

What is claimed is:

1. A gene therapy vector adapted for expressing a nucleic acid sequence within cardiomyocytes of a subject, the nucleic acid sequence comprising:
 - a first sequence encoding for PKP2 or a functional variant thereof, wherein the first sequence is codon-optimized; and
 - a second sequence comprising a cardiac-specific promoter,wherein the PKP2 or functional variant localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the gene therapy vector to cardiomyocytes that are haploinsufficient with respect to PKP2 results in at least a 1.5-fold, 2-fold, 2.5-fold, 3-fold, 4-fold, or 5-fold increase in total desmosomal expression of PKP2 by the cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.
2. A gene therapy vector adapted for expressing a nucleic acid sequence within cardiomyocytes of a subject, the nucleic acid sequence comprising:
 - a first sequence encoding for PKP2 or a functional variant thereof, wherein the first sequence is codon-optimized; and
 - a second sequence comprising a cardiac-specific promoter,wherein the PKP2 or functional variant localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the gene therapy vector to cardiomyocytes that are haploinsufficient results in total desmosomal expression of the PKP2 that is at least 50% of total desmosomal expression by non-haploinsufficient cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.
3. The gene therapy vector of either claim 1 or claim 2, wherein the gene therapy vector comprises a viral vector.
4. The gene therapy vector of claim 3, wherein the viral vector comprises one or more of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, variations thereof, and combinations thereof.
5. The gene therapy vector of claim 3, wherein the viral vector comprises AAV6 or AAV9.

6. The gene therapy vector of any one of claims 1-5, wherein the cardiac-specific promoter comprises TNNT2 or a functional sequence having at least 99%, 95%, 90%, 85%, 80%, 75%, or 70% similarity.
7. The gene therapy vector of any one of claims 1-5, wherein the subject is a human subject.
8. A therapeutic formulation for treating or preventing cardiomyopathy in a subject, the therapeutic formulation comprising:
 - a pharmaceutically acceptable excipient or carrier; and
 - a viral vector comprising a nucleic acid sequence encoding for PKP2 or a functional variant thereof, wherein the nucleic acid sequence is codon-optimized,
 - wherein the PKP2 or functional variant localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the therapeutic formulation to cardiomyocytes that are haploinsufficient with respect to PKP2 results in at least a 1.5-fold, 2-fold, 2.5-fold, 3-fold, 4-fold, or 5-fold increase in total desmosomal expression of PKP2 by the cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.
9. A therapeutic formulation for treating or preventing cardiomyopathy in a subject, the therapeutic formulation comprising:
 - a pharmaceutically acceptable excipient or carrier; and
 - a viral vector comprising a nucleic acid sequence encoding for PKP2 or a functional variant thereof, wherein the nucleic acid sequence is codon-optimized,
 - wherein the PKP2 or functional variant localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the therapeutic formulation vector to cardiomyocytes that are haploinsufficient results in total desmosomal expression of the PKP2 that is at least 50% of total desmosomal expression by non-haploinsufficient cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.
10. The therapeutic formulation of either claim 8 or claim 9, further comprising:
 - one or more additional viral vectors each comprising a nucleic acid sequence encoding for one or more non-PKP2 sarcomeric proteins or functional variants thereof.

11. The therapeutic formulation of any one of claims 8-10, wherein the subject is a human subject.

12. The gene therapy vector or therapeutic formulation of any one of claims 1-11, wherein the PKP2 is PKP2 isoform 2a.

13. The gene therapy vector or therapeutic formulation of any one of claims 1-11, wherein the PKP2 is PKP2 isoform 2b.

14. A therapeutic formulation for treating or preventing cardiomyopathy in a subject, the therapeutic formulation comprising:

a pharmaceutically acceptable excipient or carrier;

a first viral vector comprising a first nucleic acid sequence encoding for PKP2 isoform 2a or a functional variant thereof, wherein the first nucleic acid sequence is codon-optimized; and

a second viral vector comprising a second nucleic acid sequence encoding for PKP2 isoform 2b or a functional variant thereof, wherein the second nucleic acid sequence is codon-optimized,

wherein the PKP2 isoform 2a, PKP2 isoform 2b, or functional variants, localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the therapeutic formulation to cardiomyocytes that are haploinsufficient with respect to PKP2 isoform 2a or isoform 2b results in at least a 1.5-fold, 2-fold, 2.5-fold, 3-fold, 4-fold, or 5-fold increase in total desmosomal expression of PKP2 isoform 2a or isoform 2b by the cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.

15. A therapeutic formulation for treating or preventing cardiomyopathy in a subject, the therapeutic formulation comprising:

a pharmaceutically acceptable excipient or carrier;

a first viral vector comprising a first nucleic acid sequence encoding for PKP2 isoform 2a or a functional variant thereof, wherein the first nucleic acid sequence is codon-optimized;

a second viral vector comprising a second nucleic acid sequence encoding for PKP2 isoform 2b or a functional variant thereof, wherein the second nucleic acid sequence is codon-optimized,

wherein the PKP2 isoform 2a, PKP2 isoform 2b, or functional variants, localizes to the desmosome when expressed in the cardiomyocytes, and wherein delivery of the therapeutic

formulation vector to cardiomyocytes that are haploinsufficient results in total desmosomal expression of PKP2 isoform 2a or isoform 2b that is at least 50% of total desmosomal expression by non-haploinsufficient cardiomyocytes of one or more desmosomal proteins, wherein the one or more desmosomal proteins are selected from desmoplakin 1, desmoplakin 2, desmocollin 2, plakoglobin, desmoglein 2, and connexin 43.

16. An isolated cell transduced with the gene therapy vector of any one of claims 1-7.

17. The isolated cell of claim 16, wherein the cell is a human cell.

18. The isolated cell of claim 16, wherein the cell is a cardiac cell.

19. The isolated cell of claim 16, wherein the cell is a human induced pluripotent stem cell-derived cardiomyocyte.