body, thereby improving the health of the host. In general, prebiotics should be largely undigested and fermented by gut flora when they pass through the upper digestive tract. Most importantly, prebiotics can stimulate the growth of beneficial flora, but not stimulate harmful bacteria with potential pathogenicity or spoilage activity. Common prebiotics are oligosaccharides, also known as dietary fibers.

It has been a long-standing topic in this field to regulate gut flora based on probiotics/prebiotics, thereby promoting the health level of the body (e.g., improving immunity).

SUMMARY ~~OF THE INVENTION~~

In a first aspect, there is provided in the application a probiotic composition comprising *Bifidobacterium bifidum* and *Bifidobacterium longum*.

In some ~~embodiments~~examples, the ratio of the amounts of *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is 1: (0.21-2.36).

In some ~~embodiments~~examples, the probiotic composition further comprises *Bifidobacterium adolescentis*.

In some ~~embodiments~~examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36). In some specific ~~embodiments~~examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units is (0.75-1): 1: (0.75-1).

In some ~~embodiments~~examples, the probiotic composition further comprises *Lactobacillus rhamnosus*.

In some ~~embodiments~~examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units is (0.57-3.36): 1: (0.21-2.36): 1.

In some ~~embodiments~~examples, the probiotic composition is in unit dosage form, and the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units are independently in the order of 10^4 to 10^{12} CFU. In some ~~embodiments~~examples, the total amount of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* is in the order of 10^6 to 10^{12} CFU.

In some ~~embodiments~~examples, the probiotic composition is for administration to an adult

and the amount of *Bifidobacterium adolescentis* is 2.59×10^5 - 4.49×10^{11} CFU; and/or the amount of *Bifidobacterium bifidum* is 1.26×10^5 – 7.35×10^{11} CFU; and/or the amount of *Bifidobacterium longum* is 2.23×10^5 – 7.02×10^{11} CFU; and/or the amount of *Lactobacillus rhamnosus* is 1.26×10^5 – 2.59×10^{11} CFU.

In some ~~embodiments~~examples, the probiotic composition is for administration to a child, and the amount of *Bifidobacterium adolescentis* is 2.05×10^5– 4.55×10^{11} CFU; and/or the amount of *Bifidobacterium bifidum* is 1.47×10^5–3.6×10^{11} CFU; and/or the amount of *Bifidobacterium longum* is 7.55×10^4–2.5×10^{11} CFU; and/or the amount of *Lactobacillus rhamnosus* is 1.47×10^5– 3.6×10^{11} CFU.

In some ~~embodiments~~examples, the probiotic composition is free of probiotics other than the probiotics described in various ~~embodiments~~examples of the present application. In some ~~embodiments~~examples, the probiotic composition is free of probiotics other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Lactobacillus rhamnosus*. In some ~~embodiments~~examples, the probiotic composition is free of Bifidobacteria other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum*.

In a second aspect, there is provided in the application a prebiotic composition comprising xylooligosaccharide, galacto-oligosaccharide, and corn dietary fiber.

In some ~~embodiments~~examples, the ratio of the amounts of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is (0.25-5): (0.75-4): (0.5-1). In some specific ~~embodiments~~examples, the ratio of the amounts of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75).

In some ~~embodiments~~examples, the prebiotic composition is in unit dosage form, and the total amount of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is 0.1-12g. In some ~~embodiments~~examples, the prebiotic composition is in unit dosage form, and the total amount of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is 0.1-5g.

In some ~~embodiments~~examples, the amount of xylooligosaccharide is 0.01g-6g; and/or the amount of galactooligosaccharide is 0.04g-9.6g; and/or the amount of corn dietary fiber is 0.01g-6g.

In some ~~embodiments~~examples, the prebiotic composition is free of prebiotic components other than xylooligosaccharide, galactooligosaccharide, and corn dietary fiber.

In a third aspect, there is provided in the application a dietary composition,

comprising the probiotic composition of the application and the prebiotic composition of the application; preferably, the dietary composition comprises *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* as the probiotics, and xylooligosaccharide, galactooligosaccharide and corn dietary fiber as the prebiotics, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units (CFUs) is (0.75-1): 1: (0.75-1), and the total amount of the three bacteria is about 2×10^{11}CFU, and the ratio of xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75), and the total amount of xylooligosaccharide, galactooligosaccharide and corn dietary fiber is 1.2-1.5g.

In ~~a third aspect~~another example, there is provided in the application a dietary composition (in

some cases, also referred to as a synbiotic composition) comprising the probiotic composition according to the first aspect and the prebiotic composition according to the second aspect.

