Claims

1. An RNA molecule comprising at least one open reading frame (ORF) encoding a fimbrial H antigen (FimH) polypeptide and a 5' untranslated region (5' UTR), wherein the 5' UTR comprises a nucleic acid sequence set forth in any one of SEQ ID NOs: 95-101.

2. The RNA molecule of claim 1, wherein the 5' UTR comprises a nucleic acid sequence selected from the group consisting of:

SEQ ID NO: 99 (5'UTR_BMD562); and

SEQ ID NO: 101 (5'UTR_BMD576).

3. The RNA molecule of claim 2, wherein the RNA molecule further comprises a 3' untranslated region (3' UTR).

4. The RNA molecule of claim 3, wherein the 3' UTR comprises nucleotides having a sequence set forth in SEQ ID NO: 103 (3'UTR_hHBB).

5. The RNA molecule of any one of claims 1-4, wherein the FimH polypeptide encoded by the RNA molecule is full-length, truncated, fragment or variant thereof or wherein the FimH polypeptide encoded by the RNA molecule comprises at least one mutation.

6. The RNA molecule of any one of claims 1-5, wherein the FimH polypeptide encoded by the RNA molecule has at least 90%, 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence selected from SEQ ID NO: 1-64 or wherein the FimH polypeptide encoded by the RNA molecule has an amino acid sequence selected from SEQ ID NO: 1-64.

7. The RNA molecule of any one of claims 1-6, wherein the FimH polypeptide encoded by the RNA molecule is selected from the group consisting of: FimH-DSG (SEQ ID NO: 59), FimH-DSG triple mutant (G15A, G16A, V27A) (SEQ ID NO: 62), and FimHLD triple mutant (G15A, G16A, V27A) (SEQ ID NO: 54), or an immunogenic fragment thereof.

8. The RNA molecule of any one of claims 1-7, wherein the FimH polypeptide encoded by the RNA molecule is fused to a C-terminal membrane targeting domain and wherein the C-terminal membrane targeting domain is DAFgpi or a variant thereof.

9. The RNA molecule of claim 8, wherein the DAFgpi is a variant comprising a serine/glycine linker substitution of the eight DAF amino acid residues proximal to the ω site serine with a serine/glycine linker having the amino acid sequenceGSSGSGSS (SEQ ID NO:94).

10. The RNA molecule of claim 8 or 9, wherein the FimH polypeptide encoded by the RNA molecule has an amino acid sequence with at least 90%, 95, 96%, 97%, 98% or 99% identity to the amino acid sequence set forth in SEQ ID NO: 77, 79, 81 or 83 or wherein the FimH polypeptide encoded by the RNA molecule is selected from the group consisting of: SEQ ID NO: 77, 79, 81 and 83.

11. The RNA molecule of any one of claims 1-10, wherein the open reading frame is transcribed from a nucleic acid comprising a nucleotide sequence having at least 90%, 95%, 96%, 97%, 98%, or 99% identity to any one of the sequences of SEQ ID NOs: 76, SEQ ID NO: 78, SEQ ID NO: 80 or SEQ ID NO: 138 or wherein the open reading frame is transcribed from a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 76, SEQ ID NO: 78, SEQ ID NO: 80 and SEQ ID NO: 138.

12. The RNA molecule of any one of claims 1-11, wherein the open reading frame comprises a nucleic acid sequence having at least 90%, 95%, 96%, 97%, 98%, or 99% identity to any one of the sequences set forth in SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119 or SEQ ID NO: 139 or wherein the open reading frame comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, and SEQ ID NO: 139.

13. The RNA molecule of any one of claims 1-12, wherein the RNA molecule further comprises a 5’ cap moiety or a 3’ poly-A tail.

14. The RNA molecule of claim 13, wherein the 5’ cap moiety is m7G(5’)ppp(5’)(2’OMeA)pG or ($m_2^{7,3'\text{-O}}$)Gppp($m^{2'\text{-O}}$)ApG or wherein the poly-A tail comprises a sequence having SEQ ID NO: 92.

15. The RNA molecule of any one of claims 1-14, wherein the RNA molecule comprises nucleotides having the sequence set forth in SEQ ID NO: 66-75, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 86, SEQ ID NO: 88 or SEQ ID NO: 90.

