SUMMARY OF INVENTION

[0003a] In one aspect, the present disclosure provides a composition comprising a Bifidobacterium longum subsp. infantis comprising a functional H5 gene cluster and at least one oligosaccharide having a Type I or Type II core, wherein the Bifidobacterium longum subsp. infantis is Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180.

[0003b] In another aspect, the present disclosure provides a use of the composition as described herein in the manufacture of a medicament for improving the health of a mammalian gastrointestinal tract, comprising that the composition is to be administered to a mammal in need thereof.

[0003c] In another aspect, the present disclosure provides a method of preparing activated Bifidobacterium comprising cultivating Bifidobacterium by incubating the Bifidobacterium longum subsp. infantis comprising a functional H5 cluster, including the Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180, bacteria under conditions whereby one or more of the genes Blon_0042, Blon_088l, B1oh_2175, B1oh_2176, Blon_2l77, Blon_233l, Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2343, Blon_2344, Blon_2346, and Blon_2347 is upregulated, and/or Blon_2l68 is downregulated.

[0003d] In yet another aspect, the present disclosure provides a method of preparing activated commensal Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180 comprising culturing said bacterial sp. in the presence of a mammalian milk oligosaccharide (MMO) or an activator selected from the compounds listed in the group consisting of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylglucosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ, whereby bacterial cells in the culture medium are activated.

Composition with bacteria having H5 gene cluster: amount of bacteria

[0004] The invention provides a composition comprising a Bifidobacterium longum subsp. infantis comprising a functional H5 gene cluster and at least one oligosaccharide having a Type I or Type II core, where the H5 cluster comprises at least B1oh_2175, Blon_2l76, and Blon_2l77, more typically where the functional H5 cluster comprises Blon_2l7l,

B1oh_2173, B1oh_2174, B1oh_2175, B1oh_2176, Blon_2l77, and galT. An organism with a functional H5 cluster will transport and consume LNB oligosaccharides. In one preferred mode if the invention, the Bifidobacterium longum subsp. infantis is Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180. The Bifidobacterium may be present in the composition of this invention at a concentration of from 1 million cfu/g to 500 billion cfu/g, and/or the Bifidobacterium may be present at a concentration of from 5 Billion cfu/g to 100 Billion cfu/g, and/or the Bifidobacterium may be present at a concentration of from 10 Billion cfu/g to 50 Billion cfu/g. Alternatively, the Bifidobacterium may be present in the composition at a concentration of from 50 million to 4 or 5 billion cfu/g.

Activated bacteria - functionality

[0005] Preferably, the Bifidobacterium longum subsp. infantis in the compositions of this invention is activated. In the compositions of this invention, the Bifidobacterium preferably contains a LNB transport system capable of internalizing one or more oligosaccharides before the oligosaccharide is hydrolyzed and is capable of hydrolyzing the internalized oligosaccharide, where the oligosaccharide has the structure of an oligosaccharide found in a mammalian milk, and the mammalian milk may be human, bovine, pig, rabbit, goat, sheep, camel milk, or mixtures thereof. Such Bifidobacterium will have a higher binding affinity to mammalian mucosal cells than Bifidobacteria of the same species cultivated in the absence of complex oligosaccharides.

Claims

1. A composition comprising a Bifidobacterium longum subsp. infantis comprising a functional H5 gene cluster and at least one oligosaccharide having a Type I or Type II core, wherein the Bifidobacterium longum subsp. infantis is Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180.

~~2. The composition of claim 1, wherein the Bifidobacterium longum subsp. infantis is Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180.~~

~~3~~2. The composition of claim 1 ~~or 2~~, wherein the H5 cluster comprises Blon_2l75, Blon_2l76, and Blon_2l77.

~~4~~3. The composition of ~~any one of~~ claim~~s~~ 1 ~~-3~~ or 2, wherein the functional H5 cluster comprises B1oh_2171, B1oh_2173, B1oh_2174, B1oh_2175, B1oh_2176, Blon_2l77, and galT.