In some specific ~~embodiments~~examples, the dietary composition comprises *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* as the probiotics and xylooligosaccharide, galactooligosaccharide, and corn dietary fiber as the prebiotics, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units (CFUs) is (0.75-1): 1: (0.75-1), and the total amount of the three bacteria is about 2×10^{11}CFU, and, the ratio of xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75), and the total amount of xylooligosaccharide, galactooligosaccharide and corn dietary fiber is 1.2-1.5g.

In some ~~embodiments~~examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is formulated for peroral administration. In some ~~embodiments~~examples, the peroral administration comprises oral administration, mixing with oral products, and gavage.

In some ~~embodiments~~examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is a food supplement, a food additive, or a food product.

In some ~~embodiments~~examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is formulated as a powder, a granule, a tablet, or a capsule.

In a fourth aspect, there is provided in the application a use of a probiotic composition according to the application, or a prebiotic composition according to the application, or the dietary composition according to the application, in the manufacture of a medicament for preventing and/or treating a pathogen infection, or for enhancing the therapeutic effect of a pathogen infection, improving the immunity in the subject, or balancing the gut microecology in the subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).

In some ~~embodiments~~ examples according to the ~~first to third aspects~~examples herein, the probiotic composition or prebiotic composition or dietary composition is administered to a subject for assisting in preventing and/or treating a pathogen infection, or for enhancing the therapeutic effect of a pathogen infection, improving the immunity in the subject, or balancing the gut microecology in the subject (including increasing microbial abundance, increasing

desirable bacterial species, and/or reducing undesirable bacteria). In some ~~embodiments~~examples, the pathogen is a virus, a bacterium, or a fungus. In some ~~embodiments~~examples, the pathogen is a respiratory disease virus, such as COVID-19, an influenza virus, or respiratory syncytial virus.

In a fifth aspect, there is provided in the application a use of the probiotic composition according to the application, or the prebiotic composition according to the application, or the dietary composition according to the application, in the manufacture of a medicament or a dietary product for preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).

In ~~a fourth aspect~~another example, there is provided in the application use of the probiotic

composition according to the first aspect, or the prebiotic composition according to the second aspect, or the dietary composition according to the third aspect, in the preparation of a dietary product or a drug for assisting in preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria). In some ~~embodiments~~examples, the pathogen is a virus, a bacterium, or a fungus. In some ~~embodiments~~examples, the pathogen is a respiratory disease virus, such as a novel coronavirus (COVID-19), an influenza virus, or a respiratory syncytial virus.

In a sixth aspect, there is provided in the application a use of the probiotic composition according to the application, or the prebiotic composition according to the application, or the dietary composition according to the application, in the manufacture of a medicament for preventing and/or treating a pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).

In ~~a fifth aspect~~another example, there is provided in the application a method for assisting in preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria), comprising administering to the subject the probiotic composition according to the first aspect, or the prebiotic composition of the second aspect, or the dietary composition according to the third aspect. In some embodiments, the pathogen is a virus, a bacterium, or a fungus. In some embodiments, the pathogen is a respiratory disease virus, such as COVID-19, an influenza virus, or respiratory syncytial virus.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the relationship between the desirable bacterial species and various probiotics identified in previous studies. desirable bacterial species have the potential to enhance immunity and their abundances are negatively correlated with COVID-19 disease severity or SARS-CoV-2 viral load. The circle represents a positive correlation between the abundance of the desirable bacterial species and the probiotics, the size indicates the strength of the positive correlation, and the box circles the target probiotics identified in the present application.

Figure 2 shows partial results of the cohort studies in Example 2, wherein panel A shows the positive rates and the overall positive rates of *Bifidobacterium adolescentis*,

WHAT IS CLAIMED IS:

1. A probiotic composition comprising *Bifidobacterium bifidum* and *Bifidobacterium longum*.

2. The probiotic composition according to claim 1, wherein the ratio of the amounts of *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is 1: (0.21-2.36).

3. The probiotic composition according to claim 1 or 2, further comprising *Bifidobacterium adolescentis*.

4. The probiotic composition according to claim 3, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36), preferably (0.75-1): 1: (0.75-1).

5. The probiotic composition according to any one of claims 1 to 4, further comprising *Lactobacillus rhamnosus*.

6. The probiotic composition according to claim 5, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Lactobacillus rhamnosus* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36): 1.

7. The probiotic composition according to any one of claims 1 to 6, wherein the probiotic composition is in unit dosage form, and the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units are independently in the order of 10^4 to 10^{12} CFU; optionally, the total amount of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* is in the order of 10^6 to 10^{12} CFU.

8. The probiotic composition according to claim 7, wherein the probiotic composition is for administration to an adult, and

the amount of *Bifidobacterium adolescentis* is 2.59×10^5-4.49×10^{11} CFU; and/or

the amount of *Bifidobacterium bifidum* is 1.26×10^5-7.35×10^{11} CFU; and/or

the amount of *Bifidobacterium longum* is 2.23×10^5-7.02×10^{11} CFU; and/or

the amount of *Lactobacillus rhamnosus* is 1.26×10^5-2.59×10^{11} CFU.

