

CLAIMS

1. A nucleic acid comprising an expression cassette comprising a human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element, wherein the expression cassette is flanked on each side by an inverted terminal repeat sequence.
2. The nucleic acid of Claim 1, wherein:
 - (i) the human TNNT2 coding sequence is codon-optimized for expression in human cells;
 - (ii) the human TNNT2 coding sequence has at least about 85% sequence identity to the sequence set forth in SEQ ID NOs: 7-27 arranged in sequence; SEQ ID NOs: 53-71 arranged in sequence; SEQ ID NOs: 78-95 arranged in sequence; or SEQ ID NOs: 104-121 arranged in sequence; and/or
 - (iii) the promoter comprises a cardiac specific promoter, optionally wherein (a) the promoter is selected from the group consisting of: a TNNT2 promoter, a Desmin (DES1) promoter, and combinations thereof, and/or (b) the promoter sequence has at least about 85% sequence identity to the sequence of SEQ ID NO: 3, 77, or 102.
3. The nucleic acid of Claim 1, wherein:
 - (i) the expression cassette has at least about 85% sequence identity to the sequence of SEQ ID NOs: 1-31, or SEQ ID NOs: 47-75, or SEQ ID NOs: 76-98, or SEQ ID NOs: 99-124, or SEQ ID NOs: 125-132, or SEQ ID NOs: 133-141 arranged in sequence; or
 - (ii) the expression cassette comprises the sequence of SEQ ID NOs: 1-31 arranged in sequence, or SEQ ID NOs: 47-75 arranged in sequence.
4. An rAAV for use in treating dilated cardiomyopathy or hypertrophic cardiomyopathy, wherein a therapeutically effective amount of the rAAV is to be administered, wherein the rAAV comprises a nucleic acid expression construct comprising a human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element, wherein the expression construct is flanked on each side by an inverted terminal repeat sequence, and
wherein said administration results in expression of a therapeutically effective amount of human TNNT2 thereby treating the dilated cardiomyopathy or hypertrophic cardiomyopathy;

optionally wherein the rAAV is to be administered via intravenous injection, and/or between about 1×10^{13} and about 1×10^{14} rAAV vector genomes are to be administered.

5. A plurality of rAAV particles for use in inducing increased expression of human TNNT2 in a target cell,

wherein the target cell is to be contacted with the plurality of rAAV particles, wherein the rAAV particles comprise a nucleic acid expression cassette comprising a functional human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element, wherein the expression construct is flanked on each side by an inverted terminal repeat sequence, and

wherein said contacting results in the target cell increasing expression of functional human TNNT2 as compared to prior to the contacting, thereby increasing the expression of functional human TNNT2.

6. An rAAV for use in treating dilated cardiomyopathy or hypertrophic cardiomyopathy, wherein a therapeutically effective amount of rAAV comprising a nucleic acid expression construct comprising a human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element is to be administered, wherein the expression construct is flanked on each side by an inverted terminal repeat sequence, and

wherein said administration results in expression of a therapeutically effective amount of human TNNT2 thereby treating the dilated cardiomyopathy or hypertrophic cardiomyopathy;

optionally wherein a therapeutically effective amount of a silencing construct is to be further administered, optionally wherein the silencing construct comprises an shRNA.

7. A nucleic acid comprising an expression cassette comprising a silencing element and a human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element, wherein the expression cassette is flanked on each side by an inverted terminal repeat sequence, optionally wherein the silencing element encodes an shRNA; wherein:

- (i) the human TNNT2 coding sequence is codon-optimized for expression in human cells;
- (ii) the human TNNT2 coding sequence has at least about 85% sequence identity to the sequence set forth in SEQ ID NOs: 7-27 arranged in sequence; SEQ ID NOs: 53-71 arranged in

sequence; SEQ ID NOs: 78-95 arranged in sequence; or SEQ ID NOs: 104-121 arranged in sequence; and/or

(iii) the promoter comprises a cardiac specific promoter, optionally wherein (a) the promoter is selected from the group consisting of: a TNNT2 promoter, an MHCK9 (MCK) promoter, a Desmin (DES1) promoter, and combinations thereof; and/or (b) the promoter sequence has at least about 85% sequence identity to the sequence of SEQ ID NO: 3, 77, or 102 (iv) the nucleic acid has at least about 85% sequence identity to the sequence set forth in SEQ ID NOs: 1-31 arranged in sequence; or SEQ ID NOs: 47-75 arranged in sequence; or SEQ ID NOs: 76-98 arranged in sequence; or SEQ ID NOs: 99-124 arranged in sequence; or SEQ ID NOs: 125-132 arranged in sequence; or SEQ ID NOs: 133-141 arranged in sequence.

8. The nucleic acid of any one of Claims 1 to 3 and 7, wherein the nucleic acid is a recombinant adeno-associated virus (rAAV) vector, optionally wherein the nucleic acid is a single-stranded or self-complementary rAAV vector.

9. A recombinant adeno-associated virus (rAAV) particle comprising the nucleic acid of any one of claims 1 to 3, 7, and 8.

10. The rAAV particle of Claim 9, wherein the rAAV particle is an AAV9 particle, an AAVrh74 particle, or an AAVrh10 particle.

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

12. A nucleic acid comprising an expression construct comprising:
a human TNNT2 coding sequence;
a cardiac enhancer element operable linked to a promoter; and
a Kozak sequence, wherein the Kozak sequence enhances transgene expression in the heart, wherein the expression construct is flanked on each side by an inverted terminal repeat sequence, wherein the Kozak sequence is non-native with respect to the human TNNT2 coding sequence, the cardiac enhancer element, and/or the promoter.

13. The nucleic acid of claim 12, wherein the Kozak sequence is a synthetic sequence and has at least 85% sequence identity to the sequence of SEQ ID NO: 128.
14. The nucleic acid of claim 12, wherein the Kozak sequence is a synthetic sequence and has at least 85% sequence identity to the sequence of SEQ ID NO: 189.
15. Use of an rAAV in the manufacture of a medicament for the treatment of dilated cardiomyopathy or hypertrophic cardiomyopathy, wherein a therapeutically effective amount of the rAAV is to be administered, wherein the rAAV comprises a nucleic acid expression construct comprising a human TNNT2 coding sequence operably linked to a promoter and optionally an enhancer element, wherein the expression construct is flanked on each side by an inverted terminal repeat sequence, and wherein said administration results in expression of a therapeutically effective amount of human TNNT2 thereby treating the dilated cardiomyopathy or hypertrophic cardiomyopathy.