the specific complex oligosaccharides such as those found in human or bovine milk (U.S. Patent No. 8,198,872 and U.S. Pub. No. 2013/0195803, the contents of which are incorporated herein by reference). When *B. infantis* comes in contact with certain complex oligosaccharides a number of genes are specifically induced within the bacterium whose protein products as enzymes and binding proteins are responsible for the uptake and internal deconstruction of those complex oligosaccharides, and the individual sugar components are then catabolized to provide energy for the growth and reproduction of that organism (Sela et al, 2008, *PNAS*, 105(48): p. 18964-69).

SUMMARY

[0004] The instant ~~invention~~ disclosure provides compositions comprising isolated complex oligosaccharide fractions from mammalian milk sources, optionally supplemented with purified fucosylated/sialylated oligosaccharides. The mammalian milk may be from human or bovine sources, andincluding but not limited to, the bovine source is from bovine colostrum. The fucosylated oligosaccharide(s) may comprise synthetically produced and purified 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, or lacto-N-fucosylpentose.

[0005] In some ~~embodiments~~examples, the composition further comprises bifidobacteria that internalize the complex oligosaccharides or dietary glycans prior to their hydrolysis and metabolism. The combination of the bifidobacteria with the complex oligosaccharide may result in the conversion of the bifidobacteria to an activated bifidobacteria (ABI). The bifidobacteria is preferably selected from *B. longum*, *B. breve*, *B. bifidum or B. pseudocatenulatum*, and more preferably, the *B. longum* is *B. longum* subsp. *infantis*.

[0006] In other ~~embodiments~~examples, any of the compositions described herein provide a method of improving the health of a mammal comprising administering to a mammal a composition comprising a complex oligosaccharide from a mammalian milk source, optionally supplemented with a fucosylated and/or sialylated oligosaccharide, and a bifidobacteria that internalizes the complex oligosaccharide prior to its hydrolysis, and wherein the fucosylated oligosaccharide can be a synthetically produced and purified form of 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, or lacto-N-fucosylpentose, wherein the bifidobacteria is preferably selected from *B. longum*, *B. breve*, *B. bifidum or B. pseudocatenulatum*, and more

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 one aspect, the present disclosure refers to a composition comprising activated *Bifidobacterium* wherein

activated *Bifidobacterium* expresses a gene coding for a sialidase, a sialic acid transporter, a fucose transporter, and/or a fucosidase; and

wherein the composition is in the form of a dry powder or a dry powder suspended in an oil.

[0006b] In another aspect, the present disclosure refers to a use of the composition as described herein in the manufacture of a medicament for treating or preventing dysbiosis of an infant mammalian gastrointestinal tract.

[0006c] In another aspect, the present disclosure refers to a use of the composition as described herein in the manufacture of a medicament for treating or preventing dysbiosis in the gastrointestinal tract of an infant mammal in order to increase levels of *Bifidobacterium* in the feces of that mammal to greater than 20% of the total microbiome found in that feces.

[0006d] In another aspect, the present disclosure refers to a method of predicting the activated state of a *Bifidobacterium* comprising measuring whether any of the following genes are upregulated: Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2344, Blon_2346, Blon_2347, Blon_2331, and Blon_0042, and/or measuring whether the gene Blon_2168 is downregulated.

[0006e] In yet another aspect, the present disclosure refers to a method of preparing activated bifidobacteria compositions comprising (a) inoculating a fermenter with a purified strain of bifidobacteria found in infant feces, (b) incubating the bacteria in the fermenter in the presence of a mammalian milk oligosaccharide isolated from a mammalian milk source, (c) harvesting the cells, (d) purifying the bacteria cells obtained in (c), and (e) drying the bacteria cells.

[0006f] In yet another aspect, the present disclosure refers to a use of a mammalian milk oligosaccharide for upregulating 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, and downregulating the gene Blon_2168, in a *Bifidobacterium*.

[0006g] In yet another aspect, the present disclosure refers to the composition as described herein for use in therapy.

