CLAIMS

1. A recombinant adeno-associated virus (rAAV) nucleic acid vector for delivering two or more transgenes into the heart of a subject, wherein said vector comprises, from 5' to 3', in order, a first adeno-associated virus (AAV) inverted terminal repeat (ITR) sequence, two or more transgenes and a promoter operably linked to the two or more transgenes, a polyadenylation signal, and a second AAV inverted terminal repeat (ITR) sequence, wherein the two or more transgenes comprise an S100 family protein and an apoptotic inhibitor.

2. The rAAV vector of claim 1, wherein the S100 family protein is cardiac S100 calcium-binding protein A1 (cS100A1) or a variant thereof.

3. The rAAV vector of claim 1 or 2, wherein the apoptotic inhibitor is cardiac Apoptosis Repressor with Caspase Recruitment Domain (cARC) or a variant thereof.

4. The rAAV vector of any one of claims 1-3, wherein an Internal Ribosome Entry Site (IRES) is present between the S100 family protein transgene and the apoptotic inhibitor transgene.

5. The rAAV vector of any one of claims 1-4, wherein the transgenes are species-specific.

6. The rAAV vector of any one of claims 1-5, wherein the promoter is a cardiac-restricted promoter.

7. The rAAV vector of claim 6, wherein the cardiac-restricted promoter is selected from the group of genes 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 troponin C, cardiac troponin I, cardiac troponin T (cTnT), cardiac sarcoplasmic reticulum Ca-ATPase gene, and skeletal α-actin, and an artificial cardiac promoter derived from MLC-2v gene.

8. The rAAV vector of claim 6 or 7, wherein the cardiac-restricted promoter is cTnT.

9. An rAAV particle comprising the rAAV vector of any one of claims 1-8 encapsidated in an AAV capsid.

10. The rAAV particle of claim 9, wherein the AAV capsid comprises a capsid protein selected from AAV1, AAV2, AAV3, AAV6, AAV8, AAV9, and AAVrh.10 capsid proteins.

11. A composition comprising the rAAV particle of claim 9 or 10.

12. Use of the composition of claim 11, or the rAAV particle of claim 9 or 10, in the preparation of a medicament for the treatment of heart disease in a subject.

13. The use of claim 12, wherein the heart disease causes heart failure in the subject.

14. The use of claim 12 or 13, wherein the heart disease is acute ischemia or a cardiomyopathy.

15. The method of any one of claims 12-14, wherein the heart disease is hypertrophic cardiomyopathy or dilated cardiomyopathy.

16. The use of any one of claims 12-15, wherein the composition is formulated for administration via injection into the heart of the subject.

17. The use of any one of claims 12-16, wherein the subject is a mammal.

18. The method of claim 17, wherein the mammal is a human.

19. The method of claim 17, wherein the mammal is a dog or a cat.

20. The rAAV vector of any one of claims 1-8, wherein the transgene comprising an S100 family protein is positioned 5’ to the transgene comprising an apoptotic inhibitor.

21. The rAAV vector of any one of claims 1-8, wherein the transgene comprising an apoptotic inhibitor is positioned 5’ to the transgene comprising an S100 family protein.