9. The probiotic composition according to claim 7, wherein the probiotic composition is for administration to a child, and

the amount of *Bifidobacterium adolescentis* is 2.05×10^5-4.55×10^{11} CFU; and/or

the amount of *Bifidobacterium bifidum* is 1.47×10^5-3.6×10^{11} CFU; and/or

the amount of *Bifidobacterium longum* is 7.55×10^4- 2.5×10^{11} CFU; and/or

the amount of *Lactobacillus rhamnosus* is 1.47×10^5-3.6×10^{11} CFU.

10. The probiotic composition according to any one of claims 1 to 9, wherein the probiotic composition is free of probiotics other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum* and *Lactobacillus rhamnosus*, and for example, the probiotic composition is free of Bifidobacteria other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum*.

11. A prebiotic composition comprising xylooligosaccharide, galactooligosaccharide and corn dietary fiber.

12. The prebiotic composition according to claim 11, wherein the ratio of the amounts of xylooligosaccharide, galactooligosaccharides and corn dietary fiber by weight is (0.25-5): (0.75-4): (0.5-1), preferably (0.25-0.5): (2- 4): (0.5-0.75).

13. The prebiotic composition according to claim 11 or 12, wherein the prebiotic composition is in unit dosage form, and the total amount of the xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is 0.1-12g, such as 0.1-5g.

14. The prebiotic composition of claim 13, wherein

the amount of xylooligosaccharide is 0.01g-6g; and/or

the amount of galactooligosaccharide is 0.04g-9.6g; and/or

the amount of corn dietary fiber is 0.01g-6g.

15. The prebiotic composition according to any one of claims 11 to 14, which is free of prebiotic components other than xylooligosaccharide, galactooligosaccharide and corn dietary fiber.

16. A dietary composition, comprising the probiotic composition of any one of claims 1 to 10 and the prebiotic composition of any one of claims 11 to 15; preferably,

the dietary composition comprises *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* as the probiotics, and xylooligosaccharide, galactooligosaccharide and corn dietary fiber as the prebiotics, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units (CFUs) is (0.75-1): 1: (0.75-1), and the total amount of the three bacteria is about 2×10^{11}CFU, and the ratio of xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75), and the total amount of xylooligosaccharide, galactooligosaccharide and corn dietary fiber is 1.2-1.5g.

17. The probiotic composition according to any one of claims 1 to 10, or the prebiotic composition according to any one of claims 11 to 15, or the dietary composition according to claim 16, which is formulated for peroral administration, such as oral administration, mixing with oral products, or gavage.

18. The probiotic composition according to any one of claims 1 to 10 and 17, or the prebiotic composition according to any one of claims 11 to 15 and 17, or the dietary composition according to claim 16 or 17, which is a food supplement, a food additive or a food.

19. The probiotic composition according to any one of claims 1 to 10, 17 and 18, or the prebiotic composition according to any one of claims 11 to 15, 17 and 18, or the dietary composition according to any one of claims 16 to 18, which is formulated into a powder, a granule, a tablet or a capsule.

20. Use of a~~A~~ probiotic composition according to any one of claims 1 to 10 and 17 to 19, or a prebiotic composition according to any one of claims 11 to 15 and 17 to 19, or the dietary composition according to any one of claims 16 to 19, in the manufacture of a medicament for ~~which is administered to a subject for assisting in~~ preventing and/or treating a pathogen infection, or for enhancing the therapeutic effect of a pathogen infection, improving the immunity in the subject, or balancing the gut microecology in the subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).

21. The use of ~~probiotic composition, or prebiotic composition, or dietary~~

~~composition according to~~ claim 20, wherein the pathogen is a virus, a bacterium, or a fungus, such as a respiratory disease virus, such as a novel coronavirus (COVID-19), an influenza virus, or a respiratory syncytial virus.

22. Use of the probiotic composition according to any one of claims 1 to 10 and 17 to 19, or the prebiotic composition according to any one of claims 11 to 15 and 17 to 19, or the dietary composition according to any one of claims 16 to 19, in the manufacture of a medicament or ~~preparation of~~ a dietary product for ~~or a drug for assisting in~~ preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).

23. Use of ~~A method for assisting in preventing and/or treating a pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria), comprising administering to the subject~~ the probiotic composition according to any one of claims 1 to 10 and 17 to 19, or the prebiotic composition according to any one of claims 11 to 15 and 17 to 19, or the dietary composition according to any one of claims 16 to 19, in the manufacture of a medicament for preventing and/or treating a pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria).