies include, without limitation, surgery, radiation, gene therapy, and administration of additional therapeutic agents, such as chemotherapeutics, antibiotics, antivirals, anti-fungals, anti-parasitics, immunomodulatory agents, anti-inflammatory agents. In general, combination therapies can be administered simultaneously or sequentially (in any order) with the compositions and methods described herein. In some embodiments, any of the compositions described herein is administered simultaneously with one or more additional therapeutic agents, for example in a single dose or in multiple doses that are administered at substantially the same time.

[0208] In some embodiments, the compositions described herein are administered to a subject concomitantly with one or more additional therapeutic agents. In some embodiments, the compositions described herein are administered to a subject followed by administration of one or more additional therapeutic agent. In some embodiments, any of the compositions described herein is administered at least about 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 3 months, 4 months, 5 months, 6 months or more prior to administration of the one or more additional therapeutic agent. Alternatively, in some embodiments, one or more therapeutic agent administered to a subject followed by administration of any of the compositions described herein. In some embodiments, one or more therapeutic agent is administered at least about 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 3 months, 4 months, 5 months, 6 months or more prior to administration of any the compositions described herein.

[0209] Additional methods

Also within the scope of the present disclosure are methods of assessing whether one or more bacterial strains of any of the compositions described herein are present in the intestine of a subject. In some embodiments, if fewer than a threshold number of bacterial strains are detected in the intestine of the subject, any of the compositions

described herein are administered to the subject to increase the number of the bacterial strains in the intestine of the subject. In some embodiments, the method further comprises identifying the subject as a candidate for a treatment of the disease based on the number of bacterial strains detected in the intestine.

Measuring the levels of the biomarker sets may also be useful in the evaluation and treatment of a disease.

In general, the bacterial population of the intestine (e.g., presence or absence of one or more bacterial strains) may be determined by assessing a sample obtained from the subject, such as a fecal sample.

[0210] In some embodiments of the compositions provided herein, administration of the composition to a subject results in the induction of proliferation and/or accumulation of CD8+ T-cells in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in IFN γ -gamma production in the intestine of a subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in the presence of one or more bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, the one or more bacterial strains of the administered composition was not previously present in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in the engraftment of one or more bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, the one or more bacterial strains of the administered composition was not previously engrafted in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the number of the bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the engrafted number of the bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the abundance of total bacteria of the bacterial strains of the administered composition in the intestine of the subject. In some embodiments of the compositions provided herein, administration of the composition to a subject results in an increase in the engrafted total bacterial strains of the administered composition in the intestine of the subject.

[0211] In one aspect, the disclosure provides a method that includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less

than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the composition is administered to the subject.

In some embodiments of the methods provided herein, the subject is undergoing, or will be undergoing, cancer treatment.

In one aspect, the disclosure provides a method for determining if a subject is expected to respond positively to cancer treatment, wherein the method includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the subject is not expected to respond positively to cancer treatment.

In some embodiments of the methods provided herein, the cancer treatment is cancer immunotherapy treatment.

[0212] In one aspect, the disclosure provides a method for reducing the risk of a viral infection in a subject, wherein the method includes determining if one or more bacterial species of any of the compositions provided herein are present in the intestine of a subject, wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the composition is administered to the subject, thereby reducing the risk of a viral infection in the subject.

In some embodiments of the methods provided herein, determining the presence of one or more of the bacterial species is done by sequencing fecal matter of the subject.

[0213] Pharmaceutical compositions

In one aspect, the disclosure provides pharmaceutical compositions comprising the bacterial strains and combinations of bacterial strains provided herein. In some embodiments of the compositions provided herein, the composition is a pharmaceutical composition. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition comprises a pharmaceutically acceptable excipient. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for oral administration. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is formulated for rectal administration. 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 some embodiments of the pharmaceutical compositions provided herein, one or more of the bacterial strains is lyophilized. In some em-

bodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition is in the form of a capsule. In some embodiments of the pharmaceutical compositions provided herein, the pharmaceutical composition further comprises a pH sensitive composition comprising one or more enteric polymers.

[0214] 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, herein incorporated by reference in their entirety. 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.

[0215] 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.

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.

[0216] 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.

[0217] Pharmaceutical compositions 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.

[0218] 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).

[0219] 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).

[0220] 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 water-soluble 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.

[0221] 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.

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).

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.

[0222] 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).

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).

- [0223] Dosages of the active ingredients in the pharmaceutical compositions 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 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.
- [0224] 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 disclosed herein, 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.
- [0225] 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).

[0226] 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^{11} , between 10^4 and 10^{11} , between 10^5 and 10^{11} , between 10^6 and 10^{11} , 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^{11} , between 10^4 and 10^{11} , between 10^5 and 10^{11} , between 10^6 and 10^{11} , 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.

[0227] 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^{11} , between 10^4 and 10^{11} , between 10^5 and 10^{11} , between 10^6 and 10^{11} , 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^{11} , between 10^4 and 10^{11} , between 10^5 and 10^{11} , between 10^6 and 10^{11} , 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.

[0228] 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.

[0229] In one aspect, the disclosure provides a food product comprising any of the compositions provided herein and a nutrient. 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.

[0230] 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.

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.

[0231] 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 subject may be administered one or more doses of an antibiotic prior to or concurrently with a bacterial composition. Antibiotics may be administered for a variety of reasons. For instance, antibiotics may be administered to remove bacterial species from the colon and/or intestine prior to administration of the bacterial compositions provided herein. Antibiotics may also be administered to suppress unwanted infections in the case of cancer treatment. In some instances, antibiotics may be administered as a treatment method for an infectious disease.

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.

[0232] Diagnostics and prognostic methods

Also described herein are diagnostic methods (e.g., companion diagnostics) for use in determining whether a subject should receive a treatment, such as a composition as described herein and/or any of the immune checkpoint inhibitors described herein. Such methods can be used for diagnosing a disease, monitoring the progress of a disease, assessing the efficacy of a treatment for the disease, and/or identifying patients suitable for a particular treatment.

Accordingly, the methods described herein are based on the level of a marker in a

sample (e.g., a biological sample containing lymphocytes) obtained from a subject. In some embodiments, the methods involve analyzing the presence and/or level of a marker in one or more samples from a subject.

[0233] In some embodiments, the level of the marker in a sample obtained from a subject can then be compared with a reference sample or a control sample to determine a value indicating the amount of the marker in the sample. In some embodiments, a value for a marker is obtained by comparing the level of a marker in a sample to the level of another marker (e.g., an internal control or internal standard) in the sample. The value of the marker can be compared to a reference value to determine whether the subject has or is at risk for the disease. In some embodiments, the level of the marker is compared to a predetermined threshold for the marker, a deviation from which may indicate the subject has a disease. In some embodiments, if the level or value of the marker is higher than a reference level or value, the subject can be identified as having or at risk for a disease, as described herein. In some embodiments, if the level or value of the marker is lower than a reference level or value, the subject can be identified as having or at risk for a disease, as described herein.

In some embodiments, the level of the marker in a sample from a subject is compared to the level of the marker in another sample obtained from the same subject, for example, a sample obtained from the subject at a different time. In some embodiments, the level of the marker in a sample from a subject is compared to the level of the marker in a sample obtained from the subject at an earlier time, such as prior to administration of any of the compositions described herein. In some embodiments, the level of the marker in a sample from a subject is compared to the level of the marker in a sample obtained from the subject at a later time, such as after administration of any of the compositions described herein.

[0234] In some embodiments, if the level or value of the marker is higher in a sample as compared to the level or value of the marker in a sample from the subject obtained prior to administration of a composition described herein, the subject is administered an immune checkpoint inhibitor and a composition described herein. In some embodiments, if the level or value of the marker is higher in a sample as compared to the level or value of the marker in a sample from the subject obtained prior to administration of a composition described herein, the subject continues a therapy involving administration of an immune checkpoint inhibitor and a composition described herein. In some embodiments, the level or value of the marker in a sample is enhanced at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, or at least 200% as compared the level of value of the marker in a sample prior to administration of a composition as described herein.

[0235] In some embodiments, if the level or value of the marker is not increased (e.g., equal to or lower) in a sample as compared to the level or value of the marker in a sample from the subject obtained prior to administration of a composition described herein, administration of an immune checkpoint inhibitor and a composition described herein is discontinued. In some embodiments, if the level or value of the marker is not increased (e.g., equal to or lower) in a sample as compared to the level or value of the marker in a sample from the subject obtained prior to administration of a composition described herein, the administration of an immune checkpoint inhibitor and a composition described herein is reanalyzed after administration of a composition as described herein. In some embodiments, the level or value of the marker in a sample is reduced at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, or at least 200% as compared the level of value of the marker in a sample prior to administration of a composition as described herein.

In some embodiments, the level of the marker is determined by analyzing the expression of the marker (e.g., protein or nucleic acid level) and/or the cell type in which the marker is expressed. Any method known the art may be used to analyze the expression of the marker and/or cell type in which the marker is expressed.

[0236] Also provided herein are methods based on the level or degree of IFN γ production in a sample (e.g., a biological sample containing splenocytes) obtained from a subject. In some embodiments, the methods involve analyzing the presence and/or level of IFN γ production in one or more samples from a subject.

In some embodiments, the level of IFN γ production in a sample obtained from a subject can then be compared with a reference sample or a control sample to determine a value indicating the amount of the IFN γ production in the sample. In some embodiments, a value for IFN γ production is obtained by comparing the level of IFN γ production in a sample to the level of another molecule (e.g., an internal control or internal standard) in the sample. The value of IFN γ production can be compared to a reference value to determine whether the subject has or is at risk for the disease. In some embodiments, the level of IFN γ production is compared to a predetermined threshold for IFN γ production, a deviation from which may indicate the subject has a disease. In some embodiments, if the level or value of IFN γ production is higher than a reference level or value, the subject can be identified as having or at risk for a disease, as described herein. In some embodiments, if the level or value of IFN γ production is lower than a reference level or value, the subject can be identified as having or at risk for a disease, as described herein.

[0237] In some embodiments, the level of IFN γ production in a sample from a subject is compared to the level of IFN γ production in another sample obtained from the same

subject, for example, a sample obtained from the subject at a different time. In some embodiments, the level of IFN γ production in a sample from a subject is compared to the level of IFN γ production in a sample obtained from the subject at an earlier time, such as prior to administration of any of the compositions described herein. In some embodiments, the level of IFN γ production in a sample from a subject is compared to the level of IFN γ production in a sample obtained from the subject at a later time, such as after administration of any of the compositions described herein.

In some embodiments, if the level or value of IFN γ production is higher in a sample as compared to the level or value of IFN γ production in a sample from the subject obtained prior to administration of a composition described herein, the subject is administered an immune checkpoint inhibitor and a composition described herein. In some embodiments, if the level or value of IFN γ production is higher in a sample as compared to the level or value of IFN γ production in a sample from the subject obtained prior to administration of a composition described herein, the subject continues a therapy involving administration of an immune checkpoint inhibitor and a composition described herein. In some embodiments, the level or value of IFN γ production in a sample is enhanced at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, or at least 200% as compared the level of value of IFN γ production in a sample prior to administration of a composition as described herein.

[0238] In some embodiments, if the level or value of IFN γ production is not increased (e.g., equal to or lower) in a sample as compared to the level or value of IFN γ production in a sample from the subject obtained prior to administration of a composition described herein, administration of an immune checkpoint inhibitor and a composition described herein is discontinued. In some embodiments, if the level or value of IFN γ production is not increased (e.g., equal to or lower) in a sample as compared to the level or value of IFN γ production in a sample from the subject obtained prior to administration of a composition described herein, the administration of an immune checkpoint inhibitor and a composition described herein is reanalyzed after administration of a composition as described herein. In some embodiments, the level or value of IFN γ production in a sample is reduced at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, or at least 200% as compared the level of value of IFN γ production in a sample prior to administration of a composition as described herein.

[0239] In some embodiments, the level of IFN γ production is determined by analyzing the expression of IFN γ (e.g., protein or nucleic acid level) and/or the cell type by which

IFN γ is produced. Any method known the art may be used to analyze the expression of IFN γ and/or identify the cell type that produces IFN γ .

The control level can also be a predetermined level or threshold. Such a predetermined level can represent the level of the marker or IFN γ production in a population of subjects that do not have or are not at risk for the target disease. It can also represent the level of the marker or IFN γ production in a population of subjects that have the target disease.

