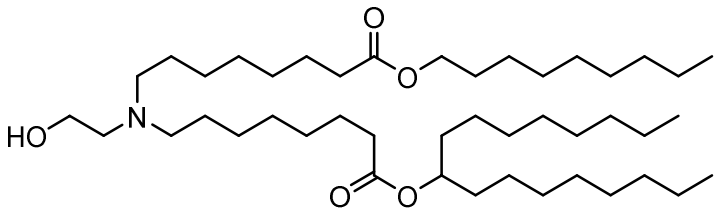
WHAT IS CLAIMED IS:

CLAIMS

1. A composition comprising an mRNA polynucleotide having an open reading frame encoding a polypeptide comprising at least one human relaxin protein formulated in an ionizable lipid nanoparticle, wherein the ionizable lipid nanoparticle comprises an ionizable lipid of Compound 18 having the structure:



a salt or a stereoisomer thereof, or any combination thereof; and

wherein the relaxin protein is a relaxin fusion protein comprising an immunoglobulin (Ig) variable chain fragment.

2. The composition of claim 1, wherein the Ig fragment comprises a variable light chain fragment.

3. The composition of claim 2, wherein the variable light chain fragment comprises a VLκ IgG region.

4. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 70%-100% identical to the sequence of SEQ ID NO:1.

5. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 85%-100% identical to the sequence of SEQ ID NO:1.

6. The composition of claim 1, wherein the composition is a unit dosage form having a dosage of 25 micrograms to 400 micrograms of the mRNA polynucleotide for a dose of up to 2 mg/kg in a human subject.

7. The composition of claim 1, wherein the open reading frame is codon optimized.

8. The composition of claim 1, wherein the mRNA comprises at least one chemical modification.

9. The composition of claim 8, wherein the chemical modification is selected from pseudouridine, 1-methylpseudouridine, 1-ethyl pseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 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-methyluridine, 5-methoxyuridine and 2'-O-methyl uridine.

10. The composition of claim 1, wherein the mRNA polynucleotide formulated in the ionizable lipid nanoparticle and administered by intravenous infusion or subcutaneous injection has a therapeutic index of greater than 60% of the therapeutic index of the mRNA polynucleotide alone.

11. The composition of claim 1, wherein the mRNA polynucleotide formulated in the ionizable lipid nanoparticle and administered by intravenous infusion or subcutaneous injection has a therapeutic index of greater than 80% of the therapeutic index of the mRNA polynucleotide alone.

12. The composition of claim 1, wherein the ionizable lipid nanoparticle comprises a molar ratio of about 20-60% ionizable lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid.

13. The composition of claim 1, wherein the ionizable lipid nanoparticle has a polydispersity value of less than 0.4.

14. The composition of claim 1, wherein the ionizable lipid nanoparticle has a net neutral charge at a neutral pH.

15. The composition of claim 1, wherein the mRNA comprises at least one chemical modification and wherein the chemical modification is N1-methylpseudouridine.

16. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 90%-100% identical to the sequence of SEQ ID NO:1.

17. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 70%-100% identical to the sequence of SEQ ID NO:6.

18. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 85%-100% identical to the sequence of SEQ ID NO:6.

19. The composition of claim 1, wherein the relaxin protein comprises an amino acid sequence that is 90%-100% identical to the sequence of SEQ ID NO:6.

20. The composition of claim 1, wherein the mRNA polynucleotide comprises the open reading frame of SEQ ID NO:5.

21. The composition of claim 1, wherein the mRNA polynucleotide comprises a polynucleotide sequence that is at least 95% identical to the sequence of SEQ ID NO:5.