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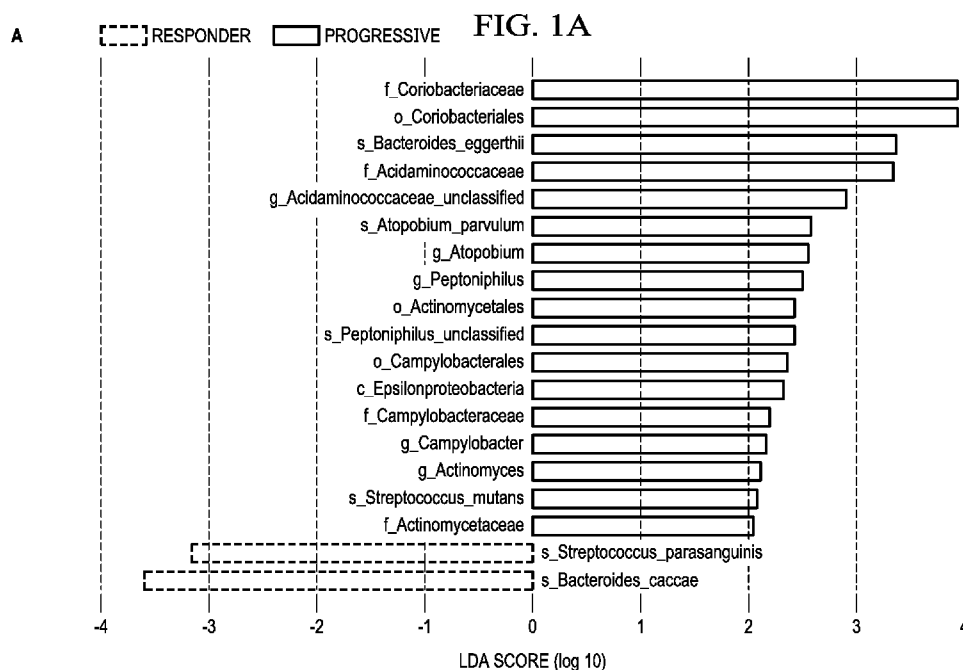
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(54) Title: SPECIFIC BACTERIAL SPECIES AND METABOLITE THAT IMPROVES IMMUNE CHECKPOINT INHIBITOR THERAPY EFFICACY



(57) Abstract: The present invention includes compositions and methods for increasing an efficacy of an immune checkpoint inhibitor comprising: identifying a human patient in need of treatment for a melanoma; providing the human patient with an effective amount of the immune checkpoint inhibitor; and providing the human patient with at least one of: a probiotic bacteria, a prebiotic agent, or a xenobiotic agent, in the amount is effective to increase the potency of the immune checkpoint inhibitor against the melanoma.

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SPECIFIC BACTERIAL SPECIES AND METABOLITE THAT IMPROVES IMMUNE CHECKPOINT INHIBITOR THERAPY EFFICACY

TECHNICAL FIELD OF THE INVENTION

The present invention relates in general to the field of cancer therapy, and more particularly, to specific bacterial species and metabolite that improves immune checkpoint inhibitor therapy efficacy.

BACKGROUND OF THE INVENTION

Without limiting the scope of the invention, its background is described in connection with checkpoint inhibitors.

Immune checkpoint inhibitor therapy, ICT, achieves durable remissions in up to half of patients with metastatic melanoma (Larkin et al. NEJM 2015). It is still unclear what host factors modulate response to ICT. Preclinical mouse studies with B16 melanoma demonstrated that ICT response was dependent on the presence of specific commensal gut bacteria (Vetizou et al. Science 2015; Sivan et al. Science 2015). In mice, these specific gut bacteria induced the maturation of dendritic cells (DCs) and T-cells needed for effective ICT.

For example, Vetizou et al., in a publication entitled "Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota," Science, 27 November 2015 • Vol. 350 (6264), 1079-1084, and International Patent Application Publication No. WO2016/063263, filed October 23, 2015, compared the relative therapeutic efficacy of a CTLA-4-specific 9D9 Ab against established MCA205 sarcomas in mice housed in specific pathogen-free (SPF) versus germ-free (GF) conditions. They further addressed the impact of the gut microbiota on the incidence and severity of intestinal lesions induced by CTLA-4 Ab treatment. To address the clinical relevance of the findings in mice, the authors analyzed the gut microbiome before and after treatment with ipilimumab in 25 individuals with metastatic myeloma. The gut microbiome was clustered into three groups, *Alloprevotella* or *Prevotella* driving the first cluster and distinct *Bacteroides* spp., driving clusters two and three. A fecal gut microbe transplantation was performed from patients with metastatic myeloma into mice with a metastatic myeloma. It was found that ipilimumab modified the abundance of immunogenic *Bacteroides* spp. in the gut, which in turn affects its anticancer efficacy. It was also found that intestinal reconstitution with *Bacteroides fragilis* and *Burkholderia cepacia* reduced histopathological signs of colitis induced by CTLA-4 blockade. The authors conclude that, "The geodistribution of Bf [*Bacteroides fragilis*] in the mucosal layer of the intestine... and its association with *Burkholderiales*—recognized through the pyrin-caspase-1 inflammasome (17) and synergizing with TLR2/TLR4 signaling pathways...—may account for the immunomodulatory effects of CTLA-4 Ab." *Id.* at 1082. In their patent application, International Patent Application Publication No. WO 2016/063263, these authors further state that the invention also pertains to the use of vancomycin or penicillin to modulate the gut microbiota to potentiate the anticancer effects of anti-CTLA4 molecules.

Thus, a need remains for identifying agents that improve the effect of immune checkpoint antagonists in human myeloma patients.

SUMMARY OF THE INVENTION

In one embodiment, the present invention includes a method of increasing the efficacy of an immune checkpoint inhibitor comprising: identifying a human patient in need of treatment for a melanoma; providing the human patient with an effective amount of the immune checkpoint inhibitor; and providing the human patient with at least one of: a probiotic bacteria, a prebiotic agent, or a xenobiotic agent, in the amount is effective to increase the potency of the immune checkpoint inhibitor against the melanoma. In one aspect, the immune checkpoint inhibitor is selected from at least one of a CTLA-4 inhibitor or a PD1 inhibitor. In another aspect, the human patient does not have a BRAF mutation. In another aspect, the immune checkpoint inhibitor is selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In another aspect, the probiotic bacteria are selected from at least one of *Alistipes shahii*, *Bacteroides caccae*, *Ruminococcaceae sp.*, *Streptococcus mutans*, or *Dorea formicigenerans*. In another aspect, the probiotic bacteria is *Dorea formicigenerans* and is provided to enhance the therapeutic effect of pembrolizumab (PD1). In another aspect, the probiotic bacteria are at least one of: *Bacteroides thetaiotamicron*, *Alistipes shahii*, *Ruminococcaceae*, or *Streptococcus mutans*, and the probiotic bacteria are provided to enhance the therapeutic effect of a combination of ipilimumab and nivolumab. In another aspect, the xenobiotic agent is an anacardic acid, a 15:2 anacardic acid, or active derivatives thereof. In another aspect, the patient is further provided with an effective amount of the probiotic and an anacardic acid in an amount sufficient to enhance the therapeutic effect of the immune checkpoint inhibitor selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In another aspect, the method further comprises providing a probiotic further comprising one or more bacteria selected from at least one of: *Methanobrevibacter smithii*, *Bacteroides thetaiotamicron*, *Lactobacillus plantarum*, or *Eubacterium limosum*, in an amount sufficient to enhance the activity of the immune checkpoint inhibitor selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In another aspect, the melanoma is metastatic melanoma. In another aspect, the melanoma is resistant or refractory to the immune checkpoint inhibitor. In another aspect, the patient did not receive a concurrent antibiotic or a probiotic therapy.

In one aspect, the probiotic bacteria that increase the effectiveness of a combination of the immune checkpoint inhibitors ipilimumab plus nivolumab is selected from at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*. In another aspect, the probiotic bacteria that increase the effectiveness of ipilimumab plus nivolumab is *Dorea formicigenerans*. In another aspect, the probiotic bacteria that increase the effectiveness of the immune checkpoint inhibitor pembrolizumab is selected from at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*.

In another embodiment, the present invention includes a method of identifying a patient that will respond to therapy with an immune checkpoint inhibitor comprising: identifying a subject in need of treatment with the immune checkpoint inhibitor for the treatment of a melanoma; obtaining a biological sample from the patient that comprises gut intestinal flora; and determining whether the intestinal flora comprises at least one of *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides*

thetaiotamicron, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis*, wherein the presence of at least one of the *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis*, is indicative that the melanoma will respond to the immune checkpoint inhibitor, or will have an improved response to the immune checkpoint inhibitor. In one aspect, the method further comprises providing the patient with an amount of *Alistipes shahii*, *Bacteroides caccae*, *Ruminococcaceae sp.*, or *Streptococcus mutans* probiotics sufficient to enhance the response to the immune checkpoint inhibitor. In another aspect, the biological sample is a fecal sample. In another aspect, the presence of the probiotic bacteria is determined by at least one of metagenomic shotgun sequencing of bacteria or metabolic LC-MS analysis of metabolites. In another aspect, the patient does not have a BRAF mutation. In another aspect, the immune checkpoint inhibitor is selected from at least one of CTLA-4 inhibitor, a PD1 inhibitor, ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In another aspect, the probiotic bacteria are selected from at least one of *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis*. In another aspect, the presence of *Dorea formicigenerans* is indicative of enhanced therapeutic effect by pembrolizumab. In another aspect, the presence of at least one of: *Bacteroides thetaiotamicron*, *Faecalibacterium prausnitzii*, or *Holdemania filiformis* is indicative of an enhanced therapeutic effect by ipilimumab plus nivolumab. In another aspect, the presence of *Bacteroides caccae* or *Streptococcus parasanguinis* is indicative of enhanced therapeutic effect by any combination of immune checkpoint inhibitor therapy. In another aspect, the presence of 15:2 anacardic acid in the biological sample is indicative of enhanced therapeutic effect by the immune checkpoint inhibitor. In another aspect, the patient is a human patient. In another aspect, the melanoma is metastatic melanoma. In another aspect, the melanoma is resistant or refractory to the immune checkpoint inhibitor. In another aspect, the patient did not receive a concurrent antibiotic or a probiotic therapy. In one aspect, the probiotic bacteria that increase the effectiveness of a combination of the immune checkpoint inhibitors ipilimumab plus nivolumab is selected from at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*. In another aspect, the probiotic bacteria that increase the effectiveness of pembrolizumab is *Dorea formicigenerans*. In another aspect, the probiotic bacteria that increase the effectiveness of any of the immune checkpoint inhibitor therapies is selected from at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*.

In another embodiment, the present invention includes a composition that increases the efficacy of an immune checkpoint inhibitor comprising: a first composition comprising at least one of a probiotic or prebiotic composition or an anacardic acid; wherein the first composition is capable of increasing the efficacy of the immune checkpoint inhibitor; and a second composition comprising a therapeutically effective amount of the immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In one aspect, the first and second compositions are provided in a single formulation, are provided concurrently, or are provided separately. In another aspect, the patient does not have a BRAF mutation.

In another aspect, the first composition further comprises at least one of *Methanobrevibacter smithii*, *Bacteroides thetaiotamicron*, *Lactobacillus plantarum*, *Eubacterium limosum*, *Bacteroides caccae*, *Streptococcus parasanguinis*, *Dorea formicigenerans*, *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*. In another aspect, the first composition comprises *Dorea formicigenerans*, when the second composition comprises pembrolizumab (PD1). In another aspect, the first composition comprises at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*, when the second composition comprises at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab. In another aspect, the first composition comprises at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*, when the second composition is ipilimumab and nivolumab. In another aspect, the first composition consists essentially of *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron* when the second composition is ipilimumab and nivolumab. In another aspect, the first composition consists essentially of *Dorea formicigenerans* when the second composition is pembrolizumab. In another aspect, the probiotic bacteria is selected from the responsive bacteria in Tables 2A to 2D having a relative response of 1.0 or greater.

In another embodiment, the present invention includes a pharmaceutical composition comprising at least one of an isolated probiotic bacteria in an amount effective to increase the effectiveness of an immune checkpoint inhibitor. In one aspect, the composition consists essentially of *Bacteroides caccae* and *Streptococcus parasanguinis*. In another aspect, the composition consists essentially of *Faecalibacterium prausnitzii*, *Holdemania filiformis* and *Bacteroides thetaiotamicron*. In another aspect, the composition consists essentially of *Dorea formicigenerans*. In one aspect, the immune checkpoint inhibitor is selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

In yet another embodiment, the present invention includes a method of increasing the efficacy of an immune checkpoint inhibitor comprising: identifying a human patient in need of treatment for a melanoma; providing the human patient with an effective amount of the immune checkpoint inhibitor; and providing the human patient with at least one of a targeted antibacterial agent in the amount effective to increase the potency of the immune checkpoint inhibitor against the melanoma. In one aspect, the antibacterial agent is directed against at least one of *actinobacteria*, *coriobacteriaceae*, *coriobacteriales*, *bacteroides eggerthii*, *parvimonas micrs*, *parvimonas*, *Bifidobacterium dentium*, or *actinomyces viscosus*. In another aspect, the antibacterial agent is directed against at least one of *lactobacillaceae*, *lactobacillus*, *acidaminococcaceae*, *anaerococcus*, *atopobium parvulum*, *anaerococcus vaginalis*, *peptoniphilus* or *lactobacillus gasseri*. In one aspect, the antibacterial agent is a bacteriophage. In one aspect, the antibacterial agent is an antimicrobial CRISP-Cas system agent

BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the features and advantages of the present invention, reference is now made to the detailed description of the invention along with the accompanying figures and in which:

FIGS. 1A to 1D show the relative abundance of gut bacterial taxa as determined by MetaPhlAn analysis of MSS data generated from fecal specimens collected from melanoma patients prior to receiving either ipilimumab/nivolumab or pembrolizumab. Differential taxonomic abundance was analyzed by linear discriminate analysis coupled with effect size measurements (LEfSe) projected as a histogram (FIG. 1A, FIG. 1C, FIG. 1E) or cladogram (FIG. 1B, FIG. 1D, FIG. 1F). FIGS. 1A and 1B are for all immune checkpoint inhibitors (all ICT), FIGS. 1C and 1D for a combination therapy of ipilimumab and nivolumab, and FIGS. 1E and 1F for pembrolizumab. All listed bacterial groups were significantly ($P < .05$, Kruskal-Wallis test) enriched for their respective groups (responder vs progressive).

FIGS. 2A and 2B shows non-targeted metabolomics analysis of stool metabolites from adult melanoma patients prior to treatment with immune checkpoint therapy with: FIG. 2A ipilimumab/nivolumab, and in FIG. 2B pembrolizumab, performed at Metabolon with four separate UHPLC-MS/MS methods. Data were log transformed and mean-centered. The heatmaps show the normalized relative abundances of stool metabolites comparing responders to those with progressive disease ($q < 0.05$, unpaired t test with Welch's correction followed by FDR correction). Orange colors indicate relative abundances above and blue indicate relative abundances below the mean of all samples.

FIG. 3 shows a study schema with I, ipilimumab. N, nivolumab. P, pembrolizumab.

FIG. 4 shows a hierarchical clustering of species abundances shown as dendrogram plots with paired samples marked in red color. Samples without numbers were non-melanoma patient fecal specimens assayed identically.

FIGS. 5A and 5B show histograms of bacterial species' abundance versus response for FIG. 5A. *Alistipes shahii* in IN patients and, FIG. 5B. *Dorea Formicigenerans* in P patients.

FIG. 6 is a scattergram of response versus 15:2 anacardic acid levels. Green dots represent patients who also report $\geq$ weekly cashew consumption.

FIG. 7 shows the structure of 15:2 anacardic acid of use with the present invention.

FIG. 8 shows an outline of *in vivo* studies and expected outcomes of the present invention.

FIG. 9 shows an outline of the detailed *in vivo* studies using the present invention.

FIG. 10 is a graph that shows the results of the precision probiotic therapy on Taconic C57BL/6 (versus a control probiotic) that promotes the activity of immune checkpoint therapy of the present invention.

FIG. 11 is a graph that shows the results of the precision probiotic therapy on Taconic C57BL/6 prolongs survival in mice with melanoma that are treated with ICT compared to mice treated with a control probiotic.

FIG. 12 is a graph that shows the results of the precision probiotic therapy on Jackson C57BL/6 (versus a control probiotic) that promotes the activity of immune checkpoint therapy against melanoma using the present invention.

FIG. 13 is a graph that shows the results of the precision probiotic therapy on Jackson C57BL/6 prolongs survival in mice with melanoma that are treated with ICT compared to mice treated with a control probiotic.

FIG. 14 is a graph that shows that Jackson C57BL/6 mice have decreased relative abundance of *Clostridial firmicutes* (which include *F. prausnitzii*, *H. filiformis*) compared to Taconic C57BL/6 Mice.

DETAILED DESCRIPTION OF THE INVENTION

While the making and using of various embodiments of the present invention are discussed in detail below, it should be appreciated that the present invention provides many applicable inventive concepts that can be embodied in a wide variety of specific contexts. The specific embodiments discussed herein are merely illustrative of specific ways to make and use the invention and do not delimit the scope of the invention.

To facilitate the understanding of this invention, a number of terms are defined below. Terms defined herein have meanings as commonly understood by a person of ordinary skill in the areas relevant to the present invention. Terms such as “a”, “an” and “the” are not intended to refer to only a singular entity, but include the general class of which a specific example may be used for illustration. The terminology herein is used to describe specific embodiments of the invention, but their usage does not delimit the invention, except as outlined in the claims.

As used herein, the term “immune checkpoint inhibitor” refers to agents that block immune checkpoints resulting in the enhancement of antigen-specific T cell responses. Non-limiting examples of immune checkpoints includes agents that target, e.g., PD1 (programmed cell death protein 1); PDL1 (PD1 ligand); BTLA (B and T lymphocyte attenuator); CTLA4 (cytotoxic T-lymphocyte associated antigen 4); TIM3 (T-cell membrane protein 3); LAG3 (lymphocyte activation gene 3); A2aR (adenosine A2a receptor A2aR); and Killer Inhibitory Receptors. Non-limiting examples of immune checkpoint inhibitor(s) for use with the present invention include but are not limited to: ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

The probiotic bacteria, prebiotic agents, and/or xenobiotics for use with the present invention can be provided in a variety of dosage forms. For example, e.g., tablets, capsules, pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions may be used to provide the probiotic bacteria, prebiotic agents, and/or xenobiotics of the present invention to a patient in need of therapy for cancer with the immune checkpoint inhibitor(s). The immune checkpoint inhibitor(s) and the probiotic bacteria, prebiotic agents, and/or xenobiotics can be provided concurrently, in the same dosage form, at the same time thorough the same or different routes, one after the other, or separately in location and/or time.

Techniques and compositions for making useful dosage forms using the present invention are described in one or more of the following references: Anderson, Philip O.; Knoben, James E.; Troutman, William G, eds., Handbook of Clinical Drug Data, Tenth Edition, McGraw-Hill, 2002; Pratt and Taylor, eds., Principles of Drug Action, Third Edition, Churchill Livingston, New York, 1990; Katzung, ed., Basic and Clinical Pharmacology, Ninth Edition, McGraw Hill, 2007; Goodman and Gilman, eds., The Pharmacological Basis of Therapeutics, Tenth Edition, McGraw Hill, 2001; Remington's Pharmaceutical Sciences, 20th Ed., Lippincott Williams & Wilkins., 2000; Martindale, The Extra

Pharmacopoeia, Thirty-Second Edition (The Pharmaceutical Press, London, 1999); all of which are incorporated by reference, and the like, relevant portions incorporated herein by reference.

For example, the probiotic bacteria, prebiotic agents, and/or xenobiotics may be included in a tablet.

Tablets may contain, e.g., suitable binders, lubricants, disintegrating agents, coloring agents, flavoring

5 agents, flow-inducing agents and/or melting agents. For example, oral administration may be in a dosage unit form of a tablet, gelcap, caplet or capsule, the active drug component being combined with an non-toxic, pharmaceutically acceptable, inert carrier such as lactose, gelatin, agar, starch, sucrose, glucose, methyl cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol, mixtures thereof, and the like. Suitable binders for use with the present invention include: starch, gelatin, natural

10 sugars (e.g., glucose or beta-lactose), corn sweeteners, natural and synthetic gums (e.g., acacia, tragacanth or sodium alginate), carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants for use with the invention may include: sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, mixtures thereof, and the like. Disintegrators may include: starch, methyl cellulose, agar, bentonite, xanthan gum, mixtures thereof, and the like.

15 In one embodiment, gelatin capsules (gelcaps) may include the probiotic bacteria, prebiotic agents, and/or xenobiotics, and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Like diluents may be used to make compressed tablets. Both tablets and capsules may be manufactured as immediate-release, mixed-release or sustained-release formulations to provide for a range of release of medication over a period of minutes to hours. Compressed tablets

20 may be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere. An enteric coating may be used to provide selective disintegration in, e.g., the gastrointestinal tract.

For oral administration in a liquid dosage form, the probiotic bacteria, prebiotic agents, and/or xenobiotics may be adapted for oral administration. Examples of suitable liquid dosage forms include

25 powders, tablets, gelcaps, solutions or suspensions in water, pharmaceutically acceptable fats and oils, alcohols or other organic solvents, including esters, emulsions, syrups or elixirs, suspensions, solutions and/or suspensions reconstituted from non-effervescent granules and effervescent preparations reconstituted from effervescent granules. Such liquid dosage forms may contain, for example, suitable solvents, emulsifying agents, suspending agents, diluents, sweeteners, thickeners, and melting agents,

30 mixtures thereof, and the like, that do not affect the viability of the probiotic bacteria or enhance the viability of the probiotic bacteria.

Liquid dosage forms for oral administration may also include coloring and flavoring agents that increase patient acceptance and therefore compliance with a dosing regimen. In general, water, a suitable oil, saline, aqueous dextrose (e.g., glucose, lactose and related sugar solutions) and glycols (e.g., propylene

35 glycol or polyethylene glycols) may be used as suitable carriers for parenteral solutions. Solutions for parenteral administration include generally, a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffering salts. Antioxidizing agents such as sodium bisulfite, sodium sulfite and/or ascorbic acid, either alone or in combination, are suitable stabilizing agents.

Citric acid and its salts and sodium EDTA may also be included to increase stability. Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field, relevant portions incorporated herein by reference.

The inventors of the present invention sought to determine whether specific gut microbiota and/or microbial metabolites are associated with improved response to ICT in melanoma patients. The present invention includes the use of specific gut microbial species and a novel plant xenobiotic enhanced ICT clinical efficacy in melanoma patients. This is the first prospective study of the effects of human gut microbiota and metabolites on immune checkpoint inhibitor (ICT) response in human metastatic melanoma patients. Whereas many melanoma patients can exhibit profound response to ICT, there are fewer options for patients failing ICT—particularly with BRAF-wild-type disease. In preclinical studies, specific mouse gut microbial species promoted regression of melanoma bearing mice. The present inventors conducted a study of the effects of pretreatment gut microbiota and metabolites on ICT RECIST response in 39 metastatic melanoma patients treated with ipilimumab (I), nivolumab (N), ipilimumab plus nivolumab (IN) or pembrolizumab (P). IN yielded 54% responses and 8% stable disease; P achieved 23% responses and 23% stable disease. Responding patients for all therapies were enriched for *Bacteroides coccae*. Among IN responders, the gut microbiome was enriched for *Bacteroides thetaiotamicron*, *Alistipes shahii*, *Ruminococcaceae* and *Streptococcus mutans*. Among P responders, the microbiome was enriched for *Dorea formicogenerans*. Shotgun metabolomics revealed high levels of anacardic acid in ICT responders. Based on these studies it was found that certain bacteria species and xenobiotics had ICT enhancing activity.

The present inventors recognized that intestinal tract bacteria, collectively known as the gut microbiota, can influence and control host immune responses. In preclinical mouse models, the composition of the host gut microbiota was found to affect ICT response [7-9]. Germ-free or antibiotic treated tumor bearing mice did not respond to immune therapy [7]. *Bifidobacterium* fed B16 melanoma bearing mice showed increased tumor dendritic cell anti-tumor immune gene expression and enhanced anti-PD-L1 immunotherapy response [8]. In one study, gut *Bacteroides thetaiotamicron* or *Bacteroides fragilis* were necessary for anti-CTLA4 antibody anti-B16 melanoma *in vivo* efficacy [9]. Further, dendritic cells (DCs) and T cells mixed with either of these *Bacteroides* species *in vitro* increased T cell interferon γ production and *in vivo* tumor growth inhibition. In all the above studies, the gut bacteria induced maturation of anti-melanoma DCs and T cells.

The present invention is the first to study metastatic melanoma patients initiating ICT. Patients were stratified for type of immunotherapy. Fecal samples were collected and analyzed. The present inventors demonstrate herein the ICT efficacy in 39 metastatic melanoma patients and correlate clinical responses with gut taxome profiles, gut metabolite levels, and patient dietary and antibiotic histories.

Patients and Methods. The study design was a single-site, correlative study of the effects of gut microbiota and metabolites on ICT efficacy in 39 patients. The study was approved by the University of Texas Southwestern Medical Center Institutional Review Board (IRB#STU012016-056). The study was conducted in accordance with the Declaration of Helsinki. The inventors enrolled patients with a

histologic diagnosis of unresectable or metastatic melanoma that were scheduled to begin ICT and able to collect stool specimens, store them in a freezer and deliver them to the University of Texas Southwestern Cancer Center facility. In addition, patients had to have measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Tumor sizes were evaluated within 4 weeks prior to beginning therapy by exams, CT scans, and/or MRIs. Therapy involved outpatient ipilimumab 3mg/kg IV every three weeks for four doses (I), nivolumab 1mg/kg IV with ipilimumab 3mg/kg IV every three weeks for four doses followed by nivolumab alone at 240mg IV every two weeks (IN), nivolumab alone at 240mg IV every two weeks (N), or pembrolizumab 2mg/kg IV every three weeks (P). After informed consent, stool samples were collected and immediately frozen until transferred to the University of Texas Southwestern Medical Center at pretreatment and various times post-therapy. Repeat exams and scans were obtained every 2-3 months. Demographics, antibiotic use, and probiotic exposure were recorded for each patient. Patient response, stable disease and progression were evaluated by RECIST v1.1 criteria as reported [10].

Fecal specimens collected at patient's homes and immediately frozen were transferred in Styrofoam containers with cold packs to the clinic and immediately transferred to -80°C freezer until assayed. Thawed 200mg fecal aliquots were suspended in 0.71mL extraction buffer consisting of 200mM NaCl, 200mM Tris pH 7.9, 20mM EDTA, 6% SDS and 0.5mL Ambion phenol/chloroform/isoamyl alcohol added. Cells were lysed by bead-beating with 0.1mm diameter Biospec zirconia/silica beads and centrifuged at 20,000xg for 3 minutes. Supernatants were reextracted with phenol/chloroform/isoamyl alcohol, adjusted to 200mM sodium acetate, and nucleic acids precipitated with equal volume isopropyl alcohol followed by an ethanol wash. Crude DNA extracts were treated with Qiagen RNase A and column-purified with the Qiagen PCR purification kit. DNA was assayed for purity by UV spectroscopy and DNA concentrations quantified by the Life Technologies Quan-iT PicoGreen dsDNA assay. Metagenomic shotgun sequencing (MSS) data was generated by pair-end sequencing of the fecal gDNA with 100bp reads on an Illumina HiSeq 2000. Raw MSS data was quality controlled using NGS-QC (www.nipgr.res.in/ngsqctoolkit.html), and human sequences removed with the NCBI BMTagger Human Contamination Screening Tool (ftp.ncbi.nlm.nih.gov/pub/agarwala/bmtagger/). Then Metagenomic bacterial taxonomic analysis was performed on the filtered sequences with the computational tool MetaPhlAn. Finally, linear discriminate analysis coupled with effect size measurements—LefSe was done to quantitate differential taxonomic abundance between responders and non-responders as previously reported by our laboratory [11].

FIGS. 1A to 1D show the relative abundance of gut bacterial taxa as determined by MetaPhlAn analysis of MSS data generated from fecal specimens collected from melanoma patients prior to receiving either ipilimumab/nivolumab or pembrolizumab. Differential taxonomic abundance was analyzed by linear discriminate analysis coupled with effect size measurements (LefSe) projected as a histogram (FIG. 1A, FIG. 1C) or cladogram (FIG. 1B, FIG. 1D). All listed bacterial groups were significantly ($P < .05$, Kruskal-Wallis test) enriched for their respective groups (responder vs progressive).

Patient gut pathway abundance was calculated by mapping the MSS sequences to the Kyoto Encyclopedia of Genes and Genomes (KEGG) Database using USEARCH and the computational tools sHUMAN and LEfSE [12]. Pathway abundance was compared for responders and stable disease patients versus progressors.

5 Gut microbial and food metabolites were also identified and quantitated by ultrahigh-performance liquid chromatography/mass spectrometry (UHPLC/MS) at Metabolon, Inc. (Durham, NC) as previously described [13]. Briefly, fecal samples were lyophilized and subjected to methanol extraction then split into aliquots for analysis for UHPLC/MS in the positive (two methods), negative, and polar ion mode, followed by normalization to account for differential volume extracted. Compounds were identified by
10 automated comparison to reference chemical library entries with subsequent visual inspection for quality control as previously described [14]. For statistical analyses and data display, any missing values were assumed to be below the limits of detection; these values were imputed with the compound minimum (minimum value imputation). Statistical tests were performed in ArrayStudio (Omicsoft) or “R” to compare data between experimental groups; $p < 0.05$ was considered significant. An estimate of the false
15 discovery rate (q-value) was also calculated to take into account the multiple comparison that normally occur in metabolomics-based studies, with $q < 0.05$ used as an indication of high confidence in a result.

FIGS. 2A and 2B shows non-targeted metabolomics analysis of stool metabolites from adult melanoma patients prior to treatment with immune checkpoint therapy with: FIG. 2A ipilimumab/nivolumab, and in FIG. 2B pembrolizumab, performed at Metabolon with four separate UHPLC-MS/MS methods. Data
20 were log transformed and mean-centered. The heatmaps show the normalized relative abundances of stool metabolites comparing responders to those with progressive disease ($q < 0.05$, unpaired t test with Welch’s correction followed by FDR correction). Orange colors indicate relative abundances above and blue indicate relative abundances below the mean of all samples.

Patient histories were interrogated for consumption of foods enriched for identified plant xenobiotic in
25 excess in ICT non-progressors based on metametabolomics.

Thirty-nine metastatic melanoma patients were enrolled, consented, provided pretreatment fecal samples, underwent ICT, and had follow-up exams and scans (Table 1). There were 30 males and 9 females. Median age was 66 years with a range of 37 years to 92 years. Sites of metastases were single organ in 22 patients including 11 lung, 4 nodes, 4 liver, 2 SQ and 1 bone. There were two sites of metastases in
30 14 patients including 3 lung/liver, 3 lung/nodes, 3 nodes/SQ, 2 nodes/bone, and one each with lung/SQ, SQ/adrenal and lung/adrenal. At least three organ sites were involved in 3 patients—lung/liver/nodes, lung/nodes/SQ and lung/liver/bone, respectively. Twenty-three patients showed RECIST response or stable disease to ICT (Table 1 and FIG. 3). I achieved 13/24 (54%) RECIST responders and 2/24 (8%)
stable disease patients 8% stable disease. P treatment led to 3/13 (23%) RECIST responders and 3/13
35 (23% stable disease patients. One patient each with I alone and N alone responded.

