process, toxicity, cost and simplicity of design. These problems and the further problems described under "Background of the Invention" were solved by the subject-matter and claims of the present invention. One exemplary solution to the problem of the invention is the provision of a a vaccine composition comprising

a) at least one nucleic acid encoding at least one antigen or fragment or variant thereof; and

b) a carrier composition, wherein the carrier composition comprises the phospholipid phosphatidylserine, wherein the amount of the phosphatidylserine is not more than 9 mol%, preferably not more than 5 mol%, of the total molar amount of all lipidic excipients in the carrier composition.

Furthermore, the above problems were solved by adding phospholipids with shorter alkyl chains to LNP formulations, specifically (07:0) PC (DHPC; 1,2-diheptanoyl-sn-glycero-3-phosphocholine), as disclosed herein.

**SUMMARY**

The inventors solved the above need in that they surprisingly found that the addition of the phospholipid phosphatidylserine to a vaccine composition, which comprises a carrier composition (preferably a lipid nanoparticle) comprising the nucleic acid encoding an antigen, results in a more effective vaccine, most likely - without wishing to be bound by theory - by targeting the vaccine compositions for phagocytosis by phagocytic cells of the immune system, ultimately resulting in the presence of the encoded antigen or fragment or variant thereof in phagocytic cells.

Further, surprisingly it was found that the above described addition of phosphatidylserine to vaccine compositions leads to a substantially increased targeting of the vaccine compositions to antigen-presenting cells (APCs), like e.g. DCs, macrophages or to the spleen as such, respectively, as when compared to vaccine compositions not comprising phosphatidylserine, preferably wherein the vaccine compositions are mRNA-LNP vaccine compositions. Also surprisingly it was found that the above described addition of phosphatidylserine to mRNA-LNP vaccine compositions leads to a substantially increased targeting of the mRNA-LNP vaccine compositions to lymph nodes, as when compared to mRNA-LNP vaccine compositions not comprising phosphatidylserine.

In one aspect, the present disclosure relates to a vaccine composition comprising a) at least one nucleic acid encoding at least one antigen or fragment or variant thereof; and b) a carrier composition, wherein the carrier composition comprises the phospholipid phosphatidylserine, wherein the amount of the phosphatidylserine is not more than 9 mol%, preferably not more than 5 mol%, of the total molar amount of all lipidic excipients in the carrier composition.

In an example, the present disclosure relates to a vaccine composition comprising

a) at least one nucleic acid encoding at least one antigen or fragment or variant thereof; and

b) a carrier composition, wherein the carrier composition comprises the phospholipid phosphatidylserine.

In another example, the present disclosure relates to a method of delivering a vaccine composition comprising at least one nucleic acid encoding at least one antigen or fragment or variant thereof to the spleen or lymph nodes, wherein the carrier composition comprises the phospholipid phosphatidylserine, as when compared to vaccine compositions not comprising phosphatidylserine.

In another example, the antigen is derived from a pathogenic antigen, a tumour antigen, an allergenic antigen or an autoimmune self-antigen.

In another example, the amount of the phosphatidylserine is not more than 9 mol%, preferably not more than 5 mol%, of the total molar amount of all lipidic excipients in the composition.

In another example, the carrier composition is a lipid nanoparticle composition. In yet another example, the lipid nanoparticle composition further comprises

(i) a cationic or ionizable lipid;

(ii) a steroid;
(iii) a further phospholipid in addition to phosphatidylserine; and
(iv) a polymer conjugated lipid.

In another aspect, the present disclosure is concerned with a pharmaceutical composition comprising the vaccine composition as described herein and a pharmaceutically acceptable carrier, diluent or excipient, preferably wherein the pharmaceutical composition is a sterile solid composition for reconstitution with a sterile liquid carrier, and wherein the composition further comprises one or more inactive ingredients selected from pH-modifying agents, bulking agents, stabilizers, non-ionic surfactants and antioxidants, and wherein the sterile liquid carrier is an aqueous carrier.