~~5~~4. The composition of any one of claims 1-~~4~~3, wherein the Bifidobacterium longum subsp. infantis is activated.

~~6~~5. The composition of any one of claims 1-~~5~~4, wherein the Bifidobacterium is activated by an activator, wherein the activator is from ~~Table 4~~the group consisting of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylglucosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ.

~~7~~6. The composition of any one of claims 1-~~5~~4, wherein the composition further comprises an activator selected from the group consisting of any one of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylgulcosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ~~Table 4~~.

~~8~~7. The composition of any one of claims 1-~~7~~6, wherein the Bifidobacterium contains a LNB transport system capable of internalizing one or more oligosaccharide having a Type I or Type II core before the oligosaccharide is hydrolyzed and is capable of hydrolyzing the internalized oligosaccharide.

~~9~~8. The composition of any one of claims 1-~~8~~7, wherein the oligosaccharide can be obtained from mammalian milk selected from human, bovine, pig, rabbit, goat, sheep, camel milk, or mixtures thereof.

~~10~~9. The composition of any one of claims 1-~~9~~8, wherein the Bifidobacterium has been cultured in the presence of at least one mammalian milk oligosaccharide.

~~11~~10. The composition of any one of claims 1-~~10~~9, wherein the Bifidobacterium has a higher binding affinity to mammalian mucosal cells than Bifidobacteria of the same species cultivated in the absence of complex oligosaccharides.

~~12~~11. The composition of any one of claims 1-~~11~~10, wherein the Bifidobacterium comprises upregulated genes selected from the group consisting of Blon_0042, Blon_R00l5, Blon_R00l7, Blon_R002l, Blon_R0022, and combinations thereof.

~~13~~12. The composition of any one of claims 1-~~12~~11, wherein the Bifidobacterium comprises downregulated genes selected from the group consisting of Blon_05l8, Blon_0785, B1oh_2167, Blon_2l68 and combinations thereof.

~~14~~13. The composition of any one of claims 1-~~13~~12, wherein the Bifidobacterium comprises an upregulated Blon_0042 gene.

~~15~~14. The composition of any one of claims 1-~~14~~13, wherein the Bifidobacterium comprises a downregulated Blon_2l68 gene.

~~16~~15. The composition of any one of claims 1-~~15~~14, wherein the Bifidobacterium comprises upregulated genes selected from the group consisting of Blon_0879, Blon_0880, Blon_088l, Blon_0882, Blon_2l77, Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2343, Blon_2344, Blon_2346, Blon_2347, and Blon_233l.

~~17~~16. The composition of any one of claims 1-~~16~~15, wherein the Bifidobacterium expresses a gene coding for a sialidase or a fucosidase.

~~18~~17. The composition of any one of claims 1-~~17~~16, wherein the Bifidobacterium expresses a gene coding for a sialic acid or a fucose transporter.

~~19~~18. The composition of any one of claims 1-~~18~~17, wherein the Bifidobacterium is present at a concentration of from 1 Million cfu/g to 500 Billion cfu/g.

~~20~~19. The composition of any one of claims 1-~~20~~19, wherein the Bifidobacterium is present at a concentration of from 5 Billion cfu/g to 100 Billion cfu/g.

~~21~~20. The composition of any one of claims 1-~~20~~19, wherein the Bifidobacterium is present at a concentration of from 10 Billion cfu/g to 50 Billion cfu/g or from 50 million cfu/g to 5 billion cfu/g.

~~22~~21. The composition of any one of claims 1-~~21~~20, further comprising an isolated complex oligosaccharide.

~~23~~22. The composition of claim ~~22~~21, wherein the complex oligosaccharide is a mammalian milk oligosaccharide (MMO).

~~24~~23. The composition of claim ~~23~~22, wherein the complex oligosaccharide is isolated from a mammalian milk source.

~~25~~24. The composition of claim ~~24~~23, wherein the mammalian milk source is human, bovine, pigs, rabbits, goats, sheep, or camel.

