Claims

What is claimed is:

1. A recombinant adeno-associated virus (rAAV) virion, comprising:
    a) an AAV5 capsid protein, wherein the capsid protein comprises an S651A substitution compared to a parental AAV5 capsid; and
    b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.

2. The rAAV virion of claim 1, wherein the AAV5 capsid protein further comprises one or more substitutions selected from T578A, T578G, T578V, T578L, T578I, T582A, T582G, T582V, T582L, and T582I.

3. The rAAV virion of claim 2, wherein the AAV5 capsid protein further comprises two or more substitutions selected from T578A, T578V, T582A and T582V.

4. The rAAV virion of claim 2, wherein the AAV5 capsid protein comprises T582A and S651A substitutions.

5. The rAAV virion of claim 2, wherein the AAV5 capsid protein comprises T578A and S651A substitutions.

6. The rAAV virion of claim 2, wherein the AAV5 capsid protein comprises S651A, T578A, and T582A substitutions.

7. The rAAV virion of any one of claims 1 to 6, wherein the AAV5 capid protein shares at least 95% identity, at least 98% identity, or at least 99% identity to SEQ ID NO: 73.

8. An AAV5 capsid protein comprising an S651A substitution compared to a parental AAV5 capsid.

9. The AAV5 capsid protein of claim 8, wherein the AAV5 capsid protein further comprises one or more substitutions selected from T578A, T578G, T578V, T578L, T578I, T582A, T582G, T582V, T582L, and T582I.

10. The AAV5 capsid protein of claim 9, wherein the capsid protein further comprises two or more substitutions selected from T578A, T578V, T582A and T582V.

11. The AAV5 capsid protein of claim 9, wherein the capsid protein comprises T582A and S651A substitutions.

12. The AAV5 capsid protein of claim 9, wherein the capsid protein comprises T578A and S651A substitutions.

13. The AAV5 capsid protein of claim 9, wherein the capsid protein comprises S651A, T578A, and T582A substitutions.

14. The AAV5 capsid protein of any one of claims 8 to 13, wherein the capid protein shares at least 90% identity to SEQ ID NO: 73.

15. The AAV5 capsid protein of any one of claims 8 to 13, wherein the capid protein shares at least 95% identity, at least 98% identity, or at least 99% identity to SEQ ID NO: 73.

16. A polynucleotide encoding the AAV5 capsid protein of any one of claims 8 to 15.

17. A pharmaceutical composition comprising the rAAV virion of any one of claims 1 to 7.

18. An *in vitro* method of transducing a cardiac cell, comprising contacting the cardiac cell with an rAAV virion according to any one of claims 1 to 7, wherein the rAAV virion transduces the cardiac cell.

19. An *in vitro* method of delivering one or more gene products to a cardiac cell, comprising contacting the cardiac cell with an rAAV virion according to any one of claims 1 to 7, wherein the cardiac cell expresses the gene product.

20. The method of claim 18 or claim 19, wherein the one or more gene products comprise a polypeptide, optionally selected from cardiac troponin T; a cardiac sarcomeric protein; β-myosin heavy chain; myosin ventricular essential light chain 1; myosin ventricular regulatory light chain 2; cardiac α-actin; a-tropomyosin; cardiac troponin I ; cardiac myosin binding protein C; four-and-a-half LIM protein 1; titin; 5'-AMP-activated protein kinase subunit gamma-2; troponin I type 3, myosin light chain 2, actin alpha cardiac muscle 1; cardiac LIM protein; caveolin 3 (CAV3); galactosidase alpha (GLA); lysosomal-associated membrane protein 2 (LAMP2); mitochondrial transfer RNA glycine (MTTG); mitochondrial transfer RNA isoleucine (MTTI); mitochondrial transfer RNA lysine (MTTK); mitochondrial transfer RNA glutamine (MTTQ); myosin light chain 3 (MYL3); troponin C (TNNC1); transthyretin (TTR); sarcoendoplasmic reticulum calcium-ATPase 2a

(SERCA2a); stromal-derived factor-1 (SDF-1); adenylate cyclase-6 (AC6); β-ARKct (β-adrenergic receptor kinase C terminus); fibroblast growth factor (FGF); platelet-derived growth factor (PDGF); vascular endothelial growth factor (VEGF); hepatocyte growth factor; hypoxia inducible growth factor; thymosin beta 4 (TMSB4X); nitric oxide synthase-3 (NOS3); apoplipoprotein-E (ApoE); and superoxide dismutase (SOD); S100A1

21. The method of claim 18 or claim 19, wherein the one or more gene products comprise one or more reprogramming factors, optionally selected from ASCL1, MYOCD, MEF2C, TBX5, CCNB1, CCND1, CDK1, CDK4, AURKB, OCT4, BAF60C, ESRRG, GATA4, GATA6, HAND2, IRX4, ISLL, MESP1, MESP2, NKX2.5, SRF, TBX20, and ZFPM2.

22. The method of claim 21, wherein the method reprograms the cardiac cell into a cardiac cardiomyocyte.

23. Use of a pharmaceutical composition according to claim 17 in the manufacture of a medicament for treating a cardiac pathology in a subject in need thereof.

24. The use of claim 23, wherein the medicament is to be administered by epicardial injection.

25. The use of claim 3, wherein the medicament is to be administered by intravenouss injection, intramuscular injection, intraperitoneal injection, intracardiac injection, intracardiac catheterization, direct intramyocardial injection, transvascular administration, antegrade intracoronary injection, retrograde injection, transendomyocardial injection, or molecular cardiac surgery with recirculating delivery (MCARD).