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 α1,2-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* wherein

activated *Bifidobacterium* expresses a gene coding for a sialidase, a sialic acid transporter, a fucose transporter, and/or a fucosidase; and

wherein the composition is in the form of a dry powder or a dry powder suspended in an oil.

~~2. The composition of claim 1, 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.~~

~~3. The composition of claim 2, wherein the mammalian milk is human, bovine, pig, rabbit, goat, sheep, camel, buffalo milk, or mixtures thereof.~~

~~4.~~2. The composition of ~~any one of claims 1-3~~claim 1, wherein the activated *Bifidobacterium* has been cultured in the presence of at least one mammalian milk oligosaccharide.

~~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.~~3. The composition of claim 1 or 2~~ any one of claims 1-5~~, wherein the activated *Bifidobacterium* has 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 ~~comprises upregulated genes selected from the group consisting of~~ Blon_0042 upregulated, gene Blon_2168 downregulated, or~~, Blon_R0015, Blon_R0017, Blon_R0021, Blon_R0022, and~~ combinations thereof.

~~7. The composition of any one of claims 1-6, wherein the *Bifidobacterium* comprises downregulated genes selected from the group consisting of Blon_0518, Blon_0785, Blon_2167, Blon_2168 and combinations thereof.~~

~~8. The composition of any one of claims 1-7, wherein the *Bifidobacterium* comprises an upregulated Blon_0042 gene.~~

~~9. The composition of any one of claims 1-8, wherein the *Bifidobacterium* comprises a downregulated Blon_2168 gene.~~

~~10. The composition of any one of claims 1-9, wherein the *Bifidobacterium* comprises upregulated genes selected from the group consisting of Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2344, Blon_2346, Blon_2347, and Blon_2331.~~

~~11. The composition of any one of claims 1-10, wherein the *Bifidobacterium* expresses a gene coding for a sialidase or a fucosidase.~~

~~12. The composition of any one of claims 1-11, wherein the *Bifidobacterium* expresses a gene coding for a sialic acid or a fucose transporter.~~

~~13.~~4. The composition of any one of claims 1-~~3~~12, wherein the *Bifidobacterium* is present at a concentration of from 1 billion cfu/g to 500 billion cfu/g.

~~14. The composition of any one of claims 1-13, wherein the *Bifidobacterium* is present at a concentration of from 1 billion cfu/g to 100 billion cfu/g.~~

~~15. The composition of any one of claims 1-14, wherein the *Bifidobacterium* is present at a concentration of from 10 billion cfu/g to 50 billion cfu/g.~~

~~16.~~5. The composition of any one of claims 1-~~4~~15, wherein the *Bifidobacterium* is *B. longum*, *B. breve*, *B. bifidum or B. pseudocatenulatum*.

~~17. The composition of claim 16, wherein the *Bifidobacterium* is *B. longum* subsp. *infantis*.~~

~~18.~~6. The composition of any one of claims 1-5~~17~~, further comprising an isolated complex oligosaccharide.

~~19. The composition of claim 18, wherein the complex oligosaccharide is isolated from a mammalian milk source.~~

~~20. The composition of claim 19, wherein the mammalian milk source is human, bovine, pigs, rabbits, goats, sheep, or camel.~~

~~21. The composition of claim 20, wherein the bovine source is from bovine milk, bovine colostrum, bovine colostrum concentrate, or mixtures thereof.~~

~~22. The composition of claim 21, wherein the complex oligosaccharide is from whey permeate.~~

~~23. The composition of any one of claims 19-22, wherein the complex oligosaccharide comprises at least one of (3Hex,4HexNac,1Fuc), (1Gal,1GlcNAc,1NeuAc), or (1Glu,1Gal,1NeuAc (3' or 6')).~~

~~24. The composition of any one of claims 19-23, wherein the complex oligosaccharide is less than 50 % fucosylated.~~

~~25. The composition of any one of claims claim 19-24, wherein the bovine colostrum oligosaccharide comprises any of Hex(4); Hex(4) HexNAc(2); or Hex(3) HexNAc(1) NeuAc(1) at levels greater than 1%.~~

~~26. The composition of any one of claims claim 19-25, wherein the complex oligosaccharide comprise one of the following ratios of constituents: 1) a ratio of Hex(2) NeuAc(1) : Hex(2)~~