~~26~~25. The composition of claim ~~23~~22, wherein the mammalian milk oligosaccharide (MMO) comprises oligosaccharide molecules found in human milk oligosaccharides (HMO), bovine milk oligosaccharides (BMO), bovine colostrum oligosaccharides (BCO), goat milk oligosaccharides (GMO), or a combination thereof.

~~27~~26. The composition of claim ~~26~~25, wherein the bovine source is from bovine milk, bovine colostrum, bovine colostrum concentrate, or mixtures thereof.

~~28~~27. The composition of claim ~~27~~26, wherein the bovine colostrum oligosaccharide comprises any of Hex(4); Hex(4) HexNAc(2); or Hex(3) HexNAc(l) NeuAc(l) at levels greater than 1%.

~~29~~28. The composition of claim ~~24~~23, wherein the complex oligosaccharide is from whey permeate.

~~30~~29. The composition of any one of claims ~~22~~21-~~29~~28, wherein the mammalian milk oligosaccharide (MMO) comprises lacto-N-biose, lacto-N-triose, N-acetyllactosamime, lacto-N-neotriose, lacto-N-tetraose, lacto-N-neotetraose, fucosyllactose, lacto-N- fucopentose, lactodifucotetraose, sialyllactose, disialyllactone-N-tetraose, 2'- fucosyllactose, 3'-sialyllactoseamin, 3'-fucosyllactose, 3'-sialyl-3-fucosyllactose, 3'- sialyllactose, 6'-sialyllactosamine, 6'-sialyllactose, difucosyllactose, lacto-N- fucosylpentose I, lacto-N-fucosylpentose II, lacto-N-fucosylpentose III, lacto-N- fucosylpentose V, sialyllacto-N-tetraose, their derivatives, or combinations thereof.

~~31~~30. The composition of any one of claims ~~22~~21-~~30~~29, wherein the complex oligosaccharide comprises at least one of (3Hex,4HexNac,lFuc), (lGal,lGlcNAc,lNeuAc), or (lGlu,lGal,lNeuAc (3' or 6')).

~~32~~31. The composition of any one of claims ~~22~~21-~~31~~30, wherein the complex oligosaccharide is less than 50 % fucosylated.

~~33~~32. The composition of any one of claims ~~22~~21-~~32~~31, wherein the complex oligosaccharide comprise one of the following ratios of constituents: 1) a ratio of Hex(2) NeuAc(l) : Hex(2)

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

~~34~~33. The composition of any one of claims ~~22~~21-~~33~~32, wherein the complex oligosaccharide is at least 20% of the weight of the composition.

~~35~~34. The composition of any one of claims ~~22~~21-~~33~~32, wherein the complex oligosaccharide is at least 50% of the weight of the composition.

~~36~~35. The composition of any one of claims ~~22~~21-~~33~~32, wherein the complex oligosaccharide is at least 80% of the weight of the composition.

~~37~~36. The composition of any one of claims ~~22~~ 21 to ~~36~~35, wherein the fucosyllactose and/or sialyllactose comprises 1-5% of the total oligosaccharides.

~~38~~37. The composition of any one of claims ~~22~~21-~~36~~35, wherein the fucosyllactose and/or sialyllactose comprises 5-20% of the total oligosaccharides.

~~39~~38. The composition of any one of claims ~~22~~21-~~36~~35, wherein the fucosyllactose and/or sialyllactose comprises 20-50% of the total oligosaccharides.

~~40~~39. The composition of any one of claims ~~22~~21-~~39~~38, where in the mass ratio of the complex oligosaccharide to the fucosyllactose and/or sialyllactose is from 20: 1 to 1: 10.

~~41~~40. The composition of any one of claims ~~22~~21-~~40~~39, wherein the complex oligosaccharide comprises a plurality of oligosaccharides with 3 to 10 residues (DP3-10 oligosaccharides).

~~42~~41. The composition of any one of claims ~~23~~22-~~41~~40, wherein the mammalian milk oligosaccharide (MMO) comprises lacto-N-biose.

