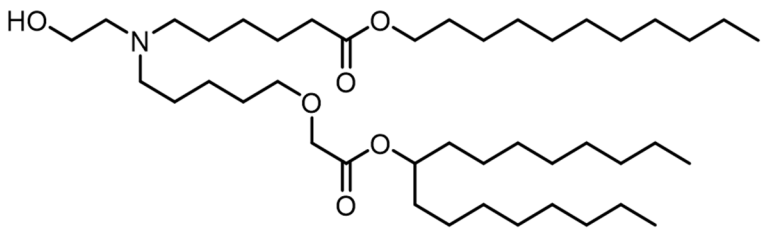
CLAIMS

1. A lipid nanoparticle, comprising a nucleic acid construct and a lipid phase, the nucleic acid construct comprises:
(a) an open reading frame (ORF), and
(b) an untranslated region element (UTR);
the lipid phase comprises a cationic lipid of Formula I,



I

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wherein (b) comprises a combination of a 3' untranslated region element (3'UTR) and a 5' untranslated region element (5'UTR);

wherein the 3'UTR comprises a sequence set forth in SEQ ID NO: 12 or a sequence having an identity of at least 90% therewith, and the 5'UTR comprises a sequence set forth in any one of SEQ ID NO: 15-47 or a sequence having an identity of at least 90% with any thereof;

preferably, the 5'UTR comprises a sequence set forth in any one of SEQ ID NO: 15, 29, 30, 32 or a sequence having an identity of at least 90% therewith.

2. The lipid nanoparticle according to claim 1, wherein the cationic lipid comprises from 20 mol% to 70 mol% of the total lipids present in the lipid nanoparticle; preferably, the cationic lipid comprises from 30 mol% to 70 mol% of the total lipids present in the lipid nanoparticle; and more preferably, the cationic lipid comprises from 40 mol% to 70 mol% of the total lipids present in the lipid nanoparticle.

3. The lipid nanoparticle according to claim 1, wherein the lipid nanoparticle comprises at least one non-cationic lipid, and preferably the non-cationic lipid is selected from a mixture of a phospholipid and a cholesterol or its derivative.

4. The lipid nanoparticle according to claim 3, wherein the non-cationic lipid comprises from 20 mol% to 70 mol% of the total lipids present in the lipid nanoparticle; preferably, the non-cationic lipid comprises 30 mol% to 60 mol% of the total lipids present in the lipid nanoparticle; and more preferably, the non-cationic lipid comprises from 20 mol% to 50 mol% of the total lipids present in the lipid nanoparticle.

5. The lipid nanoparticle according to claim 3, wherein the phospholipid comprises from 5 mol% to 30 mol% of the total lipids present in the lipid nanoparticle.

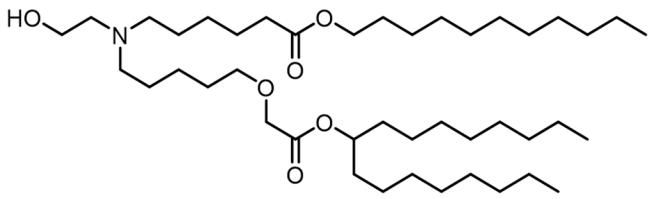
6. The lipid nanoparticle according to claim 3, wherein the cholesterol or its derivative comprises from 20 mol% to 60 mol% of the total lipids present in the lipid nanoparticle; preferably, the cholesterol or its derivative comprises from 30 mol% to 60 mol% of the total lipids present in the lipid nanoparticle; and more preferably, the cholesterol or its derivative comprises from 20 mol% to 45 mol% of the total lipids present in the lipid nanoparticle.

7. The lipid nanoparticle according to claim 1, wherein the lipid nanoparticle further comprises at least one conjugated lipid; and preferably, the conjugated lipid in the lyophilized composition comprises from 0.5 mol% to 5 mol% of the total lipids present in the lipid nanoparticle.