~~HexNAc(1) less than 5.0; 2) a ratio of Hex(2) HexNAc(1) : Hex (3) HexNAc(1) of greater than 1.0; 3) a ratio of Hex(2) HexNAc(1) : Hex (3) HexNAc(2) of greater than 2.0; 4) a ratio of Hex(3) : Hex (3) HexNAc(1) NeuAc(1) of less than 100; or 5) a ratio of Hex(2) HexNAc(1) : Hex (4) NeuAc(2) NeuGc(1) of greater than 10.~~

~~27. The composition of any one of claims 19-26, wherein the complex oligosaccharide is at least 20 % of the weight of the composition.~~

~~28. The composition of any one of claims 19-27, wherein the complex oligosaccharide is at least 50 % of the weight of the composition.~~

~~29. The composition of any one of claims 19-28, wherein the complex oligosaccharide is at least 80% of the weight of the composition.~~

~~30. The composition of any one of claims 19-29, wherein the complex oligosaccharide further comprises a fucosyllactose, sialyllactose or derivatives thereof.~~

~~31. The composition of claim 30, wherein the fucosyllactose, sialyllactose or derivatives thereof are synthetically produced and purified oligosaccharides of 2'-fucosyllactose, 3'-fucosyllactose, difucosyllactose, lacto-N-fucosylpentose I, lacto-N-fucosylpentose II, lacto-N-fucosylpentose III, lacto-N-fucosylpentose V, 3'-sialyllactose, 6'-sialyllactose, 3'-sialyl-3-fucosyllactose, sialyllacto-N-tetraose, 6'-sialyllactosamine, or mixtures thereof.~~

~~32. The composition of claim 30-31, wherein the fucosyllactose and/or sialyllactose comprises 1-5 % of the total oligosaccharides.~~

~~33. The composition of any one of claims 30-31, wherein the fucosyllactose and/or sialyllactose comprises 5-20 % of the total oligosaccharides.~~

~~34. The composition of any one of claims 30-31, wherein the fucosyllactose and/or sialyllactose comprises 20-50 % of the total oligosaccharides.~~

~~35. The composition of any one of claims 31-34, where in the mass ratio of the complex oligosaccharide to the fucosyllactose and/or sialyllactose is from 20:1 to 1:10.~~

~~36. The composition of any of claims 1-35, further comprising a secondary metabolite.~~

~~37. The composition of claim 36, wherein the secondary metabolite comprises a short chain fatty acid.~~

~~38. The composition of claim 36, wherein the secondary metabolite comprises acetate, lactate, or combinations thereof.~~

~~39.~~7. The composition of any of claims 1-6~~38~~, further comprising a stabilizer.

~~40. The composition of claim 39, wherein the stabilizer is a flow agent.~~

~~41. The composition of claim 40, wherein the stabilizer is a milk protein.~~

~~42. The composition of any one of claims 1-41, wherein the composition is in the form of a dry powder, a dry powder suspended in an oil, or as a solution.~~

~~43. The composition of claim 42, wherein the composition is spray dried or freeze-dried.~~

~~44. The composition of claim 43, wherein the composition is freeze-dried in the presence of a suitable cryoprotectant.~~

~~45. The composition of claim 44, wherein the suitable cryoprotectant is glucose, lactose, raffinose, sucrose, trehalose, adonitol, glycerol, mannitol, methanol, polyethylene glycol, propylene glycol, ribitol, alginate, bovine serum albumin, carnitine, citrate, cysteine, dextran, dimethyl sulphoxide, sodium glutamate, glycine betaine, glycogen, hypotaurine, peptone, polyvinyl pyrrolidone, or taurine.~~

~~46.~~8. The composition of any one of claims 1-7~~45~~, wherein the composition is in the form of a packet, sachet, orally disintegrating tablet, foodstuff, capsule, lozenge, effervescent tablet, suppository, or enema.