~~43~~42. The composition of any one of claims 23-~~41~~40, wherein the mammalian milk oligosaccharide (MMO) comprises lacto-N-triose.

~~44~~43. The composition of any one of claims 22-~~43~~42, wherein the complex oligosaccharide comprises a plant-derived oligosaccharide.

~~45~~44. The composition of claim ~~44~~43, wherein the plant oligosaccharide is from carrots, peas, broccoli, onions, tomatoes, peppers, rice, wheat, oats, bran, oranges, cocoa, olives, apples, grapes, sugar beets, cabbage, com, or a mixture thereof.

~~46~~45. The composition of claim ~~44~~43, wherein the plant oligosaccharide is from orange peels, cocoa hulls, olive pomace, tomato skins, grape pomace, com silage, or a mixture thereof.

~~47~~46. The composition of any one of claims ~~44~~43-~~46~~45, wherein the plant-derived oligosaccharides are between 2 and 10 sugar residues (DP2-DP10), between 3 and 10 sugar residues (DP3-DP10), between 5 and 10 sugar resides (DP5-DP10), or up to DP20.

~~48~~47. The composition of any one of claims ~~22~~21-~~47~~46, wherein the composition provides a total dietary intake of oligosaccharide in an amount of 0.001-100 grams per day.

~~49~~48. The composition of any one of claims ~~22~~21-~~47~~46, wherein the oligosaccharide is in an amount of 1-20 grams, 3-20 grams, or 5-10 grams.

~~50~~49. The composition of any one of claims ~~22~~21-~~47~~46, wherein the oligosaccharide is in an amount of 10, 15, 20, 25, 30, 35, 40, 45, or 50 grams.

~~51~~50. The composition of any one of claims 1-~~50~~49, wherein at least one of the oligosaccharide has a Type I core.

~~52~~51. The composition of any one of claims 1-~~50~~49, wherein at least one of the oligosaccharide has a Type II core.

~~53~~52. The composition of any one of claims 1-~~52~~51, further wherein the composition comprises galactooligosaccharide (GOS).

~~54~~53. The composition of any one of claims 1-~~53~~52, wherein the composition further comprises a protein source rich in threonine, N-acetyl-threonine, gamma-glutamylthreonine, or a combination thereof.

~~55~~54. The composition of any of claims 1-~~54~~53, wherein the composition further comprises a secondary metabolite.

~~56~~55. The composition of claim ~~55~~54, wherein the secondary metabolite comprises a short chain fatty acid.

~~57~~56. The composition of claim ~~55~~54, wherein the secondary metabolite comprises acetate, lactate, or combinations thereof.

~~58~~57. The composition of any one of claims 1-~~57~~56, wherein the composition is in the form of a dry powder, a dry powder suspended in an oil, or as a solution.

~~59~~58. The composition of claim ~~58~~57, wherein the dry powder is spray dried or freeze-dried.

~~60~~59. The composition of claim ~~59~~58, wherein the composition is freeze-dried in the presence of a suitable cryoprotectant.

~~61~~60. The composition of any one of claims 1-~~60~~59, wherein the composition further comprises a cryoprotectant.

~~62~~61. The composition of claim ~~61~~60, wherein the cryoprotectant is glucose, lactose, raffmose, 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, mammalian milk
oligosaccharides, chitin, chitosan, other polysaccharides, or a combination thereof.

~~63~~62. The composition of any of one of claims 1-~~62~~61, further comprising a stabilizer.

~~64~~63. The composition of claim ~~63~~62, wherein the stabilizer is a flow agent.

~~65~~64. The composition of claim ~~63~~62, wherein the stabilizer is a milk protein.

~~66~~65. The composition of any one of claims 1-~~65~~64, wherein the composition is a powder with a water activity level of less than 0.35, less than 0.30, less than 0.25, less than 0.2, less than or less than 0.1.

~~67~~66. The composition of any one of claims 1-~~66~~65, wherein the composition is an anhydrous composition.

~~68~~67. The composition of any one of claims 1-~~58~~57, wherein the composition is suspended in an oil.

