rates (70% prevalence in Africa) (Hooi *et al.*, 2017). In the United States, *H. pylori* occurs twice as frequently in the non-white population as in the white population (Everhart *et al.*, 2000) and is associated with lower socio-economic status worldwide.

[0005] No commercial vaccine exists against *H. pylori*. Though some progress has been seen in lowered *H. pylori* prevalence in some countries using antibiotic treatment, large increases in antibiotic resistance rates are now being seen in *H. pylori* isolates. The prevalence of clarithromycin-resistance in *H. pylori* rose from 11% to 60% in just 4 years (2005-2009) in Korea, with similar increases recorded in China and Japan (Thung *et al.*, 2016). Though the standard treatment is in fact a triple antibiotic therapy, antibiotic resistance rates continue to rise. Thus, it is difficult to see a path forward with *H. pylori* treatment via antibiotics. Other bacteria offer similar challenges.

SUMMARY

[0005a] In a first aspect, the present disclosure refers to a use of a probiotic in the manufacture of a medicament for the prevention or treatment of a condition caused by a target bacterium living in the gastrointestinal tract of a subject, wherein

the probiotic comprises a probiotic bacterium, wherein the probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the sequence coding for the guided antimicrobial peptide comprises the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to a protein of the target bacterium, wherein the guided antimicrobial peptide kills the target bacterium in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally disrupts other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

[0005b] In another aspect, the present disclosure refers to a use of a probiotic composition in the manufacture of a medicament for the prevention or treatment of a condition caused by *a target bacterium* living in the gastrointestinal tract of a subject, wherein the probiotic composition comprises

the probiotic as disclosed herein; and

an acceptable excipient or carrier.

[0005c] In yet another aspect, the present disclosure refers to a use of a probiotic composition in the manufacture of a medicament for preventing or treating a condition in a subject caused by a target bacterium found in the gastrointestinal tract of the subject,

wherein the probiotic composition comprises a probiotic bacterium and an acceptable excipient or carrier, wherein the probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the sequence coding for the guided antimicrobial peptide comprises the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to a protein of the target bacterium; and comprising

allowing the guided antimicrobial peptide to kill the target bacterium in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally disrupts the other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

[0005d] In a further aspect, the present disclosure refers to a use of a probiotic in the manufacture of a medicament for the prevention or treatment of a condition caused by *Helicobacter pylori* living in the gastrointestinal tract of a subject, wherein

the probiotic comprises a *Lactococcus lactis* probiotic bacterium, wherein the *Lactococcus lactis* probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the the sequence coding for the guided antimicrobial peptide comprises the the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to the VacA peptide of *H. pylori*, wherein the guided antimicrobial peptide kills *H. pylori* in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally

disrupts other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

[0006] The present disclosure pertains to a treatment strategy to combat select bacteria in the gut, such as *H. pylori*. The strategy uses a probiotic-based system for the expression and delivery of a guided antimicrobial peptide to the gut. The guided antimicrobial peptide is expressed from a hybrid gene in the probiotic bacterium's DNA, and can be the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide, with the latter peptide responsible for binding to a protein of the target bacterium. The fusing can occur with or without a linker sequence, that is, independent of the presence of a linker sequence. This technology can eliminate the target bacterium selectively and specifically from the gut microbiota. The specificity of the targeting, being at the strain, species or genus level, depends on the guide protein used to provide the targeting. The treatment can be administered orally, such as by using an ingestible probiotic.

[0007] Preferred examples described herein relate to a method for the control of a target bacterium such as *H. pylori* which does not involve antibiotics. For delivery of the active protein, this method uses engineered probiotic bacteria. Preferred examples utilize lactic acid bacteria, including *Lactococcus* and *Lactobacillus* species, such as *Lactococcus lactis* and *Lactobacillus acidophilus*, which are food grade bacterium that are safe for human consumption or have been granted GRAS status (Generally Regarded As Safe) by the FDA and are in widespread commercial use for processing dairy food products.