The predetermined level can take a variety of forms. For example, it can be single cut-off value, such as a median or mean. In some embodiments, such a predetermined level can be established based upon comparative groups, such as where one defined group is known to have a target disease and another defined group is known to not have the target disease. Alternatively, the predetermined level can be a range, for example, a range representing the levels of the metabolite in a control population.

[0240] As used herein, “an elevated level” or “an increased level” means that the level of the marker or IFN γ production is higher than a reference value or the level in another sample, such as a sample obtained from the subject prior to administration of any of the compositions described herein. An elevated level of a marker or IFN γ production includes a level of the marker or IFN γ production that is, for example, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 150%, 200%, 300%, 400%, 500% or more above a reference value or above the level in another sample from the subject. In some embodiments, the level of the marker or IFN γ production in the test sample is at least 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 7, 8, 9, 10, 50, 100, 150, 200, 300, 400, 500, 1000, 10000-fold or more, higher than the level in a reference sample or the level in another sample from the subject.

As used herein, “a decreased level” means that the level of the marker or IFN γ production is lower than a reference value or the level in another sample, such as a sample obtained from the subject prior to administration of any of the compositions described herein. A decreased level of the marker or IFN γ production includes a level of the marker or IFN γ production that is, for example, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 150%, 200%, 300%, 400%, 500% or more lower than a reference value or the level in another sample from the subject. In some embodiments, the level of the marker or IFN γ production in the test sample is at least 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 7, 8, 9, 10, 50, 100, 150, 200, 300, 400, 500, 1000, 10000-fold or more lower than the level of the marker or IFN γ production in a reference sample or the level in another sample from the subject.

[0241] A subject identified in the methods described herein may be subject to a suitable treatment, such as treatment with a combination of an immune checkpoint inhibitor

and any of the composition, as described herein.

The assay methods and kits described herein also can be applied for evaluation of the efficacy of a treatment for a disease, such as those described herein, given the correlation between the level of the marker or IFN γ production and such diseases. For examples, multiple biological samples can be collected from a subject to whom a treatment is performed either before and after the treatment or during the course of the treatment. The levels of a marker or IFN γ production may be indicative as to whether the treatment is effective.

If the subject is identified as not responsive to the treatment, a higher dose and/or frequency of dosage of the composition and/or immune checkpoint inhibitors are administered to the subject identified. In some embodiments, the dosage or frequency of dosage of the therapeutic agent is maintained, lowered, or ceased in a subject identified as responsive to the treatment or not in need of further treatment. Alternatively, a different treatment can be applied to the subject who is found as not responsive to the first treatment.

In other embodiments, the values of a marker or IFN γ production can also be relied on to identify a disease may be treatable, for example by administering the compositions described herein.

[0242] Screening methods

Provided herein are methods for screening bacteria or physiologically active substances derived from bacteria to identify bacteria or physiologically active substances thereof that produce a desired response. For example, in some embodiments, the screening methods are used to identify bacteria or physiologically active substances derived from bacteria that induce activation of CD8 $^{+}$ IFN γ -producing T cells. In some embodiments, the screening methods are used to identify bacteria or physiologically active substances derived from bacteria that induce activation of CD8 $^{+}$ IFN γ -producing T cells. In some embodiments, the screening methods are used to identify bacteria or physiologically active substances derived from bacteria as an immunostimulatory agent.

Also provided herein are methods for screening test substances to identify substances that induce activation induce or exacerbate a disease caused by CD8 $^{+}$ IFN γ -producing T cells.

In general, the screening methods may be performed in vitro (e.g., using cells) or in vivo (e.g., using non-human animal models). In some embodiments, the methods involve contacting a population of cells (e.g., intestinal epithelial cells, peripheral blood mononuclear cells) with a test substance (e.g., bacteria or physiologically active substances thereof) and assessing a response. In some embodiments, the response is the number and/or activity of a desired cell population (e.g., CD8 $^{+}$ IFN γ T cells).

[0243] In some embodiments, the methods involve inoculating a non-human animal model with a test substance (e.g., bacteria or physiologically active substances thereof) and assessing a response. In some embodiments, the non-human animal model ingests the test substance. In some embodiments, the response is the number and/or activity of a desired cell population (e.g., CD8+ IFN γ T cells). In some embodiments, the response is an improvement of a disease or symptom thereof, or induction/exacerbation of a disease or symptom thereof.

In some embodiments, the bacteria and/or the physiologically active substances derived from bacteria identified in any of the screening methods described herein may be administered to a subject, for example for the treatment of a disease.

[0244] Kits

The present disclosure also provides kits for use in evaluating the immune system activation, for example based on the degree or level of IFN γ production in splenocytes, involving administering to a subject any of the compositions as described herein. In some embodiments, a sample may be obtained from the subject prior to, during, and/or after administration of any of the compositions described herein.

In some embodiments, the kit contains one or more molecules for detecting and/or measuring the amount of IFN γ production in a sample. In some embodiments, the molecule that detects or measures the amount of IFN γ production can comprise one or more binding agents that specifically bind to IFN γ . In some embodiments, the binding agent is an antibody that specifically binds to IFN γ . In some embodiments, the binding agent is part of a reporter system, such as a receptor on a cell that binds to the IFN γ and induces expression of a gene encoding a reporter molecule. In some embodiments, the kit also contains a standard or control sample to which the amount of IFN γ in the sample(s) obtained from the subject may be compared.

[0245] In some embodiments, the kit may be for carrying out any of the companion diagnostic methods described herein.

In some embodiments, the kit contains one or more molecules for detecting and/or measuring the amount or presence of any one of the bacterial species described herein, or component thereof. In some embodiments, the molecule that detects or measures the amount of a bacterial strain can comprise one or more binding agents that specifically bind to the bacterial strain. In some embodiments, the binding agent specifically binds to a feature of one or more bacterial species that identifies the bacterial species. In some embodiments, the binding agent is a nucleic acid that specifically binds to a nucleic acid sequence of one or more of the bacterial species described herein, such as a specific 16S rRNA sequence. In some embodiments, the kit also contains a standard or control sample to which the sample(s) obtained from the subject may be compared.

[0246] The present disclosure also provides kits for use in determining a treatment method, for example, a tumor therapy, involving analyzing the expression of a marker (e.g., CD44, CD8, IFN γ , GzmB, gp70 MC38 peptide (KSPWFTTL; (SEQ ID NO: 53))-specific TCR β , or an antigen-derived ligand-specific TCR β), prior to, during, and/or after administration of any of the compositions described herein. Also provided herein are kits comprising companion diagnostics for tumor therapy with an immune checkpoint inhibitor (e.g., a PD-1 inhibitor).

In some embodiments, the kit includes one or more components for analyzing or monitoring expression levels of a marker, such as CD44, CD8, IFN γ , GzmB, or a tumor antigen-derived ligand-specific TCR β . In some embodiments, the marker is analyzed by detecting the presence of the marker, by measuring the level (amount) of the marker, and/or a specific cell type on which the marker is presented. In some embodiments, the molecule that detects or measures the amount of the marker can comprise one or more binding agents that specifically bind to the marker. In some embodiments, the binding agent is an antibody that specifically binds to the marker. In some embodiments, the binding agent is an MHC multimer that specifically binds to the marker.

[0247] In some embodiments, the marker is analyzed by detecting the presence of a nucleic acid encoding the marker, by measuring the level (amount) of a nucleic acid encoding the marker, and/or a specific cell type in which the nucleic acid encoding the marker is expressed. In some embodiments, the kit includes one or more reagents for the isolation of nucleic acids (e.g., RNA) from a sample obtained from subject.

In some embodiments, the kits further comprise a detection agent (e.g., an antibody binding to the binding agent) for detecting binding of the agent to the target (e.g., IFN γ , bacterial species) in the sample. The detection agent can be conjugated to a label. In some embodiments, the detection agent is an antibody that specifically binds to at least one of the binding agents. In some embodiments, the binding agent comprises a tag that can be identified and, directly or indirectly, bound by a detection agent.

[0248] In some embodiments, the kit may further include one or more therapeutics and/or compositions for administering to the subject. For example, in some embodiments, the kit may include one or more immune checkpoint inhibitor (e.g., PD-1 inhibitor, PD-L1 inhibitor, CTLA-4 inhibitor). In some embodiments, the kit may include a composition comprising one or more of the bacterial strains described herein.

In some embodiments, the kits may be for screening bacteria or substances derived from bacteria, for example of activation of CD8 $^{+}$ IFN γ -producing T cells. In some embodiments, the kits include cells, such as cells of a cell line. In some embodiments, the cells are intestinal epithelial cells, peripheral blood mononuclear cells.

In some embodiments, the kit or device further includes a support member. In some embodiments, the support member is a membrane, such as a nitrocellulose membrane, a polyvinylidene fluoride (PVDF) membrane, or a cellulose acetate membrane. In some examples, the immunoassay may be in a Western blot assay format or a lateral flow assay format.

[0249] In some embodiments, the support member is a multi-well plate, such as an ELISA plate. In some embodiments, the immunoassays described herein can be carried out on high throughput platforms. In some embodiments, multi-well plates, e.g., 24-, 48-, 96-, 384- or greater well plates, may be used for high throughput detection assays.

In the kit or detecting device, one or more of the binding agents may be immobilized on a support member, which can be a membrane, a bead, a slide, or a multi-well plate. Selection of an appropriate support member for the immunoassay will depend on various factor such as the number of samples and method of detecting the signal released from label conjugated to the second agent.

The kit can also comprise one or more buffers as described herein but not limited to a coating buffer, a blocking buffer, a wash buffer, and/or a stopping buffer.

[0250] In some embodiments, the kit can comprise instructions for use in accordance with any of the methods described herein. The instructions relating to the use of the kit generally include information as to the amount of each component and suitable conditions for performing the assay methods described herein. The components in the kits may be in unit doses, bulk packages (e.g., multi-dose packages), or sub-unit doses. Instructions supplied in the kits of the present disclosure are typically written instructions on a label or package insert (e.g., a paper sheet included in the kit), but machine-readable instructions (e.g., instructions carried on a magnetic or optical storage disk) are also acceptable.

The label or package insert indicates that the kit is used for evaluating the level of immune system activation, selecting a treatment, and/or diagnostic purposes. Instructions may be provided for practicing any of the methods described herein.

[0251] The kits of this present disclosure are in suitable packaging. Suitable packaging includes, but is not limited to, vials, bottles, jars, flexible packaging (e.g., sealed Mylar or plastic bags), and the like.

Kits may optionally provide additional components such as interpretive information, such as a control and/or standard or reference sample. Normally, the kit comprises a container and a label or package insert(s) on or associated with the container. In some embodiments, the present disclosure provides articles of manufacture comprising contents of the kits described above.

Table 1 below provides sequence identifier numbers (SEQ ID NOs) used in the com-

positions of the experiments disclosed herein. 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.

