more cationic lipids selected from HGT5001 (15Z, 18Z)-N,Ndimethyl-6-((9Z,12Z)-octadeca-9,12-dien-1-yl)tetracosa-4,15,18-trien-l-amine), ICE (imidazole cholesterol ester), 3-(4-(bis(2-hydroxydodecyl)amino)butyl)-6-(4-((2-hydroxydodecyl)(2-hydroxyundecyl)amino)butyl)-1,4-dioxane-2,5-dione (Target 23), and the combinations thereof.

[0003b] In one aspect, the present disclosure refers to use of a vaccine composition in the manufacture of a pharmaceutical composition for inducing an immune response *in vivo*, wherein the vaccine composition comprises a messenger RNA (mRNA) encoding an antigen derived from a virus, encapsulated in a lipid nanoparticle, wherein the lipid nanoparticle comprises one or more cationic lipids selected from HGT5001 (15Z, 18Z)-N,N-dimethyl-6-((9Z,12Z)-octadeca-9,12-dien-1-yl)tetracosa-4,15,18-trien-l-amine), ICE (imidazole cholesterol ester), 3-(4-(bis(2-hydroxydodecyl)amino)butyl)-6-(4-((2-hydroxydodecyl)(2-hydroxyundecyl)amino)butyl)-1,4-dioxane-2,5-dione (Target 23), and the combinations thereof, wherein the vaccine composition is to be administered intramuscularly or subcutaneously.

[0004] In one example, the present disclosure provides a method for inducing an immune response *in vivo* by administering to the subject a messenger RNA (mRNA) composition comprising an mRNA encoding an antigen, at a dosing regimen sufficient to induce an antigen specific T cell response and/or an antigen specific antibody response. In some examples, the mRNA is encapsulated in lipid nanoparticles (LNPs). In some examples, the composition is a vaccine composition.

[0005] In some examples, the composition is administered subcutaneously. In some examples, the composition is administered intradermally. In some examples, the composition is administered intramuscularly. In some examples, the composition is administered intravenously. In some examples, the composition is not administered intravenously.

[0006] In another example, the present disclosure provides a method of delivering a vaccine *in vivo* comprising administering to a subject a vaccine composition comprising an mRNA encoding an antigen, encapsulated in a LNP, and wherein the vaccine composition is administered intramuscularly or subcutaneously. In various examples, the vaccine composition is administered at a dosing regimen sufficient to induce an antigen specific T cell response and/or an antigen specific antibody response.

[0007] In some examples, an antigen encoded by the mRNA is a protein or a peptide.

[0008] In some examples, a composition comprising one or more than one mRNAs encoding one or more polypeptides is delivered.

[0009] In some examples, a suitable dosing regimen comprises injecting a single dose. In some examples, a suitable dosing regimen comprises administering multiple doses periodically.

CLAIMS

We claim:

1. Use of a composition in the manufacture of a medicament for inducing an immune response *in vivo*, wherein the composition comprises a messenger RNA (mRNA) encoding an antigen, encapsulated in a lipid nanoparticle, at a dosing regimen sufficient to induce an antigen specific T cell response and/or an antigen specific antibody response, wherein the lipid nanoparticle comprises one or more cationic lipids selected from HGT5001 (15Z, 18Z)-N,N-dimethyl-6-((9Z,12Z)-octadeca-9,12-dien-1-yl)tetracosa-4,15,18-trien-l-amine), ICE (imidazole cholesterol ester), 3-(4-(bis(2-hydroxydodecyl)amino)butyl)-6-(4-((2-hydroxydodecyl)(2-hydroxyundecyl)amino)butyl)-1,4-dioxane-2,5-dione (Target 23), and the combinations thereof.

2. The use of claim 1, wherein the composition is to be administered subcutaneously.

3. The use of claim 1, wherein the composition is to be administered intradermally.

4. The use of claim 1, wherein the composition is to be administered intramuscularly.

5. The use of claim 1, wherein the composition is not to be administered intravenously.

6. The use of any one of claims 1-5, wherein the composition is a vaccine composition.

7. Use of a vaccine composition in the manufacture of a pharmaceutical composition for inducing an immune response *in vivo*, wherein the vaccine composition comprises a messenger RNA (mRNA) encoding an antigen derived from a virus, encapsulated in a lipid nanoparticle, wherein the lipid nanoparticle comprises one or more cationic lipids selected from HGT5001 (15Z, 18Z)-N,N-dimethyl-6-((9Z,12Z)-octadeca-9,12-dien-1-yl)tetracosa-4,15,18-trien-l-amine), ICE (imidazole cholesterol ester), 3-(4-(bis(2-hydroxydodecyl)amino)butyl)-6-(4-((2-hydroxydodecyl)(2-hydroxyundecyl)amino)butyl)-1,4-dioxane-2,5-dione (Target 23), and the combinations thereof, wherein the vaccine composition is to be administered intramuscularly or subcutaneously.