In a further aspect, the present disclosure relates to a use of the vaccine composition as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament in the treatment or prophylaxis of infectious diseases; cancer or tumor diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease, disorder or condition; in a subject.

In a further aspect, the present disclosure relates to a use of the vaccine composition as described herein or a pharmaceutical composition comprising the vaccine composition as described herein in the manufacture of a medicament in the treatment or prophylaxis of infectious diseases including viral, bacterial or protozoological infectious diseases in a subject.

In the third example, the present disclosure relates to the vaccine composition as described herein or the pharmaceutical composition as described herein for use in the treatment or prophylaxis of infectious diseases; cancer or tumor diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease, disorder or condition; in a subject. In a very preferred example, the present disclosure relates to a vaccine composition for use in the treatment or prophylaxis of a cancer or tumor disease.

In a further aspect, the present disclosure is concerned with a kit or kit of parts, comprising the vaccine composition as described herein or the pharmaceutical composition as described herein, optionally comprising a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration and dosage of the components.

In another example, the present disclosure relates to a method of treatment or prophylaxis of infectious diseases; cancer or tumor diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease, disorder or condition; in a subject comprising the steps:

a) providing the vaccine composition as described herein or the pharmaceutical composition as described herein or the kit or kit of as described herein; and
b) applying or administering the vaccine composition or the pharmaceutical composition or the kit or kit of parts to a tissue or an organism of the subject.

In another example, the present disclosure relates to a method of inducing an immune response in a subject, the method comprising administering to the subject the vaccine composition as described herein or the

pharmaceutical composition as described herein in an amount effective to produce an antigen-specific immune response in the subject.

In anotherexample, the present disclosure is concerned with a use of a vaccine composition as described herein or the pharmaceutical composition as described herein or the kit or kit of parts as described herein for (i) inducing an immune response, for (ii) inducing an antigen specific T-cell response or preferably for (iii) inducing CD8+ T cells responses, in a subject.

**DEFINITIONS**

For the sake of clarity and readability, the following scientific background information and definitions are provided. Any technical features mentioned herein or disclosed thereby can be part of or may be read on each and every

**CLAIMS**

1. A vaccine composition comprising

a) at least one nucleic acid encoding at least one antigen or fragment or variant thereof; and

b) a carrier composition, wherein the carrier composition comprises the phospholipid phosphatidylserine, wherein the amount of the phosphatidylserine is not more than 9 mol%, preferably not more than 5 mol%, of the total molar amount of all lipidic excipients in the carrier composition.

2. The vaccine composition according to claim 1, wherein the at least one nucleic acid is not a tolerogenic nucleic acid; and/or wherein the at least one nucleic acid does not encode a tolerogenic polypeptide; and/or wherein the vaccine composition does not comprise an antigen or fragment or variant thereof; and/or wherein the vaccine composition comprises the at least one nucleic acid as the sole payload; and/or wherein the vaccine composition is not a tolerogenic composition.

3. The vaccine composition according to claim 1 or 2, wherein the carrier composition at least partly encapsulates the at least one nucleic acid.

4. The vaccine composition according to any one of claims 1 to 3, wherein the carrier composition encapsulates the at least one nucleic acid; and/or

wherein the carrier composition comprises an inner surface and an outer surface facing the outside, wherein the phosphatidylserine is located at the outer surface of the carrier composition, wherein the hydrophilic head group of the phosphatidylserine is preferably located at the outer surface of the carrier composition; and/or

wherein the hydrophilic head group of the phosphatidylserine comprised in the carrier composition is accessible from the outside of the carrier composition.

5. The vaccine composition according to any one of claims 1 to 4, wherein the phosphatidylserine is selected from the group consisting of DPhyPS, WT-PS, 16:0-PS, 14:0-PS, 10:0-PS, 6:0-PS, 18:1-PS DOPS, 18:1-Lyso PS and 18:0-Lyso PS.