[0252] [Table 1]

Table 1: Strains and species with highest homology

Strain #	SEQ ID NO		Species with highest homology	NCBI accession # of 16S locus	SEQ ID of NCBI 16S locus
	Strain ID				
1	1	2G5	<i>Phascolarctobacterium faecium</i>	LN998073	27
2	2	1A6	<i>Fusobacterium ulcerans</i>	KR822463	28
3	3	1B11	<i>Bacteroides dorei</i>	CP011531	29
4	4	2G1	<i>Bacteroides uniformis</i>	NR112945	30
5	5	2B1	<i>Subdoligranulum</i> sp.	KM098109	31
6	6	2A6	<i>Paraprevotella xylaniphila</i>	NR113078	32
7	7	2F11	<i>Parabacteroides johnsonii</i>	NR041464	33
8	8	1E7	<i>Alistipes</i> sp.	LT223566	34
9	9	1H9	<i>Parabacteroides gordonii</i>	NR112835	35
10	10	1C1	<i>Eubacterium limosum</i>	NR113248	36
11	11	2G9	<i>Parabacteroides distasonis</i>	NR041342	37
12	12	2B7	<i>Bacteroides cellulosilyticus</i>	NR112933	38
13	13	2C1	<i>Bacteroides clarus</i>	NR112893	39
14	14	1B4	<i>Anaerostipes caccae</i>	HE974918	40
15	15	2A3	<i>Bacteroides salyersiae</i>	NR043016	41
16	16	2A12	<i>Bacteroides fragilis</i>	AB618791	42
17	17	1A2	<i>Bacteroides uniformis</i>	AB215083	43
18	18	2B11	<i>Bacteroides eggerthii</i>	NR112935	44
19	19	2D2	<i>Clostridium</i> sp.	AB249652	45
20	20	2E8	<i>Parabacteroides goldsteinii</i>	NR113076	46
21	21	1H8	<i>Bacteroides</i> sp.	NR112944	47
22	22	3F2	<i>Lachnospiraceae</i> bacterium HGA0140	JX519760	48
23	23	1G1	<i>Hungatella hathewayi</i>	AJ311620	49
24	24	1E6	<i>Clostridium lavalense</i>	EF564278	50
25	25	1F3	<i>Ruminococcus</i> sp.	KT156811	51
26	26	1A1	<i>Clostridium innocuum</i>	HM008265	52

[0253] The nucleic acid sequences of the 16S rDNA, or portion thereof, for the bacterial strains described herein are provided below:

SEQ ID NO:1 strain 1 2G5_*Phascolarctobacterium faecium*_LN998073 GAC-GAACGCTGGCGGCGTGCCTAACACATGCAAGTCGAACGGAGAATTTTATTT

CGGTAGAATTCTTAGTGGCGAACGGGTGAGTAACGCGTAGGCAACCTACC
 CTTTAGACGGGGACAACATTCCGAAAGGAGTGCTAATACCGGATGTGATC
 ATCTTGCCGCATGGCAGGATGAAGAAAGATGGCCTCTACAAGTAAGCTATC
 GCTAAAGGATGGGCCTGCGTCTGATTAGCTAGTTGGTAGTGTAACGGACTA
 CCAAGGCGATGATCAGTAGCCGGTCTGAGAGGATGAACGGCCACATTGGG
 ACTGAGACACGGCCCAAACCTCCTACGGGAGGCAGCAGTGGGGAATCTTCC
 GCAATGGACGAAAGTCTGACGGAGCAACGCCGCGTGAGTGATGAAGGATT
 TCGGTCTGTAAAGCTCTGTTGTTTATGACGAACGTGCAGTGTTGTGAACAAT
 GCATTGCAATGACGGTAGTAAACGAGGAAGCCACGGCTAACTACGTGCCA
 GCAGCCGCGGTAATACGTAGGTGGCGAGCGTTGTCCGGAATTATTGGGCGT
 AAAGAGCATGTAGGCGGCTTAATAAGTCGAGCGTGAAAATGCGGGGCTCA
 ACCCGTATGGCGCTGGAACTGTTAGGCTTGAGTGCAGGAGAGGAAAGG
 GGAATTCCCAGTGTAGCGGTGAAATGCGTAGATATTGGGAGGAACACCAG
 TGGCGAAGGCGCCTTTCTGGACTGTGTCTGACGCTGAGATGCGAAAGCCAG
 GGTAGCGAACGGGATTAGATACCCCGGTAGTCCTGGCCGTAAACGATGGG
 TACTAGGTGTAGGAGGTATCGACCCCTTCTGTGCCGGAGTTAACGCAATAA
 GTACCCCGCCTGGGGAGTACGGCCGCAAGGTTGAAACTCAAAGGAATTGA
 CGGGGGCCCGCACAAAGCGGTGGAGTATGTGGTTTAATTCGACGCAACGCG
 AAGAACCTTACCAAGGCTTGACATTGATTGAACGCTCTAGAGATAGAGATT
 TCCCTTCGGGGACAAGAAAACAGGTGGTGCATGGCTGTCGTCAGCTCGTGT
 CGTGAGATGTTGGGTAAAGTCCCGCAACGAGCGCAACCCCTATCCTATGTT
 ACCAGCAAGTAAAGTTGGGGACTCATGGGAGACTGCCAGGGACAACCTGG
 AGGAAGGCGGGGATGACGTCAAGTCATCATGCCCCCTTATGTCTTGGGCTAC
 ACACGTACTACAATGGTCGGAAACAGAGGGAAGCGAAGCCGCGAGGCAG
 AGCAAACCCAGAAACCCGATCTCAGTTCGGATCGCAGGCTGCAACCCGC
 CTGCGTGAAGTCGGAATCGCTAGTAATCGCAGGTCAGCATACTGCGGTGAA
 TACGTTCCCGGGCCTTGTACACACCGCCCGTCACACCACGAAAGTTGGTAA
 CACCCGAAGCCGGTGAGGTAACTA

[0254] SEQ ID NO:2 strain 2 1A6_ *Fusobacterium ulcerans*_KR822463 GATGAACGCT-
 GACAGAATGCTTAACACATGCAAGTCTACTTGATCCTTCGGGTGAAGGTGG
 CGGACGGGTGAGTAACGCGTAAAGAACTTGCCTTACAGACTGGGACAACA
 TTTGGAAACGAATGCTAATACCGGATATTATGATTGGGTGCGATGATCTGA
 TTATGAAAGCTATATGCGCTGTGAGAGAGCTTTGCGTCCCATTAGTTAGTT
 GGTGAGGTAACGGCTCACCAAGACGATGATGGGTAGCCGGCCTGAGAGGG
 TGAACGGCCACAAGGGGACTGAGACACGGCCCTTACTCCTACGGGAGGCA
 GCAGTGGGGAATATTGGACAATGGACCAAAAGTCTGATCCAGCAATTCTGT
 GTGCACGAAGAAGTTTTTCGGAATGTAAAGTGCTTTCAGTTGGGAAGAAGT
 CAGTGACGGTACCAACAGAAGAAGCGACGGCTAAATACGTGCCAGCAGCC

GCGGTAATACGTATGTCGCAAGCGTTATCCGGATTTATTGGGCGTAAAGCG
CGTCTAGGCGGCTTAGTAAGTCTGATGTGAAAATGCGGGGCTCAACCCCGT
ATTGCGTTGGAAACTGCTAAACTAGAGTACTGGAGAGGTAGGCGGAACTA
CAAGTGTAGAGGTGAAATTCGTAGATATTTGTAGGAATGCCGATGGGGAA
GCCAGCCTACTGGACAGATACTGACGCTAAAGCGCGAAAGCGTGGGTAGC
AAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGATTACTAGG
TGTTGGGGGTCGAACCTCAGCGCCCAAGCTAACGCGATAAGTAATCCGCCT
GGGGAGTACGTACGCAAGTATGAAACTCAAAGGAATTGACGGGGACCCGC
ACAAGCGGTGGAGCATGTGGTTTAATTCGACGCAACGCGAGGAACCTTAC
CAGCGTTTGACATCCCAAGAAGTTAACAGAGATGTTTTCGTGCCTCTTCGG
AGGAACTTGGTGACAGGTGGTGATGGCTGTCGTCAGCTCGTGTCGTGAGA
TGTTGGGTTAAGTCCCGCAACGAGCGCAACCCCTTTTCGTATGTTACCATCA
TTAAGTTGGGGACTCATGCGAGACTGCCTGCGATGAGCAGGAGGAAGGTG
GGGATGACGTCAAGTCATCATGCCCCTTATACGCTGGGCTACACACGTGCT
ACAATGGGTAGTACAGAGAGCTGCAAACCTGCGAGGGTAAGCTAATCTCA
TAAAACTATTCTTAGTTCGGATTGTACTCTGCAACTCGAGTACATGAAGTT
GGAATCGCTAGTAATCGCAAATCAGCTATGTTGCGGTGAATACGTTCTCGG
GTCTTGTACACACCGCCCGTCACACCACGAGAGTTGGTTGCACCTGAAGTA
ACAGGCCTAACCGTAA

[0255] SEQ ID NO:3 strain 3 1B11_Bacteroides dorei_CP011531

AGTTTGNNNTATGGCTCAGGATGAACGCTAGCTACAGGCTTAACACATGC
AAGTCGAGGGGCAGCATGGTCTTAGCTTGCTAAGGCTGATGGCGACCGGC
GCACGGGTGAGTAACACGTATCCAACCTGCCGTCTACTCTTGGCCAGCCTT
CTGAAAGGAAGATTAATCCAGGATGGGATCATGAGTTCACATGTCCGCATG
ATTAAAGGTATTTTCCGGTAGACGATGGGGATGCGTTCCATTAGATAGTAG
GCGGGGTAACGGCCACCTAGTCAACGATGGATAGGGGTTCTGAGAGGAA
GGTCCCCCACATTGGAAGTGAAGACACGGTCCAAACTCCTACGGGAGGCAG
CAGTGAGGAATATTGGTCAATGGGCGATGGCCTGAACCAGCCAAGTAGCG
TGAAGGATGACTGCCCTATGGGTTGTAACTTCTTTTATAAAGGAATAAAG
TCGGGTATGCATACCCGTTTGCATGTACTTTATGAATAAGGATCGGCTAAC
TCCGTGCCAGCAGCCGCGGTAATACGGAGGATCCGAGCGTTATCCGGATTT
ATTGGGTTTAAAGGGAGCGTAGATGGATGTTTAAGTCAGTTGTGAAAGTTT
GCGGCTCAACCGTAAAATTGCAGTTGATACTGGATGTCTTGAGTGCAGTTG
AGGCAGGCGGAATTCGTGGTGTAGCGGTGAAATGCTTAGATATCACGAAG
AACTCCGATTGCGAAGGCAGCCTGCTAAGCTGCAACTGACATTGAGGCTCG
AAAGTGTGGGTATCAAACAGGATTAGATACCCTGGTAGTCCACACGGTAA
ACGATGAATACTCGCTGTTTTCGATATACGGCAAGCGGCCAAGCGAAAGC
GTTAAGTATTCCACCTGGGGAGTACGCCGGCAACGGTGAAACTCAAAGGA

ATTGACGGGGGCCCCGCACAAGCGGAGGAACATGTGGTTTAATTCGATGAT
ACGCGAGGAACCTTACCCGGGGCTTAAATTGCACTCGAATGATCCGGAAAC
GGTTCAGCTAGCAATAGCGAGTGTGAAGGTGCTGCATGGTTGTCGTCAGCT
CGTGCCGTGAGGTGTCGGCTTAAGTGCCATAACGAGCGCAACCCTTGTTGT
CAGTTACTAACAGGTGATGCTGAGGACTCTGACAAGACTGCCATCGTAAGA
TGTGAGGAAGGTGGGGATGACGTCAAATCAGCACGGGCCCTTACGTCCGGG
GCTACACACGTGTTACAATGGGGGGTACAGAGGGCCGCTACCACGCGAGT
GGATGCCAATCCCTAAAACCCCTCTCAGTTCGGACTGGAGTCTGCAACCCG
ACTCCACGAAGCTGGATTCGCTAGTAATCGCGCATCAGCCACGGCGCGGTG
AATACGTTCCCGGGCCTTGTACACACCGCCCGTCAAGCCATGGGAGCCGGG
GGTACCTGAAGTGCGTAACCGCGAGGAT

[0256] SEQ ID NO:4 strain 4 2G1_Bacteroides uniformis_NR_112945 GATGAACGC-
TAGCTACAGGCTTAACACATGCAAGTCGAGGGGCAGCATGAACTTAGCTTG
CTAAGTTTGATGGCGACCGGCGCACGGGTGAGTAACACGTATCCAACCTGC
CGATGACTCGGGGATAGCCTTTCGAAAGAAAGATTAATACCCGATGGCAT
AGTTCTTCCGCATGGTAGAACTATTAAGAATTTTCGGTCATCGATGGGGAT
GCGTTCCATTAGGTTGTTGGCGGGGTAAACGGCCACCAAGCCTTCGATGGA
TAGGGGTTCTGAGAGGAAGGTCCCCCACATTGGAAGTGAACACGGTCCA
AACTCCTACGGGAGGCAGCAGTGAGGAATATTGGTCAATGGACGAGAGTC
TGAACCAGCCAAGTAGCGTGAAGGATGACTGCCCTATGGGTTGTAAACTTC
TTTTATACGGGAATAAAGTGAGGCACGTGTGCCTTTTTGTATGTACCGTAT
GAATAAGGATCGGCTAACTCCGTGCCAGCAGCCGCGGTAATACGGAGGAT
CCGAGCGTTATCCGGATTTATTGGGTTTAAAGGGAGCGTAGGCGGACGCTT
AAGTCAGTTGTGAAAGTTTGCGGCTCAACCGTAAAATTGCAGTTGATACTG
GGTGTCTTGAGTACAGTAGAGGCAGGCGGAATTCGTGGTGTAGCGGTGAA
ATGCTTAGATATCACGAAGAAGTCCGATTGCGAAGGCAGCCTGCTGGACTG
TAACTGACGCTGATGCTCGAAAGTGTGGGTATCAAACAGGATTAGATACCC
TGGTAGTCCACACCAGTAAACGATGAATACTCGCTGTTTTCGATATACAGT
AAGCGGCCAAGCGAAAGCGTTAAGTATTCCACCTGGGGAGTACGCCGGCA
ACGGTGAAACTCAAAGGAATTGACGGGGGGCCCCGCACAAGCGGAGGAACAT
GTGGTTTAATTCGATGATACGCGAGGAACCTTACCCGGGCTTGAATTGCAA
CTGAATGATGTGGAGACATGTCAGCCGCAAGGCAGTTGTGAAGGTGCTGC
ATGGTTGTCGTCAGCTCGTGCCGTGAGGTGTCGGCTTAAGTGCCATAACGA
GCGCAACCCTTATCGATAGTTACCATCAGGTGATGCTGGGGACTCTGTGCA
GACTGCCGTCGTAAGATGTGAGGAAGGTGGGGATGACGTCAAATCAGCAC
GGCCCTTACGTCCGGGGGCTACACACGTGTTACAATGGGGGGTACAGAAGG
CAGCTACACGGCGACGTGATGCTAATCCCGAAAGCCTCTCTCAGTTCGGAT
TGGAGTCTGCAACCCGACTCCATGAAGCTGGATTCGCTAGTAATCGCGCAT

CAGCCACGGCGCGGTGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCA
AGCCATGAAAGCCGGGGGTACCTGAAGTGCCTAACCGCAAGGAG

[0257] SEQ ID NO:5 strain 5

2B1_ Subdoligranulum sp. 4_3_54A2FAA_NZ-ACWW00000000 GAC-
GAACGCTGGCGGCGCGCCTAACACATGCAAGTCGAACGGAGCTGTTTTCTC
TGAAGTTTTCGGATGGAAGAGAGTTTCAGCTTAGTGCGCAACGGGTGAGTA
ACACGTGAGCAACCTGCCTTTCAGTGGGGGACAACATTTGGAAACGAATG
CTAATACCGCATAAGACCACAGTGTCTGCATGGCACAGGGGTCAAAGGATT
TATCCGCTGAAAGATGGGCTCGCGTCCGATTAGCTAGATGGTGAGGTAACG
GCCCACCATGGCGACGATCGGTAGCCGGACTGAGAGGTTGAACGGCCACA
TTGGGACTGAGACACGGCCCAGACTCCTACGGGAGGCAGCAGTGGGGAAT
ATTGCACAATGGGGGAAACCCTGATGCAGCGACGCCGCGTGGAGGAAGAA
GGTCTTCGGATTGTAAACTCCTGTCCCAGGGGACGATAATGACGGTACCCT
GGGAGGAAGCACCGGCTAACTACGTGCCAGCAGCCGCGGTAAAACGTAGG
GTGCAAGCGTTGTCCGGAATTACTGGGTGTAAAGGGAGCGCAGGCGGATT
GGCAAGTTGGGAGTGAAATCTATGGGCTCAACCCATAAATTGCTTTCAAAA
CTGTCAGTCTTGAGTGGTGTAGAGGTAGGCGGAATTCCCGGTGTAGCGGTG
GAATGCGTAGATATCGGGAGGAACACCAGTGGCGAAGGCGGCCTACTGGG
CACTAACTGACGCTGAGGCTCGAAAGCATGGGTAGCAAACAGGATTAGAT
ACCCTGGTAGTCCATGCCGTAAACGATGATTACTAGGTGTGGGAGGATTGA
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[0258] SEQ ID NO:6 strain 6 2A6_Paraprevotella xylaniphila_AB331897 GATGAACGC-
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[0259] SEQ ID NO:7 strain 7 2F11_Parabacteroides johnsonii_AB261128 GATGAACGC-
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[0260] SEQ ID NO:8 strain 8 1E7_Alistipes sp. JC136_NZ-CAEG00000000 GAT-
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[0261] SEQ ID NO:9 strain 9 1H9_Parabacteroides gordonii_AB470343 GATGAACGC-
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[0262] SEQ ID NO:10 strain 10 1C1_Eubacterium limosum_AB595134 GAC-
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[0263] SEQ ID NO:11 strain 11 2G9_Parabacteroides distasonis_HE974920 GAT-
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[0264] SEQ ID NO:12 strain 12 2B7_Bacteroides cellulosilyticus_NR_112933 GAT-
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[0265] SEQ ID NO:13 strain 13 2C1_Bacteroides clarus_AB490801 GATGAACGCTAGC-
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[0266] SEQ ID NO:14 strain 14 1B4_Anaerostipes sp. 3_2_56FAA_NZ-ACWB00000000

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[0267] SEQ ID NO:15 strain 15 2A3_Bacteroides salyersiae_AY608696 GATGAACGC-
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[0268] SEQ ID NO:16 strain 16 2A12_Bacteroides fragilis_CR626927 GATGAACGC-
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GCAGCTAACGGGTGACCGTATGCTAATCCCAAAAGCCTCTCTCAGTTCGGA
TCGAAGTCTGCAACCCGACTTCGTGAAGCTGGATTTCGCTAGTAATCGCGCA
TCAGCCACGGCGCGGTGAATACGTTCCCGGGCCTTGTACACACCGCCCGTC

AAGCCATGGGAGCCGGGGGTACCTGAAGTACGTAACCGCAA

[0269] SEQ ID NO:17 strain 17 1A2_Bacteroides uniformis_AB247141 GATGAACGC-
TAGCTACAGGCTTAACACATGCAAGTCGAGGGGCATCAGGAAGAAAGCTT
GCTTTCTTTGCTGGCGACCGGCGCACGGGTGAGTAACACGTATCCAACCTG
CCGATGACTCGGGGATAGCCTTTTCGAAAGAAAGATTAATACCCGATGGTAT
ATCTGAAAGGCATCTTTTCAGCTATTAAGAATTTTCGGTCATTGATGGGGAT
GCGTTCCATTAGGTTGTTGGCGGGGTAAACGGCCACCAAGCCATCGATGGA
TAGGGGTTCTGAGAGGAAGGTCCCCACATTGGAAGTACGACACGGTCCA
AACTCCTACGGGAGGCAGCAGTGAGGAATATTGGTCAATGGACGAGAGTC
TGAACCAGCCAAGTAGCGTGAAGGATGACTGCCCTATGGGTTGTAAACTTC
TTTTATACGGGAATAAAGTTAGGCACGTGTGCCTTTTTGTATGTACCGTATG
AATAAGGATCGGCTAACTCCGTGCCAGCAGCCGCGGTAATACGGAGGATC
CGAGCGTTATCCGGATTTATTGGGTTTAAAGGGAGCGTAGGCGGATGCTTA
AGTCAGTTGTGAAAGTTTGCGGCTCAACCGTAAAATTGCAGTTGATACTGG
GTGTCTTGAGTACAGTAGAGGCAGGCGGAATTCGTGGTGTAGCGGTGAAA
TGCTTAGATATCACGAAGAACTCCGATTGCGAAGGCAGCTTGCTGGACTGT
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GCGGCCAAGCGAAAGCGTTAAGTATTCCACCTGGGGAGTACGCCGGCAAC
GGTGAAACTCAAAGGAATTGACGGGGGGCCCGCACAAAGCGGAGGAACATGT
GGTTTAATTCGATGATACGCGAGGAACCTTACCCGGGCTTAAATTGCAAAT
GAATGTTCTGGAAACAGATCAGCCGCAAGGCATTTGTGAAGGTGCTGCATG
GTTGTCGTCAGCTCGTGCCGTGAGGTGTGCGCTTAAGTGCCATAACGAGCG
CAACCCTTATCGATAGTTACCATCAGGTTATGCTGGGGACTCTGTGCGAGAC
TGCCGTCGTAAGATGTGAGGAAGGTGGGGATGACGTCAAATCAGCACGGC
CCTTACGTCCGGGGCTACACACGTGTTACAATGGGGGGTACAGAAGGCAG
CTACACGGCGACGTGATGCTAATCCCTAAAACCTCTCTCAGTTCGGATTGG
AGTCTGCAACCCGACTCCATGAAGCTGGATTGCTAGTAATCGCGCATCAG
CCACGGCGCGGTGAATACGTTCCCGGGCCTTGTAACACACCGCCCGTCAAGC
CATGAAAGCCGGGGGTACCTGAAGTGCGT

[0270] SEQ ID NO:18 strain 18 2B11_Bacteroides eggerthii_NR_112935 GATGAACGC-
TAGCTACAGGCTTAACACATGCAAGTCGAGGGGCAGCATGATTGAAGCTT
GCTTCAATCGATGGCGACCGGCGCACGGGTGAGTAACACGTATCCAACCTG
CCGATAACTCGGGGATAGCCTTTTCGAAAGAAAGATTAATACCCGATAGCAT
AGTATTTCCGCATGGTTTCACTATTAAGAATTTTCGGTTATCGATGGGGAT
GCGTTCCNTTAGATAGTTGGCGGGGTAAACGGCCACCAAGTCAACGATGG
ATAGGGGTTCTGAGAGGAAGGTCCCCACATTGGAAGTACGACACGGTCC
AACTCCTACGGGAGGCAGCAGTGAGGAATATTGGTCAATGGACGAGAGT

CTGAACCAGCCAAGTAGCGTGAAGGATGACTGCCCTATGGGTTGTAACTT
CTTTTATACGGGAATAAAGTGGAGTATGCATACTCCTTTGTATGTACCGTAT
GAATAAGGATCGGCTAACTCCGTGCCAGCAGCCGCGGTAATACGGAGGAT
CCGAGCGTTATCCGGATTTATTGGGTTTAAAGGGAGCGTAGGCGGGTGCTT
AAGTCAGTTGTGAAAGTTTGCGGCTCAACCGTAAAATTGCAGTTGATACTG
GGCGCCTTGAGTGCAGCATAGGTAGGCGGAATTCGTGGTGTAGCGGTGAA
ATGCTTAGATATCACGAAGAACTCCGATTGCGAAGGCAGCTTACTGGACTG
TAACTGACGCTGATGCTCGAAAGTGTGGGTATCAAACAGGATTAGATACCC
TGGTAGTCCACACAGTAAACGATGAATACTCGCTGTTGGCGATACACAGTC
AGCGGCCAAGCGAAAGCATTAAAGTATTCCACCTGGGGAGTACGCCGGCAA
CGGTGAAACTCAAAGGAATTGACGGGGGCCCCGCACAAGCGGAGGAACATG
TGTTTAAATTCGATGATACGCGAGGAACCTTACCCGGGCTTAAATTGCAGC
GGAATGTAGTGGAAACATTACAGCCTTCGGGCCGCTGTGAAGGTGCTGCAT
GGTTGTCGTCAGCTCGTGCCGTGAGGTGTCGGCTTAAGTGCCATAACGAGC
GCAACCCTTATCTATAGTTACTATCAGGTCATGCTGAGGACTCTATGGAGA
CTGCCGTCGTAAGATGTGAGGAAGGTGGGGATGACGTCAAATCAGCACGG
CCCTTACGTCCGGGGCTACACACGTGTTACAATGGGGGGGTACAGAAGGCA
GCTACCTGGCGACAGGATGCTAATCCCTAAAACCTCTCTCAGTTCGGATTG
GAGTCTGCAACCCGACTCCATGAAGCTGGATTTCGCTAGTAATCGCGCATCA
GCCACGGCGCGGTGAATACGTTCCCGGGCCTTGTACACACCGCCCGTCAAG
CCATGAAAGCCGGGGGTACCTGAAGTACGTAACCGCAAGGAGC