~~47. The composition of claim 46, wherein the capsule or tablet has an enteric coating.~~

~~48. The composition of claim 47, wherein the enteric coating comprises one or more of fatty acids, waxes, shellac, plastics, plant fibers, methyl acrylate-methacrylic acid copolymers, cellulose acetate succinate, hydroxy propyl methyl cellulose phthalate, hydroxy propyl methyl cellulose acetate succinate, polyvinyl acetate phthalate (PVAP), methyl methacrylate-methacrylic acid copolymers, cellulose acetate trimellitate, sodium alginate, and Zein.~~

~~49.~~9. Use of ~~A method of improving the health of a mammalian gastrointestinal tract comprising administering a therapeutically effective amount of~~ the composition of any one of claims 1-5~~18~~ in the manufacture of a medicament for treating or preventing dysbiosis of an infant mammalian gastrointestinal tract~~to a subject in need thereof~~.

~~50.~~10. Use of the ~~A method of increasing the concentration of Bifidobacterium in the gastrointestinal track of a mammal by administering an effective amount of the~~ composition of any one of claims 1-5~~18~~ in the manufacture of a medicament for treating or preventing dysbiosis in the gastrointestinal tract of an infant mammal in order to increase levels of *Bifidobacterium* in the feces of that mammal to greater than 20% of the total microbiome found in that feces~~to a subject in order to increase levels of said administered Bifidobacterium in the feces of that mammal to greater than 10% of the total microbiome found in that feces~~.

~~51. The method of claim 50, wherein the increase of the levels of said administered Bifidobacterium in the feces of that mammal is greater than 20% of the total microbiome found in that feces.~~

~~52. The method of claim 50, wherein the increase of the levels of said administered Bifidobacterium in the feces of that mammal is greater than 50% of the total microbiome found in that feces.~~

~~53. The method of claim 50, wherein the increase of the levels of said administered Bifidobacterium in the feces of that mammal is greater than 70% of the total microbiome found in that feces.~~

~~54. The method of any one of claims 49-53, further comprising administering to the subject a complex oligosaccharide.~~

~~55. The method of any one of claims 54, wherein the complex oligosaccharide and the *Bifidobacterium* are provided either together or separately.~~

~~56. The method of claim 55, wherein the complex oligosaccharide is provided as a solution and the *Bifidobacterium* is provided as an enteric-coated tablet or capsule.~~

~~57. The method of any one of claims 54-56, wherein the composition is provided in a liquid composition and comprises complex oligosaccharide at a level of from about 1 g/L to 50 g/L.~~

~~58. The method of claim 55, wherein the complex oligosaccharide and *Bifidobacterium* is provided in dry form and as an enteric-coated tablet or capsule.~~

~~59. The method of any one of claims 54-58, wherein the complex oligosaccharide is from an isolated mammalian milk source.~~

~~60. The method of claim 59, wherein the mammalian milk source is human, bovine, pigs, rabbits, goats, sheep, or camel.~~

~~61. The method of claim 60, wherein the bovine source is bovine milk, bovine colostrum or bovine colostrum concentrate.~~

~~62. The method of claim 61, wherein the complex oligosaccharide is from whey permeate.~~

~~63. The method of any one of claims 54-62, wherein the complex oligosaccharide comprises at least one of (3Hex,4HexNac,1Fuc), (1Gal,1GlcNAc,1NeuAc), or (1Glu,1Gal,1NeuAc (3' or 6')).~~

~~64. The method of any one of claims 54-63, wherein the complex oligosaccharide is less than 50 % fucosylated.~~

~~65. The method of any one of claims 61-64, wherein the bovine colostrum oligosaccharide comprises any of Hex(4); Hex(4) HexNAc(2); or Hex(3) HexNAc(1) NeuAc(1) at levels greater than 1%.~~

~~66. The method of any one of claims 54-65, wherein the complex oligosaccharide comprises one of the following ratios of constituents: 1) a ratio of Hex(2) NeuAc(1) : Hex(2) HexNAc(1) less than 5.0; 2) a ratio of Hex(2) HexNAc(1) : Hex (3) HexNAc(1) of greater than 1.0; 3) a ratio of Hex(2) HexNAc(1) : Hex (3) HexNAc(2) of greater than 2.0; 4) a ratio of Hex(3) : Hex (3) HexNAc(1) NeuAc(1) of less than 100; or 5) a ratio of Hex(2) HexNAc(1) : Hex (4) NeuAc(2) NeuGc(1) of greater than 10.~~