6. The vaccine composition according to any one of claims 1 to 5, wherein the carrier composition is a lipid nanoparticle composition.

7. The vaccine composition according to claim 6, wherein the lipid nanoparticle composition further comprises

(i) a cationic or ionizable lipid; and/or

(ii) a steroid; and/or

(iii) a further phospholipid in addition to phosphatidylserine, preferably DPhyPE; and/or

(iv) a polymer conjugated lipid.

8. The vaccine composition according to claim 6 or 7, wherein the lipid nanoparticle composition further comprises

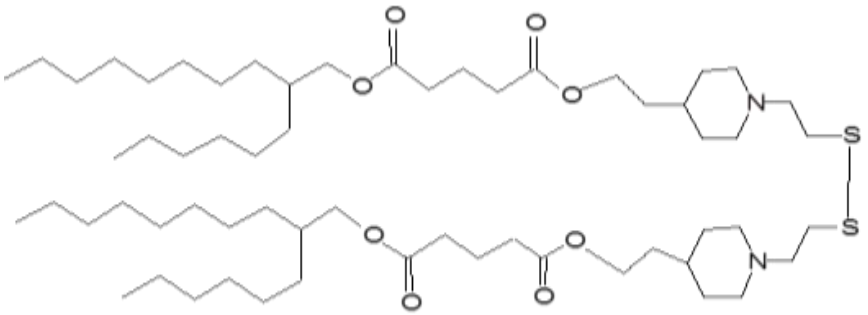
(i) a cationic or ionizable lipid;

(ii) a steroid;

(iii) a further phospholipid in addition to phosphatidylserine, preferably DPhyPE; and

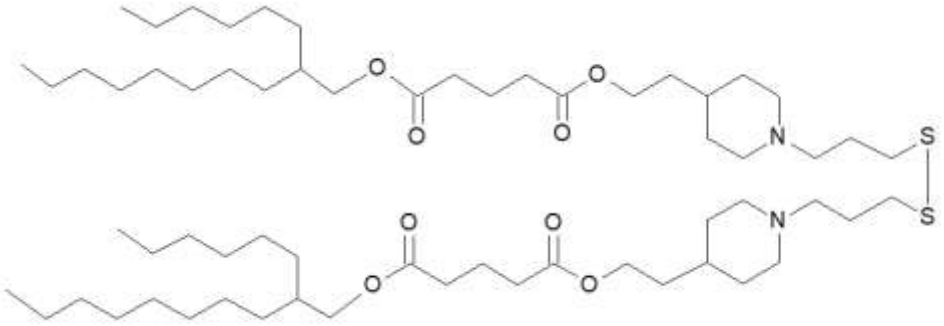
(iv) a polymer conjugated lipid.

9. The vaccine composition according to claim 7 or 8, wherein the cationic or ionizable lipid carries a net positive charge at physiological pH, preferably wherein the cationic or ionizable lipid comprises a tertiary nitrogen group or quaternary nitrogen group, more preferably wherein the cationic or ionizable lipid is selected from the group consisting of

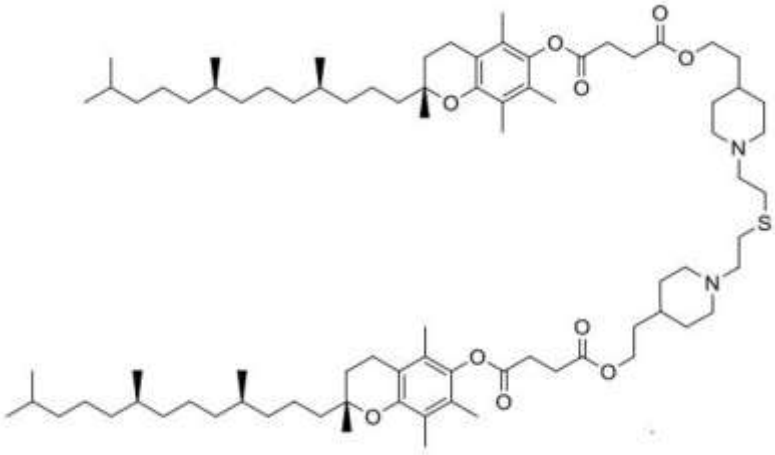
HEXA1: 