8. The use of claim 7, wherein the vaccine composition is to be administered at a dosing regimen sufficient to induce an antigen specific T cell response and/or an antigen specific antibody response.

9. The use of any one of claims 1-8, wherein the antigen is a protein.

10. The use of any one of claims 1-8, wherein the antigen is a peptide.

11. The use of any one of claims 1-10, wherein the composition comprises one or more mRNAs encoding one or more polypeptides.

12. The use of any one of claims 1-11, wherein the dosing regimen comprises that a single dose is to be injected.

13. The use of any one of claims 1-11, wherein the dosing regimen comprises that multiple doses are to be injected periodically.

14. The use of claim 12 or 13, wherein the single dose or the multiple doses range from 0.1 µg – 100 mg mRNA.

15. The use of claim 12 or 13, wherein the single dose or the multiple doses range from 0.1 µg – 50 mg, 0.1 µg – 25 mg, 0.1 µg – 10 mg, 1 µg – 1 mg, or 1 µg – 100 µg mRNA.

16. The use of claim 12 or 13, wherein the single dose is or the multiple doses are selected from 0.1µg. 0.3 µg, 0.5 µg, 1 µg, 5 µg, 10 µg, 25 µg, 50 µg, or 100 µg.

17. The use of claim 12 or 13, wherein the single dose or the multiple doses range from 0.01 µg/kg – 10 mg /kg (mRNA/body weight).

18. The use of claim 12 or 13, wherein the single dose or the multiple doses range from 0.01 µg/kg – 8 mg /kg, 0.01 µg/kg – 6 mg /kg, 0.01 µg/kg – 5 mg /kg, 0.1 µg/kg – 5 mg /kg, 0.1 µg/kg – 1 mg /kg, or 0.1 µg/kg – 0.5 mg /kg (mRNA/body weight).

19. The use of any one of claims 13-18, wherein each of the multiple doses comprise the same dosage amount of mRNA.

20. The use of any one of claims 13-18, wherein each of the multiple doses comprise a different dosage amount of mRNA.

21. The use of any one of claims 13-20, wherein each of the multiple doses are to be injected 1-3 weeks apart.

22. The use of any one of claims 13-20, wherein each of the multiple doses are to be injected weekly.

23. The use of any one of claims 13-20, wherein at least two of the multiple doses are to be injected within 3 weeks.

24. The use of any one of claims 13-20, wherein the multiple doses are to be injected at the following schedule: Dose 1 in week 0, dose 2 in week 3, and dose 3 in week 5.

25. The use of any one of claims 1-24, wherein the mRNA comprises one or more modified nucleotides.

26. The use of any one of claims 1-25, wherein the mRNA comprises a 5' untranslated region (5' UTR) and/or a 3' untranslated region (3' UTR).

27. The use of any one of claims 1-26, wherein the lipid nanoparticle further comprises one or more helper lipids and one or more PEG lipids.

28. The use of any one of claims 1-27, wherein the at least one cationic lipid comprises ICE.

29. The use of any one of claims 1-27, wherein the at least one cationic lipid comprises HGT5001.

30. The use of any one of claims 1-27, wherein the at least one cationic lipid comprises Target 23.

31. The use of any one of claims 27-30, wherein the one or more helper lipids are selected from DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine), DPPC (1,2-dipalmitoyl-sn-glycero-3-phosphocholine), DOPE (1,2-dioleyl-sn-glycero-3-phosphoethanolamine), DOPC (1,2-dioleyl-sn-glycero-3-phosphotidylcholine) DPPE (1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine), DMPE (1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine), and DOPG (1,2-dioleoyl-*sn*-glycero-3-phospho-(1'-*rac*-glycerol)).

32. The use of any one of claims 27-31, wherein the one or more PEG lipids are selected from derivatized ceramides such as N-Octanoyl-Sphingosine-l-[Succinyl(Methoxy Polyethylene Glycol)-2000] (C8 PEG-2000 ceramide), PEG-modified lipids having a polyethylene glycol chain of up to 5 kDa in length covalently attached to a lipid with alkyl chain(s) of C_6-C_{20} length, and a PEGylated cholesterol and PEG-2K.

33. The use of any one of claims 27-32, wherein the one or more PEG-modified lipids comprise at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, or at least 10% of the total lipids in the lipid nanoparticle.

34. The use of any one of claims 1-33, wherein administration of the composition results in expression of the antigen encoded by the mRNA in lymphocytes of the subject.

35. The use of any one of claims 1-34, wherein administration of the composition results in an antigen specific antibody response.

36. The use of claim 35, wherein the antigen specific antibody response is measured by the presence of antigen-specific antibodies in serum.

37. The use of any one of claims 1-36, wherein administration of the composition results in an antigen specific T-cell response.

38. The use of claim 37, wherein the antigen specific T-cell response is measured by IFN-γ ELISPOT in splenocytes.