[0271] SEQ ID NO:19 strain 19 2D2_Clostridium sp. TM-40_AB249652 GAT-

GAACGCTGGCGGCGTGCCTAATACATGCAAGTCGGACGCAATGCTTCGGC
ATTGAGTGGCGAACGGGTGAGTAATACATAAGCAACCTGCCCCCTGTGAGG
GGGATAACTGCTGGAAACGGCAGCTAAGACCGCATATGCATACATGACGC
ATGTCGAGTATGTTAAATATCCCACGGGATAGCACAGGGATGGGCTTATGA
CGCATTAGCTAGCTGGTGAGGTAGAGGCTCACCAGGGCGACGATGCGTAG
CCGGCCTGAGAGGGTGGACGGCCACACTGGGACTGAGACACGGCCCAGAC
TCCTACGGGAGGCAGCAGTAGGGAATTTTCGGCAATGGGCGAAAGCCTGA
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ATAAAGGAAGAACGGCGCCTGTAGGGAATGACAGGCGAGTGACGGTACTT
TATGAGGAAGCCACGGCTAACTACGTGCCAGCAGCCGCGGTAATACGTAG
GTGGCGAGCGTTATCCGGAATCATTGGGCGTAAAGAGGGAGCAGGCGGCA
GTGCAGGTCTGCGGTGAAAGCCCGAAGCTAACTTCGGTAAGCCGTGGAA
ACCGCACAGCTAGAGAGCATCAGAGGATCGCGGAATTCATGTGTAGCGG
TGAAATGCGTAGATATATGGAGGAACACCAGTGGCGAAGGCGGCGGTCTG
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ATACCCTAGTAGTCCACGCCGTAAACGATGAGTGCTAAGTGTTGGGGGTCA

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TGCATGGTTGTCGTCAGCTCGTGTCGTGAGATGTTGGGTAAAGTCCCGCAA
CGAGCGCAACCCCTGTTGCCAGTTGCCAGCATTAGGTGGGGACTCTGGCG
AGACTGCCTCTGCAAGGAGGAGGAAGGCGGGGATGACGTCAAATCATCAT
GCCCCCTTATGACCTGGGCTACACACGTGCTACAATGGACGGATCAGAGGG
AGGCGAAGCCGCGAGGTGGAGCGAAACCCAGAAACCCGTTTCACAGTTCGG
ACTGCAGTCTGCAACTCGACTGCACGAAGCTGGAATCGCTAGTAATCGCGA
ATCAGCATGTGCGCGGTGAATACGTTCTCGGGCCTTGTACACACCGCCCGTC
ACACCATGAGAGTTGGTAACACCCGAAGCCGGTGGCCCAACCGCAA

[0272] SEQ ID NO:20 strain 20 2E8_Parabacteroides goldsteinii_NR_113076 GAT-
GAACGCTAGCGACAGGCTTAACACATGCAAGTCGAGGGGGCAGCACGATGT
AGCAATACATTGGTGGCGACCGGCGCACGGGTGAGTAACGCGTATGCAAC
CTACCTATCAGAGGGGAATAACCCGGCGAAAGTCGGACTAATACCGCATA
AAACAGGGGTTCACATGGAAATATTTGTTAAAGAATTATCGCTGATAGAT
GGGCATGCGTTCCATTAGATAGTTGGTGAGGTAACGGCTCACCAAGTCCAC
GATGGATAGGGGTCTGAGAGGAAGGTCCCCCACACTGGTACTGAGACAC
GGACCAGACTCCTACGGGAGGCAGCAGTGAGGAATATTGGTCAATGGGCG
AGAGCCTGAACCAGCCAAGTCGCGTGAAGGATGAAGGATCTATGGTTTGT
AACTTCTTTTATATGGGAATAAAGTGAGGAACGTGTTTCTTTTGTATGTA
CCATATGAATAAGCATCGGCTAACTCCGTGCCAGCAGCCGCGGTAATACGG
AGGATGCGAGCGTTATCCGGATTTATTGGGTTTAAAGGGTGCGTAGGTGGT
TAATTAAGTCAGCGGTGAAAGTTTGTGGCTCAACCATAAAATTGCCGTTGA
AACTGGTTGACTTGAGTATATTTGAGGTAGGCGGAATGCGTGGTGTAGCGG
TGAAATGCATAGATATCACGCAGAACTCCGATTGCGAAGGCAGCTTACTAA
ACTATAACTGACACTGAAGCACGAAAGCGTGGGGATCAAACAGGATTAGA
TACCCTGGTAGTCCACGCAGTAAACGATGATTACTAGCTGTTTTCGATACA
CAGTAAGCGGCACAGCGAAAGCGTTAAGTAATCCACCTGGGGAGTACGCC
GGCAACGGTGAAACTCAAAGGAATTGACGGGGGGCCCGCACAAAGCGGAGG
AACATGTGGTTTAATTCGATGATACGCGAGGAACCTTACCCGGGTTTGAAC
GCATATTGACAGCTCTGGAAACAGAGTCTCTAGTAATAGCAATTTGCGAGG
TGCTGCATGGTTGTCGTCAGCTCGTGCCGTGAGGTGTCGGCTTAAGTGCCA
TAACGAGCGCAACCCCTTATCACTAGTTACTAACAGGTCATGCTGAGGACTC
TAGTGAGACTGCCAGCGTAAGCTGTGAGGAAGGTGGGGATGACGTCAAAT
CAGCACGGCCCTTACATCCGGGGCGACACACGTGTTACAATGGTGGGGAC
AAAGGGCAGCTACCGTGTGAGCGGATGCAAATCTCCAAACCCCATCTCAGT

TCGGATCGAAGTCTGCAACCCGACTTCGTGAAGCTGGATTCGCTAGTAATC
GCGCATCAGCCATGGCGCGGTGAATACGTTCCCGGGCCTTGTACACACCGC
CCGTCAAGCCATGGGAGTTGGGGGTACCTAAAGTCCGTAACCGC

[0273] SEQ ID NO:21 strain 21 1H8_Bacteroides sp. AR29_AF139525 GATGAACGC-
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TGCCGATAACTCGGGGATAGCCTTTTCGAAAGAAAGATTAATACCCGATGGT
ATAATNAGACCGCATGGTCTTGTTATTAAAGAATTTTCGGTTATCGATGGGG
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AATGCTTAGATATCACGAAGAACTCCGATTGCGAAGGCAGCTCACTGGACT
GCAACTGACACTGATGCTCGAAAGTGTGGGTATCAAACAGGATTAGATAC
CCTGGTAGTCCACACAGTAAACGATGAATACTCGCTGTTTGCGATATACAG
TAAGCGGCCAAGCGAAAGCATTAAAGTATTCCACCTGGGGAGTACGCCGGC
AACGGTGAAACTCAAAGGAATTGACGGGGGGCCCGCACAAGCGGAGGAAC
ATGTGGTTTAATTCGATGATACGCGAGGAACCTTACCCGGGCTTAAATTGC
ATTTGAATATATTGGAAACAGTATAGCCGTAAGGCAAATGTGAAGGTGCTG
CATGGTTGTCGTCAGCTCGTGCCGTGAGGTGTCGGCTTAAGTGCCATAACG
AGCGCAACCCTTATCTTTAGTTACTAACAGGTCATGCTGAGGACTCTAGAG
AGACTGCCGTCGTAAGATGTGA

[0274] SEQ ID NO:22 strain 22 >3F2-PREMIX.fasta

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ATTTCAANTTGACTGAGTGGCGGACGGGTGAGTAACGCGTGGGTAACCTGC
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CACAGNNCCGCATGGTGCAGGGGTAAAAACTCCGGTGGTATGGGATGGAC
CCGCGTCTGATTAGCTTGTTGGCGGGGTAAACGGCCACCAAGGCGACGATC
AGTAGCCGACCTGAGAGGGTGACCGGCCACATTGGGACTGAGACACGGCC
CAAACCTCCTACGGGAGGCAGCAGTGGGGAATATTGCACAATGGGGGAAAC
CCTGATGCAGCGACGCCGCGTGAGTGATGAAGTATTTTCGGTATGTAAAGCT
CTATCAGCAGGGAAGAAAATGACGGTACCTGACTAAGAAGCCCCGGCTAA
CTACGTGCCAGCAGCCGCGGTAATACGTAGGGGGCAAGCGTTATCCGGATT

TACTGGGTGTAAAGGGAGCGTAGACGGCTGTGCAAGTCTGGAGTGAAAGC
CCGGGGCTCAACCCCGGGACTGCTTTGGAAACTGTACGGCTGGAGTGCTGG
AGAGGCAAGCGGAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGA
GGAACACCAGTGGCGAAGGCGGCTTGCTGGACAGTAACTGACGTTGAGGC
TCGAAAGCGTGGGGAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCG
TAAACGATGAATGCTAGGTGTCGGGGAGCAAAGCTCTTCGGTGCCGCCGC
AAACGCAATAAGCATTCCACCTGGGGAGTACGTTGCAAGAATGAACTC
AAAGGANTTGACGGGGACCGCACANNGGTGGAGCATGTGGTTATTCGAGC
ACGCGAAANCTTACCAGTCTTGNNNNCCCCTGANGNNNNGTATGTCGCTNCT
NNGNNNNNGN

[0275] SEQ ID NO:23 strain 23 >1G1_3-PREMIX.fasta

AGTTTGATTATGGCTCAGGATGAACGCTGGCGGCGTGCTTAACACATGCA
AGTCGAGCGAAGCGGTTTCAATGAAGTTTTTCGGATGGATTTGAAATTGACT
TAGCGGCGGACGGGTGAGTAACGCGTGGGTAACTGCCTTACACTGGGGG
ATAACAGTTAGAAATGACTGCTAATACCGCATAAGCGCACAGGGCCGCAT
GGTCCGGTGTGAAAACTCCGGTGGTGTAAAGATGGACCCGCGTCTGATTAG
GTAGTTGGCGGGGTAAACGGCCACCAAGCCGACGATCAGTAGCCGACCTG
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CGCCGCGTGAGTGAAGAAGTATTTTCGGTATGTAAAGCTCTATCAGCAGGGA
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GGGAGCGTAGACGGTTTAGCAAGTCTGAAGTGAAAGCCCCGGGGCTCAACC
CCGGTACTGCTTTGGAAACTGTTAGACTTGAGTGCAGGAGAGGTAAAGTGA
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GAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAATA
CTAGGTGTCGGGGGGCAAAGCCCTTCGGTGCCGCCGCAAACGCAATAAGT
ATTCCACCTGGGGAGTACGTTGCAAGAATGAACTCAAAGGAATTGACG
GGGACCCGCACAAGCGGTGGAGCATGTGGTTTAATTCGAAGCAACGCGAA
GAACCTTACCAAGTCTTGACATCCCACTGAAAACACTTTAACCGGTGTCCC
TCTTCGGAGCAGTGGAGACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCG
TGAGATGTTGGGTAAAGTCCCGCAACGAGCGCAACCCTTATCCTTAGTAGC
CAGCGAGTAGAGTCGGGCACTCTGGGGAGACTGCCAGGGATAACCTGGAG
GAAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGATTTGGGCTACAC
ACGTGCTACAATGGCGTAAACAAAGGGAGGCAAAGGAGCGATCTGGAGCA
AACCCCAAAAATAACGTCTCAGTTCGGATTGCAGGCTGCAACTCGCCTGCA
TGAAGCTGGAATCGCTAGTAATCGCGAATCAGAATGTCGCGGTGAATACGT

TCCCGGGTCTTGTACACACCGCCCGTCACACCATGGGAGTTGGTAACGCCC
GAAGTCAGTGACCCAACCGCAAGGAGGNAGCTGCCGAANNNNNNN

[0276] SEQ ID NO:24 strain 24 >1E6_27Fmod-PREMIX_Length_957

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GAGTGGCGGACGGGTGAGTAACACGTGGATAACCTGCCTCACACTGGGGG
ACAACAGTTAGAAATGACTGCTAATACCGCATAAGCGCACAGTACCGCAT
GGTACAGTGTGAAAACTCCGGTGGTGTGAGATGGATCCGCGTCTGATTAG
CCAGTTGGCGGGGTAAACGGCCCAACAAAGCGACGATCAGTAGCCGACCTG
AGAGGGTGACCGGCCACATTGGGACTGAGACACGGCCCAAACCTCCTACGG
GAGGCAGCAGTGGGGAATATTGCACAATGGGCGAAAGCCTGATGCAGCGA
CGCCGCGTGAGTGAAGAAGTATTTTCGGTATGTAAAGCTCTATCAGCAGGGA
AGATAATGACGGTACCTGACTAAGAAGCCCCGGCTAACTACGTGCCAGCA
GCCGCGGTAATACGTAGGGGGGCAAGCGTTATCCGGATTTACTGGGTGTAAA
GGGAGCGTAGACGGCATGGCAAGTCTGAAGTGAAAACCCAGGGCTCAACC
CTGGGACTGCTTTGGAAACTGTCAAGCTAGAGTGCAGGAGAGGTAAGTGG
AATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGTG
GCGAAGGCGGCTTACTGGACTGTAACGTGACGTTGAGGCTCGAAAGCGTGG
GGAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAGT
GCTAGGTGTTGGGGGGCAAAGCCCTTCGGTGCCGTCGCAAACGCAATAAG
CACTCCACCTGGGGAGTACGTTTCGCAAGAATGAAACTCAAAGGAATTGAC
GGGGACCCGCACAAGCGGTGGAGCATGTGGTTTAATTCGAAGCAACGCGA
AGAACCTTACCAAGTCTTGACATCCTCTTGACCGGCGTGTAACGGCGCCTT
TCCTTCGGGACAAGAGAGACAGGTGGTGCATGGTTGTCTGTCAGCTCGTGTC
GTGAGATGTTGGGTAAAGTCCCGCAACGAGCGCAACCCTTATCCTTAGTAG
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AAGGTGGGGATGACGTCAAATCATCATGCCCCTTATGATTTGGGCTACACA
CGTGCTACAATGGCGTAAACAAAGGGAAGCGACCCTGCGAAGGTGAGCAA
ATCTCAAAAATAACGTCCCAGTTCGGACTGTAGTCTGCAACCCGACTACAC
GAAGCNNGAATCGCTAGTAATCGCGAATCAGAATGTCGCGGTGAATACGN
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[0277] SEQ ID NO:25 strain 25 >1F3_27Fmod-PREMIX.fasta