,

HEXA2:



and



THIOETHER: ; and/or

wherein the steroid is selected from the group consisting of cholesterol, cholesteryl hemisuccinate (CHEMS) and a derivate thereof, preferably wherein the steroid is cholesterol; and/or

wherein the further phospholipid is selected from the group consisting of 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (DPhyPE; 1,2-di-(3,7,11,15-tetramethylhexadecanoyl)-sn-glycero-3-phosphoethanolamine), 1,2-diphytanoyl-sn-glycero-3-phosphocholine (DPhyPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC; dioleoylphosphatidylcholine), 1,2-Di-palmitoyl-sn-glycero-3-phosphocholine (DPPC; dipalmitoylphosphatidylcholine), 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), phosphatidylethanolamines, distearoyl-phosphatidylcholines, dioleoyl-phosphatidylethanolamine (DOPEA), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE), palmitoyloleoylphosphatidylcholine (POPC), palmitoyloleoyl-phosphatidylethanolamine (POPE), 1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamine (DPPE), dioleoyl-phosphatidylethanolamine 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate (DOPE-mal), 1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine (DMPE), 1,2-Dilinoleoyl-sn-glycero-3-phosphoethanolamine (DLoPE), distearoyl-phosphatidylethanolamine (DSPE), 1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine (POPE), 1,2-Dilauroyl-sn-glycero-3-phosphoethanolamine (DLPE), 16-O-monomethylphosphoethanolamine, 16-O-dimethyl phosphatidylethanolamine, 1,2-Dierucoyl-sn-glycero-3-phosphoethanolamine (DEPE), 18-1-trans phosphatidylethanolamine, 1-stearoyl-2-oleoylphosphatidyethanolamine (SOPE), 1,2-Disqualeoyl-sn-glycero-3-phospho-ethanolamine (DSQPE), 1,2-dielaidoyl-sn-glycero-3-phosphoethanolamine (transDOPE), 1-

Stearoyl-2-linoleoyl-sn-glycero-3-phosphoethanolamine (SLPE), 1-tridecanoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1-oleoyl-2-hydroxy-sn-glycero-3-phospho-L-serine (sodium salt), 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (sodium salt) (POPS), 1-1-stearoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1,2-dioleoyl-sn-glycero-3-phospho-L-serine (sodium salt) (DOPS), 1,2-distearoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1,2-diphytanoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1-O-hexadecanyl-2-O-(9Z-octadecenyl)-sn-glycero-3-phosphoethanolamine, 1,2-distearoyl-sn-glycero-3-phosphatidylcholine or 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-di-O-phytanyl-sn-glycero-3-phosphoethanolamine, 1-palmitoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (PChemsPC), 1,2-dicholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (DChemsPC), 2-((2,3-bis(oleoyloxy)propyl)dimethylammonio)ethyl hydrogen phosphate (DOCP), 2-((2,3-bis(oleoyloxy)propyl)dimtheylammonio)ethyl ethyl phosphate (DOCPe), and 1-O-octadecyl-2-O-methyl-sn-glycero-3-phosphocholine (Edelfosine),

preferably wherein the further phospholipid is DPhyPE; and wherein the phospholipid, preferably DPhyPE, is optionally present in combination with a phospholipid having at least two alkyl chains, wherein each alkyl chain independently has a length of preferably C6, C7, C8, C9, or C10, more preferably a length of C6, C7, or C8, most preferably a length of C7, further most preferably a phospholipid selected from the group consisting of DHPC (1,2-diheptanoyl-sn-glycero-3-phosphocholine), 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyryl-sn-glycero-3-phosphocholine), 06:0 PC (1,2-dihexanoyl-sn-glycero-3-phosphocholine), 08:0 PC (1,2-dioctanoyl-sn-glycero-3-phosphocholine), and 09:0 PC (1,2-dinonanoyl-sn-glycero-3-phosphocholine), with DHPC being most preferred as the optionally present phospholipid having at least two alkyl chains; and/or

wherein the polymer conjugated lipid is a pegylated lipid or a PMOZ-lipid.

