the body in the feces. The consequence of a dysbiotic microbiome is that is skewed towards infection, inflammation, intestinal damage, and pathogenesis.

[0008] Conventional teaching with regards to the mammalian microbiome is that complexity provides stability. To be able to effectively consume the complex non-infant diet, maintaining a diversity of microorganisms in the microbiome is thought to be the key to promoting gut health. Lozupone, Nature, Vol. 489, pp. 220–230 (2012). The inventors have discovered that this is not necessarily the case and that the simplest microbiome may be of great benefit to the stabilization and recovery of the gut damaged by inflammation and/or agitation.

SUMMARY

[0009] The inventors have discovered that mucosal healing in the dysbiotic gut can be promoted by probiotic microorganisms driving the intestinal microbiome towards an infant-like state, which is simple, less diverse, and less pro-inflammatory than an adult gut microbiome particularly when inflamed by disease or dysbiosis. The inventors have also discovered that use of probiotic microorganisms for which MMOs serve as a selective energy source (carbon source), is particularly beneficial for mucosal healing. Dysbiotic mammals in need of mucosal healing would include humans that exhibit conditions such as, but not limited to, Irritable Bowel Syndrome (IBS), Crohn's Disease (CD), Ulcerative Colitis (UC) (collectively Irritable Bowel Disease or IBD), Short Gut Syndrome, colic, general diarrhea, overgrowth of certain pathogenic bacteria such as *Clostridium difficile*, or any other condition (such as extensive antibiotic use) where the gut is made susceptible to infection by pathogens, such as, but not limited to *Escherichia, Clostridium, Shigella, Campylobacter,* and *Salmonella.*

[0010] This disclosure provides methods of treating gastrointestinal dysbiosis by providing a patient with a composition comprising (i) a complex carbohydrate from a mammalian milk source and (ii) bifidobacteria which internalize the MMO prior to its hydrolysis; typically the composition is administered for a period of time (e.g., for at least 5 days). While the microorganisms and oligosaccharides are normal components of infant nutrition, the methods of this disclosure are targeted at subjects other than infants (i.e. beyond 6 months of life); therefore, the compositions of this disclosure are formulated for more mature (and typically larger) subjects and for compatibility with more complex diets. The dysbiosis may be the result of Irritable Bowel Syndrome, Crohn's Disease, Ulcerative colitis, Necrotizing Enterocolitis, bacterial overgrowth, bacterial induced diarrhea, antibiotic treatment, eating

disorders, obesity, or low diversity in dietary intake. The *Bifidobacterium* is preferably selected from *B. longum, B. pseudocatanulatum, B. adolescentis, B. animalis* (e.g., *B. animalis* subsp. *animalis*, *B. animalis* subsp. *lactis*), *B. longum* subsp. *longum, B. pseudolongum,* and *B. breve*, and more preferably, the *B. longum* is *B. longum* subs. *infantis*. The mammalian milk sources may be human, caprine, porcine, ovine, equine, or bovine, and preferably, the bovine source is from bovine colostrum. The MMO may be from whey, whey mother liquor, whey powder, whey permeates, and/or the mammalian milk oligosaccharide may be fucosylated, sialylated or be derivatives thereof. In particular, the MMO may comprise 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, 3'-sialyllactoseamin, and 6'-sialyllactosamine, produced synthetically and purified or isolated from natural sources or recombinant microorganisms. The *Bifidobacterium* is typically provided in a daily dose of from 10 million to 1 trillion cfu, preferably 10 million to 100 billion cfu, and more preferably from 4 billion to 50 billion cfu. The MMO is provided in a daily dose of from 1 to 60 g, preferably from 2 to 40 g.

[0010a] In one aspect there is provided composition described herein for use in treating gastrointestinal dysbiosis by providing a patient with said composition for at least 5 days.

[0010b] In another aspect, there is provided a composition for use in treating gastrointestinal dysbiosis, said use comprising administering a mammalian milk oligosaccharide to a patient in need thereof, wherein the patient in need thereof is a patient with a dysbiotic microbiome, particularly wherein the dysbiotic microbiome is a bacterial overgrowth of opportunistic pathogens and/or overt pathogens, more particularly wherein the dysbiotic microbiome has a reduced microbial diversity, preferably wherein the mammalian milk is from human, bovine, or caprine sources, or wherein the bovine source is from bovine colostrum, or wherein the mammalian milk oligosaccharide is from whey permeate, preferably wherein the mammalian milk oligosaccharide is selected from lacto-N-tetraose, lacto-N-neotetraose, fucosyllactose, sialyllactose, combinations thereof, and derivatives thereof, and/or wherein the mammalian milk oligosaccharide is selected from synthetically produced and purified lacto-N-tetraose, lacto-N-neotetraose, 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, lacto-N-fucosylpentaose I, lacto-N-fucosylpentaose II, lacto-N-fucosylpentaose III, lacto-N-fucosylpentaose V, 3'-sialyllactose, 6'-sialyllactose, 3'-sialyl-3-fucosyllactose, sialyllacto-N-

tetraose, N-acetylgalactosamine, 6'-sialyllactosamine, and combinations thereof, or wherein the mammalian milk is from human sources.

