

We Claim:

1. A recombinant adeno-associated virus (rAAV) vector comprising in 5' to 3' direction:
 - a) a first AAV ITR sequence;
 - b) a promoter sequence;
 - c) a transgene nucleic acid molecule, wherein the transgene nucleic acid molecule comprises a nucleic acid sequence encoding for a plakophilin-2 (PKP2) polypeptide;
 - d) a post-transcriptional regulatory element;
 - e) a polyA sequence; and
 - f) a second AAV ITR sequence.
2. An rAAV vector comprising the nucleic acid sequence set forth in SEQ ID NO: 9, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 29, or SEQ ID NO: 30.
3. The rAAV vector of claim 1, wherein the PKP2 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 13.
4. The rAAV vector of any one of the preceding claims, wherein the nucleic acid sequence encoding for a PKP2 polypeptide comprises the nucleic acid sequence set forth in SEQ ID NO: 4 or SEQ ID NO: 14.
5. The rAAV vector of any one of the preceding claims, wherein the first AAV ITR sequence comprises the nucleic acid sequence set forth in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 15, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, or SEQ ID NO: 25.
6. The rAAV vector of any one of the preceding claims, wherein the second AAV ITR sequence comprises the nucleic acid sequence set forth in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 15, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, or SEQ ID NO: 25.

7. The rAAV vector of any one of the preceding claims, wherein the promoter sequence is a cardiac-specific promoter sequence.
8. The rAAV vector of any one of the preceding claims, wherein the promoter sequence comprises a Rous sarcoma virus (RSV) LTR promoter (optionally with the RSV enhancer), a cytomegalovirus (CMV) promoter, an SV40 promoter, a dihydrofolate reductase promoter, a beta-actin promoter, a phosphoglycerol kinase (PGK) promoter, a U6 promoter, an H1 promoter, a CAG promoter, a hybrid chicken β -actin promoter, an MeCP2 promoter, an EF1 promoter, a ubiquitous chicken β -actin hybrid (CBh) promoter, a U1a promoter, a U1b promoter, an MeCP2 promoter, an MeP418 promoter, an MeP426 promoter, a minimal MeCP2 promoter, a VMD2 promoter, an mRho promoter, EFla promoter, Ubc promoter, human β -actin promoter, TRE promoter, Ac5 promoter, Polyhedrin promoter, CaMKIIa promoter, Gal1 promoter, TEF1 promoter, GDS promoter, ADH1 promoter, Ubi promoter, or α -1-antitrypsin (hAAT) promoter.
9. The rAAV vector of claim 8, wherein the promoter sequence comprises a cardiac troponin T (cTnT) promoter sequence.
10. The rAAV vector of claim 9, wherein the cTnT promoter sequence comprises the nucleic acid sequence set forth in SEQ ID NO: 2.
11. The rAAV vector of any one of the preceding claims, wherein the polyA sequence comprises a rabbit beta-globin polyA sequence.
12. The rAAV vector of claim 11, wherein the rabbit beta-globin polyA sequence comprises the nucleic acid sequence set forth in SEQ ID NO: 6.
13. The rAAV vector of any one of the preceding claims, wherein the post-transcriptional regulatory element is an oPRE post-transcriptional regulatory element.
14. The rAAV vector of claim 13, wherein the oPRE post-transcriptional regulatory element comprises the nucleic acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 27, or SEQ ID NO: 28.

15. An rAAV vector of any one of the preceding claims, comprising, in the 5' to 3' direction:

- a) a first AAV ITR sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 7;
- b) a promoter sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 2;
- c) a transgene nucleic acid molecule, wherein the transgene nucleic acid molecule comprises a nucleic acid sequence encoding for a PKP2 polypeptide, wherein the nucleic acid sequence encoding for a PKP2 polypeptide comprises the nucleic acid sequence set forth in SEQ ID NO: 4;
- d) a post-transcriptional regulatory element comprising the nucleic acid sequence set forth in SEQ ID NO: 5;
- e) a polyA sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 6; and
- f) a second AAV ITR sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 8.

16. An rAAV viral vector comprising

- (i) an AAV capsid protein; and
- (ii) an rAAV vector of any one of the preceding claims.

17. The rAAV viral vector of claim 16, wherein the AAV capsid protein is an AAV1 capsid protein, an AAV2 capsid protein, an AAV4 capsid protein, an AAV5 capsid protein, an AAV6 capsid protein, an AAV7 capsid protein, an AAV8 capsid protein, an AAV9 capsid protein, an AAV10 capsid protein, an AAV11 capsid protein, an AAV12 capsid protein, an AAV13 capsid protein, an AAVPHP.B capsid protein, an AAVrh74 capsid protein or an AAVrh10 capsid protein.

18. The rAAV viral vector of claim 17, wherein the AAV capsid protein is an AAV9 or AAVrh10 capsid protein.

19. A pharmaceutical composition comprising:
- a) the rAAV viral vector of any one of claims 16-18; and at least one pharmaceutically acceptable excipient and/or additive.
20. The rAAV viral vector of any one of claims 16-18 or the pharmaceutical composition of claim 19 for use in therapy.
21. The rAAV viral vector or the pharmaceutical composition of claim 20, wherein the rAAV viral vector or the pharmaceutical composition is to be administered to the subject at a dose ranging from about 1.0×10^{12} vg/kg to about 2.5×10^{14} vg/kg.
22. The rAAV viral vector or the pharmaceutical composition of claim 21, wherein the rAAV viral vector or the pharmaceutical composition is to be administered to the subject at a dose ranging from about 1.0×10^{12} vg/kg to about 5.0×10^{13} vg/kg.
23. The rAAV viral vector or the pharmaceutical composition of any one of claims 20-22, wherein the rAAV viral vector or the pharmaceutical composition is to be administered to the subject intravenously, intrathecally, intracerebrally, intraventricularly, intranasally, intratracheally, intra-aurally, intra-ocularly, or peri-ocularly, orally, rectally, transmucosally, inhalationally, transdermally, parenterally, subcutaneously, intradermally, intramuscularly, intracisternally, intranervally, intrapleurally, topically, intralymphatically, intracisternally or intranerve.
24. Use of the rAAV viral vector of any one of claims 16-18 or the pharmaceutical composition of claim 18 in the manufacture of a medicament for treating a disease and/or disorder involving a *PKP2* gene in a subject in need thereof.
25. The use of claim 24, wherein the disease and/or disorder involving a *PKP2* gene is ARVC.
26. The use of any one of claims 24-25, wherein the rAAV viral vector or the pharmaceutical composition is for administration to the subject at a dose ranging from about 1.0×10^{12} vg/kg to about 2.5×10^{14} vg/kg.

27. The use of any of claims 24-26, wherein the rAAV viral vector or the pharmaceutical composition is for administration to the subject at a dose ranging from about 1.0×10^{12} vg/kg to about 5.0×10^{13} vg/kg.

28. The use of any one of claims 24-27, wherein the rAAV viral vector or the pharmaceutical composition is for administration to the subject intravenously, intrathecally, intracerebrally, intraventricularly, intranasally, intratracheally, intra-aurally, intra-ocularly, or peri-ocularly, orally, rectally, transmucosally, inhalationally, transdermally, parenterally, subcutaneously, intradermally, intramuscularly, intracisternally, intranervally, intrapleurally, topically, intralymphatically, intracisternally or intranerve.

29. The use of claim 28, wherein the rAAV viral vector or pharmaceutical composition is for administration intravenously.