"dysbiosis" or disrupted symbiosis of the gut microbiome, microbiota functions can be lost or deranged, resulting in increased susceptibility to pathogens, include altered metabolic profiles, or induction of proinflammatory signals that can result in local or systemic inflammation or autoimmunity. As such, there is a need in the field of microbiology for a new and useful methods for modulating the microbiome or treating a microbiome dysbiosis.

SUMMARY

[0006] Disclosed herein is a composition comprising (a) a microbe expressing ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing ferritin and the elemental iron.

[0006a] In one aspect, the present disclosure refers to a composition comprising (a) a microbe expressing ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron; wherein at least 60% of the elemental iron is complexed with the H-ferritin. In another aspect, the present disclosure refers to an in~~di~~gestible item comprising the composition as described herein. In another aspect, the present disclosure refers to a dietary supplement comprising the composition as described herein. In another aspect, the present disclosure refers to a pharmaceutical composition comprising the composition as described herein. In another aspect, the present disclosure refers to a composition for use in therapy, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron.

In another aspect, the present disclosure refers to use of a composition in the manufacture of a medicament for the treatment of an iron deficiency disorder in a subject, comprising that the composition is to be administered to the subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron. In another aspect, the present disclosure refers to use of a composition in the manufacture of a medicament for the treatment of ~~altering the composition of the~~a gut ~~bacterial~~ microbiome disorder in a subject, comprising that the composition is to be administered to the subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron. In another aspect, the present disclosure refers to non-therapeutic use of a composition for dietary management of a subject, wherein the use comprises administering said composition to said subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron. In another aspect, the present disclosure refers to non-therapeutic use of a composition in altering the gut bacterial microbiome in a subject, wherein the use comprises administering the composition to the subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron.

[0007] Also disclosed herein is an ingestible comprising (a) a microbe expressing ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing ferritin and the elemental iron.

We claim:

1. A composition comprising (a) a microbe expressing ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron; wherein at least 60% of the elemental iron is complexed with the H-ferritin.

2. The composition of Claim 1, wherein the H-ferritin comprises mammalian H-ferritin or a homologue thereof.

3. The composition of Claim 2, wherein the mammalian H-ferritin is human H-ferritin or a homologue thereof.

4. The composition of Claim 2, wherein the homologue has at least 80% sequence identity with human H-ferritin.

5. The composition of Claim 1, wherein a source of the elemental iron is an iron salt, an organic iron complex, an elemental iron nanoparticle, or combinations thereof.

6. The composition of Claim 1, wherein the microbe comprises a fungus, an algae, a bacterium, a protozoan, a virus, a microscopic helminth, a microorganism, a lichen, or combinations thereof.

7. The composition of Claim 1, further comprising an amount of at least one filler.

8. The composition of Claim 1, consisting essentially of (a) the microbe expressing H-ferritin and (b) the elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron.

9. The composition of Claim 1, wherein the microbe further comprises intracellular elemental iron that is not complexed with the H-ferritin.

10. The composition of Claim 1, further comprising a second microbe, a probiotic, a prebiotic, or combinations thereof.

11. The composition of Claim 1, wherein the second microbe does not express ferritin.

12. An ingestible item comprising the composition of Claim 1.

13. The ingestible item of Claim 12, wherein the ingestible item is in the form of a medical food, a food, a food ingredient, or combinations thereof.

14. A dietary supplement comprising the composition of Claim 1.

15. A pharmaceutical composition comprising the composition of Claim 1.

16. A composition for use in therapy, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron.

17. Use of a composition in the manufacture of a medicament for the treatment of an iron deficiency disorder in a subject, comprising that the composition is to be administered to the subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight on a dry matter basis of the microbe expressing H-ferritin and the elemental iron.

18. The use of Claim 17, wherein at least 60% of the elemental iron is complexed with the H-ferritin.

19. The use of Claim 17, wherein the composition to be administered to the subject comprises at least 13 mg of elemental iron.

20. The use of Claim 17, wherein the administration comprises a single dose.

21. The use of Claim 17, wherein the administration comprises more than one dose to be administered sequentially.

22. The use of Claim 17, wherein at least 1 week following the administration:

(a) the average observed bacterial species richness in the subject's gut is substantially the same as the average observed bacterial species richness in the subject's gut prior to the administration;

(b) the relative abundance of *Klebsiella*, *Enterobacteriales*, *Enterobacteriaceae*, *Clostridium*, *Anaerosporobacter*, and/or *Pygmaiobacter* in the subject's gut is at least -2 as determined by linear discriminant analysis;

(c) the relative abundance of *Candidatus*, *Erysipelotrichales*, *Erysipelotrichia*, *Erysipelotrichaceae*, and/or *Ruminococcaceae* in the subject's gut is at least + 2 as determined by linear discriminant analysis;

(d) the level of biofilm formation in the subject's gut is reduced as determined by PICRUSt analysis is reduced by at least 1% relative to levels prior to the administration;

(e) the level of biofilm formation in the subject's gut as determined by PICRUSt analysis is reduced by at least 50 cpm compared to levels prior to the administration;