[0010c] In another aspect, there is provided a medicament for treating a patient with intestinal distress comprising a mammalian milk oligosaccharide and a bifidobacteria that internalizes said mammalian milk oligosaccharide prior to its hydrolysis.

[0011] Some embodiments of the instant disclosure include compositions comprising a MMO and a microorganism wherein the MMO induces a change in the microorganism such that the MMO then becomes an energy source for the organism, and when ingested by a mammal, the induced or activated microorganism provides a benefit to the gut of that mammal. Additional embodiments involve the maintenance of the induced microorganism in the gut of the mammal by maintaining the dietary supply of MMOs or other glycans that are selective for that microorganism. A further embodiment involves the subsequent clearance of the microorganism from the gut by the cessation of the supply of the MMO to the mammal.

[0011a] In another aspect, there is provided a composition comprising human milk oligosaccharides (HMO) or bovine milk oligosaccharieds (BMO) and fucosylated glycans (SPF) and/or sialylated glycans (SPS), wherein the SPF and/or SPS are not of milk origin, preferably wherein the ratio of HMO:SPF is from 20:1 to 1:5, and/or wherein the composition comprises human milk oligosaccharides and synthetically-produced and purified sialyl glycans (SPS), and wherein the ratio of HMO:SPS is from 5:1 to 1:1, particularly wherein the SPF or SPS comprises one or more 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, and 6'-sialyllactosamine, and/or wherein HMO or BMO further comprise synthetic lacto-N-tetraose and/or lacto-N-neotetraose.

[0012] In one mode of this disclosure, the MMO and the bifidobacteria are provided in a dry form which may also be enrobed in a material that would provide enteric protection. In another mode, the MMO and the bifidobacteria are encapsulated, and the capsule may further comprise an enteric coating such as a coating that is not disrupted by passage through the stomach. In another mode, the MMO is provided as a solution and the bifidobacteria is provided as an enteric-coated powder, tablet, or capsule.

[0013] In yet another mode, the method of this disclosure further comprises administering *Lactobacillus* or *Pediococcus* contemporaneously with the composition. The *Lactobacillus* may

CLAIMS

1. A medicament for treating a patient with intestinal distress comprising a mammalian milk oligosaccharide and a bifidobacteria that internalizes said mammalian milk oligosaccharide prior to its hydrolysis.
2. The medicament of claim 1, wherein the intestinal distress represents a microbial dysbiosis, which may be the result of Irritable Bowel Disease, Crohn's Disease, Ulcerative colitis, Necrotizing Enterocolitis, bacterial or viral overgrowth, bacterial induced diarrhea, antibiotic treatment, eating disorders, autism, obesity, or low diversity in dietary intake.
3. The medicament of any one of claims 1–2, wherein the bifidobacteria is selected from *B. longum, B. animalis, B. catenulatum, B. pseudolongum, B. pseudocatanulatum,* and *B. breve*, particularly wherein the *B. longum* is *B. longum* subs. *infantis* , said bifidobacteria preferably being provided in a daily dose of from 10 million to 1 trillion CFU, more preferably a daily dose of from 10 billion to 50 billion CFU.
4. The medicament of any one of claims 1–3, wherein the mammalian milk oligosaccharide is from mammalian milk, which may be from human, bovine, or caprine sources, or wherein the bovine source is from bovine colostrum, or wherein the mammalian milk oligosaccharide is from whey permeate, or wherein the mammalian milk oligosaccharide comprises lacto-N-tetraose, lacto-N-neotetraose, fucosyllactose, sialyllactose or derivatives thereof, or wherein the mammalian milk oligosaccharide comprises one or more carbohydrates selected from synthetically produced and purified lacto-N-tetraose, lacto-N-neotetraose, 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, lacto-N-fucosylpentaose I, lacto-N-fucosylpentaose II, lacto-N-fucosylpentaose III, lacto-N-fucosylpentaose V, 3'-sialyllactose, 6'-sialyllactose, 3'-sialyl-3-fucosyllactose, sialyllacto-N-tetraose, N-acetylgalactosamine, and 6'-sialyllactosamine.
5. The medicament of any one of claims 1–4, wherein the medicament further comprises Lactobacillus and/or Pediococcus, the Lactobacillus preferably being selected from *L. plantarum, L. antri, L. brevis, L. coleohominis, L. fermentum, L. gasseri, L. johnsonii, L. pentosus, L. sakei, L. salivarius, L. casei, L. rhamnosus (e.g., LGG), L. acidophilus, L. curvatus, L. reuteri, L. mucosae,* and *L. crispatus*, the Lactobacillus more preferably

being *L. reuteri* , the Lactobacillus preferably being provided in a daily dose of from 10 million to 1 trillion cfu, more preferably a daily dose of from 10 billion to 50 billion cfu.

