

CLAIMS:

1. A composition comprising a modified mRNA encoding a VEGF-A polypeptide of SEQ ID NO: 2 and a citrate saline buffer, wherein the citrate saline buffer is substantially free of divalent cations.

2. A formulation comprising a pharmaceutically acceptable amount of a modified mRNA encoding a VEGF-A polypeptide of SEQ ID NO: 2 and a citrate saline buffer, wherein the citrate saline buffer is substantially free of divalent cations.

3. The formulation of claim 2, wherein the citrate saline buffer is substantially free of calcium and magnesium.

4. The formulation of claim 2, wherein the citrate saline buffer contains no calcium or magnesium.

5. The formulation of claim 2, further comprising a pharmaceutically acceptable excipient, optionally wherein the pharmaceutically acceptable excipient is chosen from a solvent, dispersion media, diluent, dispersion, suspension aid, surface active agent, isotonic agent, thickening or emulsifying agent, preservative, core-shell nanoparticles, polymer, peptide, protein, cell, hyaluronidase, and mixtures thereof.

6. The formulation of any one of claims 2-5, wherein the formulation does not include any lipid-based complex.

7. The formulation of any one of claims 2-5, wherein the formulation does not include a liposome, lipoplex, or lipid nanoparticle.

8. A method for preparing a composition or formulation, comprising combining a modified mRNA encoding a VEGF-A polypeptide of SEQ ID NO: 2 with a citrate saline buffer, wherein the citrate saline buffer is substantially free of divalent cations, and wherein the composition or formulation is effective for treating a subject suffering from a disease responsive to VEGF-A therapy.

9. The composition or formulation of any one of claims 1-7 for use in therapy.

10. The composition or formulation of any one of claims 1-7 for use in treating a disease responsive to VEGF-A therapy, optionally wherein the disease is chosen from heart failure with reduced or preserved ejection fraction, kidney disease, a disease involving skin grafting and tissue grafting, post-MI cardiac dysfunction, ischemic heart disease, a vascular injury from trauma or surgery, a skin ulcer including a diabetic ulcer, critical limb ischemia, pulmonary hypertension, and peripheral arterial disease.

11. The composition or formulation for use according to claim 10, wherein the composition or formulation is to be administered to the subject via intramuscular, intradermal, subcutaneous, intracardiac, or epicardiac route, through a portal vein catheter, through a coronary sinus catheter, and/or by direct administration into the area to be treated.

12. The composition or formulation for use according to claim 9, wherein the composition or formulation is to be administered post myocardial infarction (MI) at peak time of epicardium-derived cell activation in the myocardium.

13. The composition or formulation for use according to claim 9 or 12, wherein the composition or formulation is to be administered about 7 days post-MI, about 10 days post-MI, about 2 weeks post-MI, about 3 weeks post-MI, or about 6 weeks post-MI.

14. The composition or formulation for use according to any one of claims 9-13, wherein the use comprises treating myocardial infarction with reduced ejection fraction or treating heart failure with preserved ejection fraction.

15. The composition or formulation for use according to claim 14, wherein the composition or formulation is to be injected at the border zone between healthy and infarcted tissue.