Table 1. Patient Characteristics

Patient Identifier	Sex	Age	Site of Metastases	ICT Therapy (I= ipilimumab, N=nivolumab, P=pembrolizumab)	Change in tumor size (%)	RECIST Category
P7	M	63	Lung	IN	-4	Stable
P8	M	70	Lung	IN	-55	Response
P10	M	75	Lung	IN	-83	Response
P14	F	69	Lung	IN	-60	Response
P16	M	80	Lung, Nodes	P	53	Progression
P17	M	68	Nodes	N	-70	Response
P22	M	64	Lung, Liver	P	81	Progression
P23	M	76	Lung	IN	-55	Response
P24	M	44	Nodes	IN	136	Progression
P25	F	60	SQ	IN	-100	Response
P28	F	68	Lung, Liver	IN	85	Progression
P30	M	54	Lung, Liver	IN	100	Progression
P32	F	57	Nodes, Bone	IN	100	Progression
P33	F	74	Nodes	P	-36	Response
P34	M	57	Liver	IN	-66	Response
P35	M	63	Nodes	IN	-30	Response
P39	M	48	Nodes, SQ	P	-68	Response
P42	M	67	SQ	P	100	Progression
P44	F	63	Nodes	P	-27	Stable
P45	M	43	Lung, Nodes, SQ	P	-14	Stable
P46	M	68	SQ, Adrenal	IN	116	Progression
P48	M	86	Lung	P	0	Stable
P49	M	84	Lung, Liver, Nodes	P	125	Progression
P52	M	41	Bone	IN	67	Progression
P53	M	74	Lung, Adrenal	IN	100	Progression
P54	M	79	Nodes, SQ	IN	100	Progression
P55	F	37	SQ, Adrenal	IN	-100	Response
P56	M	66	Lung, Nodes	P	46	Progression
P57	M	70	Liver	I	-100	Response
P58	M	52	Nodes	P	-48	Response
P59	M	78	Lung	IN	-10	Stable
P61	M	58	Lung	IN	-40	Response
P63	M	63	Nodes, SQ	IN	-100	Response
P64	F	77	Lung, Liver, Bone	P	100	Progression
P65	M	69	Liver	P	131	Progression
P66	M	80	Lung, Nodes	IN	61	Progression
P67	M	83	Lung	IN	-34	Response
P68	M	92	Lung	IN	-34	Response
P69	F	55	Lung	IN	-87	Response

Taxonomic profiles showed stability of results on repeated patient sampling in five patients based on matched hierarchical clustering of species abundances among samples (FIG. 4).

Taxonomic profiles of pretreatment samples from ICT treated patients revealed significant differences in abundance of bacterial species between responder and progressors (FIGS. 1A-1D and FIGS. 5A-5B). FIGS. 5A and 5B show histograms of bacterial species' abundance versus response for FIG. 5A. *Alistipes shahii* in IN patients and, FIG. 5B. *Dorea Formicigenerans* in P patients. Among all treated patients, responder microbiomes were significantly enriched with *Bacteroides caccae* ($p = 0.034$; linear discriminant analysis coupled with effect size measurements, LEfSe; Kruskal-Wallis test) compared to those with progression. Among those patients treated only with IN, responder microbiomes were

enriched with *Bacteroides thetaiotamicron* ($p = 0.017$), *Alistipes shahii* ($p = 0.022$), the Firmicutes family *Ruminococcaceae* ($p = 0.025$), and *Streptococcus mutans* ($p = 0.039$). Among those patients treated only with P, responder microbiomes were enriched with *Dorea Formicigenerans* ($p = 0.045$).

Next, the inventors determined if antibiotic use during ICT modified gut microbiomes and affect response. Only three patients on the study received systemic antibiotics immediately before or during the treatment course. Patient #7 received a two weeks course of ceftriaxone prior to therapy. Patient #22 received two weeks of ciprofloxacin, vancomycin and metronidazole after two ICT cycles. Patient #44 received a course of nitrofurantoin after four ICT cycles. Only patient #23 took daily doses of the probiotic *Lactobacillus rhamnosus*. The taxome profile on this patient did not show any detectable *Lactobacillus rhamnosus*. No particular response or toxicity was linked to antibiotic or probiotic exposure.

Functional pathway enrichment based on KEGG analysis did not yield statistically significant differences between responders and progressors for any of the treatment groups.

Metabolomic analysis of the patient fecal samples showed differences in metabolites between responders and non-responders (FIGS. 2A, 2B and 6). IN responders had increased levels of anacardic acids; P responders showed, to a lesser degree, increased levels of arginine.

Based on the discovery of a food metabolite increased in responders, we expanded our patient histories to include queries regarding regular consumption of plant-related products with high levels of anacardic acid including cashews. Five of six patients with high 15:2 anacardic acid levels versus two of thirty-three evaluable patients with low 15:2 anacardic acid levels consumed cashews at least weekly (significant with $P < 0.0001$ chi-squared test with Yates continuity correction).

It was found that the general disease control rate (response plus stable disease) observed in the study for both IN and P was consistent with published results. Hodi and colleagues report a 59% response rate and 13% stable disease rate in a phase 2 study of IN [15], and Wolchok and coworkers achieved a 44% response rate and 8% stable disease rate in a phase 1 study of IN [16]. These numbers are close to the findings herein of a 54% response rate and 8% stable disease rate, and suggest the patient cohort and treatment management used herein was consistent with others.

The present invention stated with snapshots of patient gut microbiomes pretreatment, which may or may not reflect potential variations in taxome distribution over days-months of therapy. However, in repeat testing on five patients, there was evidence for relative stability of the microbiome based on matched hierarchical clustering of species abundances among the patient samples. These results are consistent with those of Gordon and Relman [17, 18]. Individual patient gut bacterial community composition remains stable for months unless perturbed by antibiotics or disease or dramatic diet change.

The present invention includes the first report of human gut microbiota in melanoma patients treated with combination anti-PD1 and anti-CTLA4 immunotherapy (IN) as well as anti-PD1 therapy alone (P). The findings of distinct predictive microbes for human ICT response for IN and P is unique. Six clades of bacteria involved in modulating ICT response were found. *Bacteroides* species have been previously reported to enhance anti-CTLA4 immune checkpoint efficacy in mice [9]. From the preclinical work,

these bacteria are presumed to directly contact and stimulate host dendritic cells and T cells via pathogen-associated molecular patterns--PAMPs. The clinical findings herein differ significantly from prior studies, and show an increase of *Bacteroides caccae*, *Bacteroides thetaiotamicron*, and *Alistipes shahii* in anti-CTLA4 plus anti-PD1 responders. In addition, it was found that firmicutes of the *Clostridiales* order—*Ruminococcaceae*, *Dorea formicigenerans* and of the *Lactobacillales* order--*Streptococcus mutans* were associated with anti-CTLA4 plus anti-PD1 clinical efficacy.

The detailed molecular mechanism for immune enhancement by any of the bacteria in humans remains unknown. By way of explanation, and in no way a limitation of the present invention, *in vitro* studies with dendritic cells have implicated some of these bacterial species with immune modulation. *Streptococcus mutans* activates dendritic cells (DCs) *in vitro* [22]. In part, the *Streptococcus mutans*' Wall-associated protein A (WapA) stimulates DC TLR4-induced NF- κ B pathway [23]. *Bacteroides thetaiotamicron* releases 10nm-80nm outer membrane vesicles (OMVs) that contain mucin-degrading glycosidase hydrolases and sulfatases [24]. These enzymes degrade the gut mucin and permit the OMVs to reach and be phagocytosed by DCs. The OMVs also contain toxins, adhesins and enzymes that trigger DC activation. *Bacteroides caccae* and *thetaiotamicron* are Gram-negative organisms with surface lipopolysaccharide (LPS) that stimulate DCs in a TLR4-dependent manner [25]. Similarly, the Gram-negative *Alistipes shahii* induces TLR4-signaling and DC production of TNF α improving the response of murine tumors to CpG-oligonucleotides and platinum [7]. The six identified response related bacteria merit *in vitro* testing with human peripheral blood mononuclear cells in mixed lymphocyte reactions (MLRs). When bacterial species are combined with ipilimumab and nivolumab in the MLR and secretion of interleukin-2 and interferon γ measured in the supernatant, the results provide an indirect assay of DC activation [26].

The present inventors found that there was little if any effect of patient exposure to systemic antibiotics or probiotics. For example, the lack of effect of the probiotic on patient #23 is consistent with a baseline stable commensal community that inhibits overgrowth of the probiotic organism [28, 29]. No particular response or toxicity was linked to antibiotic or probiotic exposure in this study.

The present inventors performed metabolomics on all 39 patient samples. Surprisingly, among thousands of measured metabolites, the most dramatic correlation with response was seen with a plant xenobiotic—15:2 anacardic acid (FIG. 7). This compound is an alkyl derivative of salicylic acid and produced in the nutshell of cashews [30]. Anacardic acids stimulate neutrophils and macrophages [31, 32]. Similar to the effects of particular bacterial species, the activation of macrophages/dendritic cells may enhance T cell recruitment to tumor metastases and, consequently, enhance ICT. Recently, cashew and other tree nut consumption were linked to reduced colon cancer recurrence in an epidemiologic study [33]. The present inventors found a correlation between cashew consumption and patient fecal anacardic acid levels.

Tables 2A to 2D show additional results from the present invention. A value greater than or equal to 1.0 is indicative of a response.

Table 2A

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
k	Archaea	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
p	Euryarchaeota	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
c	Methanobacteria	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
o	Methanobacteriales	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
f	Methanobacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
g	Methanobrevibacter	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
s	Methanobrevibacter_smithii	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	5.1	0.0	0.0	0.0	2.4	0.0	2.2	0.0
k	Bacteria	100.0	100.0	100.0	100.0	100.0	100.0	95.2	100.0	100.0	94.9	100.0	100.0	100.0	97.6	100.0	97.8	100.0
p	Actinobacteria	19.5	8.9	0.2	2.7	2.1	3.5	12.0	3.2	16.7	2.6	3.0	10.2	2.3	4.9	20.4	1.4	0.7
c	Actinobacteria	19.5	8.9	0.2	2.7	2.1	3.5	12.0	3.2	16.7	2.6	3.0	10.2	2.3	4.9	20.4	1.4	0.7
o	Actinomycetales	9.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.2	0.1	0.1	0.0
f	Corynebacteriaceae	9.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Corynebacterium	9.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium_amycolatum	8.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium_striatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Bifidobacteriales	7.2	4.2	0.0	0.1	0.0	2.2	9.4	2.0	16.1	0.5	2.5	5.7	1.8	0.0	0.0	0.1	0.0
f	Bifidobacteriaceae	7.2	4.2	0.0	0.1	0.0	2.2	9.4	2.0	16.1	0.5	2.5	5.7	1.8	0.0	0.0	0.1	0.0
g	Bifidobacterium	7.2	4.2	0.0	0.1	0.0	2.2	9.4	2.0	16.1	0.5	2.5	5.7	1.8	0.0	0.0	0.1	0.0
s	Bifidobacterium_adolescentis	6.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_animalis	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	12.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_bifidum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_breve	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	3.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_catulatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_dentium	0.0	0.2	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.1	0.2	1.2	0.0	0.0	0.1	0.0
s	Bifidobacterium_longum	0.8	4.0	0.0	0.1	0.0	0.0	9.4	1.2	0.0	0.0	0.4	5.5	0.6	0.0	0.0	0.0	0.0
s	Bifidobacterium_pseudocacum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	2.1	0.0	0.0	0.0	0.0	0.0	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
	tenulatum																	
o	Coriobacteriales	3.2	4.6	0.0	2.6	2.1	1.3	2.5	1.2	0.6	2.0	0.5	4.5	0.5	4.7	20.3	1.1	0.6
f	Coriobacteriaceae	3.2	4.6	0.0	2.6	2.1	1.3	2.5	1.2	0.6	2.0	0.5	4.5	0.5	4.7	20.3	1.1	0.6
g	Collinsella	0.0	4.4	0.0	0.0	2.0	0.0	0.0	0.9	0.0	1.9	0.3	4.2	0.0	3.8	16.6	1.1	0.0
s	Collinsella aerofaciens	0.0	4.4	0.0	0.0	2.0	0.0	0.0	0.9	0.0	1.9	0.0	4.2	0.0	0.0	16.6	1.1	0.0
s	Collinsella intestinalis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.8	0.0	0.0	0.0
g	Eggerthella	2.3	0.3	0.0	1.1	0.0	1.1	1.4	0.0	0.6	0.1	0.1	0.3	0.4	0.9	2.7	0.0	0.6
s	Eggerthella lenta	2.3	0.3	0.0	1.1	0.0	1.1	1.4	0.0	0.6	0.1	0.1	0.3	0.4	0.9	2.7	0.0	0.6
g	Gordonibacter	0.9	0.0	0.0	1.5	0.0	0.2	1.2	0.3	0.0	0.1	0.1	0.0	0.0	0.1	1.1	0.0	0.1
s	Gordonibacter pamelaecae	0.9	0.0	0.0	1.5	0.0	0.2	1.2	0.3	0.0	0.1	0.1	0.0	0.0	0.1	1.1	0.0	0.1
p	Bacteroidetes	1.1	4.0	61.8	58.3	24.8	15.5	22.3	31.4	29.6	23.0	56.3	4.1	7.2	22.2	31.2	20.3	35.7
c	Bacteroidia	1.1	4.0	61.8	58.3	24.8	15.5	22.3	31.4	29.6	23.0	56.3	4.1	7.2	22.2	31.2	20.3	35.7
o	Bacteroidales	1.1	4.0	61.8	58.3	24.8	15.5	22.3	31.4	29.6	23.0	56.3	4.1	7.2	22.2	31.2	20.3	35.7
f	Bacteroidaceae	0.6	3.8	60.0	49.2	11.3	15.1	16.6	22.5	26.5	6.5	39.9	4.0	5.9	14.6	31.2	11.5	35.1
g	Bacteroides	0.6	3.8	60.0	49.2	11.3	15.1	16.6	22.5	26.5	6.5	39.9	4.0	5.9	14.6	31.2	11.5	35.1
s	Bacteroides caecae	0.0	0.0	0.2	15.7	1.3	0.0	1.0	0.9	0.0	0.4	0.0	0.0	0.9	0.0	0.0	0.1	0.0
s	Bacteroides cellulosilyticu																	
s	Bacteroides coprophilus	0.0	0.1	0.0	2.5	0.1	0.0	0.0	0.0	0.0	0.7	0.0	0.1	0.0	1.4	0.0	0.1	0.0
s	Bacteroides coprocola	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides coprophilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.7	0.0
s	Bacteroides eggerthii	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides finegoldii	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	1.5	0.0
s	Bacteroides fragilis	0.0	0.0	0.0	0.0	0.0	3.2	0.0	0.0	5.6	0.0	0.0	0.0	1.6	0.0	0.2	0.2	0.0
s	Bacteroides intestinalis	0.1	0.0	0.0	0.0	1.9	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.5	0.0
s	Bacteroides ovatus	0.0	0.1	1.3	0.2	0.0	0.0	0.0	0.2	0.0	0.1	0.0	0.1	0.1	0.7	0.0	0.0	1.7
s	Bacteroides pectinophilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides plebeius	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides stercoris	0.0	0.0	0.0	0.0	0.1	0.0	0.0	2.6	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.3	0.0
s	Bacteroides thetaotaomicr																	
s	on	0.0	0.0	1.9	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.1	0.0	0.0	0.0	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	Bacteroides_unclassified	0.1	1.7	50.3	0.0	0.0	11.9	15.6	12.0	20.8	1.2	30.6	2.0	3.2	8.7	26.9	0.0	19.7
s	Bacteroides_uniformis	0.0	0.1	0.0	16.3	1.1	0.0	0.0	0.1	0.0	1.0	2.0	0.0	0.0	1.8	4.1	0.1	0.0
s	Bacteroides_vulgatus	0.3	1.7	6.3	8.1	5.1	0.0	0.0	5.6	0.0	2.0	4.0	1.7	0.0	1.7	0.0	3.6	13.7
s	Bacteroides_xylanisolvens	0.0	0.0	0.1	6.4	0.2	0.0	0.0	1.1	0.0	0.1	2.9	0.0	0.1	0.2	0.0	0.1	0.0
f	Porphyromonadaceae	0.1	0.1	0.0	8.9	0.6	0.0	1.2	1.9	0.0	3.6	12.0	0.1	1.1	2.7	0.0	3.4	0.0
g	Odoribacter	0.0	0.0	0.0	0.0	0.3	0.0	0.2	1.0	0.0	1.1	0.0	0.0	0.2	0.8	0.0	2.0	0.0
s	Odoribacter_splanchnicus	0.0	0.0	0.0	0.0	0.3	0.0	0.2	1.0	0.0	1.1	0.0	0.0	0.2	0.8	0.0	2.0	0.0
g	Parabacteroides	0.1	0.0	0.0	8.9	0.3	0.0	1.0	0.9	0.0	2.4	12.0	0.0	0.9	1.8	0.0	0.7	0.0
s	Parabacteroides_distasonis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0
s	Parabacteroides_johnsonii	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	0.0	0.0	0.0
s	Parabacteroides_merdae	0.1	0.0	0.0	5.8	0.3	0.0	0.7	0.6	0.0	1.7	9.1	0.0	0.7	0.0	0.0	0.6	0.0
s	Parabacteroides_unclassified	0.0	0.0	0.0	3.1	0.0	0.0	0.3	0.3	0.0	0.7	2.9	0.0	0.2	0.4	0.0	0.1	0.0
g	Porphyromonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.7	0.0
s	Porphyromonas_asaccharolytica	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.7	0.0
f	Prevotellaceae	0.0	0.0	0.0	0.0	10.4	0.4	0.0	0.0	3.1	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0
g	Prevotella	0.0	0.0	0.0	0.0	10.4	0.4	0.0	0.0	3.1	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0
s	Prevotella_copri	0.0	0.0	0.0	0.0	10.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Rikenellaceae	0.4	0.1	1.7	0.2	2.4	0.0	4.5	6.9	0.0	12.9	4.4	0.1	0.1	4.6	0.0	5.4	0.6
g	Alistipes	0.4	0.1	1.7	0.2	2.4	0.0	4.5	6.9	0.0	12.9	4.4	0.1	0.1	4.6	0.0	5.4	0.6
s	Alistipes_putredinis	0.3	0.0	0.0	0.0	1.8	0.0	4.2	6.1	0.0	11.5	4.3	0.0	0.0	3.7	0.0	1.9	0.0
s	Alistipes_shahii	0.1	0.0	0.1	0.0	0.6	0.0	0.3	0.8	0.0	1.4	0.1	0.0	0.0	0.8	0.0	3.3	0.1
s	Alistipes_unclassified	0.0	0.1	1.6	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.2	0.5
p	Firmicutes	78.6	86.3	16.3	38.4	67.9	78.1	36.2	64.9	51.3	67.1	39.8	85.1	90.4	52.6	43.1	59.0	61.2
c	Bacilli	3.2	1.9	4.7	0.9	0.3	10.1	1.4	0.4	3.6	2.6	0.7	1.5	69.4	0.8	0.6	0.6	0.8
o	Lactobacillales	3.2	1.9	4.7	0.8	0.3	10.1	1.4	0.4	3.6	2.6	0.7	1.5	69.4	0.8	0.6	0.6	0.8
f	Enterococcaceae	0.0	0.0	1.4	0.0	0.0	0.1	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Enterococcus	0.0	0.0	1.4	0.0	0.0	0.1	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_casseliflavus	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	<i>Enterococcus faecalis</i>	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Enterococcus faecium</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Enterococcus unclassified</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Lactobacillaceae	0.2	0.0	2.9	0.3	0.0	9.6	0.0	0.0	3.4	0.4	0.6	0.1	65.5	0.1	0.1	0.4	0.0
g	<i>Lactobacillus</i>	0.2	0.0	2.9	0.3	0.0	9.5	0.0	0.0	2.7	0.4	0.6	0.1	65.5	0.1	0.1	0.4	0.0
s	<i>Lactobacillus casei</i>	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
s	<i>Lactobacillus crispatus</i>	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
s	<i>Lactobacillus fermentum</i>	0.0	0.0	0.2	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	5.6	0.1	0.0	0.0	0.0
s	<i>Lactobacillus gasseri</i>	0.1	0.0	0.1	0.0	0.0	1.0	0.0	0.0	0.1	0.1	0.5	0.0	12.2	0.0	0.0	0.1	0.0
s	<i>Lactobacillus paracasei</i>	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Lactobacillus reuteri</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Lactobacillus ruminis</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Lactobacillus salivarius</i>	0.0	0.0	0.0	0.1	0.0	7.9	0.0	0.0	2.1	0.0	0.0	0.0	47.2	0.0	0.1	0.3	0.0
f	Streptococcaceae	2.9	1.8	0.2	0.4	0.3	0.4	1.4	0.4	0.0	2.2	0.1	1.4	3.9	0.6	0.5	0.2	0.8
g	<i>Lactococcus</i>	1.3	1.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.2	0.2	0.0	0.0
s	<i>Lactococcus lactis</i>	1.3	1.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.2	0.2	0.0	0.0
g	<i>Streptococcus</i>	1.6	0.8	0.1	0.4	0.3	0.4	1.3	0.4	0.0	2.1	0.1	0.6	3.9	0.5	0.4	0.2	0.8
s	<i>Streptococcus anginosus</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	<i>Streptococcus infantarius</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Streptococcus mutans</i>	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	1.0	0.0	0.0	0.0	0.0
s	<i>Streptococcus parasanguinis</i>	0.1	0.1	0.0	0.2	0.1	0.0	0.0	0.2	0.0	0.2	0.0	0.1	0.7	0.1	0.0	0.0	0.2
s	<i>Streptococcus salivarius</i>	0.7	0.4	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.4	0.1	0.2	1.7	0.1	0.0	0.2	0.5
s	<i>Streptococcus thermophilus</i>	0.2	0.2	0.0	0.0	0.0	0.0	1.3	0.0	0.0	0.2	0.0	0.2	0.1	0.0	0.3	0.0	0.1
s	<i>Streptococcus vestibularis</i>	0.2	0.1	0.0	0.1	0.2	0.3	0.0	0.0	0.0	0.0	0.0	0.1	0.4	0.1	0.0	0.0	0.0
c	Clostridia	65.4	66.2	0.7	33.9	65.5	53.6	28.7	64.3	41.7	63.0	39.1	66.6	20.5	49.7	37.9	57.9	51.2
o	Clostridiales	65.4	66.2	0.7	33.9	65.5	53.6	28.7	64.3	41.7	63.0	39.1	66.6	20.5	49.7	37.9	57.9	51.2
f	Clostridiaceae	11.7	33.3	0.0	2.9	0.2	20.3	8.4	0.3	20.6	2.0	4.6	33.6	0.9	15.7	14.7	0.2	6.6
g	Clostridium	11.7	33.3	0.0	2.7	0.2	20.3	8.4	0.2	20.6	2.0	4.6	33.6	0.9	15.7	14.7	0.2	6.6

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	<i>Clostridium asparagiforme</i>	0.0	0.0	0.0	0.5	0.0	0.4	0.0	0.0	1.1	0.0	0.2	0.0	0.0	0.2	0.7	0.0	0.4
s	<i>Clostridium bartlettii</i>	7.8	2.2	0.0	0.0	0.0	1.8	0.0	0.0	3.3	0.0	0.0	2.0	0.5	0.2	4.3	0.0	0.0
s	<i>Clostridium bolteae</i>	0.0	0.2	0.0	0.6	0.0	9.9	5.1	0.0	10.5	0.1	0.5	0.2	0.1	10.9	1.1	0.0	2.4
s	<i>Clostridium cf</i>	0.1	0.1	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.1
s	<i>Clostridium hathewayi</i>	0.0	0.0	0.0	0.2	0.0	1.5	0.0	0.0	2.8	0.0	0.1	0.0	0.0	1.5	0.1	0.1	0.2
s	<i>Clostridium hiranonis</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Clostridium leptum</i>	1.6	22.5	0.0	0.2	0.0	0.0	0.1	0.0	0.0	1.2	3.1	22.5	0.0	0.2	3.8	0.1	0.0
s	<i>Clostridium nexile</i>	0.0	8.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.3	0.1	8.6	0.0	0.4	0.0	0.0	1.8
s	<i>Clostridium perfringens</i>	0.0	0.1	0.0	0.0	0.0	0.3	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
s	<i>Clostridium scindens</i>	2.1	0.1	0.0	0.6	0.0	2.5	2.7	0.0	0.7	0.3	0.4	0.1	0.1	1.6	2.2	0.0	0.8
s	<i>Clostridium symbiosum</i>	0.0	0.1	0.0	0.2	0.0	4.0	0.5	0.0	2.1	0.0	0.2	0.1	0.1	0.6	1.7	0.0	1.0
f	Clostridiales Family_XI_I ncertae Sedis	3.6	0.1	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.1	0.0	0.7
g	<i>Anaerococcus</i>	1.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.1
s	<i>Anaerococcus unclassified</i>	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0
g	Clostridiales Family_XI_I ncertae Sedis unclassified	0.6	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.1	0.0	0.6
g	<i>Finegoldia</i>	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Finegoldia magna</i>	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	<i>Parvimonas</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Parvimonas micros</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	<i>Peptoniphilus</i>	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0
s	<i>Peptoniphilus harei</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Peptoniphilus unclassified</i>	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
f	Clostridiales uncl	0.4	0.2	0.7	1.1	0.3	0.1	0.3	0.4	0.0	0.2	2.6	0.2	0.6	0.5	3.7	0.2	0.6
g	<i>Blautia</i>	0.4	0.2	0.7	1.1	0.3	0.1	0.3	0.4	0.0	0.2	2.6	0.2	0.6	0.5	3.7	0.2	0.6
s	<i>Blautia hansenii</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.4
s	<i>Blautia hydrogenotrophica</i>	0.0	0.0	0.0	0.2	0.0	0.0	0.3	0.0	0.0	0.1	0.0	0.0	0.0	0.5	3.1	0.0	0.0
s	<i>Blautia unclassified</i>	0.4	0.2	0.7	0.9	0.3	0.1	0.0	0.4	0.0	0.1	0.0	0.2	0.0	0.0	0.5	0.2	0.3
f	Eubacteriaceae	11.7	1.8	0.0	20.8	13.0	31.6	0.0	6.0	18.7	14.5	1.1	1.6	8.7	6.2	3.9	11.1	0.0
g	<i>Eubacterium</i>	11.5	1.8	0.0	20.5	13.0	0.0	0.0	5.9	0.0	14.4	1.1	1.6	8.7	6.2	3.9	11.1	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	Eubacterium eligens	0.1	0.0	0.0	4.1	4.1	0.0	0.0	0.3	0.0	2.4	0.0	0.0	0.0	0.0	3.9	2.9	0.0
s	Eubacterium hallii	3.5	1.4	0.0	0.0	3.0	0.0	0.0	2.5	0.0	8.9	0.0	1.2	1.3	0.0	0.0	1.4	0.0
s	Eubacterium limosum	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.6	0.0	0.0	0.0
s	Eubacterium rectale	7.6	0.4	0.0	0.0	0.5	0.0	0.0	3.2	0.0	2.9	0.0	0.3	7.4	5.5	0.0	6.5	0.0
s	Eubacterium siraeum	0.0	0.0	0.0	16.4	5.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.1	0.0
s	Eubacterium ventriosum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.0	0.0	0.0	0.0	0.2	0.0
g	Pseudoramibacter	0.0	0.0	0.0	0.0	0.0	31.6	0.0	0.0	18.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Pseudoramibacter_lactolyticus	0.0	0.0	0.0	0.0	0.0	31.6	0.0	0.0	18.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Lachnospiraceae	11.3	18.5	0.0	0.8	32.0	0.1	0.4	22.5	0.0	8.9	7.6	19.6	2.1	0.2	2.2	14.1	0.1
g	Anaerostipes	0.1	0.0	0.0	0.2	0.0	0.0	0.4	0.0	0.0	0.0	0.1	0.0	0.0	0.2	1.5	0.0	0.1
s	Anaerostipes cacciae	0.1	0.0	0.0	0.2	0.0	0.0	0.4	0.0	0.0	0.0	0.1	0.0	0.0	0.2	1.5	0.0	0.1
g	Butyrivibrio	0.0	0.0	0.0	0.0	25.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	8.8	0.0
s	Butyrivibrio crossotus	0.0	0.0	0.0	0.0	25.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	8.8	0.0
g	Coprococcus	2.5	0.0	0.0	0.2	2.6	0.0	0.0	1.7	0.0	0.8	0.7	0.0	0.0	0.0	0.0	0.5	0.0
s	Coprococcus catus	2.5	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.3	0.0
s	Coprococcus comes	0.0	0.0	0.0	0.2	2.0	0.0	0.0	1.7	0.0	0.2	0.7	0.0	0.0	0.0	0.0	0.2	0.0
g	Dorea	8.0	0.0	0.0	0.4	1.5	0.0	0.0	2.9	0.0	7.5	0.0	0.0	1.8	0.0	0.0	3.1	0.0
s	Dorea formicigenerans	0.5	0.0	0.0	0.4	0.6	0.0	0.0	1.2	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.9	0.0
s	Dorea longicatena	7.4	0.0	0.0	0.0	1.0	0.0	0.0	1.7	0.0	6.1	0.0	0.0	1.8	0.0	0.0	2.2	0.0
g	Roseburia	0.7	18.5	0.0	0.0	2.9	0.0	0.0	17.9	0.0	0.6	6.9	19.6	0.3	0.0	0.7	1.7	0.0
s	Roseburia intestinalis	0.5	17.9	0.0	0.0	1.1	0.0	0.0	17.6	0.0	0.3	3.8	19.0	0.0	0.0	0.7	0.0	0.0
s	Roseburia inulinivorans	0.3	0.6	0.0	0.0	1.8	0.0	0.0	0.3	0.0	0.3	3.1	0.6	0.2	0.0	0.0	1.6	0.0
f	Ruminococcaceae	26.7	12.4	0.0	8.3	20.0	1.4	19.6	35.1	2.4	37.3	23.1	11.7	8.2	25.5	13.3	32.3	43.1
g	Anaerotruncus	0.2	0.0	0.0	0.0	0.1	0.6	0.1	0.0	1.7	0.1	0.1	0.0	0.1	0.1	0.1	0.0	0.1
s	Anaerotruncus_colihomini	0.2	0.0	0.0	0.0	0.1	0.6	0.1	0.0	1.7	0.1	0.1	0.0	0.1	0.1	0.1	0.0	0.1
g	Faecalibacterium	4.4	1.8	0.0	0.9	6.3	0.0	0.0	21.6	0.0	6.7	18.3	2.1	0.6	0.0	1.1	22.1	20.5
s	Faecalibacterium cf	1.8	0.0	0.0	0.0	0.8	0.0	0.0	1.2	0.0	1.2	0.0	0.0	0.2	0.0	0.0	0.3	18.5
s	Faecalibacterium_prausnitzii	2.6	0.9	0.0	0.7	5.5	0.0	0.0	20.4	0.0	5.4	18.2	1.0	0.2	0.0	1.0	21.8	0.7

