CLAIMS

1. A polynucleotide comprising sequences encoding a S100 calcium binding protein (S100) polypeptide, a stromal cell derived factor (SDF) polypeptide, and a vascular endothelial growth factor (VEGF) polypeptide; or, fragments and variants thereof.

2. The polynucleotide of claim 1, wherein said S100 polypeptide is a S100A1 polypeptide or fragments and variants thereof.

3. The polynucleotide of claim 1, wherein said SDF polypeptide is selected from the group consisting of SDF1, SDF-1α, and SDF-1β; or fragments and variants thereof.

4. The polynucleotide of claim 1, wherein said VEGF polypeptide is selected from the group consisting of VEGF121, VEGF121b, VEGF145, VEGF165, VEGF165b, VEGF189, VEGF191, and VEGF206; or, fragments and variants thereof.

5. The polynucleotide of any one of claims 1 to 4, wherein said S100 polypeptide comprises a sequence as shown in SEQ ID NO: 104; said SDF polypeptide comprises a sequence as shown in SEQ ID NO: 102; and said VEGF polypeptide comprises a sequence as shown in SEQ ID NO: 106.

6. The polynucleotide of any one of claims 1 to 5, wherein at least two of said S100 polypeptide, said SDF polypeptide, and said VEGF polypeptide are connected by one or more linkers.

7. The polynucleotide of claim 6, wherein said one or more linkers are selected from the group consisting of a rigid linker, a flexible linker, a peptide linker, a cleavable linker, a self-cleavable linker, a linker cleavable via ribosome skipping, or any combination thereof.

8. The polynucleotide of any one of claims 6 to 7, wherein said one or more linkers are selected from the group consisting of a RAKR linker, a fp2a linker, a p2a linker, a GSG-p2a linker, and a fmdv linker, or any combination thereof.

9. The polynucleotide of any one of claims 6 to 8, wherein said one or more linkers comprise a sequence as shown in SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, or SEQ ID NO: 40.

10. The polypeptide of anyone of claims 6 to 8, wherein said one or more linkers comprise a sequence selected from the group consisting of APVKQ (SEQ ID NO: 42), GPVKQ (SEQ ID NO: 43), VPVKQ (SEQ ID NO: 44), IPVKQ (SEQ ID NO: 45), MPVKQ (SEQ ID NO: 46), APIKQ (SEQ ID NO: 47), GPIKQ (SEQ ID NO: 48), VPIKQ (SEQ ID NO: 49), IPIKQ (SEQ ID NO: 50), MPIKQ (SEQ ID NO: 51), APAKQ (SEQ ID NO: 52), GPAKQ (SEQ ID NO: 53), VPAKQ (SEQ ID NO: 54), IPAKQ (SEQ ID NO: 55), MPAKQ (SEQ ID NO: 56), APVRQ (SEQ ID NO: 57), GPVRQ (SEQ ID NO: 58), VPVRQ (SEQ ID NO: 59), IPVRQ (SEQ ID NO: 60), MPVRQ (SEQ ID NO: 61), APIRQ (SEQ ID NO: 62), GPIRQ (SEQ ID NO: 63), VPIRQ (SEQ ID NO: 64), IPIRQ (SEQ ID NO: 65), MPIRQ (SEQ ID NO: 66), APARQ (SEQ ID NO: 67), GPARQ (SEQ ID NO: 68), VPARQ (SEQ ID NO: 69), IPARQ (SEQ ID NO: 70), MPARQ (SEQ ID NO: 71), APVKN (SEQ ID NO: 72), GPVKN (SEQ ID NO: 73), VPVKN (SEQ ID NO: 74), IPVKN (SEQ ID NO: 75), MPVKN (SEQ ID NO: 76), APIKN (SEQ ID NO: 77), GPIKN (SEQ ID NO: 78), VPIKN (SEQ ID NO: 79), IPIKN (SEQ ID NO: 80), MPIKN (SEQ ID NO: 81), APAKN (SEQ ID NO: 82), GPAKN (SEQ ID NO: 83), VPAKN (SEQ ID NO: 84), IPAKN (SEQ ID NO: 85), IVIPAKN (SEQ ID NO: 86), APVRN (SEQ ID NO: 87), GPVRN (SEQ ID NO: 88), VPVRN (SEQ ID NO: 89), IPVRN (SEQ ID NO: 90), IVIPVRN (SEQ ID NO: 91), APIRN (SEQ ID NO: 92), GPIRN (SEQ ID NO: 93), VPIRN (SEQ ID NO: 94), IPIRN (SEQ ID NO: 95), MPIRN (SEQ ID NO: 96), APARN (SEQ ID NO: 97), GPARN (SEQ ID NO: 98), VPARN (SEQ ID NO: 99), IPARN (SEQ ID NO: 100) or MPARN (SEQ ID NO: 101).