WHAT IS CLAIMED IS:

1. Use of a probiotic in the manufacture of a medicament for the prevention or treatment of a condition caused by a target bacterium living in the gastrointestinal tract of a subject, wherein

the probiotic comprises a probiotic bacterium, wherein the probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the sequence coding for the guided antimicrobial peptide comprises the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to a protein of the target bacterium, wherein the guided antimicrobial peptide kills the target bacterium in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally disrupts other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

2. The use of claim 1, wherein the probiotic bacterium comprises a lactic acid bacterium.

3. The use of claim 2, wherein the lactic acid bacterium comprises a *Lactococcus* bacterium.

4. The use of claim 3, wherein the *Lactococcus* bacterium comprises *Lactococcus lactis.*

5. The use of claim 1, wherein the protein of the target bacterium is a virulence factor.

6. The use of claim 5, wherein the virulence factor is the VacA peptide.

7. The use of claim 1, wherein the antimicrobial peptide is laterosporulin, alyteserin, or cathelin-related anti-microbial peptide.

8. The use of claim 1, wherein the target bacterium comprises *H. pylori.*

9. The use of claim 1, wherein the guide peptide has a sequence comprising SEQ ID NO:5.

10. The use of claim 1, wherein the antimicrobial peptide has a sequence comprising SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:10.

11. The use of claim 1, wherein the guided antimicrobial peptide has a sequence comprising SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:11.

12. Use of a probiotic composition in the manufacture of a medicament for the prevention or treatment of a condition caused by *a target bacterium* living in the gastrointestinal tract of a subject, wherein the probiotic composition comprises

the probiotic of claim 1; and

an acceptable excipient or carrier.

13. The use of claim 12, wherein the probiotic bacterium is edible, and wherein the acceptable excipient or carrier is edible.

14. Use of a probiotic composition in the manufacture of a medicament for preventing or treating a condition in a subject caused by a target bacterium found in the gastrointestinal tract of the subject,

wherein the probiotic composition comprises a probiotic bacterium and an acceptable excipient or carrier, wherein the probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the sequence coding for the guided antimicrobial peptide comprises the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to a protein of the target bacterium; and comprising

allowing the guided antimicrobial peptide to kill the target bacterium in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally disrupts the other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

15. The use of claim 14, wherein the probiotic bacterium comprises a lactic acid bacterium.

16. The use of claim 15, wherein the lactic acid bacterium comprises a *Lactococcus* bacterium.

17. The use of claim 16, wherein the *Lactococcus* bacterium comprises *Lactococcus lactis.*

18. The use of claim 14, wherein the protein of the target bacterium is a virulence factor.

19. The use of claim 18, wherein the virulence factor is the VacA peptide.

20. The use of claim 14, wherein the antimicrobial peptide is laterosporulin, alyteserin, or cathelin-related anti-microbial peptide.

21. The use of claim 14, wherein the target bacterium comprises *H. pylori.*

22. The use of claim 14, wherein the guide peptide has a sequence comprising SEQ ID NO:5.

23. The use of claim 14, wherein the antimicrobial peptide has a sequence comprising SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:10.

24. The use of claim 14, wherein the guided antimicrobial peptide has a sequence comprising SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:11.

25. The use of claim 14, wherein the subject is an animal.

26. The use of claim 14, wherein the subject is a human.

27. The use of claim 14, wherein the probiotic bacterium is edible, and wherein the acceptable excipient or carrier is edible

28. The use of claim 14, wherein the probiotic composition is to be administered orally.

29. Use of a probiotic in the manufacture of a medicament for the prevention or treatment of a condition caused by *Helicobacter pylori* living in the gastrointestinal tract of a subject, wherein

the probiotic comprises a *Lactococcus lactis* probiotic bacterium, wherein the *Lactococcus lactis* probiotic bacterium has been transformed to comprise a DNA construct expressing a guided antimicrobial peptide, wherein the sequence coding for the guided antimicrobial peptide comprises the sequence coding for an antimicrobial peptide fused to the sequence coding for a guide peptide that binds to the VacA peptide of *H. pylori*, wherein the guided antimicrobial peptide kills *H. pylori* in the gastrointestinal tract of the subject, and wherein the guided antimicrobial peptide minimally disrupts other bacteria found in the gastrointestinal tract of the subject when compared to unguided antimicrobial peptides or antibiotics.

30. The use of claim 29, wherein the guide peptide is derived from multimerin-1 sequence.

31. The use of claim 29, wherein the antimicrobial peptide is laterosporulin, alyteserin, or cathelin-related anti-microbial peptide.