CLAIMS

1. A recombinant adeno-associated virus (rAAV) vector comprising a polynucleotide that comprises a sequence that is at least 90%, at least 95%, or at least 99.5% identical to any one of the nucleotide sequences of SEQ ID NOs: 6-8, 16, and 21.

2. The rAAV vector of claim 1, wherein the polynucleotide comprises any one of the sequences set forth as SEQ ID NOs: 6-8, 16, and 21.

3. An rAAV vector for delivering two or more transgenes into the heart of a subject, wherein said vector comprises a polynucleotide that comprises two or more transgenes, wherein a first transgene encodes an S100 family protein and a second transgene encodes a cardiac Apoptosis Repressor with Caspase Recruitment Domain (cARC),

and wherein the first transgene comprises a nucleotide sequence that is at least 90%, at least 95%, or at least 99.5% identical to any one of the sequences set forth as SEQ ID NOs: 5, 8, and 19-21, and the second transgene comprises a nucleotide sequence that is at least 90%, at least 95%, or at least 99.5% identical to any one of the sequences set forth as SEQ ID NOs: 6, 7, and 15-18.

4. The rAAV vector of claim 3, wherein the second transgene comprises any one of the sequences set forth as SEQ ID NOs: 6 and 7.

5. The rAAV vector of claim 3 or 4, wherein the S100 family protein is cardiac S100 calcium-binding protein A1 (cS100A1) or a variant thereof.

6. The rAAV vector of any one of claims 3-5, wherein the first transgene comprises the nucleotide sequence set forth as SEQ ID NO: 5.

7. The rAAV vector of any one of claims 3-5, wherein the first transgene comprises the nucleotide sequence set forth as SEQ ID NO: 8.

8. The rAAV vector of any one of claims 3-7, wherein an Internal Ribosome Entry Site (IRES) is present between the cS100A1 transgene and cARC transgene.

9. The rAAV vector of any one of claims 1-8, wherein the transgene is operably linked to a promoter; optionally wherein the promoter is a cardiac-restricted promoter selected from cardiac troponin C, cardiac troponin I, and cardiac troponin T (cTnT).

10. The rAAV vector of claim 9, wherein the promoter is a cardiac-restricted promoter derived from a gene selected from the group consisting of: α-myosin heavy chain gene, 6-myosin heavy chain gene, myosin light chain 2v gene, myosin light chain 2a gene, CARP gene, cardiac α-actin gene, cardiac m2 muscarinic acetylcholine gene, ANF, cardiac sarcoplasmic reticulum Ca-ATPase gene, and skeletal α-actin; or is an artificial cardiac promoter derived from MLC-2v gene; optionally wherein the promoter is cTnT.

11. The rAAV vector of any one of claims 1-10, wherein the rAAV vector is self-complementary.

12. The rAAV vector of any one of claims 1-11, wherein the vector comprises a nucleotide sequence that is at least 80%, at least 90%, at least 95% or at least 99.5% identical to any one of the sequences set forth in SEQ ID NOs: 9-12; optionally wherein the vector comprises the nucleotide sequence set forth as SEQ ID NO: 12.

13. An rAAV particle comprising the rAAV vector of any one of claims 1-12 encapsidated in an AAV capsid.

14. The rAAV particle of claim 13, wherein the AAV capsid comprises a capsid protein from the AAV1, AAV2, AAV3, AAV6, AAV8, AAVrh.74, AAVrh.10, AAV2/6 or AAV9 serotypes; optionally wherein the AAV capsid comprises a capsid protein from the AAVrh.10 serotype.

15. A composition comprising the rAAV particle of claim 13 or 14.

16. Use of the rAAV particle of any one of claims 13 or 14 or the composition of claim 15 for the preparation of a medicament for treating a human subject suffering from a heart disease.

17. The use of claim 16, wherein the heart disease causes heart failure in the subject.

18. The use of claim 16 or 17, wherein the heart disease is cardiomyopathy; optionally wherein the heart disease is hypertrophic cardiomyopathy or dilated cardiomyopathy.

19. The use of claim 16 or 17, wherein the heart disease is acute ischemia.

20. The use of any one of claims 16-19, wherein the medicament is to be administered via injection into the heart of the subject or intravascular injection into the coronary arteries of the subject.

21. The use of any one of claims 16-20, wherein the medicament results in expression of the two or more transgenes in the subject's heart.

22. The rAAV vector of any one of claims 3-10, wherein the transgene comprising an S100 family protein is positioned 5′ to the transgene comprising the cARC.

23. The rAAV vector of any one of claims 3-12, wherein the transgene comprising the cARC is positioned 5′ to the transgene comprising an S100 family protein.

24. The rAAV vector of any one of claims 1-15 and 22-23, wherein the vector comprises a nucleotide sequence that is at least 80%, at least 90%, at least 95% or at least 99.5% identical to any of the sequences set forth as SEQ ID NOs: 9-12; optionally wherein the vector comprises the nucleotide sequence set forth as SEQ ID NO: 11.

25. The rAAV vector of claim 24, wherein the vector comprises any one of the nucleotide sequences set forth as SEQ ID NOs: 9, 10, and 12.

26. The use of any one of claims 16-21, wherein the medicament results in improved cardiac function in the subject.

27. The use of any one of claims 16-21 and 26, wherein medicament results in improved cardiac function in the subject for more than 10 months.

28. The rAAV vector of any one of claims 1-15 and 22-25, wherein the rAAV vector encodes a protein comprising an amino acid sequence at least 90%, at least 95%, or at least

99.5% identical to SEQ ID NO: 13 or 14; optionally wherein the rAAV vector encodes a protein comprising the amino acid sequence of SEQ ID NO: 13 or 14.