AGTTTGANNTTGGCTCAGGATGAACGCTGGCGGCGTGCCTAACACATGCA
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TGAGCGGCGGACGGGTGAGTAACGCGTGGGCAACCTGCCTCATAAGGGG
GATAACAGTTAGAAATGACTGCTAATACCGCATAAGCGCACAGGACCGCA
TGGTGTAGTGTGAAAACTCCGGTGGTATGAGATGGACCCGCGTCTGATTA

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AAGAAGATGACGGTACCTGAGTAAGAAGCACCGGCTAAATACGTGCCAGC
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AGGGAGCGTAGACGGATAGGCAAGTCTGGAGTGAAAACCCAGGGCTCAAC
TCTGGGACTGCTTTGGAACTGCAGATCTGGAGTGCCGGAGAGGTAAGCG
GAATTCCTAGTGTAGCGGTGAAATGCGTAGATATTAGGAGGAACACCAGT
GGCGAAGGCGGCTTACTGGACGGTGACTGACGTTGAGGCTCGAAAGCGTG
GGGAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAC
TACTAGGTGTCGGTGTGCAAAGCACATCGGTGCCGCAGCAAACGCAATAA
GTAGTCCACCTGGGGAGTACGTTTCGCAAGAATGAACTCAAAGGAATTGA
CGGGGACCCGCACAAGCGGTGGAGCATGTGGTTTAATTCGAAGCAACGCG
AAGAACCTTACCTGGTCTTGACATCCGGATGACGGGCGAGTAATGTCGCCG
TCCCTTCGGGGCATCCGAGACAGGTGGTGATGGTTGTCGTCAGCTCGTGT
CGTGAGATGTTGGGTAAAGTCCCGCAACGAGCGCAACCCTTATCTTCAGTA
GCCAGCATATAAGGTGGGCACTCTGGAGAGACTGCCAGGGAGAACCTGGA
GGAAGGTGGGGATGACGTCAAATCATCATGCCCCCTTATGGCCAGGGCTAC
ACACGTGCTACAATGGCGTAAACAAAGGGAAGCGAGAGGGTGACCTGAAG
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[0278] SEQ ID NO:26 strain 26 1A1_27Fmod-PREMIX_Length_998

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GAAACGGTAGCTAAAACCGGATAGGTATACAGAGCGCATGCTCAGTATAT
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GGCAGCAGTAGGGAATTTTCGTCAATGGGGGAAACCCTGAACGAGCAATG
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CACTGAGGCACGAAAGCGTGGGGAGCAAATAGGATTAGATACCCTAGTAG
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AACCGGAGGAAGGTGGGGATGACGTCAAATCATCATGCCCCCTTATGGCCT
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TCGACTTCATGAAGTCGGAATCGCTAGTAATCGCAGATCAGCATGCTGCGG
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- [0279] SEQ ID NO:27 16S RNA sequence corresponding to LN998073
SEQ ID NO:28 16S RNA sequence corresponding to KR822463
SEQ ID NO:29 16S RNA sequence corresponding to CP011531
SEQ ID NO:30 16S RNA sequence corresponding to NR112945
SEQ ID NO:31 16S RNA sequence corresponding to KM098109
SEQ ID NO:32 16S RNA sequence corresponding to NR113078
SEQ ID NO:33 16S RNA sequence corresponding to NR041464
SEQ ID NO:34 16S RNA sequence corresponding to LT223566
SEQ ID NO:35 16S RNA sequence corresponding to NR112835
SEQ ID NO:36 16S RNA sequence corresponding to NR113248
SEQ ID NO:37 16S RNA sequence corresponding to NR041342
SEQ ID NO:38 16S RNA sequence corresponding to NR112933
SEQ ID NO:39 16S RNA sequence corresponding to NR112893
SEQ ID NO:40 16S RNA sequence corresponding to HE974918
SEQ ID NO:41 16S RNA sequence corresponding to NR043016
SEQ ID NO:42 16S RNA sequence corresponding to AB618791
SEQ ID NO:43 16S RNA sequence corresponding to AB215083
SEQ ID NO:44 16S RNA sequence corresponding to NR112935
SEQ ID NO:45 16S RNA sequence corresponding to AB249652
SEQ ID NO:46 16S RNA sequence corresponding to NR113076
SEQ ID NO:47 16S RNA sequence corresponding to NR112944
SEQ ID NO:48 16S RNA sequence corresponding to JX519760

SEQ ID NO:49 16S RNA sequence corresponding to AJ311620

SEQ ID NO:50 16S RNA sequence corresponding to EF564278

SEQ ID NO:51 16S RNA sequence corresponding to KT156811

SEQ ID NO:52 16S RNA sequence corresponding to HM008265

[0280] Additional sequences of interest are provided below:

SEQ ID NO:54 H81A6_16S_ribosomal_RNA

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GCTGTGAGAGAGCTTTGCGTCCCATTAGTTAGTTGGTGAGGTAACGGCTCA
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CGCAAGCGTTATCCGGATTTATTGGGCGTAAAGCGCGTCTAGGCGGCTTAG
TAAGTCTGATGTGAAAATGCGGGGCTCAACCCCGTATTGCGTTGGAACTG
CTAAACTAGAGTACTGGAGAGGTAGGCGGAACTACAAGTGTAGAGGTGAA
ATTCGTAGATATTTGTAGGAATGCCGATGGGGAAGCCAGCCTACTGGACAG
ATACTGACGCTAAAGCGCGAAAGCGTGGGTAGCAAACAGGATTAGATACC
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[0281] SEQ ID NO:55 H82F11_16S_ribosomal_RNA

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[0282] SEQ ID NO:56 H82A6_16S_ribosomal_RNA

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[0283] SEQ ID NO:57 H82G9_16S_ribosomal_RNA

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[0284] SEQ ID NO:58 H81E7_16S_ribosomal_RNA

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[0285] SEQ ID NO:59 H81C1_16S_ribosomal_RNA

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[0286] SEQ ID NO:60 H81B11_16S_ribosomal_RNA

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[0287] SEQ ID NO:61 H81H9_16S_ribosomal_RNA

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[0288] SEQ ID NO:62 H82B1_16S_ribosomal_RNA

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[0289] SEQ ID NO:63 H82G1_16S_ribosomal_RNA

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[0290] SEQ ID NO:64 H82G5_16S_ribosomal_RNA

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 CTATTAGGAGCCAGCCGTCTAAGGTGGGGCCGATGATTGGGGTGAAGTCGT
 AACAAGGTAGCCGTATCGGAAGGTGCGGCTGGATCACCTCCTTT

[0291] The invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments and of being practiced or of being carried out in various ways. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. 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.

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 shall 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.

[0292] The present invention is further illustrated by the following Examples, which in no way should be construed as further limiting. The entire contents of all of the references (including literature references, issued patents, published patent applications, and co-pending patent applications) cited throughout this application are hereby expressly incorporated by reference, in particular for the teaching that is referenced hereinabove. However, the citation of any reference is not intended to be an admission that the reference is prior art.

Examples

[0293] Example 1: Identification of a CD8⁺ T-cell inducing bacterial cocktail

C57BL/6 mice kept under specific-pathogen free (SPF) conditions which possess resident microbiota have abundant IFN γ +CD8⁺ T-cells, whereas markedly few IFN γ +CD8⁺ T-cells were found in intestinal lamina propria of germ free mice (See Figure 1). This indicates that gut microbiota induces the accumulation of IFN γ +CD8⁺ T-cells. A subset of IFN γ +CD8⁺ T cells also expressed CD103 as well as GranzymeB (see Figure 2A), suggesting that the subset was tissue-resident memory T cells. Figure 3A shows that remarkably small numbers of IFN γ +CD8⁺ T-cells were found in SPF C57BL/6 mice purchased from Charles River Laboratories Inc. and Japan SLC Inc. as compared to SPF C57BL/6 mice purchased from CLEA Japan Inc. and mice bred in RIKEN. When SPF C57BL/6 mice from Charles River Laboratories Inc. were co-housed together with CLEA mice in the same cage, an increase of IFN γ +CD8⁺ T-cells was observed in mice delivered from Charles River Laboratories Inc. (Figures 4A and 4B). This finding strongly supports a hypothesis that there are specific microbial species in the mouse microbiota which induce and accumulate IFN γ +CD8⁺ T cells in the intestine.

[0294] Next, it was investigated whether the human gut microbiota contained microbes which were able to induce IFN γ +CD8⁺ T cells. Stool samples were collected from six healthy human volunteers (A~F). The samples were individually administered orally into germ free C57BL/6 mice kept in sterile isolators (five or six mice per group). Four weeks after oral inoculation of stool samples, mice were sacrificed, and small intestine and colons were harvested and investigated for IFN γ +CD8⁺ T-cells by FACS.

As shown in Figures 5A and 5B, colonic IFN γ +CD8⁺ T-cells were most remarkably induced in mice inoculated with a stool sample collected from donor B. Among mice inoculated with the donor B stool sample, we selected a mouse that exhibited the highest frequency of IFN γ +CD8⁺ T cells (called 'mouse B#5' hereafter). In order to concentrate microbes responsible for IFN γ +CD8⁺ T cell induction, cecal contents were collected from the mouse B#5 and inoculated into another germ-free mouse. The mice were then orally administrated drinking water with or without Ampicillin, Metronidazole, Streptomycin or Tylosin (five mice per group). Alternatively, cecal contents of mouse B#5 were treated with 3% chloroform and orally inoculated into another five germ-free mice ('B#5+Chrolo'). Figures 6A and 6B show that Ampicillin treatment enhanced induction of colonic lamina propria IFN γ +CD8⁺ T-cells by the mouse B#5 microbiota, whereas other antibiotics treatment or chloroform treatment reduced the induction capability of IFN γ +CD8⁺ T-Cells by the mouse B#5 microbiota.

[0295] Figures 7A and 7B show the operational taxonomic unit (OTU) analysis of intestinal contents of mice inoculated with mouse B#5 microbiota and treated with/without antibiotics or chloroform. Cecal contents were collected from two B#5+AMP mice that exhibited the highest frequency of IFN γ +CD8+ T cells (mouse B#5+AMP-2 and mouse B#5+AMP-3) and cultured in an anaerobic chamber. 304 colonies were picked and sequencing of the 16S rRNA gene revealed that 26 strains were isolated. Twenty-one strains were selected from the 26 strains, excluding 5 strains which were included in the microbiota of B#5+Chrolo mice (therefore predicted to be unnecessary for induction of IFN γ +CD8+ T-cells). The mixture of 21 strains was orally inoculated into germ free mice and strong induction of IFN γ +CD8+ T-cells was observed (Figures 8A and 8B). IFN γ +CD8+ T cells induced by the 21 strains also expressed CD103 and a part of the IFN γ +CD8+ T-cells expressed Granzyme B as well (Figures 9A and 9B). A mixture of 11 strains with the highest correlation with IFN γ +CD8+ T-cells was inoculated into GF mice as well. The mixture of 11 strains (11 mix) was orally a strong induction of IFN γ +CD8+ T-cells, even when compared to the 21 strains mixture (21 mix) (Figures 10A and 10B). Identification of the bacterial species with the highest homology to each of the strains in the 11 mix is provided in Table 2, below.