11. A polynucleotide encoding a first polypeptide construct comprising a S100 calcium-binding protein (S100) polypeptide, and a second polypeptide, wherein said second polypeptide is at least one of a cytokine, a chemokine, an angiogenic polypeptide, and any functional variant thereof, wherein said first polypeptide and said second polypeptide is connected by a cleavable linker.

12. The polynucleotide of claim 11, further comprising a third polypeptide, wherein said third polypeptide is at least one of a cytokine, a chemokine, an angiogenic polypeptide, and any functional variant thereof, wherein said third polypeptide is different from said second polypeptide and is connected to said second polypeptide by a cleavable linker.

13. The polynucleotide of any one of claims 11 to 12, wherein at least one of said cleavable linkers comprises furin and a 2A polypeptide.

14. The polynucleotide of claim13, wherein at least one of said cleavable linkers comprises furin and P2A (fp2a), wherein said 2A polypeptide comprises a sequence that mediates a “ribosome skipping" translational effect.

15. The polynucleotide of any one of claims 11 to 14, wherein said cleavable linker comprises a sequence as shown in SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, or SEQ ID NO: 40, or SEQ ID NO: 42.

16. A polypeptide encoded by the polynucleotide of any one of claims 1 to 15.

17. A cell comprising the polynucleotide of any one of claims 1 to 15, or said polypeptide encoded by said polynucleotide.

18. An expression vector comprising the polynucleotide of any one of claims 1 to 15, wherein said polynucleotide is operably linked to a promoter.

19. The expression vector of claim 18, wherein said promotor is a constitutive promoter, a tissue specific promoter, or an inducible promoter.

20. The expression vector of claim 19, wherein said inducible promoter is a small molecule ligand-inducible two polypeptide ecdysone receptor-based gene switch.

21. The expression vector of any one of claims 18 to 20, wherein said expression vector is a cardiac expression vector.

22. A pharmaceutical composition comprising:

the polynucleotide of any one of claims 1 to 15, a polypeptide encoded by said polynucleotide of any one of claims 1 to 15, or the expression vector of any one of claims 18 to 21; and,

a pharmaceutically acceptable excipient.

23. A method comprising: contacting at least one cardiac cell with the polynucleotide of anyone of claims 1 to 15, a polypeptide encoded by said polynucleotide of any one of claims 1 to 15, or the expression vector of any one of claims 18 to 21.

24. The method of claim 23, said cardiac cell is a myocardial cell.

25. A method of treating a cardiac condition in a subject comprising providing to said subject a therapeutically effective amount of the pharmaceutical composition of claim 22.

26. The method of claim 25, wherein said cardiac condition is cardiomyopathy, vasculogenesis, congestive heart failure, arrhythmia, pericardial disease, aorta disease, Marfan syndrome, or coronary artery disease.

27. The method of any one of claims 23 to 26, wherein said subject is a human subject.

28. A method of treating a cardiac condition in a subject comprising:

administering to said subject a therapeutically effective amount of a composition comprising a microbubble complex, wherein said microbubble complex comprises a lipid, a gas, and a plasmid comprising the polynucleotide of any one of claims 1 to 15;

contacting said microbubble complex with ultrasonic energy sufficient to result in targeted microbubble destruction (UTMD).

29. The method of claim 28, wherein said lipid forms a shell enclosing said gas and said plasmid.

30. The method of any one of claims 23 to 29, wherein said contacting, providing, or administering is via retrograde coronary sinus infusion (RCSI).