~~67. The method of any one of claims 54-66, wherein the complex oligosaccharide is at least 20 % of the weight of the composition.~~

~~68. The method of any one of claims 54-67, wherein the complex oligosaccharide is at least 50 % of the weight of the composition.~~

~~69. The method of any one of claims 54-68, wherein the complex oligosaccharide is at least 80% of the weight of the composition.~~

~~70. The method of any one of claims 54-69, wherein the complex oligosaccharide further comprises a fucosyllactose, sialyllactose or derivatives thereof.~~

~~71. The method of claim 70, wherein the fucosyllactose, sialyllactose or derivatives thereof are synthetically produced and purified oligosaccharides of 2'-fucosyllactose, 3'-fucosyllactose, difucosyllactose, lacto-N-fucosylpentose I, lacto-N-fucosylpentose II, lacto-N-fucosylpentose III, lacto-N-fucosylpentose V, 3'-sialyllactose, 6'-sialyllactose, 3'-sialyl-3-fucosyllactose, sialyllacto-N-tetraose, 6'-sialyllactosamine, or mixtures thereof.~~

~~72. The method of claim 71, wherein the fucosyllactose and/or sialyllactose comprises 1-5 % of the total oligosaccharides.~~

~~73. The method of claim 72, wherein the fucosyllactose and/or sialyllactose comprises 5-20 % of the total oligosaccharides.~~

~~74. The method of claim 73, wherein the fucosyllactose and/or sialyllactose comprises 20-50 % of the total oligosaccharides.~~

~~75. The method of any one of claims 71-74, wherein the mass ratio of the complex oligosaccharide to the fucosyllactose and/or sialyllactose is from 20:1 to 1:10.~~

~~76. The method of any one of claims 54-75, wherein the complex oligosaccharide is administered prior to the administration of *Bifidobacterium*.~~

~~77. The method of any one of claims 54-76, wherein the complex oligosaccharide is administered contemporaneously with the administration of *Bifidobacterium*.~~

~~78. The method of any one of claims 54-77, wherein the complex oligosaccharide is administered after the administration of *Bifidobacterium*.~~

~~79. The method of any one of claims 54-78, wherein the complex oligosaccharide is provided in a daily dose of from 1 to 20 grams.~~

~~80. The method of any one of claims 54-79, wherein the complex oligosaccharide is provided in a daily dose of from 1 to 10 grams.~~

~~81. The method of any one of claims 49-80, wherein the *Bifidobacterium* is provided in a daily dose of from 1 to 100 billion colony forming units (CFUs).~~

~~82. The method of any one of claims 49-81, wherein the *Bifidobacterium* is provided in a daily dose of from 10 to 50 billion CFUs.~~

~~83. The method of any one of claims 49-82, wherein the subject in need thereof is administered a dose once daily or in multiple (e.g., two, three, four, five, six, or more) sub-doses administered at appropriate intervals throughout the day.~~

~~84. The method of any one of claims 49-83, wherein the composition is orally or rectally administered.~~

~~85. The method of any one of claims 49-84, further comprising monitoring the levels of the *Bifidobacterium* in the stools of the mammal.~~

~~86. The method of any of claim 49-85, wherein the composition is administered for at least 5 days.~~

~~87. The method of any one of claims 49-86, wherein the composition is administered for a duration from 30 to 360 days.~~

~~88. The method of any one of claims 49-87, comprising administering to a subject in need thereof a dose of the composition of any one of claims 1-48, in an amount, and for a duration, wherein the population of *Bifidobacterium* is established in the gut of the subject.~~

89. The method of claim 88, further comprising administering to the subject, a dose of the composition from any of claims 1-48, in an amount, and for a duration, wherein the population of *Bifidobacterium* is maintained in the gastrointestinal tract of the subject.