6. The medicament of any one of claims 1–5, wherein the mammalian milk oligosaccharide is in the form of a powder, more preferably wherein the medicament is in the form of a powder.
7. The medicament of any of claims 1–6, wherein the oligosaccharide is formulated to provide dietary fiber in an amount suitable for a non-infant patient, the non-infant patient being preferably at least 6 months of age, or wherein the medicament is formulated to provide a daily ration sufficient to support the intestinal microbiome of a patient with a body weight greater than 10 kg.
8. The medicament of any one of claims 1-7, wherein the mammalian milk oligosaccharide is provided in a daily dose of from 1-20 g, preferably a daily dose of from 1-10g.
9. The composition according to claim 1 for use in treating gastrointestinal dysbiosis by providing a patient with said composition for at least 5 days.
10. The composition of any one of claims 1-9, wherein the mammalian milk oligosaccharide and the bifidobacteria are present in a dry form and enrobed in a material that would provide enteric protection, such as when the mammalian milk oligosaccharide and the bifidobacteria are encapsulated and the capsule has an enteric coating, or wherein the mammalian milk oligosaccharide is provided as a solution and the bifidobacteria is provided as an enteric-coated tablet or capsule.
11. The composition of any one of claims 1-10, wherein the patient is on a strict diet restricting all other dietary fiber when said composition is provided to said patient.
12. The composition of any one of claims 1-11, wherein the mammalian milk oligosaccharide is in the form of a powder, and/or wherein the composition is in the form of a powder.
13. A composition comprising human milk oligosaccharides (HMO) or bovine milk oligosaccharieds (BMO) and fucosylated glycans (SPF) and/or sialylated glycans (SPS), wherein the SPF and/or SPS are not of milk origin, preferably wherein the ratio of HMO:SPF is from 20:1 to 1:5, and/or wherein the composition comprises human milk oligosaccharides and synthetically-produced and purified sialyl glycans (SPS), and wherein the ratio of HMO:SPS is from 5:1 to 1:1, particularly wherein the SPF or SPS

comprises one or more 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, and 6'-sialyllactosamine, and/or wherein HMO or BMO further comprise synthetic lacto-N-tetraose and/or lacto-N-neotetraose.

14. The composition of claim 13, wherein the composition is formulated to provide dietary fiber in an amount suitable for a non-infant patient, preferably wherein the non-infant patient is at least 6 months of age, more preferably wherein the composition is formulated to provide a daily ration sufficient to support the intestinal microbiome of a patient with a body weight greater than 10 kg.

15. A composition for use in treating gastrointestinal dysbiosis, said use comprising administering a mammalian milk oligosaccharide to a patient in need thereof, wherein the patient in need thereof is a patient with a dysbiotic microbiome, particularly wherein the dysbiotic microbiome is a bacterial overgrowth of opportunistic pathogens and/or overt pathogens, more particularly wherein the dysbiotic microbiome has a reduced microbial diversity, preferably wherein the mammalian milk is from human, bovine, or caprine sources, or wherein the bovine source is from bovine colostrum, or wherein the mammalian milk oligosaccharide is from whey permeate, preferably wherein the mammalian milk oligosaccharide is selected from lacto-N-tetraose, lacto-N-neotetraose, fucosyllactose, sialyllactose, combinations thereof, and derivatives thereof, and/or wherein the mammalian milk oligosaccharide is selected from synthetically produced and purified lacto-N-tetraose, lacto-N-neotetraose, 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, lacto-N-fucosylpentaose I, lacto-N-fucosylpentaose II, lacto-N-fucosylpentaose III, lacto-N-fucosylpentaose V, 3'-sialyllactose, 6'-sialyllactose, 3'-sialyl-3-fucosyllactose, sialyllacto-N-tetraose, N-acetylgalactosamine, 6'-sialyllactosamine, and combinations thereof, or wherein the mammalian milk is from human sources.

16. The composition of claim 15, wherein the mammalian milk oligosaccharide is in the form of a powder.

17. The composition of any one of claims 15-16, wherein the patient in need thereof is not an infant, preferably wherein the mammalian milk oligosaccharide is formulated to provide

dietary fiber in an amount suitable for a non-infant patient, and/or wherein the non-infant patient is at least 6 months of age, preferably wherein the mammalian milk oligosaccharide is formulated to provide a daily ration sufficient to support the intestinal microbiome of a patient with a body weight greater than 10 kg.