10. The vaccine composition according to claim 8 or 9, wherein the composition comprises excipients in a ratio selected from the group consisting of

(a-i) the cationic lipid at an amount of 30-70 mol%; the steroid at an amount of 20-50 mol%; the phospholipid at an amount of 5-25 mol%; and the polymer conjugated lipid at an amount of 0.5-5 mol%;

(a-ii) the cationic lipid at an amount of 40-60 mol%; the steroid at an amount of 20-40 mol%; the phospholipid at an amount of 10-20 mol%; and the polymer conjugated lipid at an amount of 1-2 mol%;

(a-iii) the cationic lipid of claim 12 at an amount of 30-70 mol%; the steroid of claim 13 at an amount of 20-50 mol%; the phospholipid phosphatidylserine and the phospholipid of claim 14 at an amount of 5-25 mol%; and the polymer conjugated lipid of claim 15 at an amount of 0.5-5 mol%; and

(a-iv) the cationic lipid of claim 12 at an amount of 40-60 mol%; the steroid of claim 13 at an amount of 20-40 mol%; the phospholipid phosphatidylserine and the

phospholipid of claim 14 at an amount of 10-20 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1-2 mol%;

preferably the composition comprising excipients in a ratio selected from the group consisting of

(b-i) the cationic lipid at an amount of 59 mol%; the steroid at an amount of 29.3 mol%; the phospholipid at an amount of 10 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-ii) the cationic lipid at an amount of 58 mol%; the steroid at an amount of 29.3 mol%; the phospholipid at an amount of 11 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-iii) the cationic lipid at an amount of 49 mol%; the steroid at an amount of 29.3 mol%; the phospholipid at an amount of 20 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-iv) the cationic lipid of claim 12 at an amount of 59 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine and the phospholipid of claim 14 at an amount of 10 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%;

(b-v) the cationic lipid of claim 12 at an amount of 58 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine and the phospholipid of claim 14 at an amount of 11 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%; and

(b-vi) the cationic lipid of claim 12 at an amount of 49 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine and the phospholipid of claim 14 at an amount of 20 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%;

more preferably the composition comprising excipients in a ratio selected from the group consisting of

(c-i) the cationic lipid of claim 12 at an amount of 59 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine at an amount of 5 mol% and DPhyPE at an amount of 5 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%;

(c-ii) the cationic lipid of claim 12 at an amount of 59 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine at an amount of 2 mol% and DPhyPE at an amount of 8 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%;

(c-iii) the cationic lipid of claim 12 at an amount of 58 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine at an amount of 5 mol%, DPhyPE at an amount of 5 mol% and DHPC at an amount of 1 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%;

(c-iv) the cationic lipid of claim 12 at an amount of 49 mol%; the steroid of claim 13 at an amount of 29.3 mol%; the phospholipid phosphatidylserine at an amount of 5 mol%, DPhyPE at an amount of 5 mol% and DHPC at an amount of 10 mol%; and the polymer conjugated lipid of claim 15 at an amount of 1.7 mol%.

11. The vaccine composition according to any one of the preceding claims, wherein the at least one nucleic acid is DNA or RNA.

12. The vaccine composition according to claim 11, wherein the at least one nucleic acid is RNA, preferably mRNA comprising a coding sequence encoding the at least one antigen or fragment or variant thereof and optionally a coding sequence encoding at least one self-amplifying enzyme.

