

preferably, the *B. longum* is *B. longum* subsp. *infantis*. The bifidobacteria is typically provided in a daily dose of from 10 thousand to 100 billion cfu, preferably 1 billion to 50 billion, and most preferably 5 billion to 25 billion, and the oligosaccharides are provided in a daily dose of from 1 to 20 g, preferably in a daily dose of from 1 to 10 g.

[0006a] In some embodiments, the instant invention provides a composition comprising activated *Bifidobacterium*.

[0006b] In some embodiments, the instant invention provides use of a therapeutically effective amount of the composition as described herein in the manufacture of a medicament for improving the health of a mammalian gastrointestinal tract.

[0006c] In some embodiments, the instant invention provides use of an effective amount of the composition as described herein in the manufacture of a medicament for increasing the concentration of *Bifidobacterium* in the gastrointestinal tract of a mammal, wherein the medicament is to be administered to a subject in order to increase levels of said *Bifidobacterium* in the feces of that mammal to greater than 10% of the total microbiome found in that feces.

[0006d] In some embodiments, the instant invention provides a method of preparing activated *Bifidobacterium* comprising cultivating *Bifidobacterium* by incubating the bacteria under conditions whereby any of the genes Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2344, Blon_2346, Blon_2347, Blon_2331, and Blon_0042 is upregulated, gene Blon_2168 is downregulated, or combinations thereof.

[0006e] In some embodiments, the instant invention provides a method of preparing activated bifidobacteria compositions comprising (a) isolating bifidobacteria from infant feces, (b) purifying the bacteria, (c) inoculating a fermenter with a purified strain of the bacteria, (d) incubating the bacteria in the fermenter in the presence of a mammalian milk oligosaccharide isolated from a mammalian milk source, (e) harvesting the cells, and (f) purifying the bacteria obtained in (e).

BRIEF DESCRIPTION OF DRAWINGS

[0007] FIG. 1 is a diagram depicting whole genome expression analysis which shows differential gene expression of *B. infantis* cells grown in the presence of bovine milk oligosaccharides (BMO) or lactose.

[0008] FIG. 2 is a diagram showing a selection of the genes of the milk oligosaccharide cluster differentially expressed in *B. infantis* during growth in the presence of bovine milk oligosaccharides (BMO) or lactose.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

I. INTRODUCTION

[0009] Human milk glycans contain a significant quantity of human milk oligosaccharides (designated herein as “HMOs”) (about 15 % of total mass) in a form that is not usable as an energy source for the baby or for most of the microorganisms in the gut of that baby. HMOs can be found as free oligosaccharides (dietary glycans) or conjugated to protein or lipids. The major HMOs in milk include lacto-N-tetraose (LNT), lacto-N-neotetraose (LNnT) and lacto-N-hexaose, which are neutral HMOs, in addition to fucosylated oligosaccharides such as 2-fucosyllactose (2FL), 3-fucosyllactose (3FL), and lacto-N-fucopentaoses I, II and III. Acidic HMOs include sialyl-lacto-N-tetraose, 3' and 6' sialyllactose (6SL). HMOs are particularly highly enriched in fucosylated oligosaccharides (Mills et al., US Patent No. 8,197,872). Among the enzymes that produce HMOs in the mammary gland is the enzyme encoded by the fucosyltransferase 2 (FUT2) gene, which catalyzes the linking of fucose residues by an α 1,2-linkage to oligosaccharides found in human milk. Fucosylated oligosaccharides are known to inhibit the binding of pathogenic bacteria in the gut. HMOs, and in particular the fucosylated HMOs, share common structural motifs with glycans on the infant's intestinal epithelia known to be receptors for pathogens. (German et al., WO 2012/009315)

CLAIMS

1. A composition comprising activated *Bifidobacterium*.
2. The composition of claim 1, wherein the activated *Bifidobacterium* has been cultured in the presence of at least one mammalian milk oligosaccharide.
3. The composition of claim 1 or 2, wherein the *Bifidobacterium* expresses a gene coding for a sialidase, a sialic acid, a fucose transporter, or a fucosidase.
4. The composition of any one of claims 1–3, wherein the activated *Bifidobacterium* contains a transport system capable of internalizing one or more oligosaccharide before said oligosaccharide is hydrolyzed and is further capable of hydrolyzing said internalized oligosaccharide, wherein said oligosaccharide has the structure of an oligosaccharide found in a mammalian milk.
5. The composition of any one of claims 1-4, wherein the activated *Bifidobacterium* has a higher binding affinity to mammalian mucosal cells than *Bifidobacteria* of the same species cultivated in the absence of complex oligosaccharides.
6. The composition of any one of claims 1-5, wherein the *Bifidobacterium* is present at a concentration of from 1 billion cfu/g to 500 billion cfu/g.
7. The composition of any one of claims 1-6, wherein the *Bifidobacterium* is *B. longum*, *B. breve*, *B. bifidum* or *B. pseudocatenulatum*.
8. The composition of any one of claims 1-7, further comprising an isolated complex oligosaccharide.
9. The composition of any of claims 1-8, further comprising a stabilizer.

10. The composition of any one of claims 1-9, wherein the composition is in the form of a dry powder, a dry powder suspended in an oil, or as a solution.
11. The composition of any one of claims 1-10, wherein the composition is in the form of a packet, sachet, orally disintegrating tablet, foodstuff, capsule, lozenge, effervescent tablet, suppository, or enema.
12. Use of a therapeutically effective amount of the composition of any one of claims 1-7 in the manufacture of a medicament for improving the health of a mammalian gastrointestinal tract.
13. Use of an effective amount of the composition of any one of claims 1-7 in the manufacture of a medicament for increasing the concentration of *Bifidobacterium* in the gastrointestinal tract of a mammal, wherein the medicament is to be administered to a subject in order to increase levels of said *Bifidobacterium* in the feces of that mammal to greater than 10% of the total microbiome found in that feces.
14. A method of preparing activated *Bifidobacterium* comprising cultivating *Bifidobacterium* by incubating the bacteria under conditions whereby any of the genes Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2344, Blon_2346, Blon_2347, Blon_2331, and Blon_0042 is upregulated, gene Blon_2168 is downregulated, or combinations thereof.
15. A method of preparing activated bifidobacteria compositions comprising (a) isolating bifidobacteria from infant feces, (b) purifying the bacteria, (c) inoculating a fermenter with a purified strain of the bacteria, (d) incubating the bacteria in the fermenter in the presence of a mammalian milk oligosaccharide isolated from a mammalian milk source, (e) harvesting the cells, and (f) purifying the bacteria obtained in (e).