~~69~~68. The composition of claim ~~68~~67, wherein the composition is in the form of a dry powder suspending in an oil.

~~70~~69. The composition of claim ~~68~~ 67 or ~~69~~68, wherein the oil is a medium chain triglyceride.

~~71~~70. The composition of any one of claims 1-~~58~~57, wherein the composition is suspended in syrup having oligosaccharide at least 57% where water activity is low enough to keep Bifidobacterium dormant.

~~72~~71. The composition of any one of claims 1-~~71~~70, wherein the composition is in the form of a packet, sachet, orally disintegrating tablet, foodstuff, capsule, lozenge, effervescent tablet, suppository, enema, capsule, dry powder, dry powder suspended in an oil, chewable composition, syrup, or gel.

~~73~~72. The composition of claim ~~72~~71, wherein the capsule or tablet has an enteric coating.

~~74~~73. The composition of claim ~~73~~72, 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.

~~75~~74. The composition of any one of claims 1-~~74~~73, wherein the composition is a pharmaceutical composition, dietary supplement, nutritional product, food product, probiotic, and/or prebiotic.

~~76~~75. The composition of claim ~~75~~74, wherein the composition is formulated as a unit dose medicament.

~~77~~76. ~~A method of improving the health of a mammalian gastrointestinal tract comprising administering a therapeutically effective amount~~ Use of the composition of any one of the preceding claims ~~1-76~~ in the manufacture of a medicament for improving the health of a mammalian gastrointestinal tract, comprising that the composition is to be administered to a mammal in need thereof.

~~78~~77. ~~A method of increasing the concentration of Bifidobacterium in the gastrointestinal tract of a mammal by administering an effective amount of the composition~~ The use of ~~any one of~~ claim~~s~~ ~~1-76~~75, wherein the use is for ~~to a subject in order to increase~~ increasing levels of said administered Bifidobacterium in the feces of that mammal to greater than 10% of the total microbiome found in that feces.

~~79. A method of improving the health of a mammalian gastrointestinal tract comprising administering to a mammal in need thereof B. longum subsp. infantis having a functional H5 gene cluster and oligosaccharide having a Type I or Type II core.~~

~~80. The method of claim 79, further comprising administering complex oligosaccharide to the mammal.~~

~~81. The method of claim 80, wherein the complex oligosaccharide and the Bifidobacterium are provided either together or separately.~~

~~82. The method of any one of claims 79 or 80, wherein the complex oligosaccharide is provided as a solution and the Bifidobacterium is provided as an enteric-coated tablet or capsule.~~

~~83. The method of any one of claims 79-81, wherein the Bifidobacterium and the oligosaccharide are provided in a liquid composition which comprises complex oligosaccharide at a level of from about 1 g/L to 50 g/L.~~

84. The method of any one of claims 79-83, wherein the complex oligosaccharide and Bifidobacterium is provided in dry form and as an enteric-coated tablet or capsule.

85. The composition of claim 79-84, wherein the complex oligosaccharide is a mammalian milk oligosaccharide (MMO).

86. The composition of claim 85, wherein the complex oligosaccharide is isolated from a mammalian milk source.

87. The composition of claim 86, wherein the mammalian milk source is human, bovine, pigs, rabbits, goats, sheep, or camel.

88. The composition of claim 85, wherein the mammalian milk oligosaccharide (MMO) comprises oligosaccharide molecules found in human milk oligosaccharides (HMO), bovine milk oligosaccharides (BMO), bovine colostrum oligosaccharides (BCO), goat milk oligosaccharides (GMO), or a combination thereof.

89. The composition of claim 88, wherein the bovine source is from bovine milk, bovine colostrum, bovine colostrum concentrate, or mixtures thereof.

90. The composition of claim 89, wherein the bovine colostrum oligosaccharide comprises any of Hex(4); Hex(4) HexNAc(2); or Hex(3) HexNAc(l) NeuAc(l) at levels greater than 1%.