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	Faecalibacterium_unclassified	0.0	0.9	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	1.1	0.1	0.0	0.1	0.0	1.3
s	Ruminococcus_bromii	0.0	0.0	0.0	0.0	6.7	0.0	0.0	0.0	0.1	26.7	0.0	0.0	2.6	22.9	0.1	4.6	10.0
s	Ruminococcus_gnavus	0.8	10.2	0.0	0.9	0.0	0.0	0.2	0.1	0.0	0.0	0.1	9.3	1.0	0.3	0.1	0.1	3.5
s	Ruminococcus_lactaris	4.7	0.0	0.0	1.0	0.0	0.0	0.0	10.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	2.1	0.0
s	Ruminococcus_obeum	11.3	0.2	0.0	0.3	1.2	0.0	19.2	0.8	0.0	2.5	0.3	0.2	0.0	0.0	0.1	1.2	0.0
s	Ruminococcus_torques	5.2	0.2	0.0	5.2	5.6	0.6	0.0	2.6	0.5	1.2	4.3	0.1	3.6	2.2	11.6	2.1	9.0
c	Erysipelotrichi	0.6	14.1	2.0	3.6	0.0	0.1	6.1	0.1	0.1	0.6	0.1	12.9	0.1	2.2	0.7	0.4	1.2
o	Erysipelotrichales	0.6	14.1	2.0	3.6	0.0	0.1	6.1	0.1	0.1	0.6	0.1	12.9	0.1	2.2	0.7	0.4	1.2
f	Erysipelotrichaceae	0.6	14.1	2.0	3.6	0.0	0.1	6.1	0.1	0.1	0.6	0.1	12.9	0.1	2.2	0.7	0.4	1.2
g	Catenibacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
s	Catenibacterium_mitsuoka	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
g	Coprobacillus	0.4	13.9	0.1	3.6	0.0	0.1	6.1	0.0	0.0	0.1	0.1	12.6	0.1	1.7	0.3	0.3	1.2
s	Coprobacillus_bacterium	0.4	13.9	0.1	3.6	0.0	0.1	6.1	0.0	0.0	0.1	0.1	12.6	0.1	1.7	0.3	0.3	1.2
g	Holdemania	0.2	0.2	1.9	0.0	0.0	0.0	0.0	0.1	0.0	0.5	0.0	0.3	0.0	0.0	0.4	0.1	0.0
s	Holdemania_filiformis	0.2	0.2	1.9	0.0	0.0	0.0	0.0	0.1	0.0	0.5	0.0	0.3	0.0	0.0	0.4	0.1	0.0
c	Negativicutes	9.4	4.1	8.9	0.0	2.1	14.3	0.0	0.0	5.9	1.0	0.0	4.1	0.4	0.0	3.9	0.1	8.1
o	Selenomonadales	9.4	4.1	8.9	0.0	2.1	14.3	0.0	0.0	5.9	1.0	0.0	4.1	0.4	0.0	3.9	0.1	8.1
f	Acidaminococcaceae	0.0	0.0	0.0	0.0	2.1	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
g	Acidaminococcaceae_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
g	Phascolarctobacterium	0.0	0.0	0.0	0.0	2.1	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Phascolarctobacterium_unclassified	0.0	0.0	0.0	0.0	2.1	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Veillonellaceae	9.4	4.1	8.9	0.0	0.0	14.3	0.0	0.0	5.9	0.0	0.0	4.1	0.4	0.0	3.8	0.1	8.1
g	Dialister	9.4	4.1	0.6	0.0	0.0	14.3	0.0	0.0	5.9	0.0	0.0	4.0	0.3	0.0	3.8	0.0	8.0
s	Dialister_invisus	9.4	4.1	0.6	0.0	0.0	14.3	0.0	0.0	5.9	0.0	0.0	4.0	0.3	0.0	3.8	0.0	8.0
g	Megamonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Megamonas_hypernegale	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Veillonella	0.0	0.0	8.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
s	Veillonella atypica	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella parvula	0.0	0.0	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella unclassified	0.0	0.0	5.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Fusobacteria	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
c	Fusobacteria	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
o	Fusobacteriales	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
f	Fusobacteriaceae	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
g	Fusobacterium	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	Fusobacterium ulcerans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
p	Proteobacteria	0.0	0.7	21.2	0.6	1.5	0.8	0.4	0.5	0.8	1.8	0.8	0.6	0.1	1.7	5.2	2.6	2.3
c	Betaproteobacteria	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Burkholderiales	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Sutterellaceae	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Sutterella	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Sutterella wadsworthensis	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
c	Deltaproteobacteria	0.0	0.0	0.0	0.0	0.1	0.1	0.4	0.4	0.1	0.8	0.8	0.0	0.0	0.1	4.3	1.2	0.0
o	Desulfovibrionales	0.0	0.0	0.0	0.0	0.1	0.1	0.4	0.4	0.1	0.8	0.8	0.0	0.0	0.1	4.3	1.2	0.0
f	Desulfovibrionaceae	0.0	0.0	0.0	0.0	0.1	0.1	0.4	0.4	0.1	0.8	0.8	0.0	0.0	0.1	4.3	1.2	0.0
g	Bilophila	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.4	0.0	0.6	0.8	0.0	0.0	0.0	4.2	0.1	0.0
s	Bilophila wadsworthia	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.4	0.0	0.6	0.8	0.0	0.0	0.0	4.2	0.1	0.0
g	Desulfovibrio	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.1	0.2	0.0	0.0	0.0	0.1	0.1	1.0	0.0
s	Desulfovibrio piger	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0
c	Gammaproteobacteria	0.0	0.7	21.2	0.6	0.0	0.1	0.0	0.1	0.2	1.0	0.0	0.6	0.1	1.6	0.9	1.5	2.3
o	Enterobacteriales	0.0	0.7	21.2	0.6	0.0	0.1	0.0	0.1	0.2	1.0	0.0	0.6	0.1	1.6	0.9	1.4	2.3
f	Enterobacteriaceae	0.0	0.7	21.2	0.6	0.0	0.1	0.0	0.1	0.2	1.0	0.0	0.6	0.1	1.6	0.9	1.4	2.3
g	Enterobacter	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterobacter cloacae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Escherichia	0.0	0.1	19.6	0.4	0.0	0.1	0.0	0.1	0.1	0.9	0.0	0.0	0.1	1.4	0.9	1.4	2.3
s	Escherichia coli	0.0	0.1	19.6	0.4	0.0	0.1	0.0	0.1	0.1	0.9	0.0	0.0	0.1	1.4	0.9	1.4	2.3
s	Escherichia unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

R a n k	Name	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
g	Klebsiella	0.0	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Klebsiella pneumoniae	0.0	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Klebsiella unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Verrucomicrobia	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0
c	Verrucomicrobiae	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0
o	Verrucomicrobiales	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0
f	Verrucomicrobiaceae	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0
g	Akkermansia	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0
s	Akkermansia muciniphila	0.8	0.2	0.3	0.0	3.8	2.0	24.3	0.0	1.6	0.2	0.0	0.0	0.0	16.0	0.0	14.2	0.0

Rank : k=kingdom p=phylum c=class o=order f=family g=genus s=species

Table 2B

Ra n k	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
k	Archaea	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
p	Euryarchaeota	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
c	Methanobacteria	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
o	Methanobacteriales	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
f	Methanobacteriaceae	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
g	Methanobrevibacter	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
s	Methanobrevibacter smithii	0.0	0.3	0.7	0.0	2.0	3.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0
k	Bacteria	100.0	99.7	99.3	100.0	98.0	96.9	100.0	99.6	100.0	100.0	100.0	100.0	100.0	99.4	100.0	100.0	100.0
p	Actinobacteria	2.2	0.1	1.3	16.6	5.7	5.0	2.0	0.6	9.2	10.6	4.0	5.8	15.6	1.4	14.3	0.5	10.3
c	Actinobacteria	2.2	0.1	1.3	16.6	5.7	5.0	2.0	0.6	9.2	10.6	4.0	5.8	15.6	1.4	14.3	0.5	10.3
o	Actinomycetales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.2	0.0	0.0
f	Corynebacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Corynebacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium amyco	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
	latum																	
s	Corynebacterium striatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Bifidobacteriales	0.1	0.0	0.0	11.7	2.5	1.3	0.1	0.0	4.3	7.9	0.0	0.1	11.3	0.6	0.3	0.0	8.8
f	Bifidobacteriaceae	0.1	0.0	0.0	11.7	2.5	1.3	0.1	0.0	4.3	7.9	0.0	0.1	11.3	0.6	0.3	0.0	8.8
g	Bifidobacterium	0.1	0.0	0.0	11.7	2.5	1.3	0.1	0.0	4.3	7.9	0.0	0.1	11.3	0.6	0.3	0.0	8.8
s	Bifidobacterium adolescentis	0.0	0.0	0.0	0.0	2.5	0.1	0.0	0.0	1.0	4.1	0.0	0.0	8.3	0.0	0.0	0.0	8.2
s	Bifidobacterium animalis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0
s	Bifidobacterium bifidum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.4	3.9	0.0	0.0	0.0	0.0	0.0	0.0	0.5
s	Bifidobacterium breve	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium catenulatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.0
s	Bifidobacterium dentium	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium longum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	0.6	0.1	0.0	0.1
s	Bifidobacterium pseudocatenulatum	0.1	0.0	0.0	6.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Coriobacteriales	2.1	0.1	1.2	4.8	3.3	3.6	1.9	0.6	4.9	2.6	3.9	5.7	4.3	0.8	13.8	0.5	1.5
f	Coriobacteriaceae	2.1	0.1	1.2	4.8	3.3	3.6	1.9	0.6	4.9	2.6	3.9	5.7	4.3	0.8	13.8	0.5	1.5
g	Collinsella	1.7	0.0	1.0	4.1	3.0	2.6	1.3	0.0	4.5	2.1	0.0	4.9	4.1	0.0	4.4	0.0	1.2
s	Collinsella aerofaciens	0.0	0.0	1.0	4.1	3.0	2.6	1.3	0.0	4.5	2.1	0.0	4.9	4.1	0.0	4.4	0.0	1.2
s	Collinsella intestinalis	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Eggerthella	0.3	0.1	0.1	0.3	0.2	0.9	0.5	0.4	0.3	0.4	2.6	0.8	0.1	0.5	8.7	0.0	0.2
s	Eggerthella lenta	0.3	0.1	0.1	0.3	0.2	0.9	0.5	0.4	0.3	0.4	2.6	0.8	0.1	0.5	8.7	0.0	0.2
g	Gordonibacter	0.1	0.0	0.0	0.4	0.1	0.0	0.0	0.2	0.1	0.1	1.3	0.0	0.0	0.4	0.6	0.5	0.1
s	Gordonibacter pamela	0.1	0.0	0.0	0.4	0.1	0.0	0.0	0.2	0.1	0.1	1.3	0.0	0.0	0.4	0.6	0.5	0.1
p	Bacteroidetes	37.5	21.3	36.9	16.3	10.0	26.4	21.7	45.4	1.0	46.9	45.5	21.8	46.9	39.1	6.6	41.2	20.6
c	Bacteroidia	37.5	21.3	36.9	16.3	10.0	26.4	21.7	45.4	1.0	46.9	45.5	21.8	46.9	39.1	6.6	41.2	20.6
o	Bacteroidales	37.5	21.3	36.9	16.3	10.0	26.4	21.7	45.4	1.0	46.9	45.5	21.8	46.9	39.1	6.6	41.2	20.6
f	Bacteroidaceae	33.1	18.0	20.3	14.6	7.0	12.8	6.4	19.4	0.2	31.8	24.9	15.9	40.9	20.8	3.9	23.9	16.4

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
g	Bacteroides	33.1	18.0	20.3	14.6	7.0	12.8	6.4	19.4	0.2	31.8	24.9	15.9	40.9	20.8	3.9	23.9	16.4
s	Bacteroides caccae	0.0	0.0	11.7	0.5	0.0	0.0	1.0	2.7	0.0	4.6	0.0	0.0	0.0	0.2	1.6	1.8	0.5
s	Bacteroides cellulosityti	0.9	0.0	0.1	0.0	0.2	0.0	0.1	1.1	0.0	0.1	0.0	5.5	0.1	0.7	0.1	0.0	0.3
s	Bacteroides coprocola	10.7	7.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides coprophilus	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides eggerthii	0.0	0.0	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	10.5	0.0	0.1	0.0	0.7	0.0	0.0
s	Bacteroides finegoldii	1.4	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4
s	Bacteroides fragilis	0.4	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0
s	Bacteroides intestinalis	0.0	0.0	1.9	0.0	0.0	2.8	0.0	0.0	0.0	7.2	0.0	0.0	0.0	0.0	0.9	0.0	0.0
s	Bacteroides ovatus	0.5	0.2	0.6	0.7	0.0	0.0	0.3	0.6	0.0	0.1	0.4	0.0	0.6	0.5	0.2	0.5	0.7
s	Bacteroides pectinophilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides plebeius	0.0	8.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	9.4
s	Bacteroides stercoris	3.1	0.3	0.0	3.8	0.0	0.0	0.5	0.2	0.0	0.4	0.0	2.9	21.0	10.0	0.1	0.0	1.7
s	Bacteroides thetaiotaomicron	0.0	0.0	0.3	0.4	0.0	0.6	0.1	0.4	0.0	0.6	0.0	0.2	0.0	0.0	0.0	0.0	0.0
s	Bacteroides unclassified	4.7	0.0	0.0	0.0	0.0	3.8	2.5	10.5	0.2	0.0	10.8	0.3	14.4	9.3	0.0	2.3	0.0
s	Bacteroides uniformis	0.0	0.0	0.0	4.3	0.1	0.0	0.0	0.2	0.0	7.2	0.3	6.5	0.0	0.0	0.1	0.0	0.4
s	Bacteroides vulgatus	8.9	1.1	4.5	4.7	4.3	5.2	1.6	3.0	0.0	10.6	2.7	0.0	3.4	0.0	0.1	19.1	2.5
s	Bacteroides xylanisolve	1.2	0.0	1.2	0.2	0.0	0.3	0.3	0.5	0.0	0.9	0.1	0.3	1.4	0.0	0.1	0.3	0.5
f	Porphyromonadaceae	3.6	0.7	4.6	1.2	1.0	0.6	0.7	6.9	0.8	8.1	8.9	0.6	5.5	2.6	0.7	8.4	3.1
g	Odoribacter	0.0	0.4	1.6	0.4	0.9	0.6	0.3	1.7	0.8	0.6	1.1	0.0	0.0	0.3	0.5	2.1	0.0
s	Odoribacter splanchnicus	0.0	0.4	1.6	0.4	0.9	0.6	0.3	1.7	0.8	0.6	1.1	0.0	0.0	0.3	0.5	2.1	0.0
g	Parabacteroides	3.6	0.3	1.9	0.9	0.0	0.0	0.5	5.3	0.0	7.5	7.8	0.6	5.5	2.3	0.2	6.3	3.1
s	Parabacteroides distasonis	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.1	0.0	0.0	5.2	0.0	0.0	0.0	0.0	0.0	0.0
s	Parabacteroides johnsonii	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.6	0.0	0.0	0.0	0.0	0.9	0.0
s	Parabacteroides merdae	2.7	0.3	1.5	0.7	0.0	0.0	0.5	3.5	0.0	5.6	0.0	0.4	4.2	1.6	0.1	3.2	3.0
s	Parabacteroides unclassified	0.9	0.0	0.4	0.0	0.0	0.0	0.0	1.7	0.0	1.9	0.0	0.2	1.3	0.7	0.1	2.2	0.0

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
g	Porphyromonas	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Porphyromonas_asaccharolytica	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Prevotellaceae	0.0	0.0	0.0	0.0	0.0	0.0	14.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Prevotella	0.0	0.0	0.0	0.0	0.0	0.0	14.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Prevotella_copri	0.0	0.0	0.0	0.0	0.0	0.0	14.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Rikenellaceae	0.9	2.6	12.1	0.4	2.0	13.1	0.2	19.1	0.0	7.0	11.7	5.2	0.5	15.7	1.9	8.9	1.2
g	Alistipes	0.9	2.6	12.1	0.4	2.0	13.1	0.2	19.1	0.0	7.0	11.7	5.2	0.5	15.7	1.9	8.9	1.2
s	Alistipes_putredinis	0.0	2.1	10.6	0.0	0.8	7.3	0.0	18.7	0.0	5.0	9.2	4.3	0.0	13.3	0.0	6.9	0.0
s	Alistipes_shahii	0.6	0.5	1.5	0.2	1.3	0.7	0.2	0.3	0.0	2.0	2.5	0.9	0.3	2.4	0.4	1.9	0.9
s	Alistipes_unclassified	0.4	0.0	0.0	0.2	0.0	5.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	1.6	0.0	0.2
p	Firmicutes	60.1	76.9	53.5	46.9	66.5	63.0	75.7	45.7	82.3	42.2	49.9	43.6	36.3	25.7	68.1	53.7	54.5
c	Bacilli	0.4	0.2	1.3	3.2	0.1	0.7	0.5	0.1	12.4	5.3	1.0	9.8	1.1	0.1	23.0	0.1	0.1
o	Lactobacillales	0.4	0.2	1.3	3.2	0.1	0.7	0.5	0.1	12.4	5.3	1.0	9.8	1.1	0.1	22.8	0.1	0.1
f	Enterococcaceae	0.0	0.0	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Enterococcus	0.0	0.0	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_casseliflavus	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_faecalis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_faecium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_unclassified	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Lactobacillaceae	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	4.2	0.0	0.0	0.7	0.0	0.0
g	Lactobacillus	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	4.2	0.0	0.0	0.7	0.0	0.0
s	Lactobacillus_casei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0
s	Lactobacillus_crispatus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_fermentum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_gasseri	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_paracasei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0
s	Lactobacillus_reuteri	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_ruminis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
s	Lactobacillus salivarius	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	0.0	0.0	0.0	0.0	0.0
f	Streptococcaceae	0.2	0.2	0.5	3.2	0.1	0.7	0.4	0.1	12.3	5.3	1.0	5.6	1.1	0.1	22.0	0.1	0.1
g	Lactococcus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
s	Lactococcus lactis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
g	Streptococcus	0.2	0.2	0.5	3.2	0.1	0.7	0.4	0.1	12.3	5.2	1.0	5.6	1.1	0.1	21.9	0.1	0.1
s	Streptococcus anginosus	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.8	0.0	0.0
s	Streptococcus infantarii	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Streptococcus mutans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	9.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Streptococcus parasanguinis	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
s	Streptococcus salivarius	0.1	0.0	0.0	0.2	0.0	0.0	0.2	0.0	0.1	1.0	0.3	2.3	0.3	0.0	0.5	0.0	0.0
s	Streptococcus thermophilus	0.1	0.0	0.2	0.1	0.0	0.0	0.1	0.1	0.0	3.6	0.3	1.8	0.2	0.0	0.3	0.1	0.0
s	Streptococcus vestibularis	0.0	0.1	0.0	2.4	0.0	0.7	0.0	0.0	2.0	0.1	0.3	0.1	0.0	0.0	19.5	0.0	0.0
s	Clostridia	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	1.0	0.2	0.0	0.5	0.0	0.0
c	Clostridiales	58.9	73.7	51.9	43.5	61.9	51.5	69.3	33.4	68.0	35.9	44.5	33.2	32.2	25.1	36.9	53.4	54.2
o	Clostridiaceae	58.9	73.7	51.9	43.5	61.9	51.5	69.3	33.4	68.0	35.9	44.5	33.2	32.2	25.1	36.9	53.4	54.2
f	Clostridium	6.1	0.7	7.8	10.0	3.0	2.1	14.5	1.7	1.2	3.9	11.2	6.9	0.5	3.1	10.2	0.1	2.7
g	Clostridium asparagiforme	6.1	0.7	7.8	10.0	3.0	2.1	14.5	1.7	0.9	3.9	11.0	6.9	0.5	3.1	10.2	0.1	2.7
s	Clostridium bartlettii	0.2	0.0	0.0	0.2	0.0	0.1	0.0	0.4	0.1	0.3	1.0	0.2	0.1	0.3	0.1	0.0	0.1
s	Clostridium bolteae	4.6	0.2	0.2	1.9	0.0	0.3	14.2	0.3	0.1	0.6	0.0	0.0	0.1	0.0	1.2	0.0	1.6
s	Clostridium cf	0.1	0.0	0.0	0.5	0.1	0.1	0.1	0.3	0.1	0.9	4.1	3.7	0.1	0.7	0.4	0.0	0.2
s	Clostridium hathewayi	0.0	0.0	0.2	0.0	0.1	0.0	0.0	0.2	0.0	0.2	1.4	0.0	0.0	0.0	0.0	0.0	0.0
s	Clostridium hiranonis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.1	0.0	0.1	5.3	0.0	0.2
s	Clostridium leptum	0.8	0.3	1.8	7.1	2.4	1.0	0.0	0.2	0.0	0.0	0.6	0.1	0.1	0.0	0.6	0.0	0.2
s	Clostridium nexile	0.0	0.1	5.2	0.0	0.4	0.2	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Clostridium perfringens	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.3	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.2
s	Clostridium scindens	0.2	0.0	0.0	0.4	0.0	0.0	0.0	0.1	0.2	0.1	3.5	1.3	0.0	1.6	2.2	0.0	0.2
s	Clostridium symbiosum	0.1	0.0	0.3	0.0	0.0	0.0	0.2	0.1	0.1	0.5	0.2	0.8	0.1	0.3	0.3	0.0	0.1
f	Clostridiales Family XI	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3	0.0	0.0

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
	Incertae Sedis																	
g	Anaerococcus	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0
s	Anaerococcus_unclassified	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0
g	Clostridiales Family_XI_Incertae Sedis_unclassified																	
g	Finegoldia	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
s	Finegoldia magna	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
g	Parvimonas	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Parvimonas micros	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Peptoniphilus	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0
s	Peptoniphilus harei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
s	Peptoniphilus_unclassified																	
f	Clostridiales uncl	0.2	0.1	0.1	0.3	0.0	0.2	0.1	0.1	1.1	0.2	1.4	5.8	0.2	0.2	3.6	0.2	0.2
g	Blautia	0.2	0.1	0.1	0.3	0.0	0.2	0.1	0.1	1.1	0.2	1.4	5.8	0.2	0.2	3.6	0.2	0.2
s	Blautia hansenii	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.7	5.8	0.1	0.0	0.0	0.0	0.0
s	Blautia_hydrogenotrophica	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.1	3.6	0.0	0.0
s	Blautia unclassified	0.1	0.1	0.0	0.3	0.0	0.1	0.1	0.1	0.4	0.2	0.4	0.0	0.1	0.1	0.0	0.2	0.2
f	Eubacteriaceae	6.1	22.6	0.4	12.0	8.4	17.9	2.3	15.2	51.5	5.0	8.5	4.6	15.9	1.0	3.4	11.1	9.9
g	Eubacterium	6.0	22.6	0.4	12.0	8.4	17.9	2.2	15.2	51.5	5.0	8.5	4.6	15.9	1.0	3.4	11.1	9.8
s	Eubacterium eligens	0.0	0.0	0.0	0.0	5.0	1.6	0.0	7.2	6.5	1.0	8.4	0.2	0.0	0.0	0.0	0.0	1.6
s	Eubacterium hallii	5.9	1.5	0.3	10.0	2.0	0.7	0.9	0.3	0.0	3.7	0.0	4.1	1.9	0.0	3.3	3.7	0.6
s	Eubacterium limosum	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Eubacterium rectale	0.0	14.7	0.0	2.0	0.0	11.3	0.7	7.7	45.0	0.2	0.0	0.0	12.1	0.9	0.0	6.5	6.2
s	Eubacterium siraeum	0.0	6.0	0.0	0.0	1.4	4.1	0.6	0.0	0.0	0.0	0.0	0.0	1.9	0.0	0.0	0.0	0.0
s	Eubacterium ventriosum	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.0	0.0	0.0	0.9	1.4
g	Pseudoramibacter	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Pseudoramibacter_alactolyticus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Lachnospiraceae	12.4	12.0	4.3	0.1	7.8	0.9	19.4	3.6	7.8	0.2	3.2	4.2	6.1	2.2	4.2	6.8	1.2

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
g	Anaerostipes	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.2	2.9	0.1	0.0	0.0	0.1	0.1	0.0
s	Anaerostipes cacciae	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.2	2.9	0.1	0.0	0.0	0.1	0.1	0.0
g	Butyrivibrio	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Butyrivibrio crossotus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Coprococcus	0.4	2.0	2.7	0.0	3.1	0.0	1.2	0.6	1.2	0.0	0.0	0.0	2.1	0.5	2.6	3.6	0.0
s	Coprococcus catus	0.4	0.7	0.3	0.0	1.5	0.0	0.0	0.0	1.2	0.0	0.0	0.0	0.6	0.0	1.3	1.1	0.0
s	Coprococcus comes	0.0	1.4	2.4	0.0	1.6	0.0	1.2	0.6	0.0	0.0	0.0	0.0	1.5	0.5	1.3	2.4	0.0
g	Dorea	1.0	4.7	0.2	0.0	4.6	0.2	9.0	1.7	3.2	0.0	0.1	0.0	0.3	0.2	1.4	3.2	0.9
s	Dorea formicigenerans	1.0	0.5	0.2	0.0	0.8	0.2	2.9	0.2	0.0	0.0	0.0	0.0	0.3	0.0	0.2	1.6	0.0
s	Dorea longicatena	0.0	4.2	0.0	0.0	3.7	0.0	6.1	1.4	3.2	0.0	0.0	0.0	0.0	0.2	1.2	1.6	0.9
g	Roseburia	11.0	5.2	1.5	0.1	0.2	0.6	9.3	1.3	3.4	0.0	0.2	4.1	3.6	1.6	0.0	0.0	0.3
s	Roseburia intestinalis	9.8	4.2	0.9	0.0	0.0	0.6	1.3	0.4	1.9	0.0	0.2	4.1	0.0	1.0	0.0	0.0	0.1
s	Roseburia inulinivorans	1.2	1.0	0.6	0.1	0.1	0.0	8.0	0.9	1.5	0.0	0.0	0.0	3.6	0.6	0.0	0.0	0.2
f	Ruminococcaceae	34.1	38.3	38.2	21.0	42.7	30.4	32.9	12.7	6.5	26.6	20.2	11.7	9.5	18.5	14.2	35.3	40.2
g	Anaerotruncus	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.1	0.2	0.4	0.4	0.2	0.1	0.2	0.0	0.0	0.1
s	Anaerotruncus colihomi nis	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.1	0.2	0.4	0.4	0.2	0.1	0.2	0.0	0.0	0.1
g	Faecalibacterium	7.6	13.2	1.3	16.0	8.7	2.1	12.5	12.3	0.0	12.8	0.0	0.0	4.8	5.6	0.1	11.1	5.8
s	Faecalibacterium cf	3.0	1.9	0.1	8.5	0.1	0.1	4.5	5.8	0.0	8.1	0.0	0.0	0.8	3.5	0.0	2.6	0.5
s	Faecalibacterium prausnitzii	3.0	11.3	1.2	6.6	8.5	1.8	5.0	4.7	0.0	2.9	0.0	0.0	2.6	0.6	0.1	8.4	4.9
s	Faecalibacterium uncclassified	1.7	0.0	0.0	0.9	0.2	0.2	2.9	1.8	0.0	1.7	0.0	0.0	1.4	1.6	0.0	0.1	0.3
s	Ruminococcus bromii	11.8	20.2	32.3	0.1	31.8	13.8	0.1	0.0	0.0	8.4	0.0	0.0	0.0	10.4	0.0	0.0	27.5
s	Ruminococcus gnavus	13.8	0.0	0.1	0.0	0.0	10.6	0.3	0.0	0.0	0.0	0.6	5.1	0.1	0.1	0.6	0.6	0.2
s	Ruminococcus lactaris	0.7	0.0	0.0	3.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	2.5
s	Ruminococcus obeum	0.0	0.7	1.7	0.8	1.8	0.0	0.3	0.1	0.0	1.0	0.0	0.1	0.1	2.0	2.0	14.3	0.0
s	Ruminococcus torques	0.1	4.0	2.7	0.1	0.2	3.9	19.7	0.1	6.3	3.9	19.2	6.3	3.8	0.2	11.5	9.3	4.1
c	Erysipelotrichi	0.2	0.0	0.4	0.1	3.7	7.9	2.5	0.2	0.0	0.3	4.4	0.5	0.0	0.5	8.2	0.1	0.2
o	Erysipelotrichales	0.2	0.0	0.4	0.1	3.7	7.9	2.5	0.2	0.0	0.3	4.4	0.5	0.0	0.5	8.2	0.1	0.2
f	Erysipelotrichaceae	0.2	0.0	0.4	0.1	3.7	7.9	2.5	0.2	0.0	0.3	4.4	0.5	0.0	0.5	8.2	0.1	0.2
g	Catenibacterium	0.0	0.0	0.0	0.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
s	Catenibacterium_mitsuo kai	0.0	0.0	0.0	0.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Coprobacillus	0.0	0.0	0.2	0.1	0.0	7.9	2.4	0.1	0.0	0.1	4.4	0.3	0.0	0.4	8.1	0.0	0.0
s	Coprobacillus bacterium	0.0	0.0	0.2	0.1	0.0	7.9	2.4	0.1	0.0	0.1	4.4	0.3	0.0	0.4	8.1	0.0	0.0
g	Holdemania	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.1	0.0	0.3	0.0	0.1	0.0	0.1	0.1
s	Holdemania filiformis	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.1	0.0	0.3	0.0	0.1	0.0	0.1	0.1
c	Negativicutes	0.6	2.9	0.0	0.1	0.7	2.8	3.5	12.0	1.9	0.7	0.0	0.0	2.9	0.0	0.0	0.1	0.0
o	Selenomonadales	0.6	2.9	0.0	0.1	0.7	2.8	3.5	12.0	1.9	0.7	0.0	0.0	2.9	0.0	0.0	0.1	0.0
f	Acidaminococcaceae	0.0	0.0	0.0	0.0	0.3	0.0	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Acidaminococcaceae_un classified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Phascolarctobacterium	0.0	0.0	0.0	0.0	0.0	0.0	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Phascolarctobacterium_un classified	0.0	0.0	0.0	0.0	0.0	0.0	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Veillonellaceae	0.6	2.9	0.0	0.1	0.4	2.8	0.1	12.0	1.9	0.7	0.0	0.0	2.9	0.0	0.0	0.1	0.0
g	Dialister	0.0	2.4	0.0	0.0	0.4	2.8	0.0	12.0	1.9	0.7	0.0	0.0	2.8	0.0	0.0	0.0	0.0
s	Dialister invisus	0.0	2.4	0.0	0.0	0.4	2.8	0.0	12.0	1.9	0.7	0.0	0.0	2.8	0.0	0.0	0.0	0.0
g	Megamonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Megamonas_hypermegale	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Veillonella	0.6	0.5	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0
s	Veillonella atypica	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella parvula	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0
s	Veillonella unclassified	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
c	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
o	Fusobacteriales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
f	Fusobacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
g	Fusobacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
s	Fusobacterium ulcerans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.4	0.0	0.0	0.0	0.0	0.0
p	Proteobacteria	0.2	1.4	7.6	1.0	15.8	1.8	0.6	0.7	7.4	0.3	0.5	1.4	1.1	1.7	10.5	4.6	14.5
c	Betaproteobacteria	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Rank	Name	P18	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34
o	Burkholderiales	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Sutterellaceae	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Sutterella	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Sutterella wadsworthensis	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
c	Deltaproteobacteria	0.2	0.0	0.3	0.0	0.1	0.3	0.5	0.7	0.0	0.3	0.5	0.6	0.8	1.7	0.5	0.0	0.3
o	Desulfovibrionales	0.2	0.0	0.3	0.0	0.1	0.3	0.5	0.7	0.0	0.3	0.5	0.6	0.8	1.7	0.5	0.0	0.3
f	Desulfovibrionaceae	0.2	0.0	0.3	0.0	0.1	0.3	0.5	0.7	0.0	0.3	0.5	0.6	0.8	1.7	0.5	0.0	0.3
g	Bilophila	0.2	0.0	0.2	0.0	0.1	0.3	0.4	0.6	0.0	0.2	0.4	0.6	0.8	1.2	0.1	0.0	0.3
s	Bilophila wadsworthia	0.2	0.0	0.2	0.0	0.1	0.3	0.4	0.6	0.0	0.2	0.4	0.6	0.8	1.2	0.1	0.0	0.3
g	Desulfovibrio	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.4	0.0	0.0
s	Desulfovibrio piger	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0
c	Gammaproteobacteria	0.0	1.4	7.3	1.0	15.3	1.5	0.1	0.0	7.2	0.0	0.1	0.8	0.3	0.0	10.0	4.6	14.2
o	Enterobacteriales	0.0	1.4	7.3	1.0	15.3	1.5	0.0	0.0	7.2	0.0	0.1	0.8	0.0	0.0	10.0	4.6	14.1
f	Enterobacteriaceae	0.0	1.4	7.3	1.0	15.3	1.5	0.0	0.0	7.2	0.0	0.1	0.8	0.0	0.0	10.0	4.6	14.1
g	Enterobacter	0.0	1.4	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterobacter cloacae	0.0	1.4	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Escherichia	0.0	0.0	5.7	1.0	1.2	1.3	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	9.5	4.6	0.2
s	Escherichia coli	0.0	0.0	3.8	1.0	1.2	1.3	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	9.5	2.9	0.2
s	Escherichia unclassified	0.0	0.0	1.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.7	0.0
g	Klebsiella	0.0	0.0	1.6	0.0	13.7	0.0	0.0	0.0	7.2	0.0	0.0	0.8	0.0	0.0	0.4	0.0	14.0
s	Klebsiella pneumoniae	0.0	0.0	1.6	0.0	10.9	0.0	0.0	0.0	6.1	0.0	0.0	0.6	0.0	0.0	0.4	0.0	2.5
s	Klebsiella unclassified	0.0	0.0	0.0	0.0	2.9	0.0	0.0	0.0	1.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	11.5
p	Verrucomicrobia	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0
c	Verrucomicrobiae	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0
o	Verrucomicrobiales	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0
f	Verrucomicrobiaceae	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0
g	Akkermansia	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0
s	Akkermansia muciniphila	0.0	0.0	0.0	19.3	0.0	0.8	0.0	7.2	0.0	0.0	0.0	22.0	0.1	31.4	0.5	0.0	0.0

Rank : k=kingdom p=phylum c=class o=order f=family g=genus s=species

Table 2C

Ran k	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
k	Archaea	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.6	4.4	2.4	2.5
p	Euryarchaeota	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.6	4.4	2.4	2.5
c	Methanobacteria	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.6	4.4	2.4	2.5
o	Methanobacteriales	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.6	4.4	2.4	2.5
f	Methanobacteriaceae	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.6	4.4	2.4	2.5
g	Methanobrevibacter	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.5	4.4	2.4	2.5
s	Methanobrevibacter_s mithii	0.0	8.0	0.0	10.2	0.0	0.0	0.0	0.0	0.0	23.4	0.0	0.0	0.0	21.0	3.5	4.4	2.4	2.5
k	Bacteria	100. 0	92.0	100. 0	89.8	100. 0	100. 0	100. 0	100. 0	100. 0	100. 0	100. 0	100. 0	100. 0	79.0	96.4	95.6	97.6	97.5
p	Actinobacteria	1.7	1.9	3.1	8.9	21.8	30.5	0.9	4.5	0.1	1.4	1.2	2.5	8.2	22.0	4.1	5.7	5.4	35.5
c	Actinobacteria	1.7	1.9	3.1	8.9	21.8	30.5	0.9	4.5	0.1	1.4	1.2	2.5	8.2	22.0	4.1	5.7	5.4	35.5
o	Actinomycetales	0.0	1.6	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.0	0.3	0.0
f	Corynebacteriaceae	0.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Corynebacterium	0.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium_amy colatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium_striat um	0.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Bifidobacteriales	0.2	0.0	2.7	3.3	0.9	26.6	0.0	2.8	0.0	0.0	0.0	0.0	2.8	14.9	0.0	1.6	0.0	29.1
f	Bifidobacteriaceae	0.2	0.0	2.7	3.3	0.9	26.6	0.0	2.8	0.0	0.0	0.0	0.0	2.8	14.9	0.0	1.6	0.0	29.1
g	Bifidobacterium	0.2	0.0	2.7	3.3	0.9	26.6	0.0	2.8	0.0	0.0	0.0	0.0	2.7	14.9	0.0	1.6	0.0	29.1
s	Bifidobacterium_adole scents	0.0	0.0	0.0	0.0	0.9	20.2	0.0	1.4	0.0	0.0	0.0	0.0	0.0	14.8	0.0	0.1	0.0	12.6
s	Bifidobacterium_anim alis	0.0	0.0	0.0	3.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_bifidu m	0.0	0.0	2.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.0
s	Bifidobacterium_breve	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
s	Bifidobacterium_caten	0.0	0.0	0.0	0.0	0.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
	ulatum																		
s	Bifidobacterium_dentium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.1	0.0	0.0	0.0	0.0
s	Bifidobacterium_longum	0.2	0.0	0.0	0.0	0.0	2.8	0.0	1.2	0.0	0.0	0.0	0.0	1.9	0.0	0.0	1.4	0.0	9.5
s	Bifidobacterium_pseudocatenulatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0
o	Coriobacteriales	1.5	0.3	0.4	5.5	21.0	3.9	0.9	1.7	0.0	1.4	1.1	2.5	5.3	7.1	4.1	4.1	5.1	6.4
f	Coriobacteriaceae	1.5	0.3	0.4	5.5	21.0	3.9	0.9	1.7	0.0	1.4	1.1	2.5	5.3	7.1	4.1	4.1	5.1	6.4
g	Collinsella	0.8	0.3	0.0	5.2	19.7	0.0	0.0	1.4	0.0	0.0	0.0	0.0	4.7	7.0	3.5	3.0	4.1	6.4
s	Collinsella_aerofaciens	0.8	0.3	0.0	5.2	19.7	0.0	0.0	1.3	0.0	0.0	0.0	0.0	4.7	7.0	3.5	3.0	0.0	6.4
s	Collinsella_intestinalis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.1	0.0
g	Eggerthella	0.5	0.0	0.3	0.3	0.7	3.3	0.0	0.4	0.0	1.4	1.0	1.8	0.6	0.1	0.6	1.0	1.0	0.0
s	Eggerthella_lenta	0.5	0.0	0.3	0.3	0.7	3.3	0.0	0.4	0.0	1.4	1.0	1.8	0.6	0.1	0.6	1.0	1.0	0.0
g	Gordonibacter	0.2	0.0	0.1	0.0	0.6	0.6	0.9	0.0	0.0	0.0	0.1	0.7	0.0	0.0	0.0	0.0	0.0	0.0
s	Gordonibacter_pamelae	0.2	0.0	0.1	0.0	0.6	0.6	0.9	0.0	0.0	0.0	0.1	0.7	0.0	0.0	0.0	0.0	0.0	0.0
p	Bacteroidetes	35.5	78.2	23.7	37.1	13.7	10.6	27.9	41.8	54.7	54.4	1.2	32.1	23.1	26.0	8.3	20.1	20.3	34.2
c	Bacteroidia	35.5	78.2	23.7	37.1	13.7	10.6	27.9	41.8	54.7	54.4	1.2	32.1	23.1	26.0	8.3	20.1	20.3	34.2
o	Bacteroidales	35.5	78.2	23.7	37.1	13.7	10.6	27.9	41.8	54.7	54.4	1.2	32.1	23.1	26.0	8.3	20.1	20.3	34.2
f	Bacteroidaceae	18.6	49.4	22.8	31.0	12.6	6.8	17.9	26.6	48.6	54.4	0.8	32.1	22.8	12.2	6.8	9.0	12.0	5.1
g	Bacteroides	18.6	49.4	22.8	31.0	12.6	6.8	17.9	26.6	48.6	54.4	0.8	32.1	22.8	12.2	6.8	9.0	12.0	5.1
s	Bacteroides_caccae	1.0	0.1	0.0	6.4	6.6	0.0	2.7	0.0	0.0	0.0	0.2	0.0	2.2	1.9	0.0	0.0	0.0	0.3
s	Bacteroides_cellulosilyticus	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	1.6	0.0
s	Bacteroides_coprocola	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6
s	Bacteroides_coprophilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5
s	Bacteroides_eggerthii	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0
s	Bacteroides_finegoldii	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	11.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides_fragilis	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.9	0.0	0.1	0.0	0.1	0.0	0.0
s	Bacteroides_intestinalis	0.0	0.3	0.0	0.0	0.0	0.1	0.0	11.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0	0.0

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
s	Bacteroides ovatus	0.2	0.0	0.0	1.0	0.1	0.1	0.3	0.2	0.0	6.3	0.1	2.0	0.1	0.1	0.1	0.0	0.6	0.0
s	Bacteroides pectinophilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides plebeius	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8
s	Bacteroides stercoris	0.0	0.0	0.0	2.0	0.8	4.2	0.0	14.2	31.3	17.6	0.1	0.0	0.0	2.7	0.8	0.0	0.0	0.3
s	Bacteroides thetaiotaomicron	0.0	1.1	7.3	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.1	1.1	0.4	0.0	0.0
s	Bacteroides unclassified	0.0	47.2	15.4	0.0	1.9	0.3	3.0	0.0	0.0	0.0	0.0	22.6	15.5	4.2	3.5	3.3	6.3	0.0
s	Bacteroides uniformis	0.6	0.0	0.0	1.4	0.2	0.1	0.0	0.3	0.0	19.2	0.1	4.2	1.1	0.6	0.0	0.0	1.3	0.1
s	Bacteroides vulgatus	16.1	0.1	0.0	19.2	0.9	1.3	11.5	0.0	5.9	5.7	0.4	0.0	3.1	2.0	0.0	3.1	2.0	1.4
s	Bacteroides xylophilus	0.5	0.4	0.0	0.9	0.1	0.1	0.5	0.0	0.0	4.9	0.0	2.4	0.8	0.1	0.3	0.2	0.3	0.1
f	Porphyromonadaceae	6.6	14.7	0.7	2.3	0.5	0.4	5.9	8.7	4.4	0.0	0.1	0.0	0.0	6.3	1.0	0.5	3.0	2.6
g	Odoribacter	2.3	8.2	0.7	1.7	0.1	0.1	0.6	1.0	0.8	0.0	0.0	0.0	0.0	3.6	0.7	0.5	0.8	0.3
s	Odoribacter splanchnicus	2.3	8.2	0.7	1.7	0.1	0.1	0.6	1.0	0.8	0.0	0.0	0.0	0.0	3.6	0.7	0.5	0.8	0.3
g	Parabacteroides	4.3	6.5	0.0	0.0	0.4	0.3	5.3	7.7	3.6	0.0	0.1	0.0	0.0	2.8	0.3	0.0	1.8	2.3
s	Parabacteroides distans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.2	0.0
s	Parabacteroides johnsonii	0.0	0.6	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	0.0
s	Parabacteroides merdarius	3.8	5.0	0.0	0.0	0.3	0.2	2.7	6.4	2.5	0.0	0.1	0.0	0.0	2.5	0.2	0.0	0.0	1.6
s	Parabacteroides unclassified	0.4	1.0	0.0	0.0	0.1	0.0	1.8	1.3	1.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.4	0.7
g	Porphyromonas	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0
s	Porphyromonas asaccharolytica	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0
f	Prevotellaceae	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.3	25.4
g	Prevotella	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.3	25.4
s	Prevotella copri	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	25.4

Ran k	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
f	Rikenellaceae	10.3	14.1	0.2	3.8	0.7	3.3	4.1	6.6	1.7	0.0	0.3	0.0	0.3	7.5	0.5	10.6	5.0	1.0
g	Alistipes	10.3	14.1	0.2	3.8	0.7	3.3	4.1	6.6	1.7	0.0	0.3	0.0	0.3	7.5	0.5	10.6	5.0	1.0
s	Alistipes putredinis	8.0	5.4	0.0	3.2	0.6	2.7	2.2	4.9	1.7	0.0	0.3	0.0	0.0	2.6	0.0	6.8	4.1	0.8
s	Alistipes shahii	2.4	3.8	0.0	0.6	0.1	0.6	1.9	1.6	0.0	0.0	0.0	0.0	0.0	4.9	0.4	0.4	0.9	0.2
s	Alistipes unclassified	0.0	4.9	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	3.4	0.0	0.0
p	Firmicutes	50.6	9.5	65.4	43.0	63.9	56.5	63.3	51.3	17.8	44.1	90.8	59.0	68.1	27.1	37.0	67.5	53.7	25.5
c	Bacilli	2.1	5.1	2.6	11.0	1.7	1.9	0.5	0.1	10.0	0.6	8.8	2.1	15.9	0.1	1.3	0.5	0.6	8.8
o	Lactobacillales	2.1	5.1	2.6	11.0	1.7	1.9	0.5	0.1	10.0	0.6	8.8	2.1	15.9	0.1	1.3	0.5	0.6	8.8
f	Enterococcaceae	0.1	4.5	0.0	0.0	0.0	0.0	0.1	0.0	9.6	0.0	2.4	2.1	0.0	0.0	0.1	0.0	0.0	0.0
g	Enterococcus	0.1	4.5	0.0	0.0	0.0	0.0	0.1	0.0	9.6	0.0	2.4	2.1	0.0	0.0	0.1	0.0	0.0	0.0
	Enterococcus casselifl																		
s	avus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus faecalis	0.0	4.5	0.0	0.0	0.0	0.0	0.0	0.0	9.6	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	Enterococcus faecium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.1	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus unclassified																		
f	Lactobacillaceae	0.3	0.6	0.0	1.8	0.0	0.3	0.0	0.0	0.0	0.0	0.3	0.0	7.3	0.0	0.4	0.0	0.1	8.7
g	Lactobacillus	0.3	0.6	0.0	1.8	0.0	0.3	0.0	0.0	0.0	0.0	0.3	0.0	7.3	0.0	0.3	0.0	0.1	8.7
s	Lactobacillus casei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus crispatus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus fermentum																		
s	Lactobacillus gasseri	0.0	0.0	0.0	0.5	0.0	0.2	0.0	0.0	0.0	0.0	0.2	0.0	1.5	0.0	0.1	0.0	0.1	0.0
s	Lactobacillus paracasei	0.0	0.6	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	Lactobacillus reuteri	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus ruminis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus salivarius	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3	0.0	0.0	0.0	0.0	8.7
f	Streptococcaceae	1.3	0.0	2.6	9.2	1.7	1.6	0.4	0.1	0.4	0.6	6.1	0.0	8.5	0.1	0.8	0.5	0.5	0.0
g	Lactococcus	0.1	0.0	0.0	0.3	0.2	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.3	0.0	0.0	0.0	0.1	0.0

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
s	Lactococcus lactis	0.1	0.0	0.0	0.3	0.2	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.3	0.0	0.0	0.0	0.1	0.0
g	Streptococcus	1.2	0.0	2.6	8.9	1.4	1.6	0.4	0.0	0.3	0.5	6.1	0.0	8.2	0.1	0.8	0.5	0.4	0.0
s	Streptococcus_anginosus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.1	0.0
s	Streptococcus_infantarius	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Streptococcus_mutans	0.0	0.0	0.0	3.2	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0
s	Streptococcus_paraniguis	0.5	0.0	0.0	0.8	0.1	0.1	0.0	0.0	0.0	0.2	0.4	0.0	0.4	0.0	0.3	0.0	0.1	0.0
s	Streptococcus_salivarius	0.2	0.0	0.1	1.0	0.3	0.4	0.2	0.0	0.0	0.1	0.6	0.0	4.0	0.0	0.0	0.0	0.1	0.0
s	Streptococcus_thermophilus	0.0	0.0	0.0	0.4	0.9	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.2	0.0	0.3	0.4	0.0	0.0
s	Streptococcus_vestibularis	0.0	0.0	0.0	3.6	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.6	0.0	0.2	0.0	0.1	0.0
c	Clostridia	48.2	1.9	56.2	27.8	61.9	51.4	62.7	49.4	6.8	40.5	79.7	56.1	25.8	26.7	29.4	54.9	51.2	12.3
o	Clostridiales	48.2	1.9	56.2	27.8	61.9	51.4	62.7	49.4	6.8	40.5	79.7	56.1	25.8	26.7	29.4	54.9	51.2	12.3
f	Clostridiaceae	0.6	0.6	4.4	2.6	2.5	7.6	0.1	1.6	0.0	1.0	2.2	5.6	2.1	10.2	6.2	2.2	13.7	0.5
g	Clostridium	0.6	0.5	4.4	2.6	2.5	7.6	0.1	1.6	0.0	1.0	2.2	5.6	2.1	10.2	6.2	2.2	13.7	0.5
s	Clostridium_asparagiforme	0.0	0.0	0.3	0.5	0.0	0.1	0.0	0.1	0.0	0.2	0.1	0.6	0.1	0.0	0.9	0.0	0.2	0.0
s	Clostridium_bartlettii	0.2	0.0	0.1	0.1	0.0	4.6	0.0	0.0	0.0	0.0	0.0	0.4	0.0	2.7	0.0	0.3	0.2	0.1
s	Clostridium_bolteae	0.0	0.0	1.4	1.3	0.9	0.2	0.0	0.3	0.0	0.3	0.0	2.1	1.0	0.0	1.4	0.0	9.2	0.0
s	Clostridium_cf	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.0	0.0
s	Clostridium_hathewayi	0.0	0.0	0.2	0.2	0.2	0.1	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.6	1.4	0.0	1.5	0.0
s	Clostridium_hiranonis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Clostridium_leptum	0.0	0.5	0.3	0.0	1.2	0.5	0.1	0.8	0.0	0.2	0.3	2.4	0.0	0.7	0.0	0.8	0.1	0.4
s	Clostridium_nexile	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.1	0.0	0.6	0.4	0.0
s	Clostridium_perfringens	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.8	0.0	0.1	4.0	0.0	0.2	0.0	0.0
s	Clostridium_scindens	0.1	0.0	1.7	0.3	0.0	1.9	0.0	0.2	0.0	0.0	0.0	0.0	0.4	0.0	2.0	0.0	1.5	0.0
s	Clostridium_symbiosum	0.0	0.0	0.2	0.0	0.0	0.1	0.0	0.1	0.0	0.2	0.0	0.0	0.4	0.0	0.2	0.0	0.5	0.0

Ran k	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
f	Clostridiales Family_ XI Incertae Sedis	0.0	0.7	0.0	0.0	0.0	0.2	0.0	1.5	6.7	0.0	0.0	1.4	0.0	0.0	0.0	0.0	7.0	0.0
g	Anaerococcus	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.1	0.4	0.0	0.0	0.3	0.0	0.0	0.0	0.0	2.7	0.0
s	Anaerococcus_unclassi fied	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.2	0.0	0.0	0.0	0.0	2.0	0.0
g	Clostridiales Family_ XI Incertae Sedis_unc lassified	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.4	0.0	0.0	0.0	0.0	1.6	0.0
g	Finegoldia	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.2	0.0
s	Finegoldia magna	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.2	0.0
g	Parvimonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Parvimonas micros	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Peptoniphilus	0.0	0.3	0.0	0.0	0.0	0.1	0.0	0.3	4.8	0.0	0.0	0.5	0.0	0.0	0.0	0.0	2.5	0.0
s	Peptoniphilus harei	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	2.6	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.2	0.0
s	Peptoniphilus_unclassi fied	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.3	2.3	0.0	0.0	0.3	0.0	0.0	0.0	0.0	2.2	0.0
f	Clostridiales_uncl	0.9	0.0	0.4	0.2	1.8	0.1	0.2	0.3	0.0	0.2	0.2	0.9	0.5	0.1	0.1	0.1	0.4	0.1
g	Blautia	0.9	0.0	0.4	0.2	1.8	0.1	0.2	0.3	0.0	0.2	0.2	0.9	0.5	0.1	0.1	0.1	0.4	0.1
s	Blautia hansenii	0.0	0.0	0.3	0.0	0.5	0.0	0.0	0.2	0.0	0.0	0.0	0.6	0.4	0.0	0.0	0.0	0.0	0.0
s	Blautia_hydrogenotrop hica	0.3	0.0	0.1	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.4	0.0
s	Blautia_unclassified	0.6	0.0	0.0	0.2	0.0	0.1	0.2	0.1	0.0	0.2	0.1	0.4	0.1	0.1	0.1	0.0	0.0	0.1
f	Eubacteriaceae	17.3	0.1	0.5	1.2	15.6	16.3	24.1	19.6	0.0	28.4	26.9	0.9	13.1	5.2	1.9	15.0	5.9	2.1
g	Eubacterium	17.3	0.1	0.5	1.2	15.5	16.3	24.1	19.5	0.0	28.4	26.9	0.9	13.1	5.1	1.8	15.0	5.8	2.1
s	Eubacterium eligens	2.2	0.0	0.0	0.0	4.0	2.4	0.0	0.0	0.0	0.0	0.2	0.3	0.0	0.0	0.0	1.0	0.0	0.1
s	Eubacterium hallii	1.7	0.0	0.0	0.3	2.7	6.6	2.2	9.2	0.0	0.9	2.0	0.6	0.0	0.0	0.0	0.7	0.0	1.2
s	Eubacterium limosum	0.0	0.0	0.5	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.1	0.2	0.7	0.0
s	Eubacterium rectale	6.4	0.1	0.0	0.9	4.0	7.1	21.4	10.3	0.0	27.5	23.2	0.0	13.1	0.1	0.0	9.4	5.1	0.9
s	Eubacterium siraeum	6.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.6	1.7	3.7	0.1	0.0
s	Eubacterium_ventriosu m	0.3	0.0	0.0	0.0	4.7	0.0	0.5	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Pseudoramibacter	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ran k	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
s	<i>Pseudoramibacter_alac tolyticus</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	<i>Lachnospiraceae</i>	14.4	0.1	3.4	12.6	14.6	5.3	6.8	8.2	0.0	4.8	33.5	22.1	1.1	4.2	3.2	0.7	0.2	2.6
g	<i>Anaerostipes</i>	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.1	0.1	0.2	0.0
s	<i>Anaerostipes cacciae</i>	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.1	0.1	0.2	0.0
g	<i>Butyrivibrio</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.1	0.0	0.0	0.0	0.0
s	<i>Butyrivibrio crossotus</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.1	0.0	0.0	0.0	0.0
g	<i>Coprococcus</i>	4.1	0.0	0.8	0.5	0.1	2.1	4.2	0.3	0.0	1.6	4.9	0.0	0.0	0.0	1.6	0.0	0.0	0.4
s	<i>Coprococcus catus</i>	1.5	0.0	0.8	0.3	0.0	2.1	0.9	0.3	0.0	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.0	0.1
s	<i>Coprococcus comes</i>	2.5	0.0	0.0	0.2	0.1	0.0	3.3	0.0	0.0	1.6	4.0	0.0	0.0	0.0	1.6	0.0	0.0	0.3
g	<i>Dorea</i>	4.5	0.0	0.0	0.2	10.3	2.2	2.6	4.4	0.0	2.2	13.7	0.0	1.0	0.0	0.1	0.2	0.0	1.9
s	<i>Dorea formicigenerans</i>	1.0	0.0	0.0	0.0	4.5	0.5	1.4	0.4	0.0	1.1	2.6	0.0	1.0	0.0	0.1	0.2	0.0	0.9
s	<i>Dorea longicatena</i>	3.4	0.0	0.0	0.2	5.8	1.6	1.2	4.0	0.0	1.1	11.1	0.0	0.0	0.0	0.0	0.0	0.0	1.0
g	<i>Roseburia</i>	5.9	0.0	2.6	11.8	4.2	1.0	0.0	3.5	0.0	1.0	14.9	21.8	0.0	0.0	1.4	0.4	0.0	0.4
s	<i>Roseburia intestinalis</i>	4.8	0.0	1.8	0.0	0.4	0.3	0.0	2.8	0.0	1.0	14.9	21.7	0.0	0.0	0.0	0.4	0.0	0.1
s	<i>Roseburia inulinivoran s</i>	1.1	0.0	0.8	11.8	3.9	0.7	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.3
f	<i>Ruminococcaceae</i>	15.0	0.4	47.4	11.1	27.4	21.8	31.5	18.3	0.1	6.1	16.9	25.2	9.0	7.1	17.9	36.9	24.0	7.0
g	<i>Anaerotruncus</i>	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.3	0.0	0.1	0.0
s	<i>Anaerotruncus colih o</i>	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.3	0.0	0.1	0.0
g	<i>Faecalibacterium</i>	3.9	0.0	0.0	0.7	3.5	2.7	11.6	9.2	0.0	0.0	8.5	0.0	0.1	0.5	1.9	1.5	0.0	5.0
s	<i>Faecalibacterium cf snitzii</i>	0.6	0.0	0.0	0.0	0.0	0.9	1.4	2.1	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.9
s	<i>Faecalibacterium uncl assified</i>	2.9	0.0	0.0	0.6	3.5	1.9	10.0	6.8	0.0	0.0	6.5	0.0	0.0	0.4	1.9	1.5	0.0	4.1
s	<i>Ruminococcus bromii</i>	0.0	0.0	41.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.1	0.0	0.0	0.0	0.0	0.0
s	<i>Ruminococcus gnavus</i>	0.6	0.0	3.6	0.0	0.0	1.9	0.1	0.1	0.0	0.4	4.7	6.3	2.0	0.2	0.1	10.3	0.3	0.0
s	<i>Ruminococcus lactaris</i>	0.0	0.0	0.0	5.8	0.0	0.0	0.0	0.0	0.0	4.1	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	<i>Ruminococcus obeum</i>	4.7	0.1	2.3	0.8	5.9	3.8	12.5	5.5	0.0	1.5	1.1	0.0	0.0	2.0	5.9	0.0	0.0	1.1

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
s	Ruminococcus torques	5.7	0.3	0.4	3.6	17.8	13.2	7.3	3.5	0.1	0.1	1.2	11.3	6.9	4.3	4.5	5.8	2.1	0.4
c	Erysipelotrichi	0.2	2.6	2.3	0.0	0.3	1.7	0.0	0.3	0.8	0.5	0.1	0.8	0.8	0.3	4.8	10.2	1.8	1.6
o	Erysipelotrichales	0.2	2.6	2.3	0.0	0.3	1.7	0.0	0.3	0.8	0.5	0.1	0.8	0.8	0.3	4.8	10.2	1.8	1.6
f	Erysipelotrichaceae	0.2	2.6	2.3	0.0	0.3	1.7	0.0	0.3	0.8	0.5	0.1	0.8	0.8	0.3	4.8	10.2	1.8	1.6
g	Catenibacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.2	0.0	0.0	1.6
s	Catenibacterium_mitsuokai	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.2	0.0	0.0	1.6
g	Coprobacillus	0.0	2.6	2.3	0.0	0.2	0.5	0.0	0.0	0.8	0.5	0.0	0.8	0.7	0.1	1.6	10.2	1.4	0.0
s	Coprobacillus_bacterium	0.0	2.6	2.3	0.0	0.2	0.5	0.0	0.0	0.8	0.5	0.0	0.8	0.7	0.1	1.6	10.2	1.4	0.0
g	Holdemania	0.2	0.0	0.0	0.0	0.2	0.9	0.0	0.2	0.0	0.0	0.1	0.0	0.1	0.1	0.0	0.0	0.0	0.0
s	Holdemania_filiformis	0.2	0.0	0.0	0.0	0.2	0.9	0.0	0.2	0.0	0.0	0.1	0.0	0.1	0.1	0.0	0.0	0.0	0.0
c	Negativicutes	0.0	0.0	4.3	4.2	0.0	1.5	0.0	1.4	0.2	2.5	2.3	0.0	25.7	0.0	1.6	1.9	0.0	2.9
o	Selenomonadales	0.0	0.0	4.3	4.2	0.0	1.5	0.0	1.4	0.2	2.5	2.3	0.0	25.7	0.0	1.6	1.9	0.0	2.9
f	Acidaminococcaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	2.9
g	Acidaminococcaceae_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Phascolarctobacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	2.9
s	Phascolarctobacterium_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	2.9
f	Veillonellaceae	0.0	0.0	4.3	4.2	0.0	1.5	0.0	1.4	0.2	2.5	2.3	0.0	25.7	0.0	0.0	1.9	0.0	0.0
g	Dialister	0.0	0.0	4.3	3.9	0.0	1.5	0.0	0.0	0.0	2.5	0.0	0.0	2.1	0.0	0.0	1.9	0.0	0.0
s	Dialister_invisus	0.0	0.0	4.3	3.9	0.0	1.5	0.0	0.0	0.0	2.5	0.0	0.0	2.1	0.0	0.0	1.9	0.0	0.0
g	Megamonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	23.2	0.0	0.0	0.0	0.0	0.0
s	Megamonas_hypermegale	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	23.2	0.0	0.0	0.0	0.0	0.0
g	Veillonella	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.2	0.0	2.3	0.0	0.4	0.0	0.0	0.0	0.0	0.0
s	Veillonella_atypica	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella_parvula	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0
s	Veillonella_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
p	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
c	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
o	Fusobacteriales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
f	Fusobacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
g	Fusobacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
s	Fusobacterium_ulceran s	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
p	Proteobacteria	0.7	2.4	0.7	0.7	0.4	0.2	7.8	2.1	3.9	0.1	6.8	6.4	0.5	2.9	2.3	1.7	1.6	2.3
c	Betaproteobacteria	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9
o	Burkholderiales	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9
f	Sutterellaceae	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9
g	Sutterella	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9
s	Sutterella_wadsworthie nsis	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9
c	Deltaproteobacteria	0.3	0.0	0.4	0.6	0.0	0.1	0.0	0.3	0.0	0.0	0.1	1.3	0.4	0.4	1.2	0.3	0.1	0.0
o	Desulfovibrionales	0.3	0.0	0.4	0.6	0.0	0.1	0.0	0.3	0.0	0.0	0.1	1.3	0.4	0.4	1.2	0.3	0.1	0.0
f	Desulfovibrionaceae	0.3	0.0	0.4	0.6	0.0	0.1	0.0	0.3	0.0	0.0	0.1	1.3	0.4	0.4	1.2	0.3	0.1	0.0
g	Bilophila	0.3	0.0	0.3	0.3	0.0	0.1	0.0	0.3	0.0	0.0	0.1	1.3	0.4	0.1	0.0	0.3	0.0	0.0
s	Bilophila_wadsworthia	0.3	0.0	0.3	0.3	0.0	0.1	0.0	0.3	0.0	0.0	0.1	1.3	0.4	0.1	0.0	0.3	0.0	0.0
g	Desulfovibrio	0.0	0.0	0.1	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	1.2	0.0	0.1	0.0
s	Desulfovibrio_piger	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.0	0.0	0.0	0.0
c	Gammaproteobacteria	0.4	2.4	0.3	0.0	0.3	0.1	7.8	1.8	3.9	0.1	6.7	5.1	0.1	2.5	1.0	1.4	1.5	1.4
o	Enterobacteriales	0.4	2.4	0.3	0.0	0.3	0.1	7.8	1.7	3.9	0.1	6.7	5.1	0.0	2.5	1.0	1.4	1.5	1.4
f	Enterobacteriaceae	0.4	2.4	0.3	0.0	0.3	0.1	7.8	1.7	3.9	0.1	6.7	5.1	0.0	2.5	1.0	1.4	1.5	1.4
g	Enterobacter	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterobacter_cloacae	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Escherichia	0.2	1.5	0.3	0.0	0.3	0.1	5.9	0.0	3.9	0.1	0.0	5.1	0.0	2.4	1.0	1.3	1.2	1.4
s	Escherichia_coli	0.2	1.5	0.3	0.0	0.3	0.1	3.3	0.0	3.9	0.1	0.0	5.1	0.0	2.4	1.0	1.3	1.2	1.4
s	Escherichia_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Klebsiella	0.2	0.0	0.0	0.0	0.0	0.0	2.0	1.7	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0

Rank	Name	P35	P36	P37	P38	P39	P40	P41	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52
s	Klebsiella pneumoniae	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	Klebsiella unclassified	0.0	0.0	0.0	0.0	0.0	0.0	1.9	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Verrucomicrobia	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5
c	Verrucomicrobiae	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5
o	Verrucomicrobiales	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5
f	Verrucomicrobiaceae	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5
g	Akkermansia	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5
s	Akkermansia_muciniphila	11.5	0.0	7.1	0.0	0.1	2.2	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1.0	44.7	0.6	16.5

Rank : k=kingdom p=phylum c=class o=order f=family g=genus s=species

Table 2D

Rank	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
k	Archaea	0.4	0.0	0.0	1.3	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
p	Euryarchaeota	0.4	0.0	0.0	1.3	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
c	Methanobacteria	0.4	0.0	0.0	1.3	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
o	Methanobacteriales	0.4	0.0	0.0	1.3	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
f	Methanobacteriaceae	0.4	0.0	0.0	1.3	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
g	Methanobrevibacter	0.4	0.0	0.0	1.3	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
s	Methanobrevibacter_smithii	0.4	0.0	0.0	1.3	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.1	0.0	0.0	0.0	0.0	0.0
k	Bacteria	99.6	100.0	100.0	98.7	96.5	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	94.9	100.0	100.0	100.0	100.0	100.0
p	Actinobacteria	2.9	7.2	5.6	8.4	1.6	7.3	1.2	8.8	1.5	5.8	2.0	8.0	10.6	6.9	1.6	1.7	1.6	1.2	6.5
c	Actinobacteria	2.9	7.2	5.6	8.4	1.6	7.3	1.2	8.8	1.5	5.8	2.0	8.0	10.6	6.9	1.6	1.7	1.6	1.2	6.5
o	Actinomycetales	0.3	0.1	0.0	0.1	0.0	0.0	0.2	0.1	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1
f	Corynebacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Corynebacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
s	Corynebacterium_ am ycolatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Corynebacterium_ str iatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Bifidobacteriales	0.0	2.4	0.3	3.7	0.1	5.2	0.0	4.3	0.0	2.3	0.3	1.5	0.5	1.1	0.0	0.0	0.2	0.0	2.7
f	Bifidobacteriaceae	0.0	2.4	0.3	3.7	0.1	5.2	0.0	4.3	0.0	2.3	0.3	1.5	0.5	1.1	0.0	0.0	0.2	0.0	2.7
g	Bifidobacterium	0.0	2.4	0.3	3.7	0.1	5.2	0.0	4.3	0.0	2.3	0.3	1.5	0.5	1.1	0.0	0.0	0.2	0.0	2.7
s	Bifidobacterium_ ado lescentis	0.0	0.6	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8
s	Bifidobacterium_ ani malis	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0
s	Bifidobacterium_ bifi dum	0.0	0.0	0.0	0.0	0.0	4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_ bre ve	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_ cate nulatum	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_ den tium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bifidobacterium_ lon gum	0.0	1.7	0.3	1.9	0.0	0.0	0.0	4.2	0.0	2.2	0.2	1.4	0.0	1.1	0.0	0.0	0.0	0.0	1.8
s	Bifidobacterium_ pse udocatenuatum	0.0	0.1	0.0	1.7	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1
o	Coriobacteriales	2.6	4.6	5.2	4.7	1.4	2.0	1.0	4.3	1.5	3.5	1.7	6.3	10.0	5.8	1.6	1.6	1.5	1.1	3.7
f	Coriobacteriaceae	2.6	4.6	5.2	4.7	1.4	2.0	1.0	4.3	1.5	3.5	1.7	6.3	10.0	5.8	1.6	1.6	1.5	1.1	3.7
g	Collinsella	0.0	4.4	4.0	4.6	1.4	1.9	0.0	4.2	0.0	0.0	1.6	6.0	10.0	5.4	0.0	0.8	0.0	0.0	3.5
s	Collinsella_ aerofacie ns	0.0	4.3	4.0	4.6	1.4	1.9	0.0	4.2	0.0	0.0	1.6	6.0	0.0	5.4	0.0	0.8	0.0	0.0	3.5
s	Collinsella_ intestinal is	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	9.9	0.0	0.0	0.0	0.0	0.0	0.0
g	Eggerthella	2.2	0.1	0.8	0.0	0.0	0.1	1.0	0.1	1.0	3.5	0.0	0.2	0.0	0.3	1.0	0.3	1.3	1.1	0.1
s	Eggerthella_ lenta	2.2	0.1	0.8	0.0	0.0	0.1	1.0	0.1	1.0	3.5	0.0	0.2	0.0	0.3	1.0	0.3	1.3	1.1	0.1
g	Gordonibacter	0.3	0.2	0.4	0.0	0.0	0.1	0.0	0.0	0.5	0.0	0.1	0.1	0.0	0.1	0.6	0.5	0.1	0.0	0.1
s	Gordonibacter_ pame	0.3	0.2	0.4	0.0	0.0	0.1	0.0	0.0	0.5	0.0	0.1	0.1	0.0	0.1	0.6	0.5	0.1	0.0	0.1

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
	laeae																			
p	Bacteroidetes	45.3	27.2	45.6	14.5	31.1	49.6	20.1	43.2	25.0	56.6	27.3	50.7	51.3	19.5	41.7	36.2	33.2	48.5	30.0
c	Bacteroidia	45.3	27.2	45.6	14.5	31.1	49.6	20.1	43.2	25.0	56.6	27.3	50.7	51.3	19.5	41.7	36.2	33.2	48.5	30.0
o	Bacteroidales	45.3	27.2	45.6	14.5	31.1	49.6	20.1	43.2	25.0	56.6	27.3	50.7	51.3	19.5	41.7	36.2	33.2	48.5	30.0
f	Bacteroidaceae	21.4	15.9	36.8	13.2	20.7	9.0	9.2	32.8	20.6	45.9	11.0	35.6	48.0	18.1	26.5	26.5	27.6	45.9	20.3
g	Bacteroides	21.4	15.9	36.8	13.2	20.7	9.0	9.2	32.8	20.6	45.9	11.0	35.6	48.0	18.1	26.5	26.5	27.6	45.9	20.3
s	Bacteroides cacciae	0.0	1.1	0.0	0.9	0.7	0.1	0.7	2.4	4.2	0.0	0.5	0.0	0.0	0.0	3.1	0.8	0.0	0.0	0.4
s	Bacteroides_cellulosi																			
s	lyticus	0.1	0.2	0.0	0.0	2.0	0.1	0.6	0.5	0.0	0.0	0.3	0.1	3.4	0.0	0.0	0.0	0.0	0.0	0.2
s	Bacteroides_coproco																			
s	la	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides_coprophi																			
s	ilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides_eggerthi																			
s	i	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2
s	Bacteroides_finegold																			
s	ii	0.0	1.9	1.5	1.2	0.0	0.3	0.0	0.8	0.0	0.0	2.2	0.0	3.8	0.0	0.2	0.0	0.0	0.0	2.1
s	Bacteroides_fragilis	0.4	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
s	Bacteroides_intestina																			
s	lis	0.0	0.0	0.0	0.0	7.0	0.0	0.0	0.0	1.8	0.0	0.0	1.4	0.0	0.0	0.0	6.2	10.1	0.0	0.0
s	Bacteroides_ovatus	1.3	0.1	1.1	0.1	0.1	0.1	0.9	0.1	0.4	0.0	0.1	0.9	0.0	1.3	0.5	1.1	0.0	1.3	0.1
s	Bacteroides_pectinop																			
s	hilus	0.0	0.0	0.0	0.0	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Bacteroides_plebeius	0.0	0.0	4.8	0.0	0.0	7.5	0.0	6.8	0.0	0.0	0.0	0.0	8.2	0.0	7.5	0.0	0.0	0.0	0.0
s	Bacteroides_stercoris	10.8	8.1	18.2	2.7	0.0	0.2	0.0	0.0	0.0	0.0	0.4	13.3	5.3	0.0	3.6	1.0	6.6	9.2	12.2
s	Bacteroides_thetaiota																			
s	omicron	0.0	0.4	0.3	0.4	0.0	0.0	1.9	0.2	0.2	0.0	0.1	0.0	6.5	0.0	0.0	0.3	4.7	8.4	0.3
s	Bacteroides_unclassi	2.8	3.7	8.8	3.6	0.0	0.0	3.2	3.0	0.1	41.3	0.5	9.2	5.4	11.0	6.5	0.0	6.2	19.3	4.6
s	Bacteroides_uniform																			
s	is	2.0	0.0	0.1	0.2	0.1	0.0	0.0	0.3	0.6	4.6	0.1	0.0	4.8	0.1	1.0	2.6	0.0	0.0	0.0
s	Bacteroides_vulgatus	2.6	0.0	1.6	2.9	7.6	0.6	1.6	18.0	12.7	0.0	6.0	10.7	7.0	4.8	3.6	14.3	0.0	6.8	0.0
s	Bacteroides_xylaniso	1.3	0.0	0.2	1.1	0.1	0.0	0.3	0.7	0.5	0.0	0.3	0.0	3.0	0.8	0.1	0.1	0.0	0.6	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
	lvens																			
f	Porphyromonadaceae	8.5	2.6	2.4	0.6	0.7	1.0	0.8	7.3	0.9	5.5	1.8	5.1	1.4	1.3	2.7	2.5	1.6	2.6	2.2
g	Odoribacter	6.7	0.6	0.5	0.0	0.5	0.3	0.7	0.0	0.9	0.0	0.6	0.0	0.0	0.0	2.1	0.5	0.0	0.0	0.6
s	Odoribacter_splanch	6.7	0.6	0.5	0.0	0.5	0.3	0.7	0.0	0.9	0.0	0.6	0.0	0.0	0.0	2.1	0.5	0.0	0.0	0.6
g	Parabacteroides	1.8	2.0	1.8	0.6	0.2	0.7	0.1	7.3	0.1	5.5	1.2	5.1	1.4	1.3	0.6	2.0	1.6	2.6	1.6
s	Parabacteroides_dist	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.3	0.0
s	Parabacteroides_john	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.4	0.5	0.0	0.9	0.4	0.0	0.6	0.0	0.0
s	Parabacteroides_mer	1.4	1.5	1.5	0.5	0.0	0.6	0.0	5.7	0.0	3.8	0.5	3.8	0.0	0.0	0.0	1.6	0.3	2.3	1.3
s	Parabacteroides_uncl	0.3	0.5	0.3	0.1	0.0	0.1	0.1	1.5	0.0	1.7	0.3	0.8	0.0	0.3	0.2	0.4	0.7	0.0	0.3
g	Porphyromonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Porphyromonas_asac	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Prevotellaceae	0.0	0.0	0.0	0.0	0.0	39.2	0.0	0.0	0.0	0.1	6.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Prevotella	0.0	0.0	0.0	0.0	0.0	39.2	0.0	0.0	0.0	0.1	6.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Prevotella_copri	0.0	0.0	0.0	0.0	0.0	39.2	0.0	0.0	0.0	0.0	6.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Rikenellaceae	15.4	8.7	6.4	0.7	9.7	0.5	10.0	3.1	3.4	5.2	8.4	9.9	1.8	0.1	12.5	7.2	4.0	0.1	7.5
g	Alistipes	15.4	8.7	6.4	0.7	9.7	0.5	10.0	3.1	3.4	5.2	8.4	9.9	1.8	0.1	12.5	7.2	4.0	0.1	7.5
s	Alistipes_putredinis	13.5	8.0	5.7	0.0	7.6	0.5	5.3	0.0	0.0	0.0	7.4	9.0	0.0	0.0	9.2	5.9	0.0	0.0	6.9
s	Alistipes_shahii	1.0	0.7	0.8	0.1	2.0	0.0	4.8	2.5	0.7	0.6	1.0	0.9	0.3	0.0	3.3	1.4	4.0	0.0	0.6
s	Alistipes_unclassified	0.8	0.0	0.0	0.5	0.0	0.0	0.0	0.6	2.8	4.5	0.0	0.0	1.4	0.1	0.0	0.0	0.0	0.0	0.0
p	Firmicutes	36.5	60.7	48.0	75.1	63.5	41.6	78.6	45.9	67.9	25.6	63.8	40.9	35.3	66.1	54.4	61.6	64.2	37.5	55.7
c	Bacilli	2.2	2.4	0.3	6.2	0.1	0.3	41.8	5.3	0.1	0.6	0.2	3.4	2.9	0.6	3.9	3.2	0.3	0.1	2.4
o	Lactobacillales	2.2	2.4	0.3	6.1	0.1	0.3	41.8	5.3	0.1	0.6	0.2	3.4	2.9	0.6	3.9	3.2	0.3	0.1	2.4
f	Enterococcaceae	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Enterococcus	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_casseli	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
	flavus																			
s	Enterococcus_faecalis	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_faecium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Enterococcus_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Lactobacillaceae	0.0	1.7	0.0	3.5	0.1	0.0	14.3	0.8	0.0	0.0	0.0	0.1	0.7	0.1	0.1	0.0	0.0	0.0	1.4
g	Lactobacillus	0.0	1.7	0.0	3.5	0.1	0.0	14.3	0.8	0.0	0.0	0.0	0.1	0.7	0.1	0.1	0.0	0.0	0.0	1.4
s	Lactobacillus_casei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
s	Lactobacillus_crispat	0.0	0.6	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
s	Lactobacillus_fermentum	0.0	0.9	0.0	0.0	0.0	0.0	11.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8
s	Lactobacillus_gasseri	0.0	0.1	0.0	0.0	0.0	0.0	1.2	0.5	0.0	0.0	0.0	0.1	0.3	0.0	0.0	0.0	0.0	0.0	0.1
s	Lactobacillus_paracasei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_reuteri	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_ruminis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactobacillus_salivarius	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Streptococcaceae	2.1	0.7	0.3	2.6	0.0	0.3	26.0	4.5	0.1	0.6	0.1	3.3	2.2	0.5	3.8	3.1	0.3	0.1	1.0
g	Lactococcus	0.5	0.0	0.1	0.1	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Lactococcus_lactis	0.5	0.0	0.1	0.1	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Streptococcus	1.6	0.7	0.2	2.5	0.0	0.3	25.8	4.5	0.1	0.5	0.1	3.2	2.2	0.5	3.7	3.1	0.3	0.1	1.0
s	Streptococcus_anginosus	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Streptococcus_infantarius	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Streptococcus_mutans	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0
s	Streptococcus_parasanguinis	1.1	0.3	0.1	0.8	0.0	0.1	8.4	3.1	0.0	0.1	0.0	1.7	0.6	0.1	0.1	0.3	0.1	0.0	0.4

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
s	Streptococcus_saliva rius	0.3	0.2	0.1	1.1	0.0	0.1	14.7	0.5	0.1	0.2	0.1	0.6	0.5	0.2	0.2	2.0	0.1	0.0	0.4
s	Streptococcus_therm ophilus	0.1	0.0	0.0	0.0	0.0	0.1	2.3	0.2	0.0	0.1	0.0	0.0	0.1	0.0	3.4	0.1	0.0	0.1	0.0
s	Streptococcus_vestib ularis	0.1	0.1	0.0	0.2	0.0	0.0	0.3	0.3	0.0	0.0	0.0	0.1	0.8	0.0	0.0	0.1	0.1	0.0	0.1
c	Clostridia	34.3	57.7	45.2	61.8	63.3	41.2	36.2	36.9	64.1	24.3	63.6	36.1	11.7	64.6	50.1	58.1	60.6	37.0	52.9
o	Clostridiales	34.3	57.7	45.2	61.8	63.3	41.2	36.2	36.9	64.1	24.3	63.6	36.1	11.7	64.6	50.1	58.1	60.6	37.0	52.9
f	Clostridiaceae	1.2	6.8	2.5	1.8	0.5	0.2	6.3	4.7	3.2	9.3	1.0	3.7	10.0	1.9	3.1	0.4	3.5	18.3	5.8
g	Clostridium	1.2	6.8	2.5	1.8	0.5	0.1	6.3	4.7	3.2	9.3	1.0	3.7	10.0	1.9	3.1	0.4	3.3	18.3	5.8
s	Clostridium_asparagi forme	0.0	0.1	0.3	0.0	0.0	0.0	0.1	2.3	0.1	0.9	0.1	0.1	0.0	0.1	0.6	0.1	0.6	0.0	0.1
s	Clostridium_bartlettii	0.0	2.2	0.0	1.5	0.4	0.1	0.0	0.0	0.0	0.1	0.7	1.5	0.0	0.0	0.0	0.0	0.0	3.5	3.4
s	Clostridium_boleae	0.1	0.1	0.9	0.0	0.0	0.0	0.2	0.6	0.6	3.1	0.0	0.5	1.5	0.3	0.9	0.0	0.8	14.6	0.1
s	Clostridium_cf	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.1	0.1	0.0	0.1	0.1	0.0	0.2	0.0	0.0
s	Clostridium_hathewa yi	0.2	0.0	0.2	0.0	0.0	0.0	0.9	0.1	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.2	0.0
s	Clostridium_hiranoni s	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.7	0.0	0.0	0.0	0.0	0.0	0.0
s	Clostridium_leptum	0.5	1.2	0.1	0.3	0.0	0.0	0.3	0.0	1.6	0.2	0.0	0.1	3.3	0.7	0.1	0.2	0.1	0.0	1.3
s	Clostridium_nexile	0.0	2.9	0.0	0.0	0.0	0.0	0.0	0.2	0.0	2.1	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.0	0.6
s	Clostridium_perfring ens	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Clostridium_scinden s	0.1	0.1	0.9	0.0	0.0	0.0	4.4	1.0	0.4	0.5	0.0	0.5	0.3	0.5	1.2	0.0	0.7	0.0	0.1
s	Clostridium_symbios um	0.0	0.0	0.1	0.0	0.0	0.0	0.3	0.1	0.3	0.7	0.1	0.1	0.1	0.2	0.1	0.0	0.8	0.0	0.0
f	Clostridiales_Family XI Incertae Sedis	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0
g	Anaerococcus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Anaerococcus_uncla ssified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Clostridiales_Family	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
	XI Incertae Sedis_unclassified																			
g	Finegoldia	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Finegoldia magna	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Parvimonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Parvimonas micros	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Peptoniphilus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Peptoniphilus harei	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Peptoniphilus_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Clostridiales uncl	2.9	0.1	0.9	0.1	0.8	0.1	9.7	0.5	1.6	1.6	0.1	0.4	1.0	0.2	0.1	0.7	1.2	0.1	0.1
g	Blautia	2.9	0.1	0.9	0.1	0.8	0.1	9.7	0.5	1.6	1.6	0.1	0.4	1.0	0.2	0.1	0.7	1.2	0.1	0.1
s	Blautia hansemii	0.0	0.0	0.0	0.0	0.0	0.0	6.3	0.3	1.1	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Blautia_hydrogenotr	2.9	0.1	0.0	0.0	0.0	0.0	3.4	0.0	0.4	0.8	0.1	0.4	0.0	0.1	0.0	0.7	1.2	0.0	0.1
s	Blautia unclassified	0.0	0.0	0.8	0.1	0.8	0.1	0.0	0.2	0.0	0.0	0.1	0.0	1.0	0.2	0.1	0.0	0.0	0.1	0.0
f	Eubacteriaceae	5.6	10.6	0.7	26.4	37.6	22.7	2.7	6.6	1.5	11.0	20.1	9.1	0.3	35.1	10.2	17.2	10.5	0.0	12.1
g	Eubacterium	5.6	10.6	0.7	26.4	37.6	22.7	2.5	6.6	1.5	11.0	20.1	9.1	0.3	35.1	10.2	17.2	10.4	0.0	12.1
s	Eubacterium eligens	1.9	0.4	0.0	0.0	0.8	7.2	0.0	0.0	0.6	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
s	Eubacterium hallii	0.2	0.3	0.7	1.3	1.6	1.7	0.0	3.9	0.4	0.0	1.0	0.0	0.0	0.5	0.0	1.3	0.0	0.0	0.2
s	Eubacterium_limosu	0.0	0.1	0.0	0.0	0.0	0.0	2.4	0.1	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.6	0.0	0.1
s	Eubacterium rectale	0.0	8.0	0.0	25.1	6.4	13.5	0.1	2.6	0.0	11.0	16.7	7.9	0.0	20.4	4.9	12.9	0.0	0.0	8.4
s	Eubacterium_siraeu	3.4	1.9	0.0	0.0	28.5	0.2	0.1	0.0	0.4	0.0	1.2	0.0	0.0	14.2	5.3	3.0	9.8	0.0	2.7
s	Eubacterium_ventrio	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Pseudoramibacter	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Pseudoramibacter_al	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	actolyticus	10.2	2.5	3.8	9.6	6.1	6.7	0.2	10.1	17.1	0.9	4.1	10.5	0.0	17.1	11.5	6.5	11.7	0.2	2.2
g	Lachnospiraceae	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.1	0.0
g	Anaerostipes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
s	Anaerostipes caccacae	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.1	0.0
g	Butyrivibrio	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Butyrivibrio crossotus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Coprococcus	9.1	1.7	0.2	3.9	1.7	1.2	0.0	0.6	0.0	0.0	0.6	1.3	0.0	2.1	8.9	0.6	0.0	0.0	1.4
s	Coprococcus catus	0.4	0.6	0.2	0.3	0.9	0.0	0.0	0.2	0.0	0.0	0.6	0.6	0.0	0.0	3.7	0.6	0.0	0.0	0.5
s	Coprococcus comes	8.7	1.1	0.0	3.6	0.7	1.2	0.0	0.4	0.0	0.0	0.0	0.7	0.0	2.1	5.2	0.0	0.0	0.0	0.9
g	Dorea	1.1	0.8	3.6	3.3	1.6	1.2	0.0	0.9	0.0	0.0	1.5	1.1	0.0	3.4	0.0	5.1	9.6	0.0	0.8
s	Dorea formicigenerans	0.0	0.2	3.6	0.5	0.7	0.6	0.0	0.7	0.0	0.0	1.1	0.0	0.0	1.1	0.0	1.4	5.5	0.0	0.2
s	Dorea longicatena	1.1	0.6	0.0	2.8	0.9	0.6	0.0	0.2	0.0	0.0	0.4	1.1	0.0	2.3	0.0	3.7	4.1	0.0	0.6
g	Roseburia	0.0	0.0	0.0	2.4	2.8	4.2	0.0	8.5	17.1	0.0	2.0	8.2	0.0	11.6	1.6	0.8	2.0	0.0	0.0
s	Roseburia intestinalis	0.0	0.0	0.0	0.8	2.7	2.2	0.0	0.0	13.9	0.0	0.4	4.0	0.0	8.1	1.6	0.7	0.0	0.0	0.0
s	Roseburia inulinivorans	0.0	0.0	0.0	1.6	0.1	2.0	0.0	8.5	3.1	0.0	1.5	4.2	0.0	3.5	0.0	0.1	2.0	0.0	0.0
f	Ruminococcaceae	14.3	37.7	37.2	23.8	18.3	11.6	17.2	15.0	40.6	1.4	38.3	12.3	0.3	10.3	25.1	33.2	33.8	18.4	32.6
g	Anaerotruncus	0.0	0.0	0.1	0.0	0.0	0.0	0.4	0.4	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
s	Anaerotruncus colihominis	0.0	0.0	0.1	0.0	0.0	0.0	0.4	0.4	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
g	Faecalibacterium	0.1	5.7	6.6	20.6	13.3	10.8	0.0	6.8	1.6	0.0	21.1	2.2	0.0	0.0	4.4	11.7	20.1	0.0	5.6
s	Faecalibacterium cf	0.1	3.1	0.0	4.0	1.2	4.9	0.0	0.6	0.0	0.0	1.8	1.7	0.0	0.0	0.8	0.7	10.7	0.0	3.1
s	Faecalibacterium prausnitzii	0.0	1.9	1.1	16.5	11.3	5.0	0.0	5.5	1.3	0.0	19.3	0.2	0.0	0.0	2.9	11.0	6.6	0.0	1.9
s	Faecalibacterium unclassified	0.0	0.7	5.4	0.0	0.8	0.9	0.0	0.6	0.3	0.0	0.0	0.3	0.0	0.0	0.7	0.0	2.7	0.0	0.7
s	Ruminococcus bromii	0.0	13.6	0.0	0.0	0.0	0.0	0.0	3.2	28.7	0.0	12.3	0.0	0.0	0.2	0.0	11.3	0.0	0.0	13.7
s	Ruminococcus gnavus	0.0	10.2	0.9	0.0	0.0	0.0	0.2	0.0	0.5	1.3	0.0	0.8	0.2	0.0	0.0	0.0	0.0	7.5	10.3
s	Ruminococcus lactaris	0.0	0.0	0.0	0.0	0.8	0.0	0.0	0.0	0.0	0.0	2.5	0.0	0.0	8.4	0.0	2.8	0.0	0.0	0.0
s	Ruminococcus obeum	14.0	0.4	10.6	1.0	3.9	0.7	12.5	0.5	0.0	0.0	0.8	0.4	0.0	1.6	5.0	2.9	0.0	0.0	0.4

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
s	Ruminococcus_torques	0.0	7.7	19.0	2.2	0.1	0.0	4.1	4.1	9.7	0.0	1.6	8.9	0.0	0.0	15.6	4.4	13.7	10.9	2.6
c	Erysipelotrichi	0.1	0.4	2.6	0.1	0.1	0.0	0.6	0.2	0.2	0.2	0.0	0.0	1.1	0.8	0.4	0.0	2.5	0.3	0.3
o	Erysipelotrichales	0.1	0.4	2.6	0.1	0.1	0.0	0.6	0.2	0.2	0.2	0.0	0.0	1.1	0.8	0.4	0.0	2.5	0.3	0.3
f	Erysipelotrichaceae	0.1	0.4	2.6	0.1	0.1	0.0	0.6	0.2	0.2	0.2	0.0	0.0	1.1	0.8	0.4	0.0	2.5	0.3	0.3
g	Catenibacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Catenibacterium_mitsuokai	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Coprobacillus	0.1	0.4	2.4	0.0	0.0	0.0	0.6	0.0	0.1	0.2	0.0	0.0	1.1	0.2	0.0	0.0	1.5	0.3	0.3
s	Coprobacillus_bacterium	0.1	0.4	2.4	0.0	0.0	0.0	0.6	0.0	0.1	0.2	0.0	0.0	1.1	0.2	0.0	0.0	1.5	0.3	0.3
g	Holdemania	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.6	0.4	0.0	1.0	0.0	0.0
s	Holdemania_filiformis	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.6	0.4	0.0	1.0	0.0	0.0
c	Negativicutes	0.0	0.1	0.1	7.0	0.0	0.1	0.0	3.5	3.5	0.5	0.0	1.4	19.6	0.0	0.0	0.3	0.8	0.0	0.1
o	Selenomonadales	0.0	0.1	0.1	7.0	0.0	0.1	0.0	3.5	3.5	0.5	0.0	1.4	19.6	0.0	0.0	0.3	0.8	0.0	0.1
f	Acidaminococcaceae	0.0	0.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	1.8	0.0	0.0	0.3	0.0	0.0	0.1
g	Acidaminococcaceae_unclassified	0.0	0.1	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	1.8	0.0	0.0	0.3	0.0	0.0	0.1
g	Phascolarctobacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Phascolarctobacterium_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Veillonellaceae	0.0	0.0	0.1	6.6	0.0	0.1	0.0	3.5	3.5	0.0	0.0	1.4	17.7	0.0	0.0	0.0	0.8	0.0	0.0
g	Dialister	0.0	0.0	0.0	6.6	0.0	0.0	0.0	3.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.0
s	Dialister_invisus	0.0	0.0	0.0	6.6	0.0	0.0	0.0	3.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.0
g	Megamonas	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	17.7	0.0	0.0	0.0	0.0	0.0	0.0
s	Megamonas_hypermegale	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	17.7	0.0	0.0	0.0	0.0	0.0	0.0
g	Veillonella	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.5	0.0	0.0	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella_atypica	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
s	Veillonella parvula	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Veillonella unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
c	Fusobacteria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
o	Fusobacteriales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
f	Fusobacteriaceae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Fusobacterium	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Fusobacterium ulcerans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p	Proteobacteria	2.3	4.9	0.8	0.7	0.3	1.5	0.0	2.1	0.5	5.3	3.5	0.5	1.4	0.8	2.3	0.5	1.0	12.8	7.7
c	Betaproteobacteria	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
o	Burkholderiales	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
f	Sutterellaceae	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Sutterella	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
s	Sutterella wadsworthensis	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
c	Deltaproteobacteria	1.6	0.2	0.8	0.0	0.2	0.1	0.0	1.9	0.0	0.0	1.4	0.0	1.1	0.0	1.4	0.5	1.0	0.0	0.2
o	Desulfovibrionales	1.6	0.2	0.8	0.0	0.2	0.1	0.0	1.9	0.0	0.0	1.4	0.0	1.1	0.0	1.4	0.5	1.0	0.0	0.2
f	Desulfovibrionaceae	1.6	0.2	0.8	0.0	0.2	0.1	0.0	1.9	0.0	0.0	1.4	0.0	1.1	0.0	1.4	0.5	1.0	0.0	0.2
g	Bilophila	1.4	0.1	0.8	0.0	0.2	0.1	0.0	1.9	0.0	0.0	0.5	0.0	1.1	0.0	1.2	0.5	1.0	0.0	0.1
s	Bilophila wadsworthia	1.4	0.1	0.8	0.0	0.2	0.1	0.0	1.9	0.0	0.0	0.5	0.0	1.1	0.0	1.2	0.5	1.0	0.0	0.1
g	Desulfovibrio	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.9	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0
s	Desulfovibrio piger	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
c	Gammaproteobacteria	0.7	4.7	0.0	0.7	0.1	0.1	0.0	0.2	0.5	5.3	2.1	0.5	0.3	0.5	0.8	0.0	0.0	12.8	7.5
o	Enterobacteriales	0.7	4.7	0.0	0.5	0.0	0.0	0.0	0.2	0.5	5.3	2.1	0.3	0.3	0.5	0.8	0.0	0.0	12.8	7.5
f	Enterobacteriaceae	0.7	4.7	0.0	0.5	0.0	0.0	0.0	0.2	0.5	5.3	2.1	0.3	0.3	0.5	0.8	0.0	0.0	12.8	7.5
g	Enterobacter	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
s	Enterobacter cloacae	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Ra nk	Name	P53	P54	P55	P56	P57	P58	P59	P60	P61	P62	P63	P64	P65	P66	P67	P68	P69	P70	P71
g	Escherichia	0.7	4.3	0.0	0.3	0.0	0.0	0.0	0.0	0.5	5.1	2.1	0.2	0.0	0.5	0.8	0.0	0.0	12.4	6.7
s	Escherichia coli	0.7	4.3	0.0	0.3	0.0	0.0	0.0	0.0	0.5	3.5	2.1	0.2	0.0	0.5	0.8	0.0	0.0	12.4	6.7
s	Escherichia_unclassified	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
g	Klebsiella	0.0	0.4	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.3	0.8
s	Klebsiella_pneumoniae	0.0	0.3	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.1	0.6
s	Klebsiella_unclassified	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.1
p	Verrucomicrobia	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0
c	Verrucomicrobiae	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0
o	Verrucomicrobiales	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0
f	Verrucomicrobiaceae	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0
g	Akkermansia	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0
s	Akkermansia_muciniphila	12.5	0.0	0.0	0.0	0.1	0.0	0.0	0.0	5.1	6.6	3.4	0.0	1.4	1.6	0.0	0.0	0.0	0.0	0.0

The patients as set forth in Table 1 were followed through treatment using the present invention and the results tracked as set forth in Tables 3 to 9.

Table 3. Repeat Responders+Stable vs Progressors For IPI+NIVO (In) Melanoma.

5	<u>Responders+Stable</u>	<u>Progressors</u>
	P7	P24
	P8	P28
	P10	P30
	P14	P32
10	P23	P46
	P25	P53
	P34	P54
	P35	P66
	P52	
15	P55	
	P59	
	P61	
	P63	
	P67	
20	P68	
	P69	

This repeat analysis was conducted as P52 had a large bone lesion that on resection which, after one week, showed only dead tumor cells, as such, P52 is listed as a responder.

Table 4. Second Analysis—By Percent Change In Tumor Size For All Treated Melanomas (IPI+NIVO, PEMBRO, IPI, NIVO).

	<u>Patient</u>	<u>Percent Change Tumor</u>
	P25	-100
	P42	-100
30	P52	-100
	P55	-100
	P57	-100
	P63	-100
	P69	-87
35	P10	-83
	P17	-70
	P39	-68
	P34	-66
	P61	-65
40	P14	-60
	P23	-55
	P8	-55
	P58	-48
	P33	-36
45	P67	-34
	P68	-34
	P35	-20
	P45	-14
	P59	-10

	P7	-4
	P30	0
	P44	0
	P53	0
5	P48	0
	P46	+24
	P49	+25
	P64	+31
	P56	+46
10	P16	+53
	P32	+60
	P66	+61
	P54	+70
	P22	+81
15	P28	+85
	P64	+100
	P24	+136

Table 5. Responders+Stable vs Progressors with NIVO (N) in RCC

20	<u>Responders+Stable</u>	<u>Progressors</u>
	P1	P5
	P3	P11
	P6	P26
	P27	P38
25		P43
		P47
		P60
		P62

30 Table 6. Severe Autoimmune Toxicities vs None In All Treated Melanoma Patients (IN, P, I, N)

	<u>With GR3/4 Toxicities</u>	<u>No Toxicities</u>
	P7	P14
	P8	P16
	P10	P17
35	P23	P22
	P23	P25
	P28	P32
	P30	P34
	P33	P35
40	P42	P39
	P53	P44
	P56	P45
	P57	P46
	P58	P48
45	P59	P49
	P63	P52
	P66	P54
	P68	P55
50		P61
		P64
		P65
		P67

P69

Table 7. Severe Autoimmune Toxicities vs None In All Treated RCC Patients (N)

	<u>With GR3/4 Toxicities</u>	<u>No Toxicities</u>
5	P5 P27	P1 P3 P6 P1 P26
10		P38 P43 P47 P60 P62
15		

Table 8. Specific Toxicities Among Melanoma Patients

	<u>Pneumonitis</u>	<u>Hepatitis</u>	<u>Colitis</u>	<u>Hypophysitis</u>	<u>Rare</u>	<u>None</u>
	P24	P7	P8	P42	P10	P14
	P28	P33	P23	P56	P53	P16
20	P30	P58	P57		P63	P17
	P59		P68			P22
	P66					P25
						P32
						P34
25						P35
						P39
						P44
						P45
						P46
30						P48
						P49
						P52
						P54
						P55
35						P61
						P64
						P65
						P67
40						P69

Table 9. Specific Toxicities Among Patients

	<u>Pneumonitis</u>	<u>Rare</u>	<u>None</u>
	P27	P5	P1
			P3
45			P6
			P11
			P26
			P38
			P43
50			P47
			P60

P62

Using next generation sequencing techniques, the present inventors identified specific species of gut commensal bacteria that were associated with response to immune checkpoint inhibitor therapy (ICT) in melanoma patients. For example, patients receiving ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) combination ICT for melanoma who showed a positive response had increased abundance of three specific gut bacterial species (*Faecalibacterium prausnitzii*, *Bacteroides thetaiotaomicron*, and *Holdemania filiformis*) compared to counterparts with progressive disease. Next, the inventors used a preclinical melanoma model (immunocompetent C57BL/6 mice with B16-F10 melanoma) to investigate whether we could recapitulate our clinical findings and establish causality. Indeed, mice with melanoma who were treated with combination ICT and a precision probiotic cocktail (*B. thetaiotaomicron* and *F. prausnitzii*) had smaller tumor growth and increased length of survival compared to mice who were treated with *Lactobacillus acidophilus*, a probiotic commonly found in yogurt. These data show that administration of a precision probiotic cocktail increases efficacy of ICT (ipilimumab and nivolumab) against melanoma as an adjunctive therapy to ICT that optimize therapeutic efficacy.

FIG. 8 shows an outline of *in vivo* studies and expected outcomes of the present invention. FIG. 9 shows an outline of the detailed *in vivo* studies using the present invention.

FIG. 10 is a graph that shows the results of the precision probiotic therapy on Taconic C57BL/6 versus control that promotes the activity of immune checkpoint therapy of the present invention. ICT was 200 micrograms anti-PD1 and 200 micrograms anti-CTLA4 IP injections. B16-F10 melanoma cells from C57BL/6, 1×10^5 cells were injected subcutaneously in the right flank. Probiotic therapy was 2×10^8 cfu of bacteria administered by oral gavage.

FIG. 11 is a graph that shows the results of the precision probiotic therapy on Taconic C57BL/6 prolongs survival in mice with melanoma that are treated with ICT compared to mice treated with control. It was found that precision probiotic therapy (*B. theta*, *F. prausnitzii*) prolongs survival in mice with melanoma that are treated with ICT compared to mice treated with *L. acidophilus* (probiotic commonly found in yogurt).

FIG. 12 is a graph that shows the results of the precision probiotic therapy on Jackson C57BL/6 versus control that promotes the activity of immune checkpoint therapy against melanoma using the present invention. It was found that precision probiotic therapy (*B. theta*, *F. prausnitzii*) promoted ICT in Mice (Jackson, n=4) with melanoma.

FIG. 13 is a graph that shows the results of the precision probiotic therapy on Jackson C57BL/6 prolongs survival in mice with melanoma that are treated with ICT compared to mice treated with control. These results show that precision probiotic therapy significantly increases the length of survival in mice (Jackson) with melanoma treated with ICT.

FIG. 14 is a graph that shows that Jackson C57BL/6 mice have decreased relative abundance of *Clostridial firmicutes* (which include *F. prausnitzii*, *H. filiformis*) compared to Taconic C57BL/6 Mice.

It is contemplated that any embodiment discussed in this specification can be implemented with respect to any method, kit, reagent, or composition of the invention, and vice versa. Furthermore, compositions of the invention can be used to achieve methods of the invention.

It will be understood that particular embodiments described herein are shown by way of illustration and not as limitations of the invention. The principal features of this invention can be employed in various embodiments without departing from the scope of the invention. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific procedures described herein. Such equivalents are considered to be within the scope of this invention and are covered by the claims.

All publications and patent applications mentioned in the specification are indicative of the level of skill of those skilled in the art to which this invention pertains. All publications and patent applications are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

The use of the word “a” or “an” when used in conjunction with the term “comprising” in the claims and/or the specification may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.” The use of the term “or” in the claims is used to mean “and/or” unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and “and/or.” Throughout this application, the term “about” is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

As used in this specification and claim(s), the words “comprising” (and any form of comprising, such as “comprise” and “comprises”), “having” (and any form of having, such as “have” and “has”), “including” (and any form of including, such as “includes” and “include”) or “containing” (and any form of containing, such as “contains” and “contain”) are inclusive or open-ended and do not exclude additional, unrecited elements or method steps. In embodiments of any of the compositions and methods provided herein, “comprising” may be replaced with “consisting essentially of” or “consisting of”. As used herein, the phrase “consisting essentially of” requires the specified integer(s) or steps as well as those that do not materially affect the character or function of the claimed invention. As used herein, the term “consisting” is used to indicate the presence of the recited integer (e.g., a feature, an element, a characteristic, a property, a method/process step or a limitation) or group of integers (e.g., feature(s), element(s), characteristic(s), propertie(s), method/process steps or limitation(s)) only.

The term “or combinations thereof” as used herein refers to all permutations and combinations of the listed items preceding the term. For example, “A, B, C, or combinations thereof” is intended to include at least one of: A, B, C, AB, AC, BC, or ABC, and if order is important in a particular context, also BA, CA, CB, CBA, BCA, ACB, BAC, or CAB. Continuing with this example, expressly included are combinations that contain

repeats of one or more item or term, such as BB, AAA, AB, BBC, AAABCCCC, CBBAAA, CABABB, and so forth. The skilled artisan will understand that typically there is no limit on the number of items or terms in any combination, unless otherwise apparent from the context.

As used herein, words of approximation such as, without limitation, “about”, “substantial” or “substantially” refers to a condition that when so modified is understood to not necessarily be absolute or perfect but would be considered close enough to those of ordinary skill in the art to warrant designating the condition as being present. The extent to which the description may vary will depend on how great a change can be instituted and still have one of ordinary skilled in the art recognize the modified feature as still having the required characteristics and capabilities of the unmodified feature. In general, but subject to the preceding discussion, a numerical value herein that is modified by a word of approximation such as “about” may vary from the stated value by at least $\pm 1, 2, 3, 4, 5, 6, 7, 10, 12$ or 15% .

All of the compositions and/or methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

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WHAT IS CLAIMED IS:

1. A method of increasing an efficacy of an immune checkpoint inhibitor comprising:
 identifying a human patient in need of treatment for a melanoma;
 providing the human patient with an effective amount of the immune checkpoint inhibitor; and
 5 providing the human patient with at least one of: a probiotic bacteria, a prebiotic agent, or a
 xenobiotic agent, in an amount is effective to increase a potency of the immune checkpoint inhibitor against
 the melanoma.
2. The method of claim 1, wherein the immune checkpoint inhibitor is selected from at least one of a
 CTLA-4 inhibitor or a PD1 inhibitor.
- 10 3. The method of claim 1, wherein the human patient does not have a BRAF mutation.
4. The method of claim 1, wherein the immune checkpoint inhibitor is selected from at least one of
 ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.
5. The method of claim 1, wherein the probiotic bacteria are selected from at least one of
Faecalibacterium prausnitzii, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*,
 15 *Bacteroides caccae* or *Streptococcus parasanguinis*.
6. The method of claim 1, wherein the probiotic bacteria is *Dorea formicigenerans* and is provided to
 enhance a therapeutic effect of pembrolizumab (PD1).
7. The method of claim 1, wherein the probiotic bacteria are at least one of: *Faecalibacterium*
prausnitzii, or *Holdemania filiformis*, and the probiotic bacteria are provided to enhance a potency of a
 20 combination of ipilimumab and nivolumab.
8. The method of claim 1, wherein the xenobiotic agent is an anacardic acid, a 15:2 anacardic acid, or
 active derivatives thereof.
9. The method of claim 1, wherein the probiotic bacteria that increase an effectiveness of a combination
 of the immune checkpoint inhibitors ipilimumab plus nivolumab is selected from at least one of:
 25 *Faecalibacterium prausnitzii*, *Holdemania filiformis*, or *Bacteroides thetaiotamicron*.
10. The method of claim 1, wherein the probiotic bacteria that increase an effectiveness of the immune
 checkpoint inhibitor pembrolizumab is *Dorea formicigenerans*.
11. The method of claim 1, wherein the probiotic bacteria that increase an effectiveness of any immune
 checkpoint inhibitor is selected from at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*.
- 30 12. The method of claim 1, wherein the human patient is further provided with an effective amount of
 the probiotic bacteria, the prebiotic agent, and an anacardic acid in an amount sufficient to enhance the
 potency of the immune checkpoint inhibitor selected from at least one of ipilimumab, nivolumab, ipilimumab
 plus nivolumab, or pembrolizumab.
13. The method of claim 1, further comprising providing a probiotic further comprising one or more
 35 bacteria selected from at least one of: *Methanobrevibacter smithii*, *Bacteroides thetaiotamicron*,

Lactobacillus plantarum, *Eubacterium limosum*, *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis* in an amount sufficient to enhance the potency of the immune checkpoint inhibitor selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

14. The method of claim 1, wherein the melanoma is metastatic melanoma.

15. The method of claim 1, wherein the melanoma is resistant or refractory to the immune checkpoint inhibitor.

16. The method of claim 1, wherein the human patient did not receive a concurrent antibiotic or a probiotic therapy.

17. The method of claim 1, wherein the probiotic bacteria is listed as responsive in Tables 2A to 2D.

18. A method of identifying a patient that will respond to a therapy with an immune checkpoint inhibitor comprising:

identifying a subject in need of treatment with the immune checkpoint inhibitor to treat a melanoma; obtaining a biological sample from the patient that comprises gut intestinal flora; and

15 determining whether the gut intestinal flora in the biological sample comprises a probiotic bacteria, wherein the presence of at least one of the *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis*, is indicative that the melanoma will respond to the immune checkpoint inhibitor, or will have an improved response to the immune checkpoint inhibitor.

19. The method of claim 18, further comprising providing the patient with an amount of *Faecalibacterium prausnitzii*, *Holdemania filiformis*, *Bacteroides thetaiotamicron*, *Dorea formicigenerans*, *Bacteroides caccae* or *Streptococcus parasanguinis* probiotic bacteria sufficient to enhance the response to the immune checkpoint inhibitor.

20. The method of claim 18, further comprising providing the patient with a combination of the immune checkpoint inhibitors ipilimumab plus nivolumab and the probiotic bacteria is selected from at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*.

21. The method of claim 18, further comprising providing the patient with pembrolizumab and the probiotic bacteria is *Dorea formicigenerans*.

22. The method of claim 18, wherein the probiotic bacteria that increase the effectiveness of the immune checkpoint inhibitor selected from at least one of least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab and the probiotic bacteria is selected from at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*.

23. The method of claim 18, wherein the patient is further provided with an effective amount of the probiotic bacteria and an anacardic acid in an amount sufficient to enhance a potency of the immune

checkpoint inhibitor selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

24. The method of claim 18, wherein the biological sample is a fecal sample.

25. The method of claim 18, wherein a presence of the probiotic bacteria is determined by at least one of metagenomic shotgun sequencing of bacteria or metabolic LC-MS analysis of metabolites.

26. The method of claim 18, wherein the patient does not have a BRAF mutation.

27. The method of claim 18, wherein the immune checkpoint inhibitor is selected from at least one of CTLA-4 inhibitor, PD1 inhibitor, ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

28. The method of claim 18, wherein a presence of *Dorea formicigeneran* is indicative of an enhanced therapeutic effect by pembrolizumab (PD1).

29. The method of claim 18, wherein a presence of at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*, is indicative of an enhanced therapeutic effect by ipilimumab plus nivolumab.

30. The method of claim 18, wherein a presence of at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*, is indicative of an enhanced therapeutic effect by an immune checkpoint inhibitor selected from at least one of least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

31. The method of claim 18, wherein a presence of 15:2 anacardic acid in the biological sample is indicative of enhanced therapeutic effect by the immune checkpoint inhibitor.

32. The method of claim 18, wherein the patient is a human patient.

33. The method of claim 18, wherein the melanoma is metastatic melanoma.

34. The method of claim 18, wherein the melanoma is resistant or refractory to the immune checkpoint inhibitor.

35. The method of claim 18, wherein the patient did not receive a concurrent antibiotic or a probiotic therapy.

36. The method of claim 18, wherein the probiotic bacteria is selected from the responsive probiotic bacteria in Tables 2A to 2D having a relative response of 1.0 or greater.

37. A composition that increases an efficacy of an immune checkpoint inhibitor for a treatment of cancer comprising:

a first composition comprising at least one of a probiotic bacteria, a prebiotic composition, or an anacardic acid, wherein the first composition is capable of increasing the efficacy of the immune checkpoint inhibitor; and

a second composition comprising a therapeutically effective amount of the immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is selected from at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.

38. The composition of claim 37, wherein the first and second compositions are provided in a single formulation, are provided concurrently, or are provided separately.

39. The composition of claim 37, wherein the first composition further comprises at least one of *Bacteroides caccae*, *Streptococcus parasanguinis*, *Dorea formicigenerans*, *Faecalibacterium prausnitzii*,
5 *Holdemania filiformis* or *Bacteroides thetaiotamicron*.

40. The composition of claim 37, wherein the first composition comprises *Dorea formicigenerans*, when the second composition comprises pembrolizumab.

41. The composition of claim 37, wherein the first composition comprises at least one of: *Bacteroides caccae* or *Streptococcus parasanguinis*, when the second composition comprises at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.
10

42. The composition of claim 37, wherein the first composition comprises at least one of: *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron*, when the second composition is ipilimumab and nivolumab.

43. The composition of claim 37, wherein the first composition consists essentially of *Bacteroides caccae* or *Streptococcus parasanguinis* when the second composition is comprises at least one of ipilimumab, nivolumab, ipilimumab plus nivolumab, or pembrolizumab.
15

44. The composition of claim 37, wherein the first composition consists essentially of *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron* when the second composition is ipilimumab and nivolumab.

45. The composition of claim 37, wherein the first composition consists essentially of *Dorea formicigenerans* when the second composition is pembrolizumab.
20

46. The composition of claim 37, wherein the probiotic bacteria are selected from those responsive in Tables 2A to 2D.

47. A pharmaceutical composition comprising at least one of an isolated *Bacteroides caccae*,
25 *Streptococcus parasanguinis*, *Dorea formicigenerans*, *Faecalibacterium prausnitzii*, *Holdemania filiformis* or *Bacteroides thetaiotamicron* in an amount effective to increase an effectiveness of an immune checkpoint inhibitor against a cancer.

48. The composition of claim 47, wherein the composition consists essentially of *Bacteroides caccae* and *Streptococcus parasanguinis*.

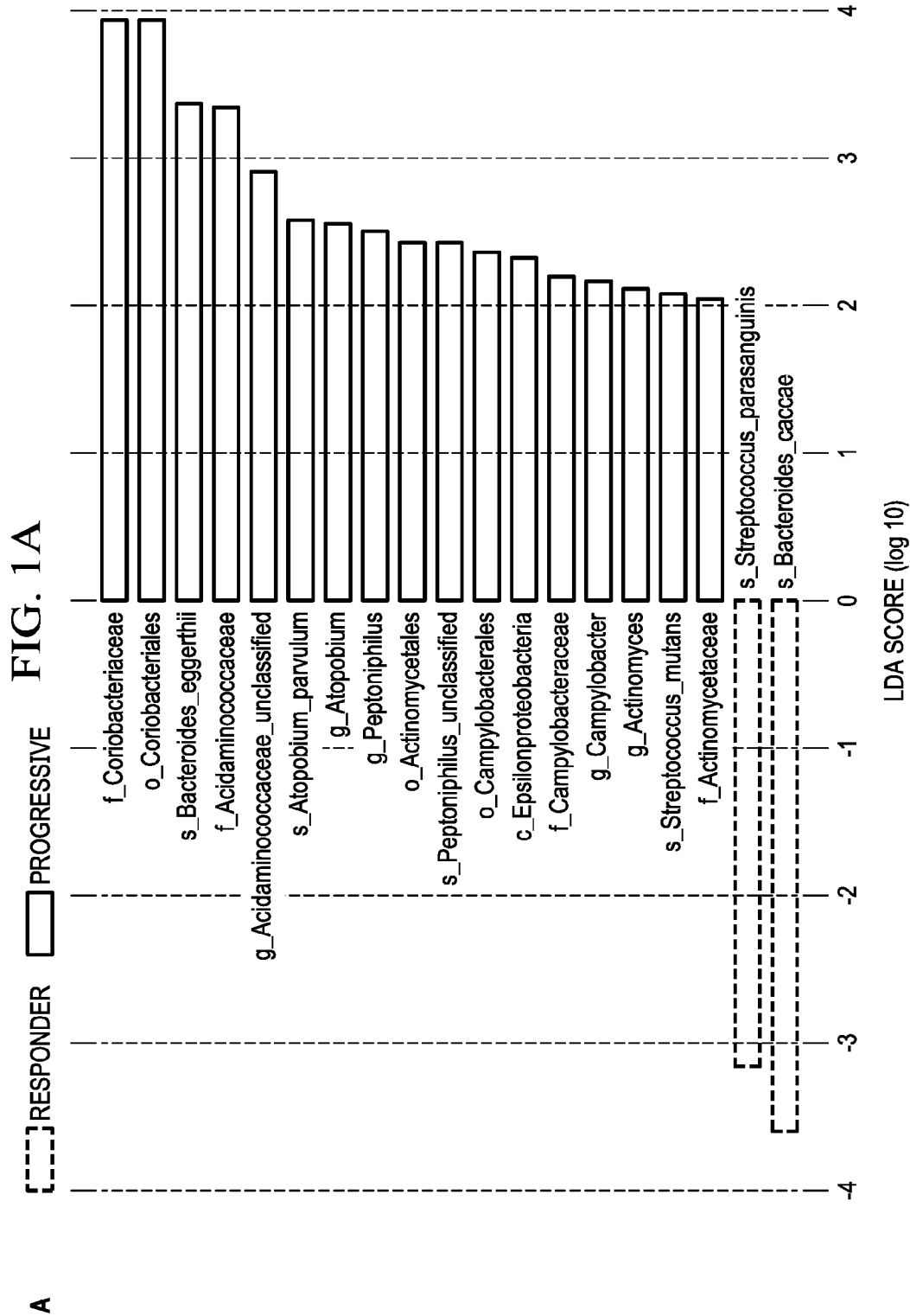
49. The composition of claim 47, wherein the composition consists essentially of *Faecalibacterium prausnitzii*, *Holdemania filiformis* and *Bacteroides thetaiotamicron*.
30

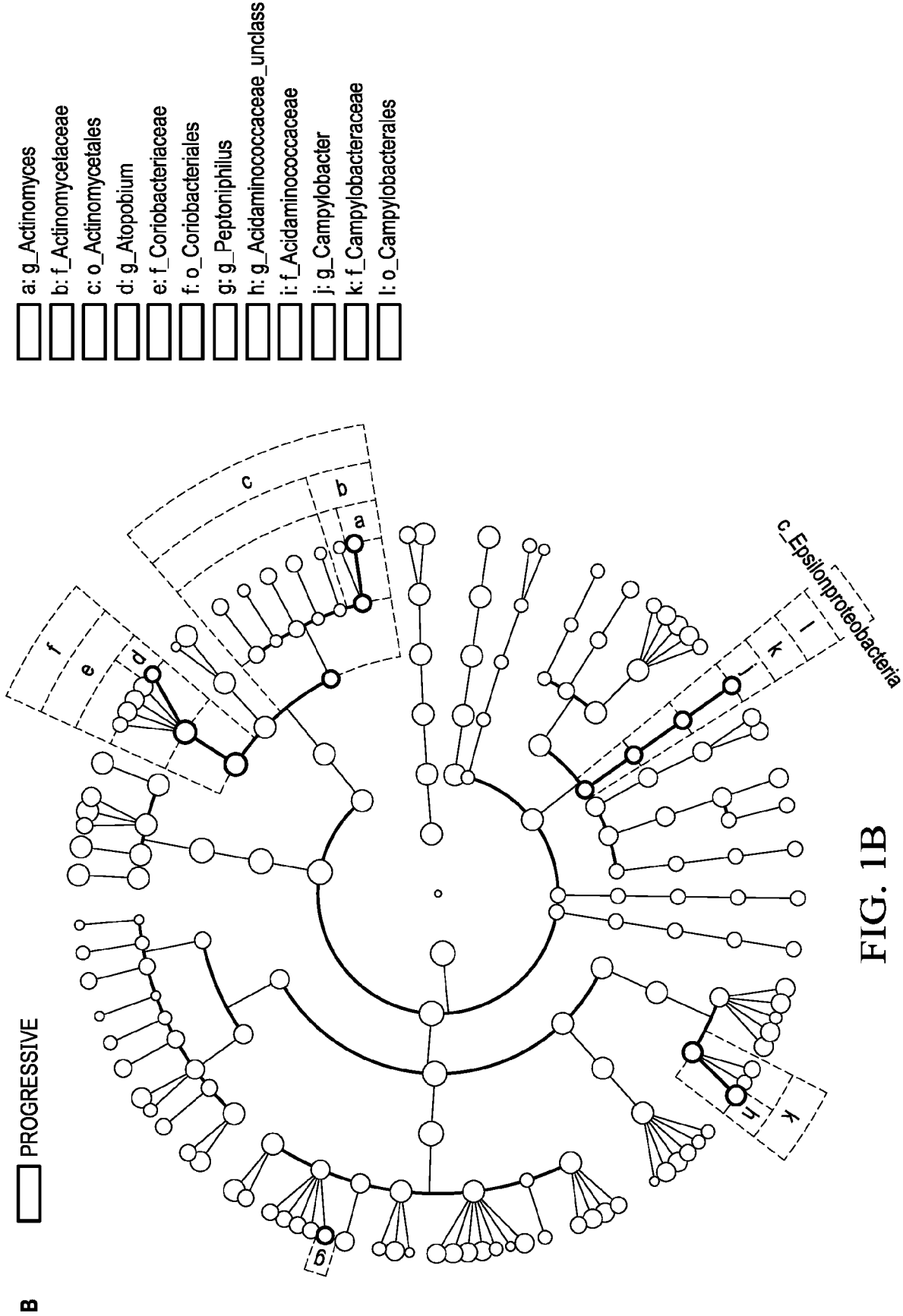
50. The composition of claim 47, wherein the composition consists essentially of *Dorea formicigenerans*.

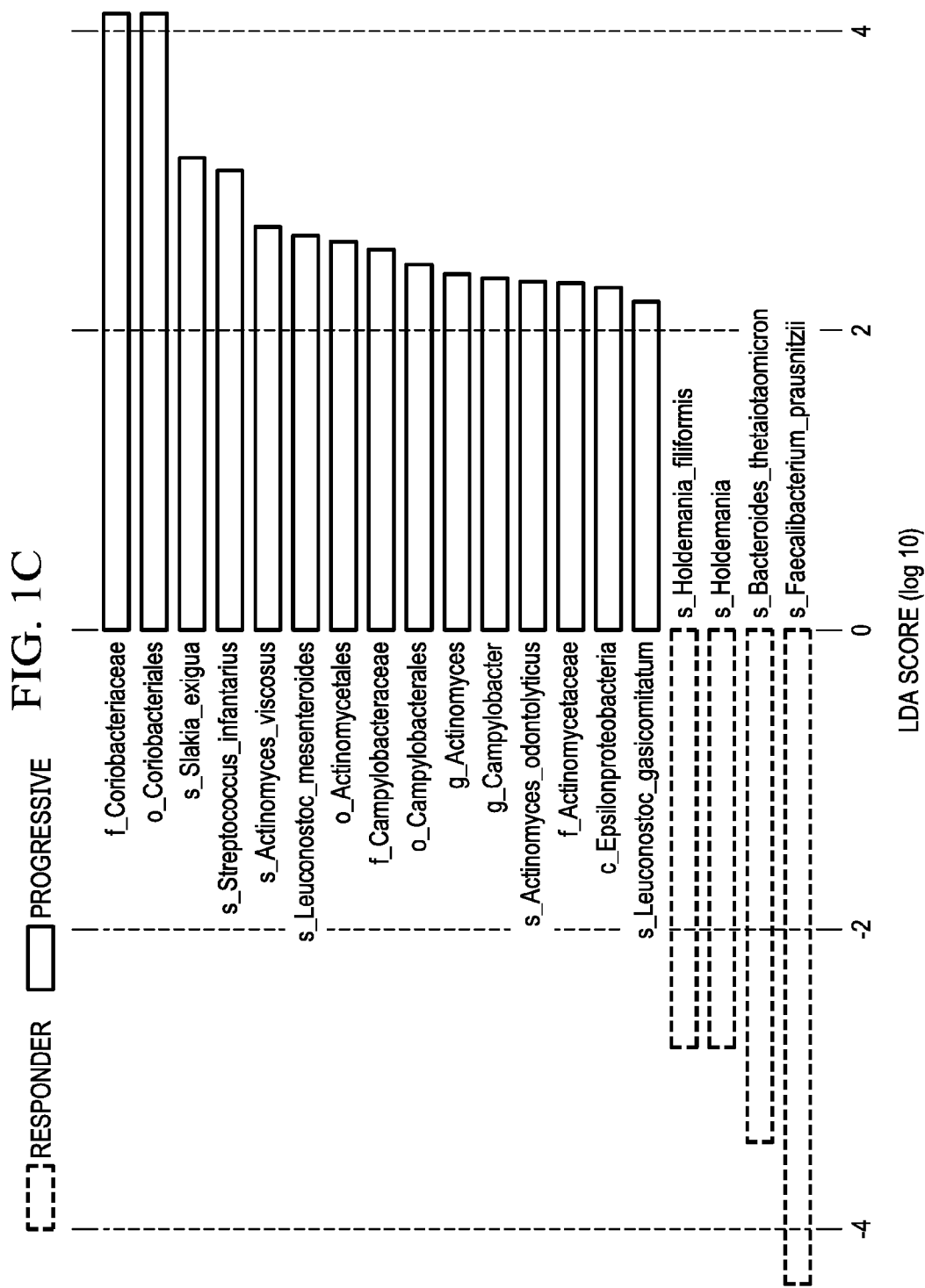
51. A method of increasing an efficacy of an immune checkpoint inhibitor against melanoma
35 comprising:

identifying a human patient in need of treatment for melanoma;
providing the human patient with an effective amount of the immune checkpoint inhibitor; and
providing the human patient with at least one of a targeted antibacterial agent in the amount effective
to increase the potency of the immune checkpoint inhibitor against the melanoma.

- 5 52. The method of claim 51, wherein the antibacterial agent is directed against at least one of
actinobacteria, *coriobacteriaceae*, *coriobacteriales*, *bacteroides eggerthii*, *parvimonas micrs*, *parvimonas*,
Bifidobacterium dentium, or *actinomyces viscosues*.
53. The method of claim 51, wherein the antibacterial agent is directed against at least one of
lactobacillaceae, *lactobacillus*, *acidaminococcaceae*, *anaerococcus*, *atopobium parvulum*, *anaerococcus*
10 *vaginalis*, *peptoniphilus* or *lactobacillus gasseri*.
54. The method of claim 51, wherein the antibacterial agent is a bacteriophage.
55. The method of claim 51, wherein the antibacterial agent is an antimicrobial CRISP-Cas system
agent.