(f) the predicted bacterial chemotaxis in the subject's gut as determined by PICRUSt analysis is reduced by at least 1% relative to levels prior to the administration;

(g) the predicted bacterial chemotaxis in the subject's gut as determined by PICRUSt analysis is reduced by at least 200 cpm compared to the predicted cpm prior to the administration;

(h) the subject's hemoglobin concentration is increased by at least 1% relative to the hemoglobin concentration prior to the administration;

(i) the subject's hemoglobin concentration is increased by at least 0.1 g/dL relative to the hemoglobin concentration prior to the administration;

(j) the subject's total iron binding capacity is decreased by at least 2.5% relative to the total iron binding capacity prior to the administration

(k) the subject's total iron binding capacity is decreased by at least 40 μg/dL relative to the total iron binding capacity prior to the administration;

(l) the subject's FACIT Fatigue Score is increased by at least 5 points relative to the FACIT Fatigue Score prior to the administration;

(m) the subject's SF-36 Bodily Pain Score is increased by at least 5 points relative to the SF-36 Bodily Pain Score prior to the administration;

(n) the subject's SF-36 Vitality Score is increased by at least 5 points relative to the SF-36 Vitality Score prior to the administration; and/or

(o) the mean incidence of the subject's gastrointestinal symptoms per week are less than a two-fold increase relative to the mean incidence of the subject's gastrointestinal symptoms per week prior to the administration.

23. The use of Claim 22, wherein the administration comprises an average of at least 13 mg of elemental iron per day.

24. Non-therapeutic use of a composition for ~~The use of Claim 17, wherein the treatment comprises~~ dietary management in a subject, wherein the use comprises administering said composition to said subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron.

25. The use of Claim 21 or Claim 24, wherein the subject is not iron deficient.

26. Use of a composition in the manufacture of a medicament for the treatment of ~~altering the composition of the~~a gut ~~bacterial~~ microbiome disorder in a subject, comprising that the composition is to be administered to the subject,

wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron.

27. The use of Claim ~~23~~26, wherein at least 60% of the elemental iron is complexed with the H-ferritin.

28. The use of Claim ~~23~~26, wherein at least 1 week following the administration:

(a) the average observed bacterial species richness in the subject's gut is substantially the same as the average observed bacterial species richness in the subject's gut prior to the administration;

(b) the relative abundance of *Klebsiella*, *Enterobacteriales*, *Enterobacteriaceae*, *Clostridium*, *Anaerosporobacter*, and/or *Pygmaiobacter* in the subject's gut is at least -2 as determined by linear discriminant analysis;

(c) the relative abundance of *Candidatus*, *Erysipelotrichales*, *Erysipelotrichia*, *Erysipelotrichaceae*, and/or *Ruminococcaceae* in the subject's gut is at least + 2 as determined by linear discriminant analysis;

(d) the level of biofilm formation in the subject's gut is reduced as determined by PICRUSt analysis is reduced by at least 1% relative to levels prior to the administration;

(e) the level of biofilm formation in the subject's gut as determined by PICRUSt analysis is reduced by at least 50 cpm compared to levels prior to the administration;

(f) the predicted bacterial chemotaxis in the subject's gut as determined by PICRUSt analysis is reduced by at least 1% relative to levels prior to the administration;

(g) the predicted bacterial chemotaxis in the subject's gut as determined by PICRUSt analysis is reduced by at least 200 cpm compared to the predicted cpm prior to the administration;

(h) the subject's hemoglobin concentration is increased by at least 1% relative to the hemoglobin concentration prior to the administration;

(i) the subject's hemoglobin concentration is increased by at least 0.1 g/dL relative to the hemoglobin concentration prior to the administration;

(j) the subject's total iron binding capacity is decreased by at least 2.5% relative to the total iron binding capacity prior to the administration;

(k) the subject's total iron binding capacity is decreased by at least 40 μg/dL relative to the total iron binding capacity prior to the administration;

(l) the subject's FACIT Fatigue Score is increased by at least 5 points relative to the FACIT Fatigue Score prior to the administration;

(m) the subject's SF-36 Bodily Pain Score is increased by at least 5 points relative to the SF-36 Bodily Pain Score prior to the administration;

(n) the subject's SF-36 Vitality Score is increased by at least 5 points relative to the SF-36 Vitality Score prior to the administration; and/or

(o) the mean incidence of the subjects gastrointestinal symptoms per week are less than a two-fold increase relative to the mean incidence of the subject's gastrointestinal symptoms per week prior to the administration.

29. The use of Claim 2~~5~~8, wherein the administration comprises an average of at least 13 mg of elemental iron per day.

30. Non-therapeutic use of a composition in altering the gut bacterial microbiome in a subject, wherein the use comprises administering the composition to the subject, wherein the composition comprises (a) a microbe expressing H-ferritin and (b) elemental iron in an amount of at least 3% by weight based on dry weight of the microbe expressing H-ferritin and the elemental iron. ~~The use of Claim 23, wherein the treatment comprises dietary management.~~