91. The composition of claim 87, wherein the complex oligosaccharide is from whey permeate.

92. The composition of any one of claims 85-91, wherein the mammalian milk oligosaccharide (MMO) comprises lacto-N-biose, lacto-N-triose, N-acetyllactosamime, lacto-N-neotriose, lacto-N-tetraose, lacto-N-neotetraose, fucosyllactose, lacto-N- fucopentose, lactodifucotetraose, sialyllactose, disialyllactone-N-tetraose, 2'- fucosyllactose, 3'-sialyllactoseamin, 3'-fucosyllactose, 3'-sialyl-3-fucosyllactose, 3'- sialyllactose, 6'-sialyllactosamine, 6'-sialyllactose, difucosyllactose, lacto-N- fucosylpentose I, lacto-N-fucosylpentose II, lacto-N-fucosylpentose III, lacto-N- fucosylpentose V, sialyllacto-N-tetraose, their derivatives, or combinations thereof.

93. The composition of any one of claims 80-92, wherein the complex oligosaccharide comprises at least one of (3Hex,4HexNac,lFuc), (lGal,lGlcNAc,lNeuAc), or (lGlu,lGal,lNeuAc (3' or 6')).

94. The composition of any one of claims 80-93, wherein the complex oligosaccharide is less than 50 % fucosylated.

~~95. The composition of any one of claims 80-94, wherein the complex oligosaccharide comprise one of the following ratios of constituents: 1) a ratio of Hex(2) NeuAc(l) : Hex(2) HexNAc(l) less than 5.0; 2) a ratio of Hex(2) HexNAc(l) : Hex (3) HexNAc(l) of greater than 1.0; 3) a ratio of Hex(2) HexNAc(l) : Hex (3) HexNAc(2) of greater than 2.0; 4) a ratio of Hex(3) : Hex (3) HexNAc(l) NeuAc(l) of less than 100; or 5) a ratio of Hex(2) HexNAc(l) : Hex (4) NeuAc(2) NeuGc(l) of greater than 10.~~

~~96. The method of any one of claims 80-95, wherein the complex oligosaccharide is at least 20 % of the weight administered daily.~~

~~97. The method of any one of claims 80-95, wherein the complex oligosaccharide is at least 50 % of the weight administered daily.~~

~~98. The method of any one of claims 80-95, wherein the complex oligosaccharide is at least 80% of the weight administered daily.~~

~~99~~78. The ~~method~~ use of ~~any one of~~ claim~~s~~ ~~80-98~~76 or 77, wherein ~~the~~ a complex oligosaccharide is to be administered prior to the administration of Bifidobacterium.

~~100~~79. The ~~method~~ use of ~~any one of~~ claim~~s 80-98~~76 or 77, wherein ~~the~~ a complex oligosaccharide is to be administered contemporaneously with the administration of Bifidobacterium.

~~101~~80. The ~~method~~ use of ~~any one of~~ claim~~s~~ 76 or 77~~80-98~~, wherein ~~the~~ a complex oligosaccharide is to be administered after the administration of Bifidobacterium.

~~102~~81. The use~~method~~ of any one of claims ~~80-101~~76-80, wherein the complex oligosaccharide is provided in a daily dose of from 1 to 20 grams.

~~103~~82. The ~~method~~ use of any one of claims ~~80-101~~76-80, wherein the complex oligosaccharide is provided in a daily dose of from 1 to 10 grams.

~~104~~83. The ~~method~~ use of any one of claims ~~80-103~~76-82, wherein the Bifidobacterium is provided in a daily dose of from 1 million to 100 billion colony forming units (CFUs).

~~105~~84. The ~~method~~ use of any one of claims ~~80-104~~76-83, wherein the Bifidobacterium is provided in a daily dose of from 5 to 50 billion CFUs.

~~106~~85. The ~~method~~ use of any one of claims ~~80-105~~76-84, wherein the subject in need thereof is to be administered a dose once daily or in multiple, optionally two, three, four, five, six, sub doses to be administered at appropriate intervals throughout the day.