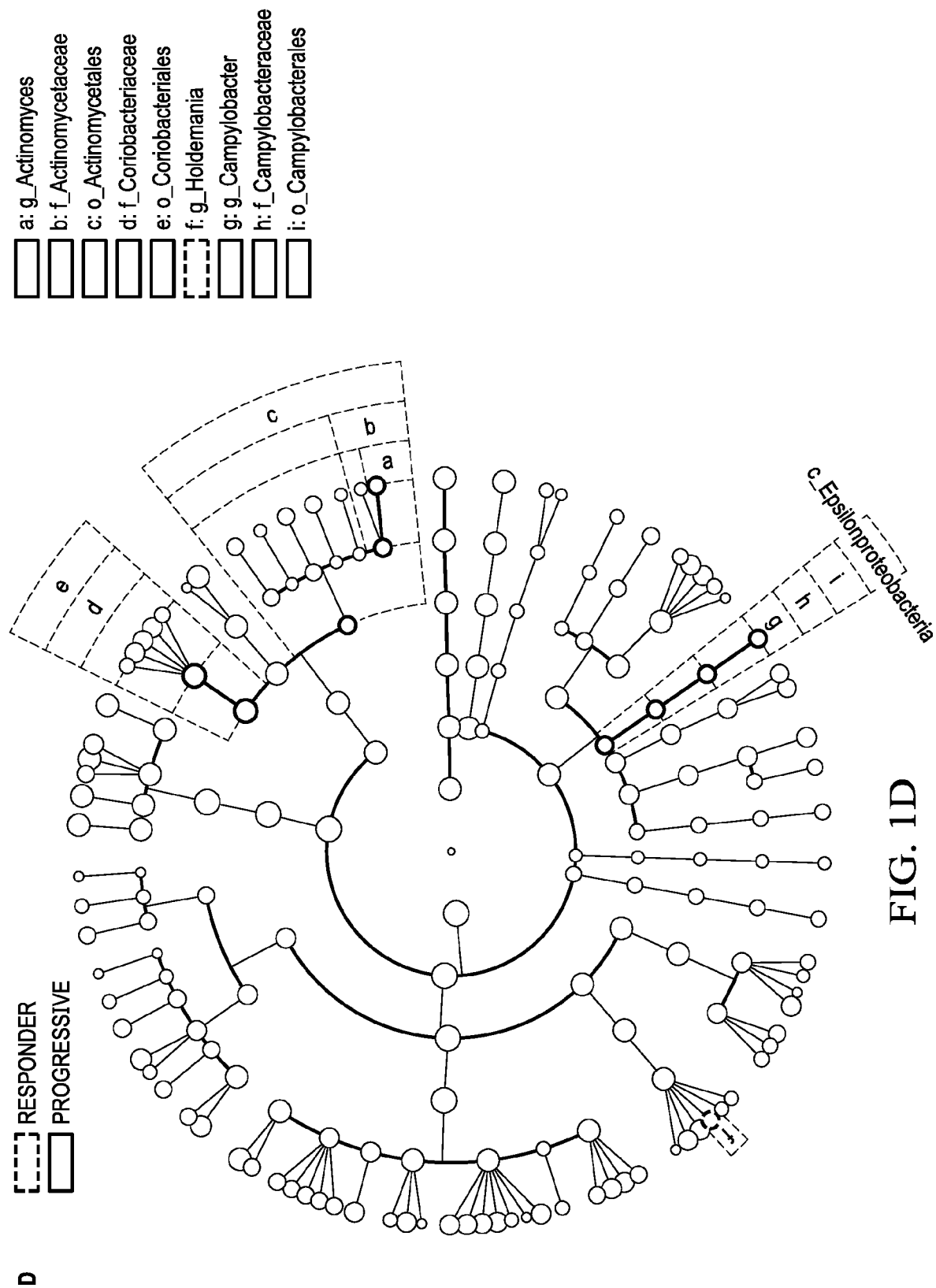
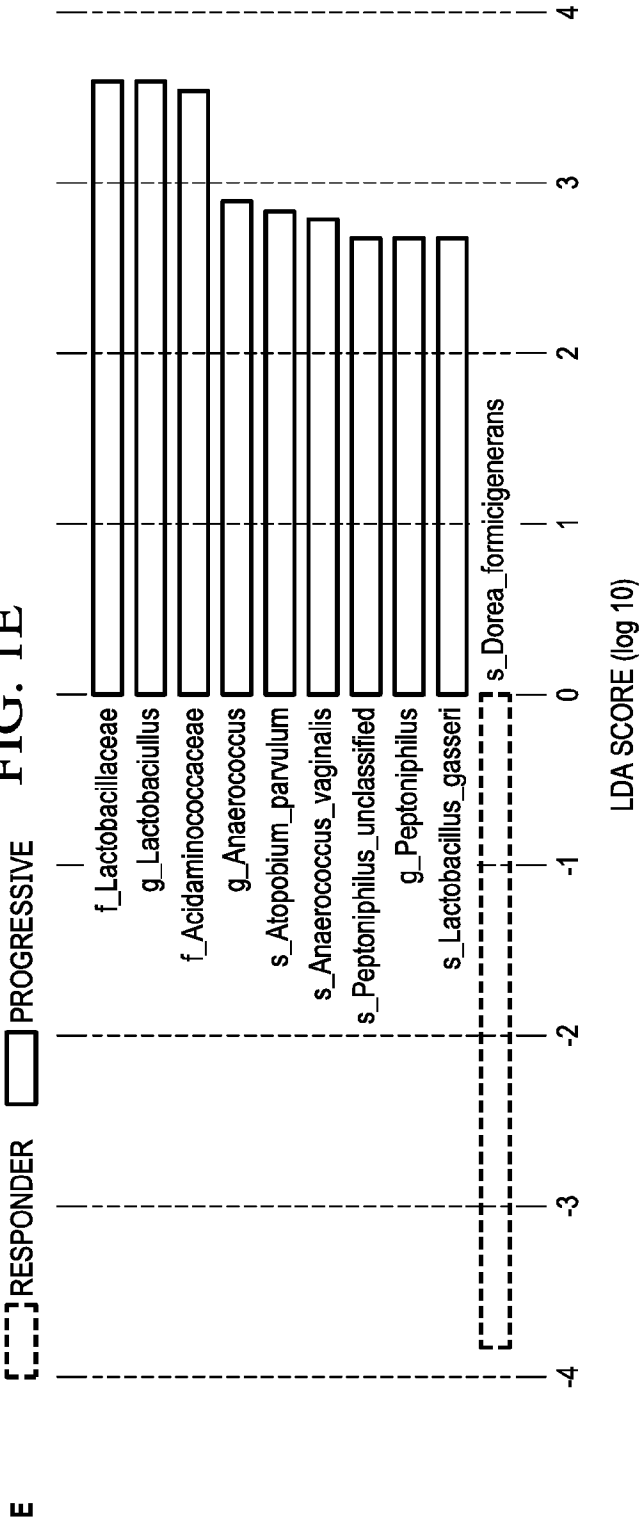
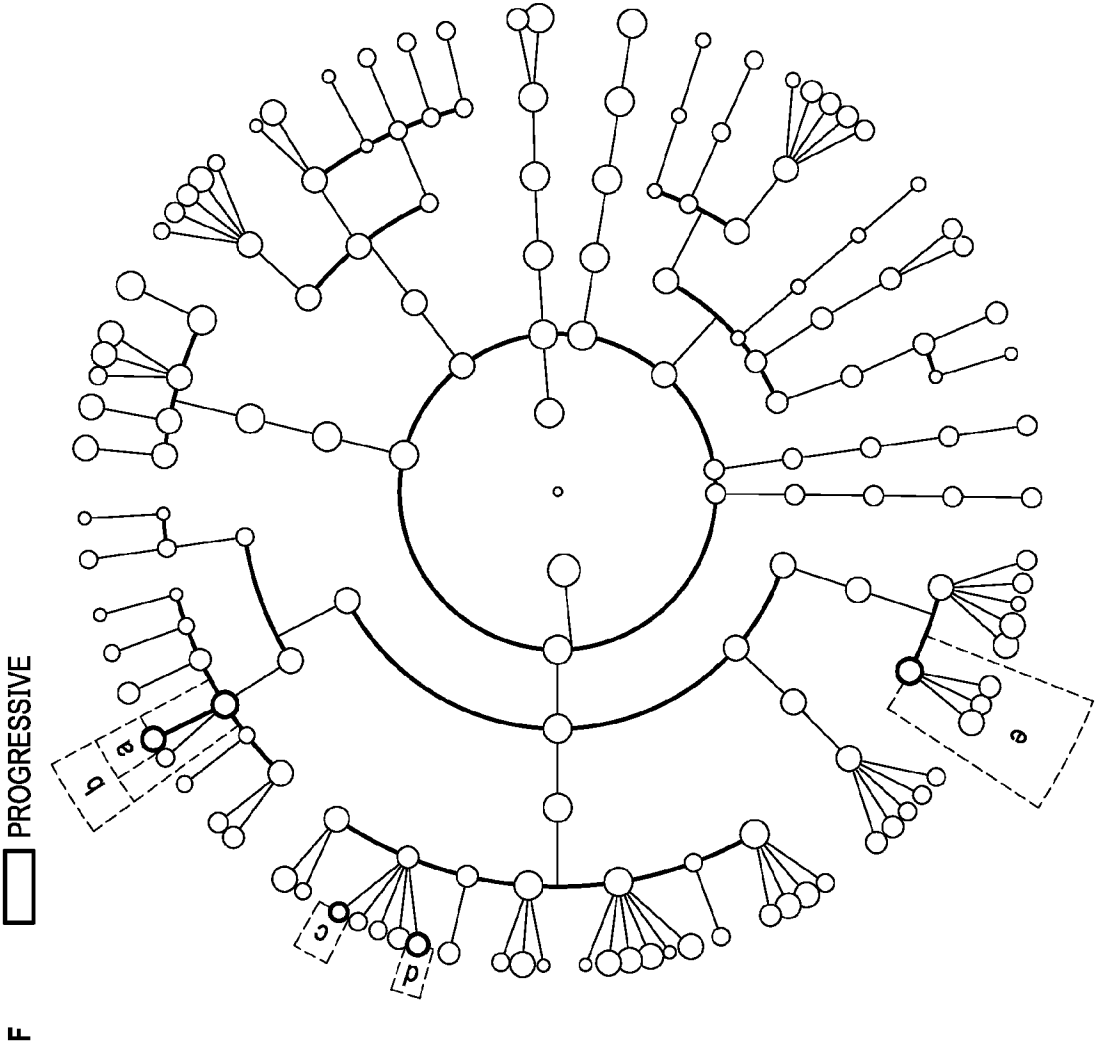


FIG. 1E



- ☐ a: g_Lactobacillus
- ☐ b: f_Lactobacillaceae
- ☐ c: g_Anaerococcus
- ☐ d: g_Peptoniphilus
- ☐ e: f_Acidaminococcaceae



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Ipilimumab and Nivolumab

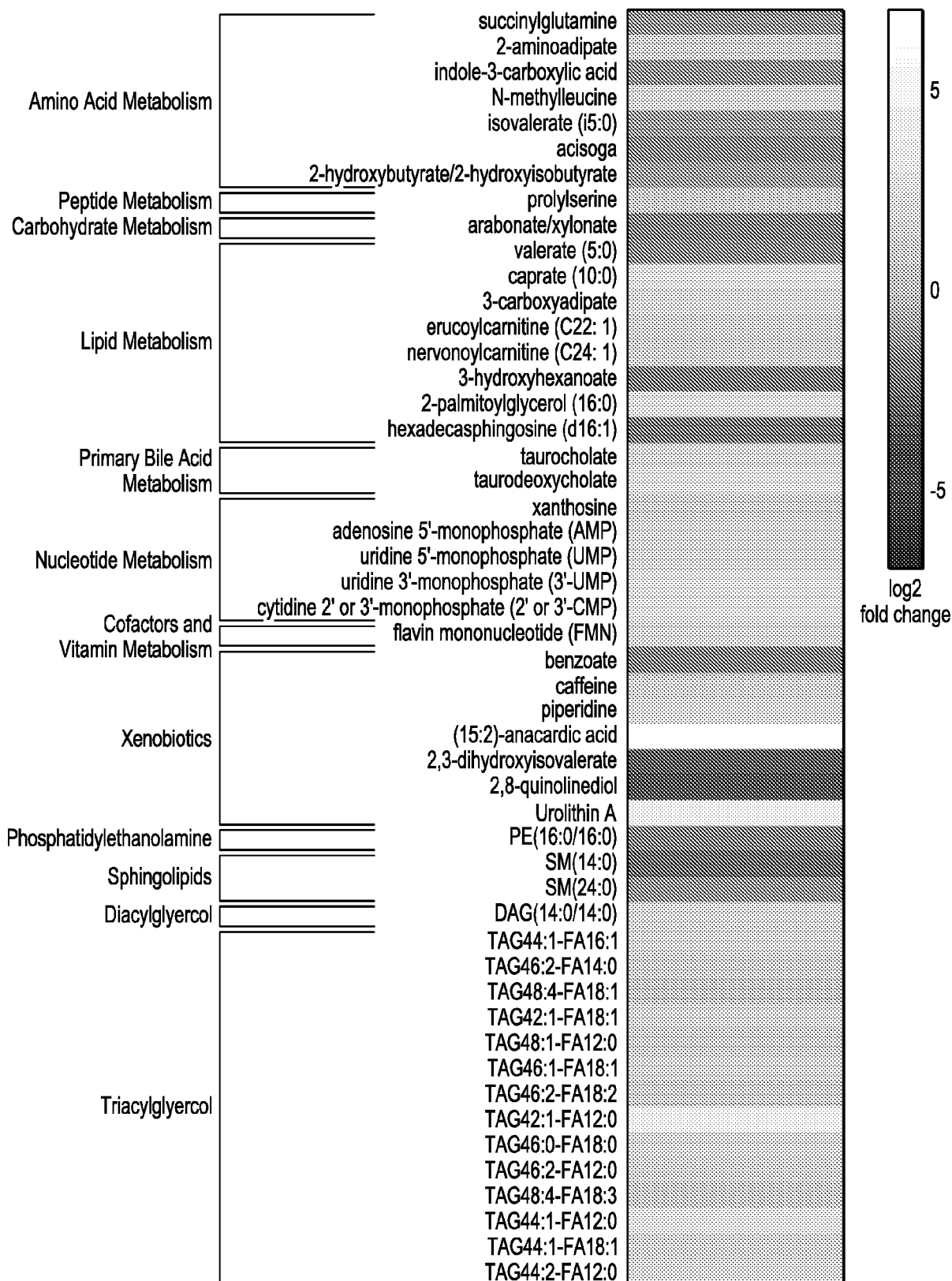


FIG. 2A

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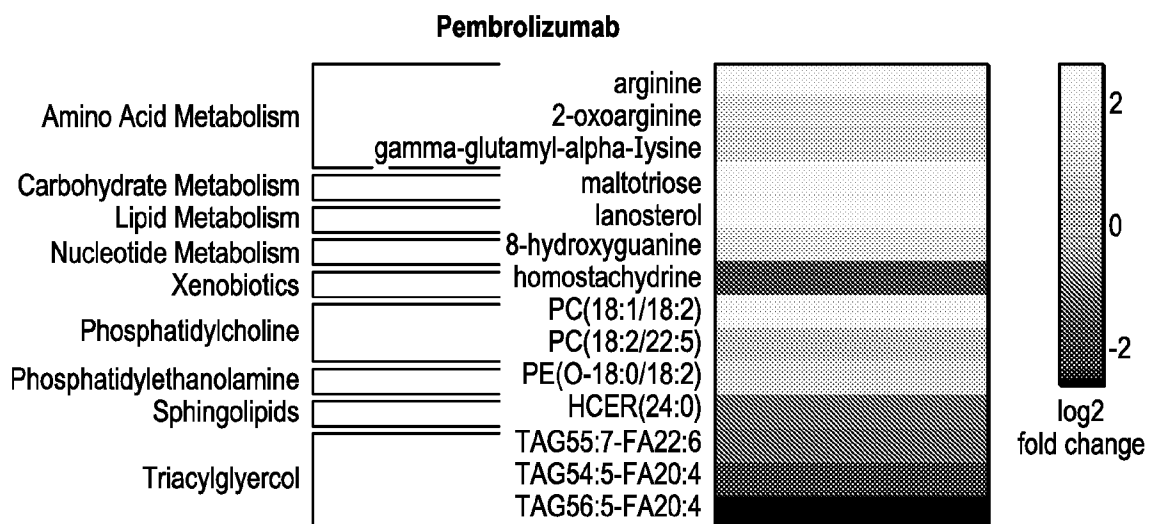


FIG. 2B

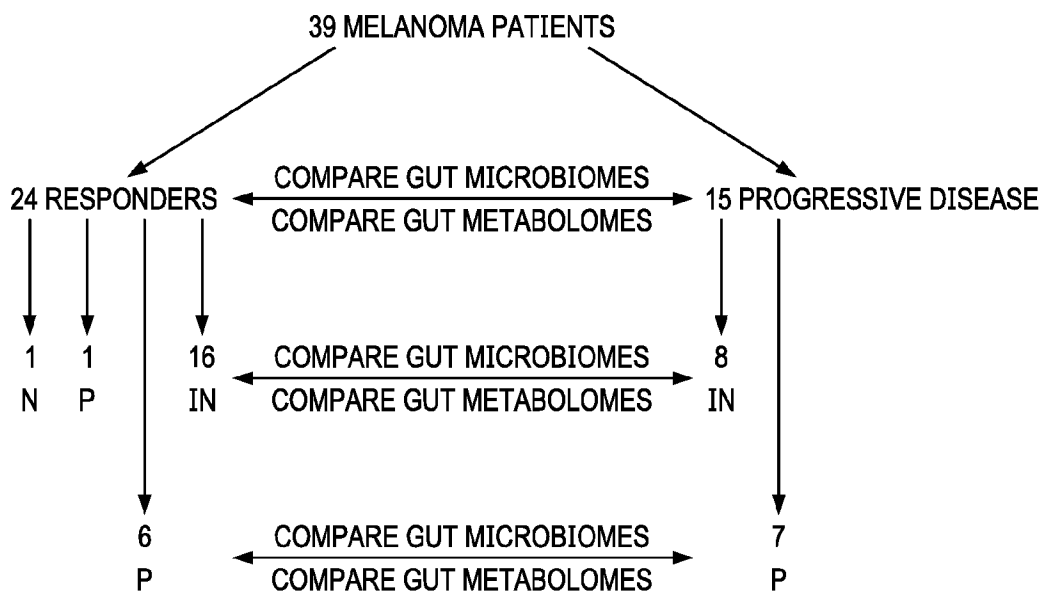


FIG. 3

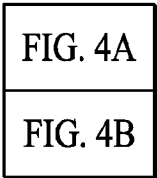
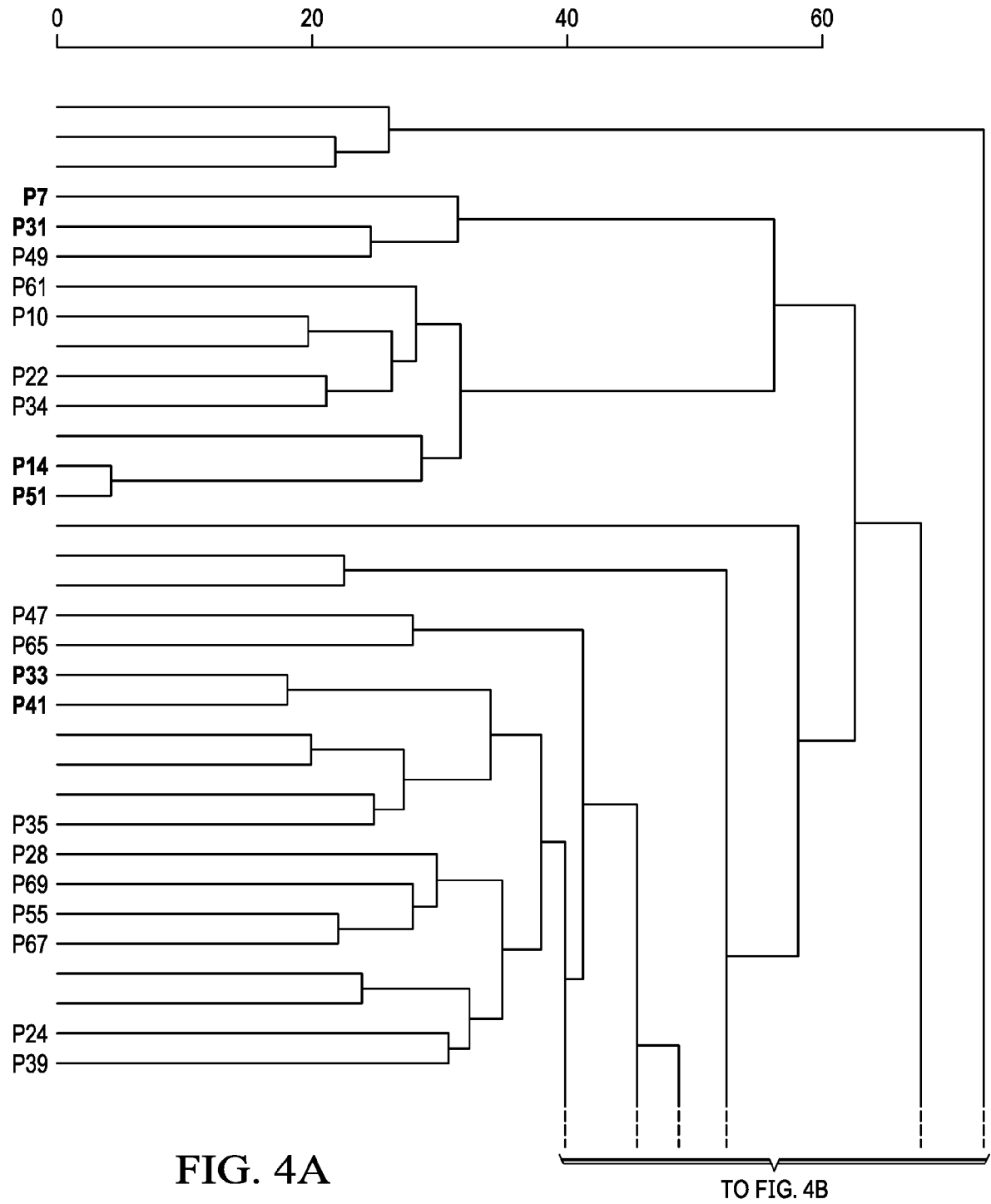


FIG. 4



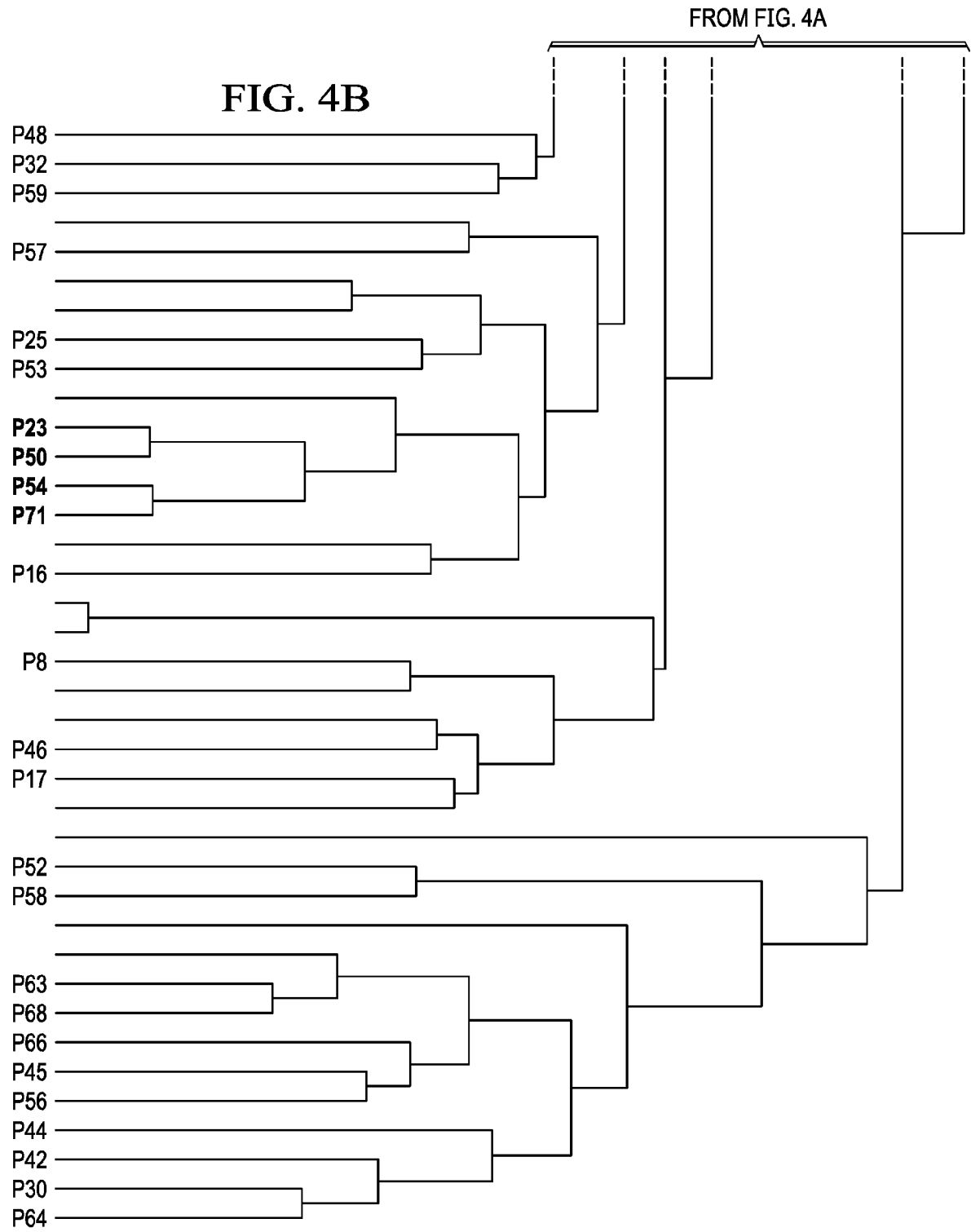


FIG. 5A 11/19

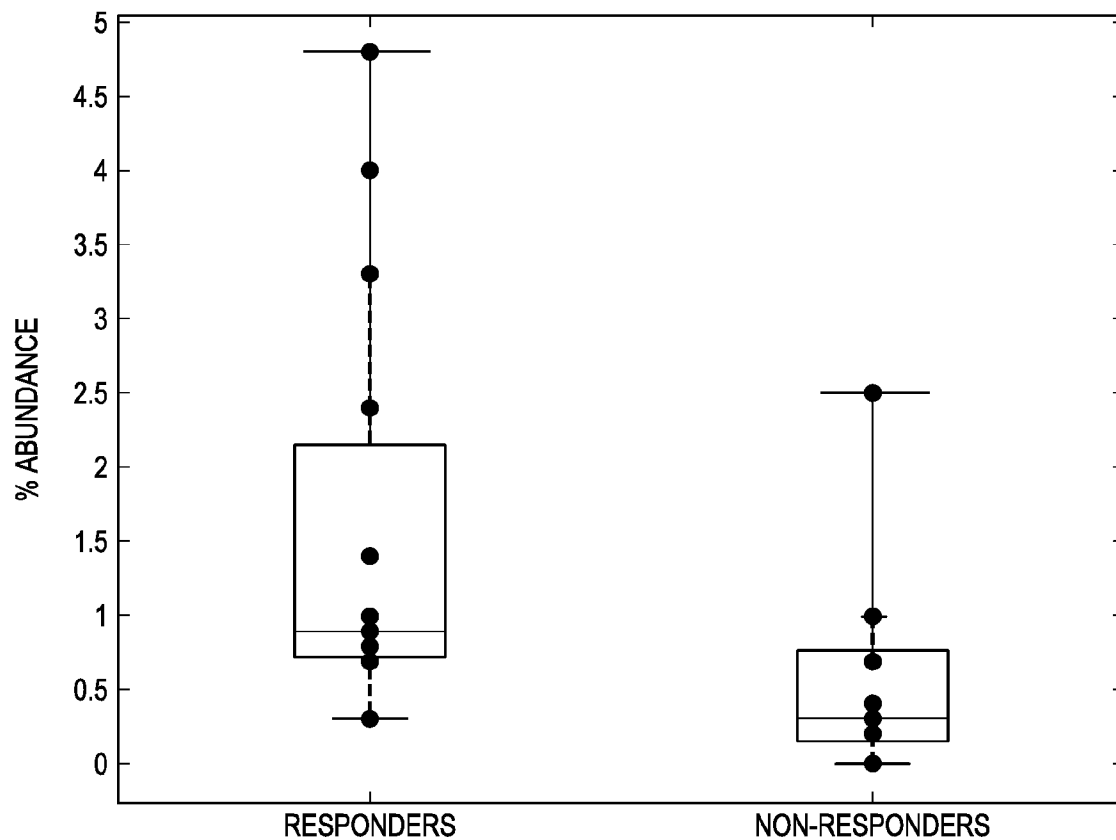
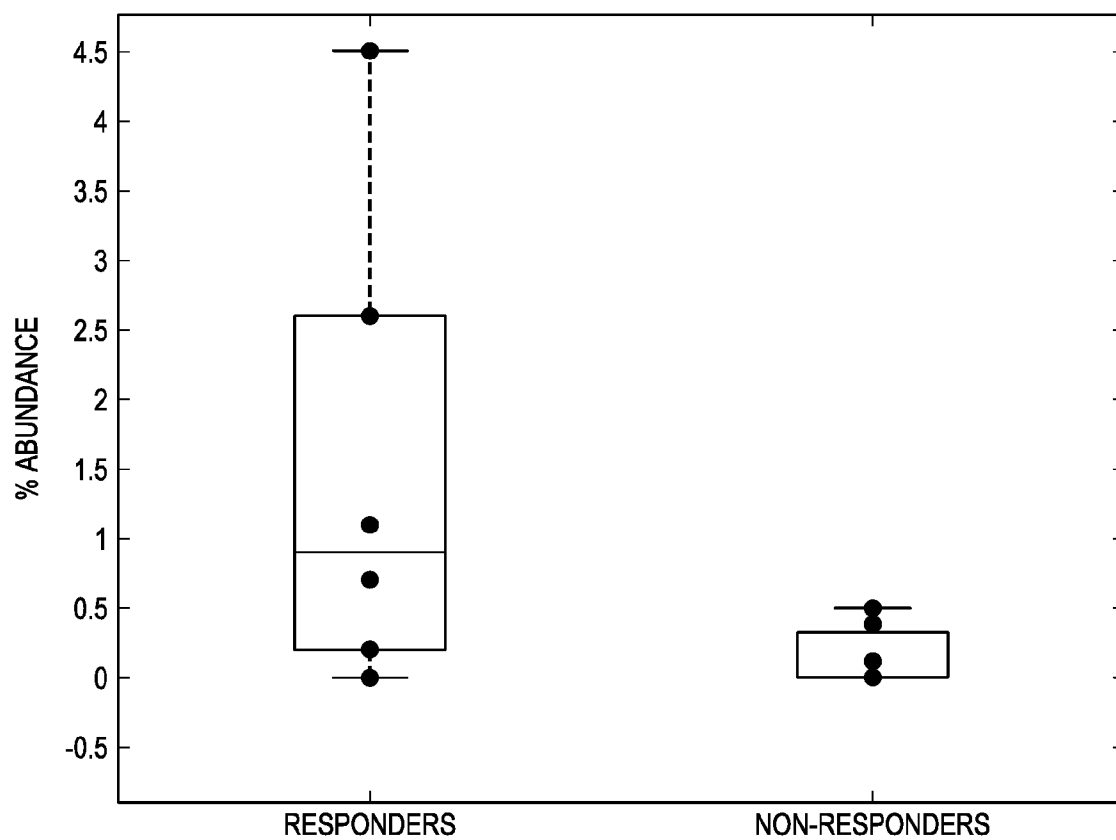