16. The RNA molecule of claim 15, wherein the RNA molecule is transcribed from a nucleic acid sequence having at least 90%, 95%, 96%, 97%, 98% or 99% identity to any one of sequences selected from SEQ ID NO: 107-116 or SEQ ID NO: 120-124.

17. The RNA molecule of any one of claims 1-16, wherein the open reading frame comprises a G/C content of at least 55%, 60%, 65%, 70%, or 75%, or of or of about 50% to 75% or 55% to 70%.

18. The RNA molecule of any one of claims 1-17, wherein the encoded FimH polypeptide localizes in the cellular membrane, localizes in the Golgi and/or is secreted.

19. The RNA molecule of any one of claims 1-18, wherein the RNA comprises at least one modified nucleotide and wherein the modified nucleotide is pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4′-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine OR 2′-O-methyl uridine.

20. The RNA molecule of claim 19, wherein the modified nucleotide is pseudouridine (Ψ) or N^1-methylpseudouridine (m1Ψ) and wherein each uridine of the RNA molecule is replaced with pseudouridine (Ψ) or N^1-methylpseudouridine (m1Ψ).

21. The RNA molecule of any one of claims 1-20, wherein the RNA is mRNA or modRNA.

22. A composition comprising the RNA molecule of any one of claims 1-21, wherein the RNA molecule is formulated in a lipid nanoparticle (RNA-LNP).

23. The composition of claim 22, wherein lipid nanoparticle comprises at least one of a cationic lipid, a PEGylated lipid, a neutral lipid, and a steroid or steroid analog.

24. The composition of claim 23, wherein the cationic lipid is (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315).

25. The composition of claim 23 or 24, wherein the PEGylated lipid is 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159).

26. The composition of any one of claims 23-25, wherein the neutral lipid is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC).

27. The composition of any one of claims 23-26, wherein the steroid or steroid analog is cholesterol.

28. The composition of any one of claims 22 to 27, wherein the composition is a vaccine.

29. A mutant FimH polypeptide comprising at least 80% identity to any one of amino acid sequences set forth in SEQ ID NO: 77, SEQ ID NO: 81 or SEQ ID NO: 83.

30. The mutant FimH polypeptide of claim 29, wherein the mutant FimH polypeptide comprises amino acids having the sequence set forth in SEQ ID NO: 81 or SEQ ID NO: 83.

31. A polynucleotide encoding a mutant FimH polypeptide comprising at least 80% identity to any one of amino acid sequences set forth in SEQ ID NO: 77, 81 or 83.

32. A polynucleotide encoding a mutant FimH polypeptide comprising nucleic acids having a sequence set forth in SEQ ID NO: 117, SEQ ID NO: 118 or SEQ ID NO: 139.

33. The polynucleotide of claim 32, wherein the polynucleotide encoding the mutant FimH polypeptide is transcribed from a nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO: 76, SEQ ID NO: 78 or SEQ ID NO: 138.

34. Use of the RNA molecule or composition of any one of claims 1 to 28 in the manufacture of a medicament for (i) inducing an immune response in a subject against extra-intestinal

pathogenic *E. coli*, or (ii) inducing the production of opsonophagocytic and/or neutralizing antibodies in a subject that are specific to extra-intestinal pathogenic E. coli.

35. The use of claim 34, wherein the subject is at risk of developing a urinary tract infection, bacteremia, sepsis, or cystitis.

36. The use of claim 34 or 35, wherein the subject is less than about 1 year of age, about 1 year of age or older, about 5 years of age or older, about 10 years of age or older, about 20 years of age or older, about 30 years of age or older, about 40 years of age or older, about 50 years of age or older, about 60 years of age or older, or about 70 years of age or older.

37. The use of any one of claims 34 to 36, wherein the subject is a pregnant woman.

38. The use of any one of claims 34 to 37, wherein the RNA molecule or composition is to be administered as a vaccine.

39. The use of any one of claims 34 to 38, wherein the RNA molecule or composition is to be administered by intradermal or intramuscular injection.

40. The use of any one of claims 34-39, wherein the subject is to be administered a single dose, two doses, three doses, or more, and optionally, a booster dose of the RNA molecule or composition.

41. The RNA molecule or composition of any one of claims 1 to 28, for use in therapy.