90. The method of claims 79-89, wherein the dose is administering for at least 10 days in order to maintain the levels of *Bifidobacterium* greater than at least 5% of the total fecal microbiome of the mammal.

91. The method of claims 79-90, wherein the dose is administered for at least 10 days in order to maintain the levels of *Bifidobacterium* greater than at least 20% of the total fecal microbiome of the mammal.

92. The method of claims 79-91, wherein the dose is administered for at least 10 days in order to maintain the levels of *Bifidobacterium* greater than at least 50% of the total fecal microbiome of the mammal.

93. The method of any one of claims 49-92, wherein the mammal is a human, a cow, a pig, a rabbit, a goat, a sheep, a cat, a dog, a horse, buffalo, or a camel.

94. The method of claim 93, wherein the mammal is a human infant.

95. The method of claim 94, wherein the infant was delivered via cesarean section.

96. The method of claim 94, wherein the infant was delivered vaginally.

97. The method of any of claims 94-96, wherein the infant is being fed with infant formula which contains no appreciable quantity of mammalian milk oligosaccharides.

98. The method of any one of claims 94-97, wherein the infant is from birth to about 36 months post-conception.

~~99. The method of any of claim 94-97, wherein the infant is from birth to weaning age.~~

~~100. The method of any of claim 94-99, wherein the infant is nursed by a mother who is FUC-2 deficient as measured by a genetic test or the absence of complex fucosylated oligosaccharides in her milk.~~

~~101. The method of claim 93, wherein the human is a pregnant woman.~~

~~102. The method of claim 101, wherein the pregnant woman is in at least the third trimester of pregnancy.~~

~~103. The method of any one of claims 49-101, wherein the improvement of the health of the mammal is a reduction of colic in an infant.~~

~~104. The method of any one of claims 49-103, wherein the improvement of the health of the mammal is accelerating the development of the immune system in a baby.~~

~~105. The method of any one of claims 49-104, wherein the improvement of the health of the mammal is the result of the colonization of the GI tract of the baby with *B. infantis* at levels that represent more than 20% of the total gut microbiome as measured by fecal analysis.~~

~~106. A method of preparing activated *Bifidobacterium* comprising cultivating *Bifidobacterium* by incubating the bacteria under conditions whereby gene Blon_0042 is upregulated, gene Blon_2168 is downregulated, or combinations thereof.~~

~~107.~~11. A method of predicting the~~preparing~~ activated state of a *Bifidobacterium* comprising measuring whether any of the following genes are upregulated: ~~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, ~~and~~ Blon_2331, and Blon_0042, and/or measuring whether the gene Blon_2168 is downregulated~~is upregulated~~.

~~108.~~12. 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 bifidobacteria found in infant feces~~the bacteria~~, (b~~d~~) incubating the bacteria in the fermenter in the presence of a mammalian milk oligosaccharide isolated from a mammalian milk source, (c~~e~~) harvesting the cells, ~~and~~ (d~~f~~) purifying the bacterial cells obtained in (c~~e~~), and (e) drying the bacteria cells.

13. Use of a mammalian milk oligosaccharide for upregulating 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, and downregulating the gene Blon_2168, in a *Bifidobacterium*.

14. The composition of any one of claims 1-5 for use in therapy.

~~109. The method of claim 108, wherein the mammalian milk oligosaccharide is from a human.~~

~~110. The method of claim 108, wherein the mammalian milk oligosaccharide is from a bovine source.~~

~~111. The method of claim 110, wherein the bovine source is bovine colostrum.~~

~~112. The method of claim 108, wherein the complex oligosaccharide is present during incubation for at least late log phase.~~

~~113. The method of any one of claims 108-112, wherein the complex oligosaccharide is present at a level of from about 1 g/L to 50 g/L as a carbon source.~~

~~114. The method of any one of claims 108-113, further comprising combining the purified *Bifidobacterium* from step (c) with a complex oligosaccharide.~~

~~115. The method of any one of claims 108-114, further comprising measuring gene expression of fucosidase or sialidase, wherein the detection of the presence of fucosidase or sialidase is indicative of activated bifidobacteria.~~

~~116. The method of any one of claims 108-115, further comprising drying the cells.~~