13. The vaccine composition according to claim 12, wherein the lipid nanoparticles comprise the mRNA

(i) at an amount such as to achieve an N/P ratio in the range of 10 to 20, preferably 2 to 15, more preferably 3 to 10, even more preferably 4 to 9, most preferably 6; or

(ii) at an amount such as to achieve an N/P ratio in the range of 5 to 20, more preferably 10 to 18, even more preferably 12 to 16, most preferably 14; and/or

(iii) at an amount such as to achieve a lipid : mRNA weight ratio in the range of 20 to 60, preferably from 3 to 15, 5 to 13, 4 to 8 or from 7 to 11; and/or

wherein the lipid nanoparticles have a mean hydrodynamic diameter as determined by dynamic laser scattering from 50nm to 300nm, or from 60nm to 250nm, or from 60nm to 200nm, or from 70nm to 200nm, or from 75nm to 160nm, or from 90nm to 140nm, or from 100nm to 140nm; and/or

wherein the lipid nanoparticles exhibit a zeta potential in the range of -50 mV to +50 mV, preferably in the range of -25 mV to +25 mV, more preferably in the range of -10 mV to +10 mV, most preferably in the range of -5 mV to +5 mV.

14. The vaccine composition according to claim 12 or 13, wherein the mRNA is a mono-, bi-, or multicistronic mRNA; and/or

wherein the mRNA comprises at least one chemical modification, wherein the chemical modification preferably is selected from the group consisting of base modifications, sugar modifications, backbone modifications and lipid modifications, more preferably wherein the chemical modification is a base modification, most preferably wherein the base modification preferably is selected from the group consisting of pseudouridine (psi or ψ), N1-methylpseudouracil (N1MPU, N1Mpsi or N1Mψ), 1-ethylpseudouracil, 2-thiouracil (s2U), 4-

thiouracil, 5-methylcytosine, 5-methyluracil, 5-methoxyuracil, and any combination thereof; and/or.

wherein the coding sequence exhibits a sequence modification wherein the sequence modification preferably is selected from a G/C content modification, a codon modification, a codon optimization or a C-optimization of the sequence; more preferably wherein, compared with the coding sequence of the corresponding wild-type mRNA, the

a) G/C content of the coding sequence is increased;

b) C content of the coding sequence is increased;

c) codon usage in the coding sequence is adapted to the human codon usage; and/or

d) codon adaptation index (CAI) is increased or maximised in the coding sequence.

15. The vaccine composition according to any one of claims 12 to 14, wherein the mRNA further comprises

a) a 5'-CAP structure, preferably m7GpppN, more preferably CAP1 or m7G(5')ppp(5')(2'OMeA)pG;

b) at least one miRNA binding site sequence, preferably wherein the microRNA binding site is for a microRNA selected from the group consisting of a miR-126, miR-142, miR-144, miR-146, miR-150, miR-155, miR-16, miR-21, miR-223, miR-24, miR-27, miR-26a binding site, preferably a miR-122 or miR-142 binding site, or any combination of the aforementioned miRNA binding sites thereof;

c) at least one 5'-UTR element;

d) at least one 3'-UTR element;

e) at least one poly(A) sequence;

f) at least one poly(C) sequence;

g) optionally, a histone stem-loop selected from SEQ ID NO:3 or 4;

h) optionally, a 3'-terminal sequence element selected from SEQ ID NO:41-70;

or any combinations of these.

16. The vaccine composition according to any one of claims 12 to 15, wherein the mRNA comprises a 5'-CAP structure, preferably m7G, CAP0, CAP1, CAP2, a modified CAP0 or a modified CAP1 structure.