8. The lipid nanoparticle according to claim 1, comprising:

a) a nucleic acid construct;

b) a cationic lipid, wherein the cationic lipid comprises a compound of Formula I or a pharmaceutically acceptable salt thereof, and the cationic lipid comprises from 10 mol% to 75 mol% of the total lipids present in the lipid nanoparticle,



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c) a non-cationic lipid, wherein the non-cationic lipid is selected from a phospholipid and/or a cholesterol or its derivative, wherein the phospholipid comprises from 5 mol% to 40 mol% of the total lipids present in the lipid nanoparticle, and the cholesterol or its derivative comprises from 15 mol% to 60 mol% of the total lipids present in the lipid nanoparticle;

and d) a conjugated lipid, wherein the conjugate comprises from 0.5 mol% to 2 mol% of the total lipids present in the lipid nanoparticle.

9. The lipid nanoparticle according to any one of claims 1 to 8, wherein the nucleic acid construct further comprises:

(c) a polyadenylation (poly-A) tail;

preferably, the poly-A tail is selected from the group consisting of A120, A30L70, HGH polyA, SV40 polyA, BGH polyA, rbGlob polyA, and SV40late polyA;

preferably, the poly-A tail is selected from the group consisting of A120 and A30L70, the A120 comprises 120 adenine nucleotides, and the A30L70 comprises a sequence set forth in SEQ ID NO: 52 or a sequence having an identity of at least 90% therewith.

10. The lipid nanoparticle according to any one of claims 1 to 9, wherein the ORF encodes hepatocyte growth factor (HGF), an antibody, or an antigen-binding fragment thereof, and preferably human hepatocyte growth factor (hHGF), an anti-PD-1 antibody, or an antigen-binding fragment thereof.

11. The lipid nanoparticle according to claim 10, comprising a sequence set forth in any one of SEQ ID NO: 115, 116, 127, 132 or a sequence having an identity of at least 90% therewith; or, comprising a sequence set forth in SEQ ID NO: 124 or a sequence having an identity of at least 90% therewith and/or a sequence set forth in SEQ ID NO: 125 or a sequence having an identity of at least 90% therewith.

12. The lipid nanoparticle according to any one of claims 1 to 11, wherein the nucleic acid construct is DNA or RNA, preferably RNA, and more preferably mRNA.

13. A lyophilized composition, comprising the lipid nanoparticle according to any one of claims 1 to 12.

14. The lyophilized composition according to claim 13, comprising the lipid nanoparticle according to any one of claims 1 to 8 and sodium chloride, preferably the weight ratio of sodium chloride to the cationic lipid is 1:10 to 10:1; more preferably, the weight ratio of sodium chloride to the cationic lipid is 1:5 to 10:1; more preferably, the weight ratio of sodium chloride to the cationic lipid is 1:5 to 5:1; more preferably, the weight ratio of sodium chloride to the cationic lipid is 1:3 to 5:1; more preferably, the weight ratio of sodium chloride to the cationic lipid is 1:2 to 5:1; and more preferably, the weight ratio of sodium chloride to the cationic lipid is 1:2 to 4:1.

15. Use of the lipid nanoparticle according to any one of claims 1-12, the lyophilized composition according to any one of claims 13-14 in the manufacture of a medicament for the treatment of a disease in a subject in need thereof;

wherein the disease is selected from the group consisting of ischemic disease, metabolic syndrome, diabetes and complications thereof, restenosis, and a nerve injury;

preferably, the ischemic disease is selected from the group consisting of coronary artery disease (CAD), peripheral artery disease (PAD), myocardial infarction, limb ischemia, thromboangiitis obliterans (TAO), and diabetic artery obliterans (DAO); more preferably, the limb ischemia is Lower limb ischemia, and most preferably, the limb ischemia is critical limb ischemia (CLI);

preferably, the diabetes and complications thereof are selected from the group consisting of diabetic peripheral neuropathy, diabetic foot ulcer (DFU), and diabetic artery obliterans (DAO);

preferably, the restenosis is selected from the group consisting of post-surgical

restenosis and post-perfusion restenosis;

preferably, the nerve injury is selected from the group consisting of neurodegenerative disease, traumatic nerve injury, and peripheral neuropathy; more preferably, the neurodegenerative disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), Parkinson's disease, and dementia, and the peripheral neuropathy is diabetic peripheral neuropathy.