[0296] [Table 2]

Table 2: Mixture of 11 strains

SEQ ID NO				NCBI	SEQ ID of
Strain #	Strain ID	Species with highest homology	accession #	of 16S locus	NCBI 16S locus
1	1	2G5	<i>Phascolarctobacterium faecium</i>	LN998073	27
2	2	1A6	<i>Fusobacterium ulcerans</i>	KR822463	28
3	3	1B11	<i>Bacteroides dorei</i>	CP011531	29
4	4	2G1	<i>Bacteroides uniformis</i>	NR112945	30
5	5	2B1	<i>Subdoligranulum</i> sp.	KM098109	31
6	6	2A6	<i>Paraprevotella xylaniphila</i>	NR113078	32
7	7	2F11	<i>Parabacteroides johnsonii</i>	NR041464	33
8	8	1E7	<i>Alistipes</i> sp.	LT223566	34
9	9	1H9	<i>Parabacteroides gordonii</i>	NR112835	35
10	10	1C1	<i>Eubacterium limosum</i>	NR113248	36
11	11	2G9	<i>Parabacteroides distasonis</i>	NR041342	37

[0297] Example 1A: Further characterization of the mixture of 11 strains (Composition A)
The strains of Table 2 were characterized further by resequencing of the 16S sequences and by whole genome sequencing. The results of the further characterization are found in Table 3.

[Table 3]

Table 3: Further characterization of the 11-mix (the mixture of 11 strains)

Strain #	SEQ ID NO	Strain ID	species with highest homology based on original 16S analysis	NCBI accession ID	species with highest homology based on 16S resequencing	16S identity (%) of re-sequencing	species with highest homology based on whole genome sequencing (WGS)	WGS identity (%)	WGS Coverage (%)	Alternative species with high(est) homology
2	2	1A6	<i>Fusobacterium ulcerans</i>	KRE22463	<i>Fusobacterium varium</i>	99	<i>Fusobacterium ulcerans</i>	93.2	78.6	
7	7	2F11	<i>Parabacteroides johnsonii</i>	NR041464	<i>Parabacteroides johnsonii</i>	99	<i>Parabacteroides johnsonii</i>	99.9	90.5	
6	6	2A6	<i>Paraprevotella xylaniphila</i>	NR113078	<i>Paraprevotella xylaniphila</i>	99	<i>Paraprevotella xylaniphila</i>	98.9	92.1	
11	11	2G9	<i>Parabacteroides distasonis</i>	NR041342	<i>Parabacteroides distasonis</i>	99	<i>Parabacteroides sp. CAG:2</i>	99.4	95.4	
8	8	1E7	<i>Alistipes sp.</i>	LT223566	<i>Alistipes senegalensis</i>	99	<i>Alistipes senegalensis</i>	98.7	72.2	<i>Alistipes timonensis</i>
10	10	1C1	<i>Eubacterium limosum</i>	NR113248	<i>Eubacterium limosum</i>	99	<i>Eubacterium limosum</i>	95	81	
3	3	1B11	<i>Bacteroides dorei</i>	CP011531	<i>Bacteroides dorei</i>	99	<i>Bacteroides dorei</i>	99.3	79.5	<i>Bacteroides fluxus</i>
9	9	1H9	<i>Parabacteroides gordonii</i>	NR112835	<i>Parabacteroides gordonii</i>	97	<i>Parabacteroides sp. HG50025</i>	90	50	
5	5	2B1	<i>Subdoligranulum sp.</i>	KM098109	<i>Gemminger formicilis</i>	99	<i>Ruminococcaceae bacterium cv2</i>	99.2	73.9	<i>Ruthenibacterium lactatiformans</i>
4	4	2G1	<i>Bacteroides uniformis</i>	NR112945	<i>Bacteroides uniformis</i>	99	<i>Bacteroides sp. D20</i>	98.5	81	
1	1	2G5	<i>Phascolarctobacterium faecium</i>	LN598073	<i>Phascolarctobacterium faecium</i>	99	<i>Phascolarctobacterium sp. CAG:207</i>	99.2	87	

[0298] Example 2: Further characterization of a CD8+ T-cell inducing bacterial cocktail

Twenty six strains isolated from cecal contents of B#5+AMP mice that exhibited high frequencies of IFN γ +CD8+ T cells are shown in Figure 11. Among the 26 strains, 11 strains (“11 mix”) were positively correlated with the frequency of IFN γ +CD8+ T cells. Therefore, these 11 strains were selected for further experiments, and the mixture of 11 strains (“11-mix”) was inoculated into germ-free mice (see also Table 2). Colonization with the 11-mix resulted in a strong induction of colonic IFN γ + CD8+ T cells (Figures 10A, 10B, 12A, and 12B), whereas the other 10 strains (“10-mix”) weakly induced IFN γ + CD8+ T cells compared to the levels induced by the 11-mix (Figures 12A and 12B). Mice inoculated with a mixture of 17 Treg-inducing bacterial strains (See e.g., WO2013/080561; Atarashi et al., Nature (2013) 500 (7461): 232-236; Narushima et al. Gut Microbes (2014)5(3): 333-339) did not accumulate IFN γ +CD8+ T cells (Figures 12A and 12B).

A phylogenetic comparison using 16S rRNA gene sequences showed that the 11 strain mixture (also referred to as “the 11 mix”) consists of 7 strains falling within Bacteroidales (“7 strains”) and 4 strains of non-Bacteroidales: 2 Clostridiales, 1 Fusobacteriales and 1 Selenomonadales (“4 strains”) (See Figure 13 and Table 4).

[0299] Inoculation with the mixture of 4 non-Bacteroidales strains (“4-mix”) resulted in a strong accumulation of colonic IFN γ +CD8+ T cells, comparable to the level of colonic IFN γ +CD8+ T cells observed in mice colonized with the 11 mix. In contrast, colonization with 7 Bacteroidales strains (“7-mix”) weakly induced IFN γ +CD8+ T cells (Figures 14A and 14B).

A repeat of the experiment is shown in Figure 47, which shows that the 11-mix is

more effective than either the 7-mix or the 4-mix. The data of the experiment shown in Figure 47 have strong statistical support.

Identification of the bacterial species with the highest homology to each of the strains in the 4 mix is provided in Table 4, below.

[Table 4]

Table 4: Mixture of 4 strains

Strain #	SEQ ID NO	Strain ID	Species with highest homology	NCBI accession # of 16S locus	SEQ ID of NCBI 16S locus
1	1	2G5	Phascolarctobacterium faecium	LN998073	27
2	2	1A6	Fusobacterium ulcerans	KR822463	28
5	5	2B1	Subdoligranulum sp.	KM098109	31
10	10	1C1	Eubacterium limosum	NR113248	36

[0300] Example 3: Anti-cancer characteristics of CD8+ T-cell inducing bacterial cocktail

To investigate whether colonization with the 11 mix could enhance anticancer immune responses, a subcutaneous tumor model was used. SPF mice were treated with mixture of antibiotics (1 g/L ampicillin, 0.5 g/L vancomycin, 1g/L metronidazole, and 1 g/L neomycin) via the drinking water from day -7 to day 2. A MC38 colon cancer cell line (3×10^5 cells per mouse) was subcutaneously injected into the right flank of mice at day 0. Antibiotics treatment was stopped at day 2, and mice were gavaged with fecal microbiota from SPF mice mixed with or without 11-mix on day 3. For the 11-mix treatment groups, mice were gavaged with the 11 mix two or three times per week until the end of the experiment. For the anti-PD-1 antibody (Ab) treatment groups, mice were intraperitoneally injected with 200 μ g of anti-PD1 monoclonal Ab (clone J43) at days 3, 5 and 9. Tumor size was measured using a caliper and tumor volume was determined as length $\times$ width 2×0.5 .

[0301] Treatment with the 11 mix alone (i.e., without anti-PD1 Ab) significantly suppressed MC38 tumor growth (see Figure 15). The combination of the 11 mix and anti-PD1 Ab exhibited the strongest suppressive effect on the growth of tumor cells (see Figure 15). Treatment with the 11 mix and anti-PD1 Ab resulted in elevated accumulation of IFN γ +CD8+ T cells in the MC38 tumor mass (see Figures 16A and 16B). A subset of the IFN γ +CD8+ T cells in tumors expressed T- cell receptors specific for gp70p15E604-611 (KSPWFTTL; SEQ ID NO: 53), which is an immunodominant epitope of MC38 (Figure 17A). Furthermore, a subset of IFN γ +CD8+ T cells expressed CD44 and Granzyme B, suggesting that the IFN γ +CD8+ T cells accumulated in the tumor included tumor-specific and memory-type cytotoxic CD8+ T cells (see Figures 17A and 17B). The effect on IFN γ +CD4 T cells is shown in Figure 18.

Oral inoculation with the 11 mix resulted in the increased numbers of IFN γ -producing splenocytes, even in the absence of tumor antigen stimulation (see Figure 19).

These results show that treatment with 11 mix in combination with, or without, anti-PD1 Ab systemically activate CD8 T cells that respond to tumor cells.

[0302] Example 4: Anti-cancer characteristics of CD8+ T-cell inducing bacterial cocktail in combination with CTLA-4 immune checkpoint inhibitor

To investigate whether colonization with the 11-mix in combination with immune checkpoint inhibitor CTLA4 could enhance anticancer immune response, a subcutaneous tumor model was used (Fig. 24). Mice were treated with mixture of antibiotics for 5 days (from day -21 to day -16), followed by a two-day period to wash out the antibiotics. A MC38 colon cancer cell line (3×10^5 cells per mouse) was subcutaneously injected into the right flank of mice at day -14. The animals were randomized into the following treatment groups:

Group 1: No antibiotics, no treatments (provides a reference for standard progression of MC38 tumor model);

Group 2: Antibiotic pre-treatment, no treatment (provides a reference for the progression of the MC38 tumor model with antibiotic pre-treatment);

Group 3: 11-mix monotherapy (referred to as AAM1 in Figs. 25 and 26);

Group 8: anti-CTLA-4 antibody (9H10) and 11-mix (referred to as AAM1 in Figs. 25 and 26) combination;

Group 9: anti-CTLA-4 antibody (9H10) monotherapy.

Bacterial cocktail treatments were also begun on day -14 and administered biweekly 4 times. For groups receiving the CTLA-4 immune checkpoint inhibitor, the treatment was begun once the tumor volume reached approximately 100 mm^3 ($100\text{-}150 \text{ mm}^3$). The anti-CTLA-4 antibody was administered on days 1, 4, and 7. The mice were assessed for weight and survival through the course of the experiment. Tumor size and volume were measured.

[0303] Tumor Measurements

The group of mice that received the anti-CTLA-4 antibody alone (Group 9) had slightly reduced tumor growth compared to control mice. The combination of the 11-mix (referred to as “AAM1” in Fig. 25) and the anti-CTLA-4 antibody (Group 8) significantly reduced the tumor growth as compared to the 11-mix on its own and as compared to the anti-CTLA-4 antibody on its own. See Fig. 25. Tumor volume plots of individual mice are shown in Fig. 27.

[0304] Survival

The group of mice that received the anti-CTLA-4 antibody alone had slightly increased survival compared to control mice. The 11-mix by itself had no impact on survival. The combination of the 11-mix (referred to as “AAM1” in Fig. 26) and the

anti-CTLA-4 antibody significantly enhanced survival of the treated mice (Group 8). See Fig. 26.

[0305] Example 5: Anti-cancer characteristics of CD8⁺ T-cell inducing bacterial cocktails in combination with an anti-PD1 antibody

To investigate whether colonization with the 4-mix or 11-mix in combination with immune checkpoint inhibitor anti-PD1 could enhance anticancer immune responses in the absence of antibiotic pretreatment and prior engraftment, a MC38 colon cancer cell line (3×10^5 cells per mouse) was subcutaneously injected into the right flank of mice at day -14 (See Fig. 28). The animals were randomized into the following treatment groups:

Group 1: No treatment;

Group 3: 11-mix monotherapy (referred to as "AAM1" in Figs. 28 and 29);

Group 4: 4-mix monotherapy (referred to as "AAM2" in Figs. 28 and 29);

Group 5: anti-PD1 antibody (RMP1-14) monotherapy;

Group 6: anti-PD1 antibody (RMP1-14) and 11-mix (referred to as "AAM1" in Figs. 28 and 29) combination; and

Group 7: anti-PD1 antibody (RMP1-14) and 4-mix (referred to as "AAM2" in Figs. 28 and 29) combination.