FIG. 5B



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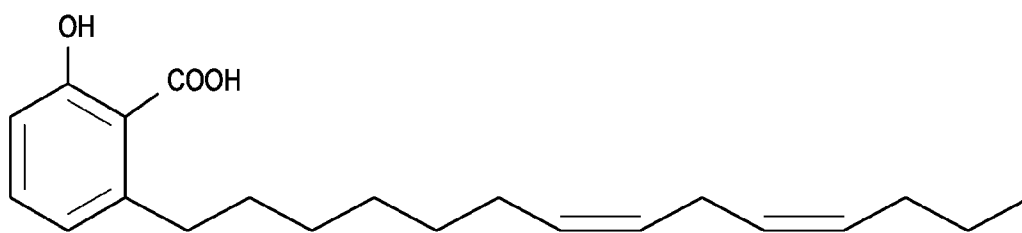
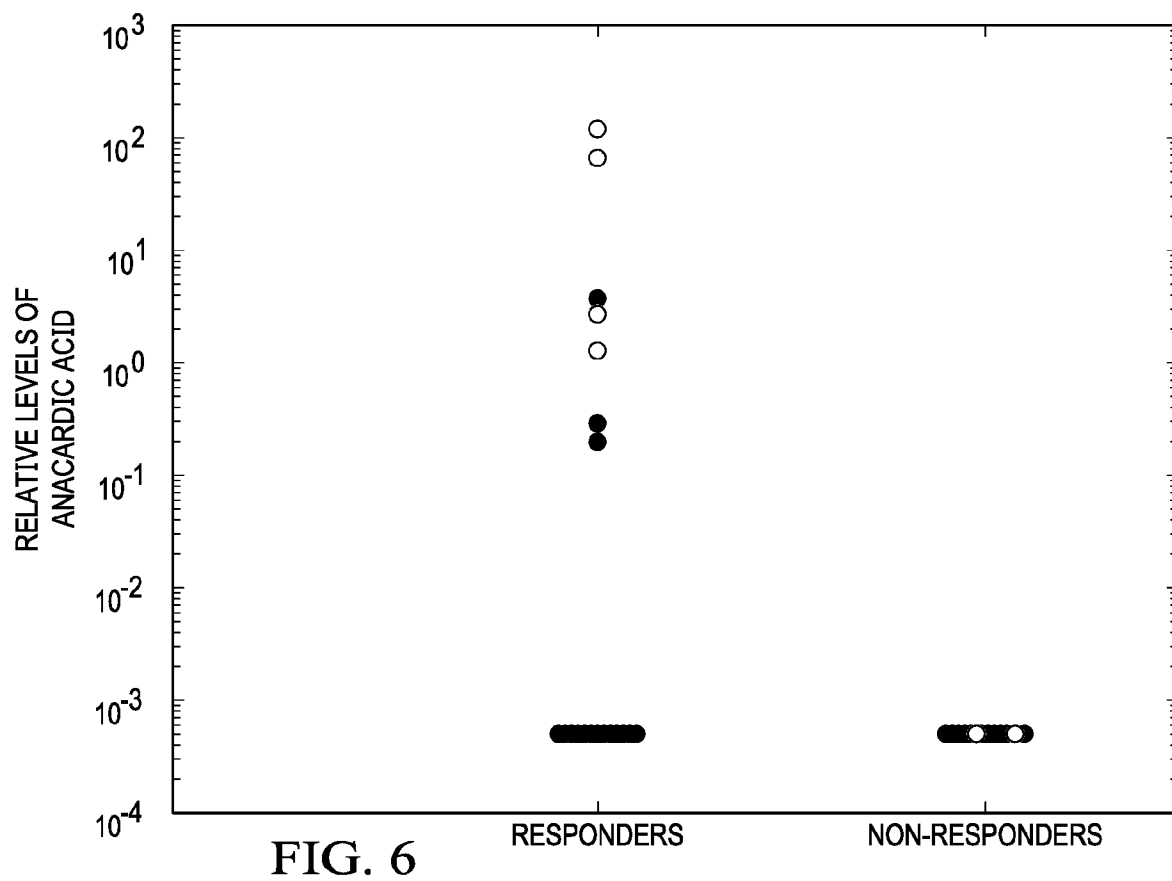


FIG. 7

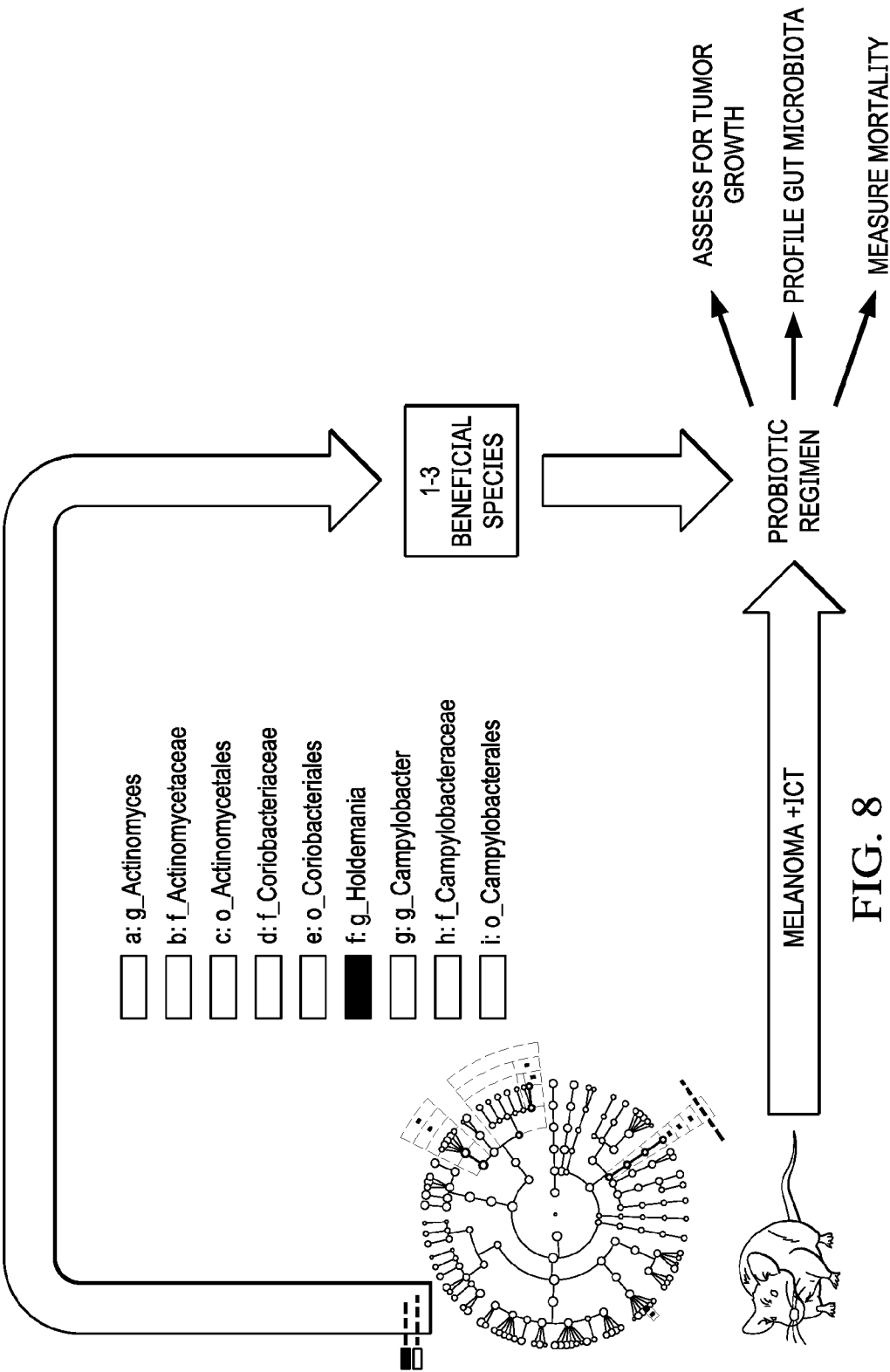


FIG. 8

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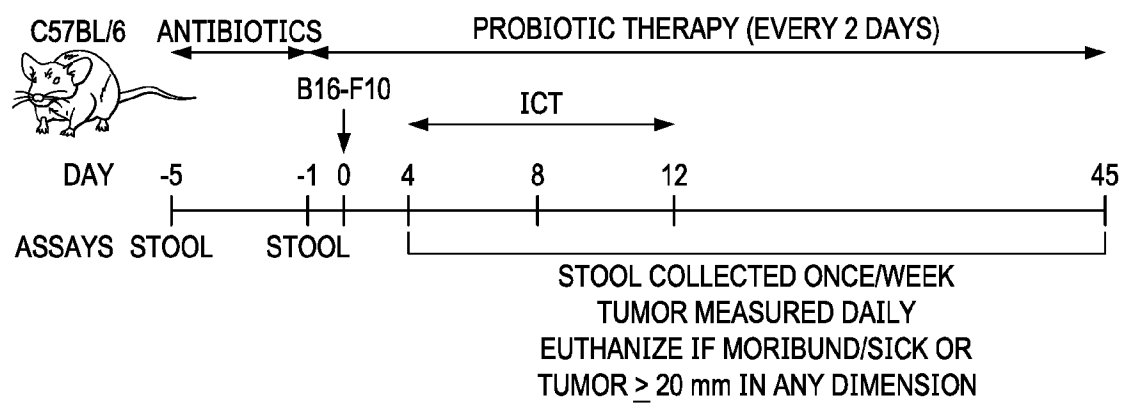
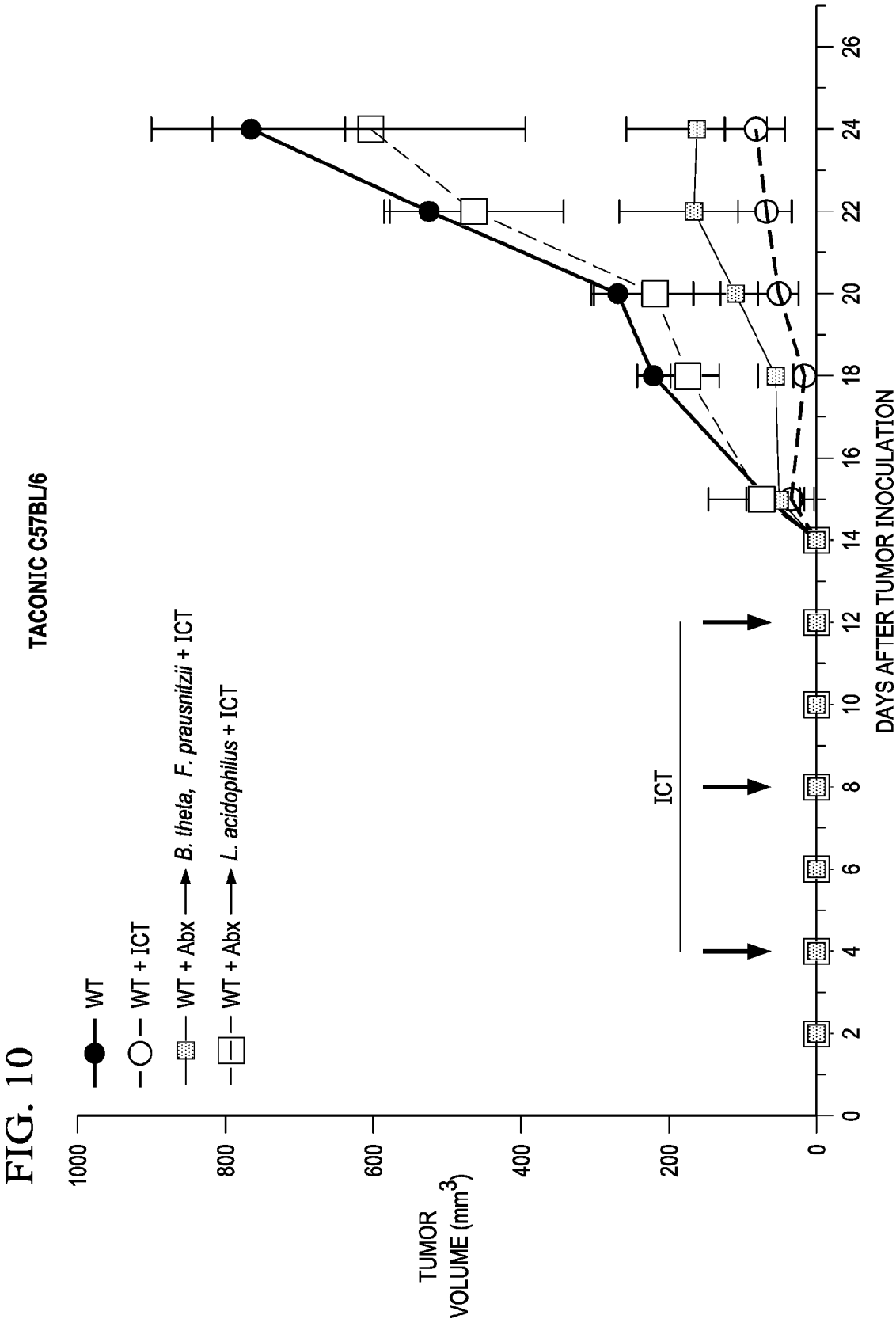
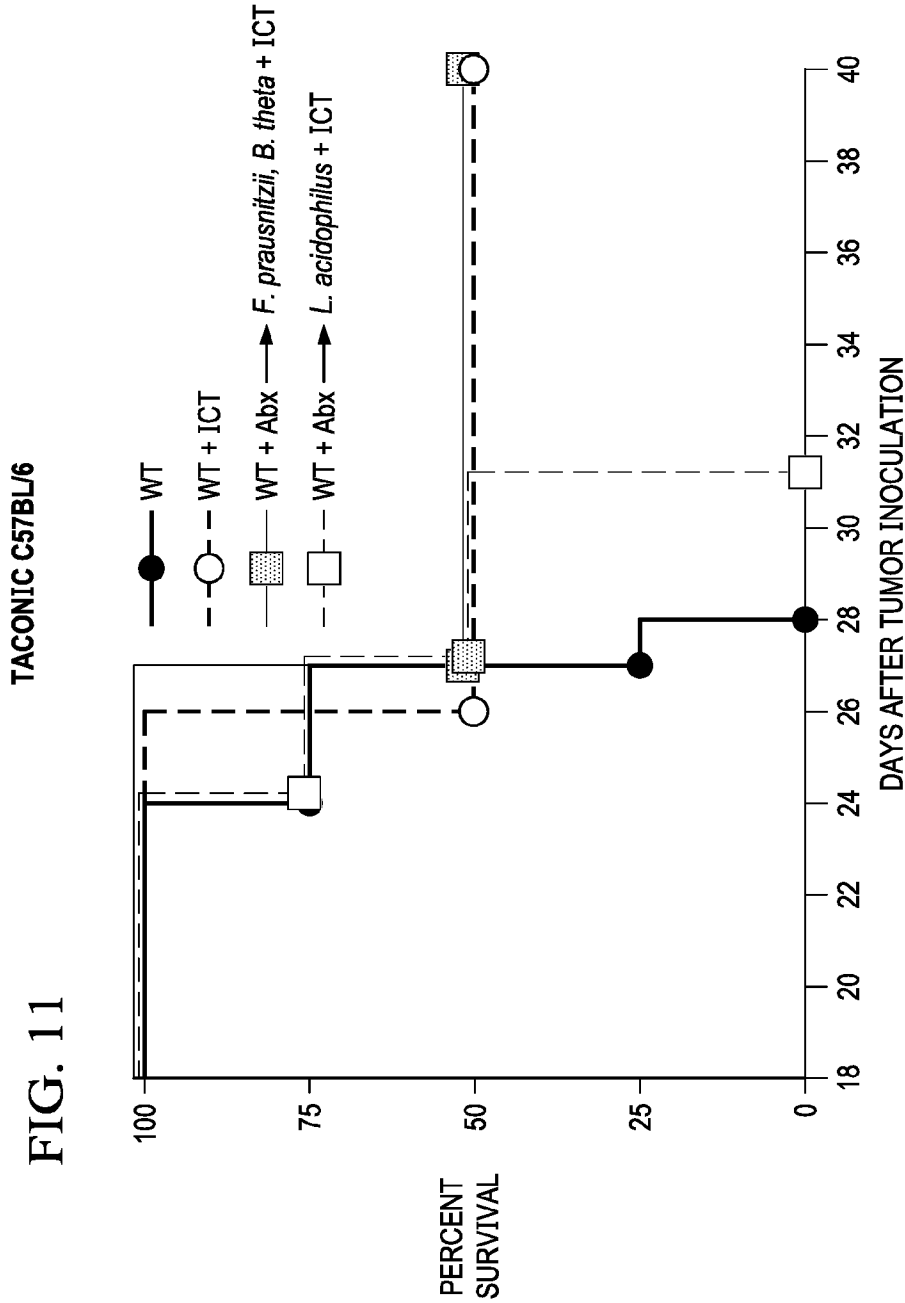
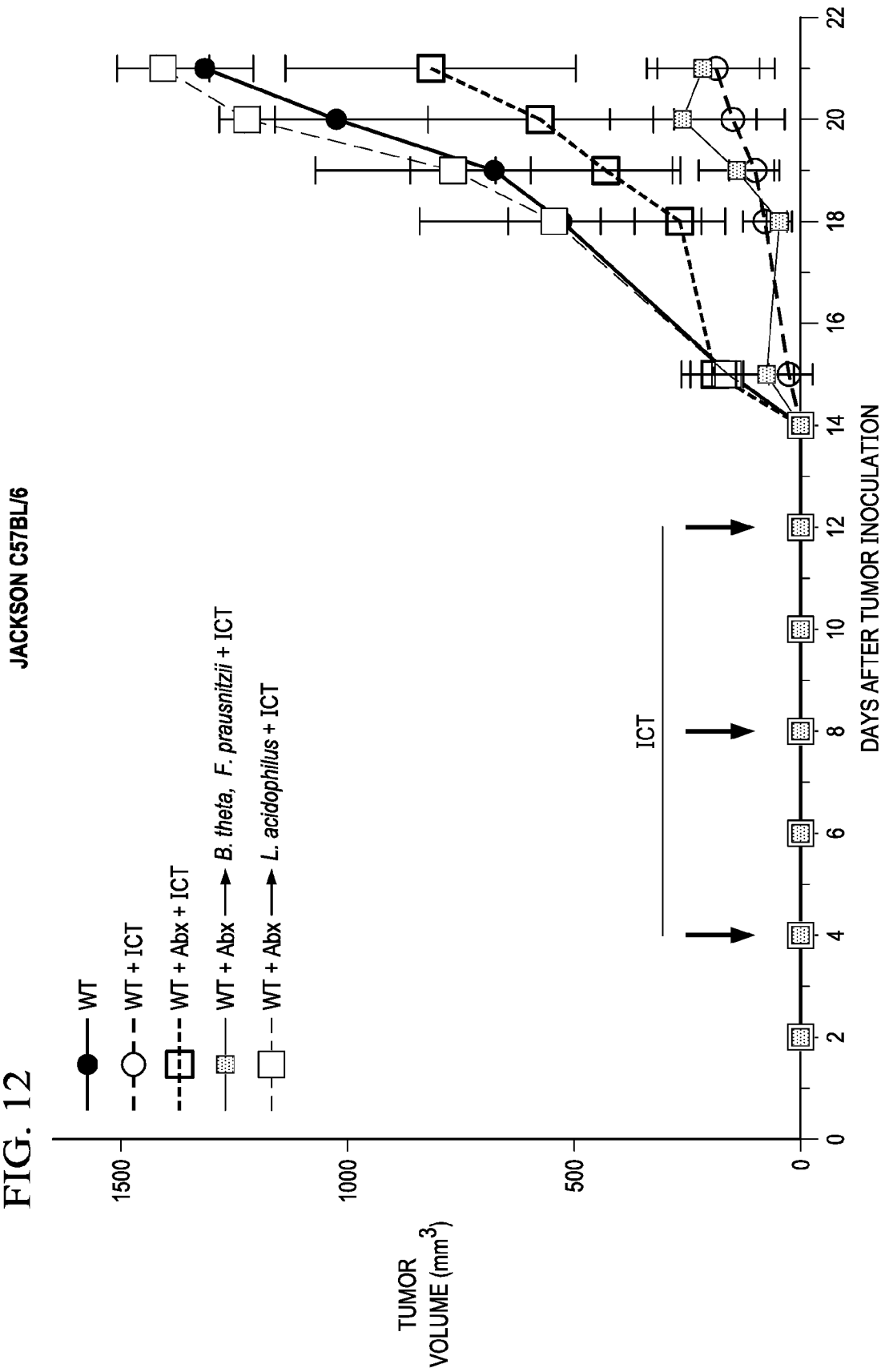


FIG. 9

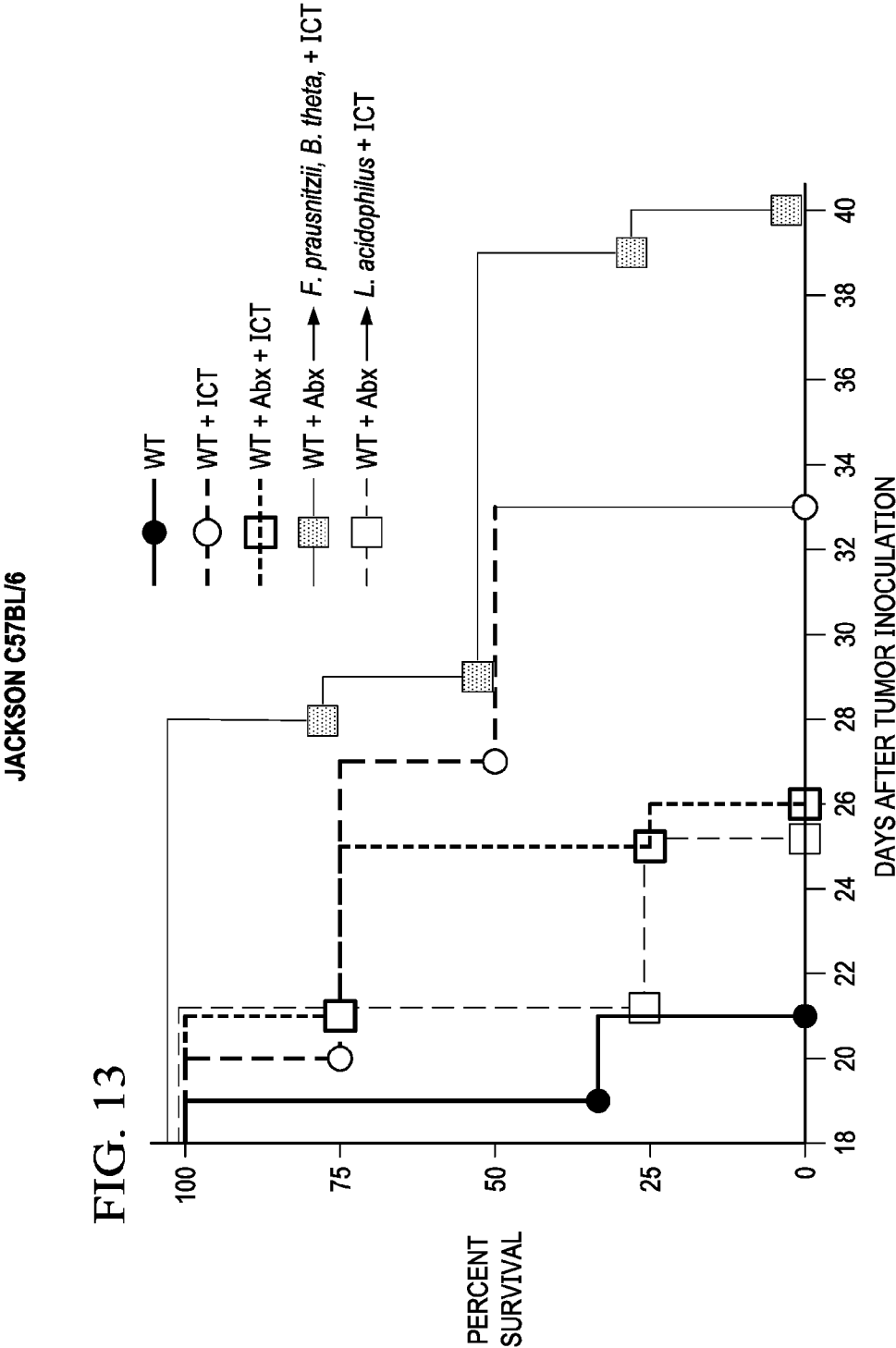




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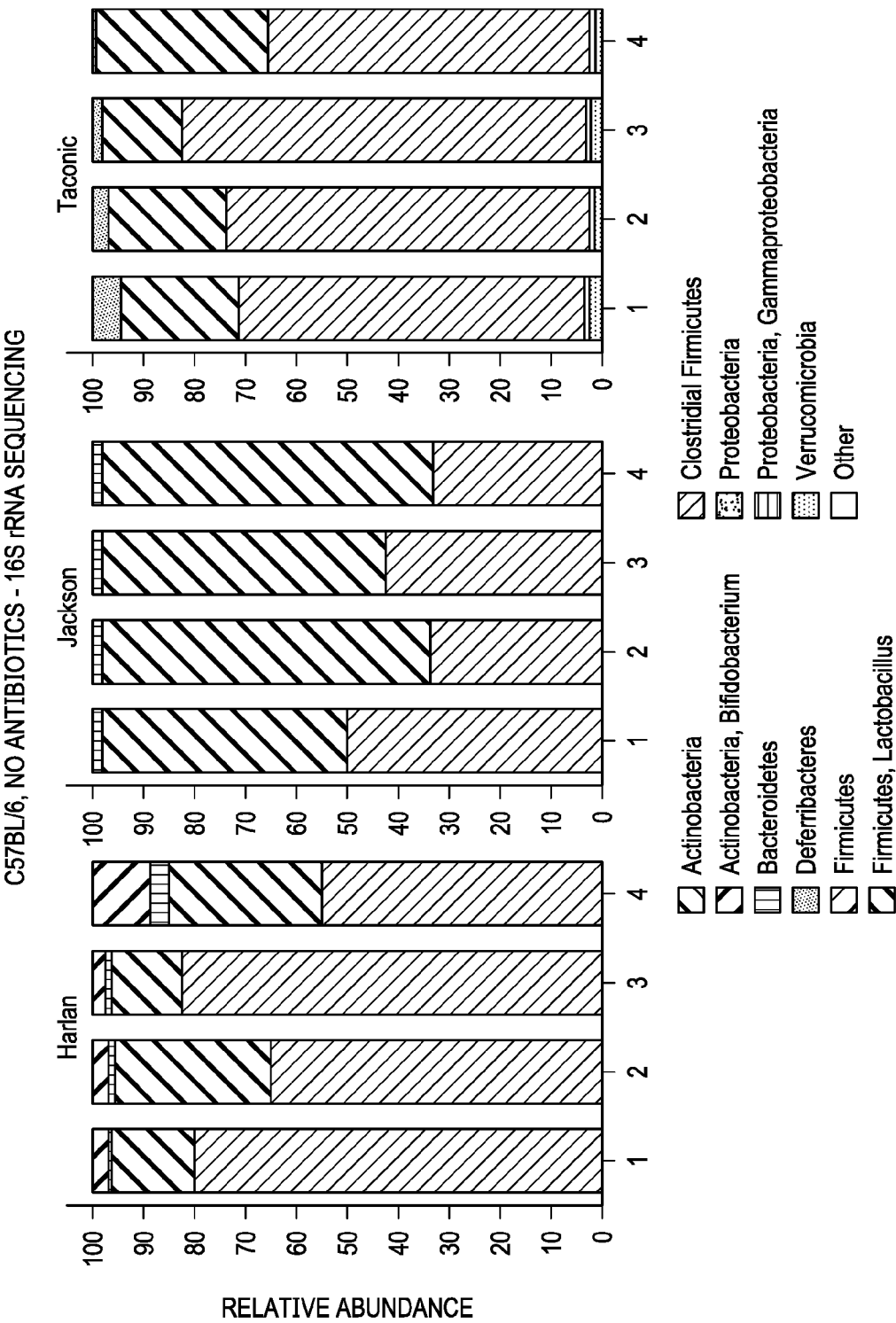


FIG. 14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 18/35564

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - A61K 31/444, A61K 39/395, C07K 16/28 (2018.01)
 CPC - A61K 2039/507, A61K 2300/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y --- A	BASHIARDES et al. "The microbiome in anti-cancer therapy, April 5, 2017, Seminars in Immunology", Pgs. 1-8 Pg. 1, Para [1]; Pg. 4, Full Para [3]; Pg. 4, Full Para [4];	1-4, 14-17, 37-38, 46 ----- 5, 7, 8-9, 12-13, 18-20, 23-27, 29, 31-36, 39, 42, 44, 51-55 ----- 6, 10-11, 21-22, 28, 30, 40-41, 43, 45, 48, 50
X --- Y	CHAPUT et al., "Baseline gut microbiota predicts clinical response and colitis in metastatic melanoma patients treated with ipilimumab", March 27, 2017, Annals of Oncology Vol. 28: pgs. 1368-1379 Pg. 1369, Para [1]; Pg. 1369, Full Para [8]; Pg. 1370, Full Para [4]; Pg. 1375, Para [1]; Pg. 1377, Para [1];	47, 49 ----- 5, 7, 9, 13, 18-20, 23-27, 29, 31-36, 39, 42, 44
Y	LEGUT et al., "Anacardic acid enhances the anticancer activity of liposomal mitoxantrone towards melanoma cell lines ? in vitro studies", January 23, 2014, International Journal of Nanomedicine, Vol. 9, pgs. 653-668 Pg. 653, Abstract; Pg. 663, Full Para [1]; Pg. 664, Para [1]; Pg. 664, Full Para [1];	8, 12, 23, 31
Y	KRYDER et al., "The CRISPR-Cas9 Toolkit: Moving From Bench to Bedside", June 01, 2017, IASLC Lung Cancer News, pgs. 1-4 Pg. 2, Full Para [3]; Pg. 2, Full Para [4];	51-55
Y	HODI et al., "Two-year overall survival rates from a randomised phase 2 trial evaluating the combination of nivolumab and ipilimumab versus ipilimumab alone in patients with advanced melanoma", November 2016, Lancet Oncol., Vol. 17 (11): pgs. 1558-1568 Pg. 2, Para [1]; Pg. 2, Para [4];	7, 9, 20, 29, 42, 44

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

07 August 2018

Date of mailing of the international search report

10 SEP 2018

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 18/35564

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	✓ OH et al., "CRISPR-Cas9-assisted recombineering in <i>Lactobacillus reuteri</i> ," June 27, 2014, <i>Nucleic Acids Research</i> , Vol. 42 (17): pgs. 1-11 Pg. 1, Para [1]; Pg. 1, Para [2]; Pg. 2, Para [2];	52-53
Y	✓ YIN et al., "Boosting Immunity to Small Tumor-Associated Carbohydrates with Bacteriophage Q[Beta] Capsids", June 21, 2013, <i>ACS Chem Biol.</i> Vol. 8 (6): pgs. 1253-1262 Pg. 1, Abstract;	54
A	✗ DUBIN et al., "Intestinal microbiome analyses identify melanoma patients at risk for checkpoint-blockade-induced colitis, February 02, 2016, <i>Nature Communications</i> ", pgs. 1-8 Pg. 3, Para [1]	25
A	✓ SAULNIER et al. "The intestinal microbiome, probiotics and prebiotics in neurogastroenterology", February 2013, <i>Gut Microbes</i> , Vol. 4 (1): pgs. 17-27 Pg. 17, Para [2];	12