~~107. The method of any one of claims 77 to 106, wherein subsequent to said administration, the level of the administered Bifidobacterium in the feces of that mammal is greater than 20% of the total microbiome found in that feces.~~

~~108. The method of any one of claims 77-106, wherein subsequent to said administration, the level of the administered Bifidobacterium in the feces of that mammal is greater than 50% of the total microbiome found in that feces.~~

~~109. The method of claim any one of claims 77-106, wherein subsequent to said administration, the level of the administered Bifidobacterium in the feces of that mammal is greater than 70% of the total microbiome found in that feces.~~

~~110. The method of any one of claims 77-109, further comprising monitoring the levels of the Bifidobacterium in the stools of the mammal.~~

~~111. The method of any one of claims 77-110, wherein the Bifidobacterium is administered for at least 5 days.~~

~~112. The method of any one of claims 77-110, wherein the oligosaccharide is administered for a duration from 30 to 360 days.~~

~~113. The method of any one of claims 77-112, wherein said administration to the mammal in need thereof continues for a duration, whereby the population of Bifidobacterium is established in the gut of the subject.~~

~~114. The method of any one of claims 77-112, wherein said administration to the mammal in need thereof continues so that the population of Bifidobacterium is maintained in the gut of the subject.~~

~~115. The method of claim 114, wherein the dose is administering in order to maintain the levels of Bifidobacterium greater than at least 5% of the total fecal microbiome of the mammal.~~

~~116. The method of claim 114, wherein the dose is administered in order to maintain the levels of Bifidobacterium greater than at least 20% of the total fecal microbiome of the mammal.~~

~~117. The method of claim 114, wherein the dose is administered in order to maintain the levels of Bifidobacterium greater than at least 50% of the total fecal microbiome of the mammal.~~

~~118~~86. The ~~method~~ use of any one of claims 76-80~~77-117~~, wherein the mammal is a human, a cow, a pig, a rabbit, a goat, a sheep, a cat, a dog, a horse, or a camel.

~~119~~87. The use~~method~~ of claim ~~118~~86, wherein the mammal is a human infant.

~~120~~88. The use~~method~~ of claim ~~119~~87, wherein the infant was delivered via cesarean section.

~~121~~89. The use~~method~~ of claim ~~119~~87, wherein the infant was delivered vaginally.

~~122~~90. The use~~method~~ of claim ~~119~~87, wherein the infant is being fed with infant formula which contains no appreciable quantity of mammalian milk oligosaccharides.

~~123~~91. The use~~method~~ of any one of claims ~~119-122~~87-90, wherein the infant is from birth to about 36 months post-conception.

~~124~~92. The use~~method~~ of any one of claims ~~119-112~~87-90, wherein the infant is from birth to weaning age.

~~125~~93. The use~~method~~ of any one of claims 87-92~~119-124~~, 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.

~~126~~94. The use~~method~~ of claim ~~118~~86, wherein the human is a pregnant woman.

~~127~~95. The use~~method~~ of claim ~~126~~94, wherein the pregnant woman is in at least the third trimester of pregnancy.

~~128. The method of any one of claims 118-125, wherein the improvement of the health of the mammal is a reduction of colic in an infant.~~

~~129. The method of any one of claims 77-125, wherein the improvement of the health of the mammal is accelerating the development of the immune system in a baby.~~

~~130. The method of any one of claims 77-125, 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.~~

~~131. A method of preparing activated Bifidobacterium comprising cultivating Bifidobacterium by incubating the Bifidobacterium longum subsp. infantis comprising a functional H5 cluster, including the Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180, bacteria under conditions whereby gene Blon_0042 is upregulated, gene Blon_2168 is downregulated, or combinations thereof.~~

~~132~~96. A method of preparing activated Bifidobacterium comprising cultivating Bifidobacterium by incubating the Bifidobacterium longum subsp. infantis comprising a functional H5 cluster, including the Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180, bacteria under conditions whereby one or more of the genes Blon_0042, Blon_088l, B1oh_2175, B1oh_2176, Blon_2l77, Blon_233l, Blon_2334,

Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2343, Blon_2344, Blon_2346, and Blon_2347 is upregulated, and/or Blon_2l68 is downregulated.