17. The vaccine composition according to claim 15, wherein the at least one coding RNA comprises at least one heterologous 5'-UTR and/or at least one heterologous 3'-UTR, preferably wherein the at least one heterologous 5'-UTR comprises a nucleic acid sequence derived from a 5'-UTR of a gene selected from HSD17B4, RPL32, ASAH1, ATP5A1, MP68, NDUFA4, NOSIP, RPL31, SLC7A3, TUBB4B and UBQLN2, or from a homolog, a fragment or variant of any one of these genes; and/or preferably wherein the at least one heterologous 3'-UTR comprises a nucleic acid sequence derived from a 3'-UTR of a gene selected from PSMB3, ALB/albumin, alpha-globin, CASP1 (preferably SEQ ID NO:81 (DNA) or SEQ ID

NO:82 (RNA)), COX6B1 (preferably SEQ ID NO:83 (DNA) or SEQ ID NO:84 (RNA)), GNAS (preferably SEQ ID NO:85 (DNA) or SEQ ID NO:86 (RNA)), NDUFA1 (preferably SEQ ID NO:87 (DNA) or SEQ ID NO:88 (RNA)) and RPS9 (preferably SEQ ID NO:79 (DNA) or SEQ ID NO:80 (RNA)), or from a homolog, a fragment or a variant of any one of these genes.

18. The vaccine composition according to claim 17, wherein the at least one coding RNA comprises a (i) HSD17B4 5'-UTR and a PSMB3 3'-UTR or (ii) a RPL32 5'-UTR and an ALB/albumin 3'-UTR, preferably a mutated alpha-globin 3'-UTR (SEQ ID NO:11, 12), more preferably a HSD17B4 5'-UTR (SEQ ID NO:21, 22) and a PSMB3 3'-UTR (SEQ ID NO:19, 20).

19. The vaccine composition according to any one of claims 12 to 14, wherein the mRNA comprises the following elements in the 5' to 3' direction:

a) a 5'-CAP structure, preferably selected from the group consisting of m7G(5'), m7G(5')ppp(5')(2'OMeA) and m7G(5')ppp(5')(2'OMeG);

b) a 5'-UTR element comprising a nucleic acid sequence derived from the 5'-UTR of a TOP gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26 or preferably SEQ ID NO:77/78 (SLC7A3) or SEQ ID NO:75/76 (RPL31), or a homolog, a fragment or a variant thereof; most preferably according to SEQ ID NO:22 (HSD17B4);

c) the at least one coding sequence;

d) a 3'-UTR element comprising a nucleic acid sequence derived from an α-globin gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:6, 8 or SEQ ID NO:10, 12, 14, 16, 18, or preferably SEQ ID NO:20, or a homolog, a fragment or a variant thereof; and/or a 3'-UTR element comprising a nucleic acid sequence derived from an albumin gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:18 (ALB/albumin) or preferably SEQ ID NO:79/80 (RPS9), or a homolog, a fragment or a variant thereof; most preferably according to SEQ ID NO:20 (PSMB3);

e) optionally, at least one poly(A) sequence, preferably consisting of 10 to 200, 10 to 100, 40 to 80, or 50 to 70 adenosine nucleotides, more preferably at least 70 adenosine nucleotides, even more preferably 100 adenosine nucleotides;

f) optionally, at least one poly(C) sequence, preferably consisting of 10 to 200, 10 to 100, 20 to 70, 20 to 60 or 10 to 40 cytosine nucleotides; and

g) optionally, at least one histone stem-loop, preferably comprising the RNA sequence according to SEQ ID NO:4.

20. The vaccine composition according to any one of the preceding claims, wherein the antigen is derived from a pathogenic antigen, a tumour antigen, an allergenic antigen or an autoimmune self-antigen,
wherein the pathogenic antigen is preferably selected from the group consisting of a bacterial antigen, a viral antigen, a fungal antigen and a protozoal antigen.