The treatments were begun at day 1 (tumor volume approximately 100-150 mm³). Bacterial cocktail treatment and the anti-PD1 antibody were administered biweekly twice. The mice were assessed for weight and survival through the course of the experiment. Tumor size and volume were measured.

[0306] Tumor Measurement

Treatment with the anti-PD1 antibody alone or in combination with either the 4-mix or the 11-mix resulted in a reduction in tumor growth as compared to no treatment. Fig. 30 shows tumor volume plots of the individual mice treated in experiments of Example 5 (control, 11-mix; α PD-1 Ab; 11-mix + α PD-1 Ab). The tumor volume did not increase in multiple animals in the 11-mix + α PD-1 Ab treatment group (bottom right panel). Fig. 32 shows tumor volume plots of individual mice treated in experiments of Example 5 (control, 4-mix; α PD-1 Ab; 4-mix + α PD-1 Ab). The tumor volume did not increase in multiple animals in the 4-mix + α PD-1 Ab treatment group (bottom right panel).

[0307] Survival

Survival data are shown in Fig. 31 for the control, 11-mix; PD-1 Ab; and 11-mix + PD-1 Ab groups. The combination of the 11-mix and the α PD-1 Ab showed increased survival when compared to either the 11-mix or the α PD-1 Ab on its own.

The combined survival data of mice in the control, 4-mix; α PD-1 Ab; 4-mix + α PD-1 Ab, 11-mix, and 11-mix + α PD-1 Ab groups are shown in Fig. 33. Both the com-

combination of the 4-mix and the α PD-1 Ab and the combination of the 11-mix and the α PD-1 antibody showed increased survival when compared to the α PD-1 Ab on its own.

[0308] Example 6: Anti-cancer characteristics of CD8⁺ T-cell inducing bacterial cocktail combination with an anti-PD1 antibody in a melanoma model

A melanoma engraftment mouse model was used to evaluate the efficacy of the 11-mix in combination with a PD-1 antibody in the treatment of melanoma. As shown in the timelines in Figs. 34 and 35, mice received antibiotics (Ampicillin, Vancomycin, Metronidazole, and Neomycin: "AVMN") from day -3 to day 2. On day 0, the mice were engrafted with 7×10^5 Braf Pten melanoma cells. The mice were grouped in the following treatment groups:

- Specific Pathogen Free (SPF) feces;
- SPF feces + anti-PD1 antibody;
- SPF feces + 11-mix; and
- SPF feces + 11-mix + anti-PD1 antibody.

On days 3, 6, and 9, the mice were administered SLC SPF feces from specific-pathogen free (SPF) mice obtained from Japan SLC (SLC SPF feces), an anti-PD1 antibody (arrows on the timelines in Figs. 34 and 35) and/or the 11-mix (arrows with asterisk on the timelines in Figs. 34 and 35). The 11-mix was administered to the indicated groups of mice 2 or 3 times per week by gavage. Mice that received the combination of the anti-PD1 antibody and the 11-mix had reduced tumor volume (Fig. 34), tumor area (Fig. 35), and tumor weight (Fig. 36) as compared to the other groups of mice.

[0309] Lymphocytes were isolated from tumors obtained from the mice on days 22 and 24 and stained using antibodies to cell markers, including CD3, TCR β , CD8, CD4, IFN γ , Granzyme, and IL-17. Treatment with the 11-mix and anti-PD1 antibody combination resulted in elevated accumulation of IFN γ +CD8⁺ T cells in the melanoma tumor. Figs. 37A-37C and 38. In this experiment, there was no significant difference in the number of IFN γ + GzmB⁺ cells, Th1 cells, Th17 cells, or Treg cells between the groups of mice. Figs. 39A-39D.

These results show that treatment with 11-mix in combination with the anti-PD1 antibody systemically activates CD8 T cells in the melanoma.

[0310] Example 7: CD8 T-cell Induction in Specific-Pathogen Free (SPF) mice

Experimental parameters were evaluated for the induction of CD8 T cells by the 11-mix bacterial cocktail. The animals used in this study were specific pathogen free mice (SPF mice) as compared to germ-free mice.

As shown in Fig. 40, the mice were grouped in the following treatment groups:

- 11-mix multi-dose;

- AVMN + SPF feces;
- AVMN + SPF feces + 11-mix single dose; and
- AVMN + SPF feces + 11-mix multi-dose.

The indicated groups of mice received antibiotics (Ampicillin, Vancomycin, Metronidazole, and Neomycin: "AVMN") in their drinking water from day -5 to day -1. Mice were inoculated with SPF feces with or without the 11-mix on day 0. For groups that received multiple doses of the 11-mix, the bacterial cocktail was also administered in the water on days 3, 7, 10, 14, 17, 21, 24, and 28.

[0311] Lymphocytes were isolated from the mice on days 22 and 24 and stained using antibodies to cell markers, including CD3, TCR β , CD8, CD4, IFN γ , Granzyme, and IL-17. Mice that received the antibiotic pretreatment and multiple doses of the 11-mix showed enhanced levels of IFN γ +CD8+ T cells. Figs. 41A-41C. The mice that received the antibiotic pretreatment and multiple doses of the 11-mixes also had enhanced levels of CD103+ IFN γ + cells in the CD8T cell population of cells (Fig. 42A) and slightly enhanced levels of Th17 cells (Fig. 42B). There was no significant difference in the number of Th1 cells between the groups of mice. (Fig. 42C). These data show that the 11-mix can induce CD8+ T cells in a complex background: a specific pathogen free mouse (as compared to a germ free mouse).

[0312] Example 8: The role of transcription factor BATF3

The 11-mix was administered to mice that have the BATF3 transcription factor and mice that do not have the BATF3 transcription factor. Mice that do not have the transcription factor BATF3 are not susceptible to CD8 T cell induction by the 11-mix. (Figs. 43A and 43B). It is likely that CD103-CD11b dendritic cells are required for stimulation of IFN γ -gamma producing CD8 and Th1 cells. The induction of Th17 cells by the 11-mix cocktail is independent of BATF3 status. (Fig. 43C). Figs. 43 and 44 show the results from the experiments of Example 8. The experiments show that BATF3 is required for the 11-mix to induce CD8-T cells. BATF3 is not required to induce Th17.

[0313] Example 9: Treatment of *Listeria* infected mice.

Since IFN γ +CD8+ T cells have been reported to play critical roles in controlling intracellular pathogens, it was evaluated whether oral supplementation with the 11 strain mixture in a multiple dosing regimen could augment host protective immunity against *Listeria monocytogenes* infection. SPF mice were treated with AVMN (ampicillin, vancomycin, metronidazole, neomycin) for 5 days via the drinking water. After one day washout of antibiotics, multiple oral administrations of the 11-mix (4 times) were performed. To reconstitute complex microbiota, fecal microbiota from SPF mice were introduced together with the first administration of 11-mix. The mice were then orally infected with *Listeria monocytogenes* on day 0. Fecal *Listeria* CFU and body weight

of mice were determined. Treatment with 11-mix significantly reduced *Listeria monocytogenes* colonization of the gut lumen (Fig. 45) and maintained the body weight of the mice (Fig. 46). Thus, administration of the 11 strain-mixture can provide protective immunity against an intracellular, infectious pathogen.

[0314] Example 10: Localization of the CD8 T-cells induced by the 11-mix

The 11-mix was administered to normal healthy mice (i.e., mice that were not otherwise stressed). Various organs and compartments in the mice were investigated for the presence of CD8 positive T- cells. As shown in Fig. 48, the CD8 positive T-cell induction effect of the 11-mix is limited to the intestine / gut (SI = small intestine, CIEL = colonic intraepithelial lymphocytes, LN = lymph nodes).

[0315] Example 11: Selective and temporal activation of subsets of lamina propria dendritic cells.

As CD8 cells can be activated through certain subclasses of dendritic cells, the number and activation state of lamina propria CD11b- CD103+ dendritic cells was investigated following administration of the 11-mix. As shown in Fig. 49, the administration of the 11-mix did not change the proportion of the lamina propria CD11b- CD103+ dendritic cell subset.

The temporality / kinetics of activation was also investigated. GF mice were colonized with the 11-mix for 1, 2, 3, and 4 weeks. The frequency of colonic LP and MLN dendritic cells (DCs)/ macrophage subsets were not affected by the colonization with 11 mix. However, expression of MHC class I on colonic LP DCs (but not MLN DCs), particularly on colonic LP CD103+ DC subset (namely, Batf3-dependent DC subset), was significantly enhanced by the colonization with 11-mix. Upregulation of MHC class I expression most strongly occurred at 1 week after colonization. (See Figs. 50-54) Without being limited to a particular mechanism it is likely that induction of the CD8 positive T cells is mostly due to proliferation rather than antigen-specific de novo differentiation.

Ki67 staining revealed that expansion of CD8 positive T cells occurred at 1 week, accompanied by increase with IFN γ + CD8+ T in the colonic LP (See Figure 55). CD103 staining revealed that induced IFN γ + CD8+ T at 1 week post colonization were mostly CD103 negative, and that CD103+ IFN γ + CD8 T (tissue resident memory phenotype CD8+ T) were gradually increased (See Figs. 56 and 57).

CLAIMS

1. A composition comprising a purified bacterial mixture consisting of bacterial strains *Phascolarctobacterium faecium*, *Fusobacterium ulcerans*, *Bacteroides dorei*, *Bacteroides uniformis*, *Subdoligranulum sp.*, *Paraprevotella xylaniphila*, *Parabacteroides johnsonii*, *Alistipes sp.*, *Parabacteroides gordonii*, *Eubacterium limosum*, and *Parabacteroides distasonis*, wherein the bacterial strains are lyophilized.
2. A pharmaceutical composition comprising a purified bacterial mixture consisting of bacterial strains comprising 16S rDNA sequences of at least 99% sequence identity with SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11, wherein the bacterial strains are lyophilized.
3. The composition of claim 1, wherein the composition is a pharmaceutical composition.
4. The composition of claims 2 or 3, wherein the pharmaceutical composition comprises a pharmaceutically acceptable excipient.
5. The composition of any one of claims 2 to 4, wherein the pharmaceutical composition is in the form of a capsule.
6. The composition of any one of claims 2 to 5, wherein the pharmaceutical composition further comprises a pH sensitive composition comprising one or more enteric polymers.
7. The composition of any one of the preceding claims, wherein the composition further comprises an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor.

8. Use of the composition of any one of the preceding claims in the manufacture of a medicament for the treatment of cancer in a subject.
9. The use of claim 8, wherein the cancer is carcinoma, glioma, mesothelioma, melanoma, lymphoma, leukemia, adenocarcinoma, breast cancer, ovarian cancer, cervical cancer, glioblastoma, multiple myeloma, prostate cancer, Burkitt's lymphoma, head and neck cancer, colon cancer, colorectal cancer, non-small cell lung cancer, small cell lung cancer, cancer of the esophagus, stomach cancer, pancreatic cancer, hepatobiliary cancer, cancer of the gallbladder, cancer of the small intestine, rectal cancer, kidney cancer, bladder cancer, prostate cancer, penile cancer, urethral cancer, testicular cancer, vaginal cancer, uterine cancer, thyroid cancer, parathyroid cancer, adrenal cancer, pancreatic endocrine cancer, carcinoid cancer, bone cancer, skin cancer, retinoblastomas, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Kaposi's sarcoma, multicentric Castleman's disease, AIDS-associated primary effusion lymphoma, neuroectodermal tumors, or rhabdomyosarcoma.
10. The use of claim 9, wherein the cancer is melanoma, head and neck cancer, stomach cancer, esophageal cancer, non-small cell lung cancer or colorectal cancer.
11. The use of any one of claims 8-10, wherein one or more anticancer agents is further to be administered to the subject.
12. The use of claim 11, wherein the anticancer agent is an immune checkpoint inhibitor wherein the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor.
13. The use of any one of claims 8-12, wherein an antibiotic is to be administered to the subject prior to the composition.
14. The use of claim 13, wherein the antibiotic is vancomycin.
15. A method, the method comprising

Determining, from a fecal matter sample obtained from a subject, if the bacterial mixture of the composition in any of claims 1 to 7 are present in the intestine of a subject,

wherein if less than 100%, less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or none of the bacterial species are present, the composition is to be administered to the subject.

16. The method of claim 15, wherein determining the presence of the bacterial mixture is done by sequencing the fecal matter sample obtained from the subject.