~~133~~97. A method of preparing activated commensal Bifidobacterium longum subsp. infantis EVC001 deposited under ATCC Accession No. PTA-125180 comprising culturing said bacterial sp. in the presence of a mammalian milk oligosaccharide (MMO) or an activator selected from the compounds listed in the group consisting of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylglucosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ~~Table 4~~, whereby bacterial cells in the culture medium are activated.

~~134~~98. The method of any one of claims ~~132~~ 96 or ~~133~~97, wherein the MMO or the compound the group consisting of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylglucosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ~~from Table 4~~ is added in an amount sufficient to induce expression of a gene and/or a protein encoding for a sialidase, a fucosidase, or an alpha-N-acetylgalactosaminidase, or genes listed in Table 1 or Table 2 in the bacterial cells.

~~135~~99. The method of any one of claims ~~132~~96-~~134~~98, wherein the starting media composition comprises one or more compounds from the group consisting of N-acetyl-glucosamine/galactosamine (NAG), Dimeric N-acetylglucosamine, Fucose, Sialic Acid, Lacto-N-biose, Galacto-N-biose and Fuc α1,2Galβ~~Table 4~~ in an amount from 0.1 to 3% by weight/vol of the media composition.

~~136~~100. The method of any one of claims ~~132~~96-~~135~~99, wherein the MMO and/or the activator constitutes a carbon source and consumption of the carbon source by Bifidobacterium cells both increases cellular biomass and activates a transport system capable of internalizing one or more oligosaccharides before the oligosaccharide is hydrolyzed and consequently the Bifidobacterium cells are further capable of hydrolyzing the internalized oligosaccharide, wherein the oligosaccharide has the structure of an oligosaccharide found in a mammalian milk.

~~137~~101. The method of claim ~~136~~100, wherein the mammalian milk is human, bovine, pig, rabbit, goat, sheep, camel, buffalo milk, or mixtures thereof.

~~138~~102. The method of any one of claims ~~132~~96-~~137~~101, wherein the activated bacterial cells have a higher binding affinity to mammalian mucosal cells than bacterial cells of the same species cultivated on non-activating monomers or dimers.

~~139~~103. The method of any one of claims ~~132~~96-~~138~~102, wherein activation of the bacterial cells comprises upregulating Blon_088l and Blon_2343 in B. infantis or the functional homologs in other bacterial species, the homologs being expressed during activation of the other bacterial species.

~~140~~104. The method of any one of claims ~~132~~96-~~138~~102, wherein activation comprises upregulating expression of glucosamine-6-phosphate isomerase and carbohydrate ABC transporter membrane protein from B. infantis.

~~141~~105. The method of any one of claims ~~132~~96-~~138~~102, wherein activation of the Bifidobacterium cells comprises upregulating the genes selected from the group consisting of Blon_0042 , Blon_R00l5, Blon_R00l7, Blon_R002l, Blon_R0022, Blon_2l77and combinations thereof, and/or downregulating genes selected from the group consisting of Blon_05l8, Blon_0785, B1oh_2167, Blon_2l68 from B. infantis.

~~142~~106. The method of any one of claims ~~132~~96-~~138~~102, wherein the Bifidobacterium cells comprise an upregulated Blon_0042 gene from B. infantis.

~~143~~107. The method of any one of claims ~~132~~96-~~138~~102, wherein the Bifidobacterium cells comprise a downregulated Blon_2l68 and/or Blon_2l77 gene from B. infantis.

108. The method of any one of claims ~~132~~96-~~138~~102, wherein activation of the Bifidobacterium cells comprise upregulating genes selected from the group consisting of Blon_0882, Blon_088l, Blon 0880, Blon_0879, Blon_2334, Blon_2335, Blon_2336, Blon_2337, Blon_2338, Blon_2339, Blon_2344, Blon_2346, Blon_2347, Blon_233l, and combinations thereof.