21. The vaccine composition according to claim 20, wherein the pathogenic antigen

(i) is derived from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), Bunyavirales virus, Cytomegalovirus (CMV), Dengue viruses (DENV-1, DENV-2, DENV-3 and DENV-4), Ebola virus (EBOV), Flavivirus, Hepatitis B virus (HBV), Herpes simplex virus (HSV), Human immunodeficiency virus (HIV), Human metapneumovirus (HMPV), Human Papilloma virus (HPV), Human parainfluenza viruses (HPIV), Influenza virus, extraintestinal pathogenic E. coli (ExPEC), Lassa mammarenavirus (LASV), MERS coronavirus, Mycobacterium tuberculosis, Nipah virus, Norovirus, Rabies virus (RABV), Respiratory Syncytial virus (RSV), Rhinovirus, Rotavirus, Vaccinia virus, Yellow Fever virus (YFV), Zika virus (ZIKV), Chlamydia trachomatis (i.e. bacterium chlamydia causing chlamydia), or Malaria parasite (e.g. Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, or Plasmodium ovale); and/or

(ii) is derived from a structural protein, an accessory protein, or a replicase protein from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), or an immunogenic fragment or immunogenic variant of any of these; and/or

(iii) is derived from a spike protein (S), an envelope protein (E), a membrane protein (M) or a nucleocapsid protein (N) from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), or an immunogenic fragment or immunogenic variant of any of these, preferably wherein the spike protein (S) comprises or consists of spike protein fragment S1 or spike protein fragment S2, more preferably spike protein fragment S1, or an immunogenic fragment or immunogenic variant thereof; and/or

(iv) is derived from a pre-fusion stabilized spike protein (S) (S_stab) from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV) comprising at least one pre-fusion stabilizing mutation.

22. A pharmaceutical composition comprising the vaccine composition according to claim 20 or 21 and a pharmaceutically acceptable carrier, diluent or excipient, preferably wherein the pharmaceutical composition is a sterile solid composition for reconstitution with a sterile liquid carrier, and wherein the composition further comprises one or more inactive ingredients

selected from pH-modifying agents, bulking agents, stabilizers, non-ionic surfactants and antioxidants, and wherein the sterile liquid carrier is an aqueous carrier.

23. Use of the vaccine composition according to claim 20 or 21 or the pharmaceutical composition according to claim 22 in the manufacture of a medicament in the treatment or prophylaxis of infectious diseases; cancer or tumor diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease, disorder or condition; in a subject.

24. Use of the vaccine composition according to claim 21 or a pharmaceutical composition comprising the vaccine composition according to claim 21 in the manufacture of a medicament in the treatment or prophylaxis of infectious diseases including viral, bacterial or protozoological infectious diseases in a subject.

25. The use according to claim 23 or 24, wherein the vaccine composition or pharmaceutical composition is to be administered via local or locoregional injection, infusion or implantation, in particular intradermal, subcutaneous, intramuscular, intracameral, subconjunctival, suprachoroidal injection, subretinal, subtenon, retrobulbar, topical, posterior juxtascleral administration, or intrapulmonal inhalation, interstitial, locoregional, intravitreal, intratumoral, intralymphatic, intranodal, intra-articular, intrasynovial, periarticular, intraperitoneal, intra-abdominal, intracardial, intralesional, intrapericardial, intraventricular, intrapleural, perineural, intrathoracic, epidural, intradural, peridural, intrathecal, intramedullary, intracerebral, intracavernous, intracorporus cavernosum, intraprostatic, intratesticular, intracartilaginous, intraosseous, intradiscal, intraspinal, intracaudal, intrabursal, intragingival, intraovarian, intrauterine, periocular, periodontal, retrobulbar, subarachnoid, subconjunctival, suprachoroidal injection, infusion, implantation, nasal, buccal, sublingual, otic or auricular, ophthalmic, conjunctival, vaginal, rectal, intracervical, endosinusial, laryngeal, oropharyngeal, ureteral, urethral administration, more preferably said lipid nanoparticle is to be administered intramuscularly, intravenously, intradermally, subcutaneously, intratumorally, intranasally, or by inhalation to a subject, preferably via local or locoregional injection or infusion to a subject.

26. A kit or kit of parts, comprising the vaccine composition according to claim 20 or 21 or the pharmaceutical composition according to claim 22, optionally comprising a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration and dosage of the components.

27. The use according to claim 23 or 24, wherein the subject is a mammalian subject, preferably a human subject.