CLAIMS

1. A modified cardiac troponin T promoter, comprising a polynucleotide having between 300 bp and 500 bp.

2. The promoter of claim 1, wherein the polynucleotide comprises a sequence that shares at least 80%, at least 90%, or 100% identity to any one of SEQ ID NOs: 1-85.

3. The promoter of claim 1, wherein the polynucleotide comprises a sequence that shares at least 80%, at least 90%, or 100% identity to SEQ ID NO: 3.

4. The promoter of claim 1, wherein the polynucleotide shares at least 80%, 90%, 95%, 96%, 97%, 98%, 99%, or and 100% sequence identity with a genomic polynucleotide sequence:

(i) upstream of and including the transcription start site of a troponin T gene; or

(ii) -450 bp to +1 bp, -350 bp to +1 bp, -250 bp to +1 bp, -450 bp to +50 bp, -350 bp to +50 bp, or -250 bp to +50 bp relative to the transcription start site of a troponin T gene;

optionally wherein the troponin T gene is a human troponin T gene.

5. The promoter of any one of claims 1-4, wherein the promoter is:

(i) a muscle-specific promoter; and/or

(ii) a cardiac cell-specific promoter; and/or

(iii) a cardiomyocyte-specific promoter.

6. The promoter of any one of claims 1-5, wherein the promoter has the same cell-type specificity as:

(i) a native troponin T promoter of about 600 bp; and/or

(ii) a reference promoter comprising SEQ ID NO: 1.

7. The promoter of any one of claims 1-6, wherein the promoter expresses a gene product operatively linked thereto at least about 10%, at least about 20%, at least about 30% more than a native troponin T promoter; optionally wherein the native troponin T promoter is a reference promoter comprising SEQ ID NO: 1.

8. A vector comprising the promoter of any one of claims 1-7 operatively linked to a polynucleotide encoding a gene product.

9. The vector of claim 8, wherein the vector is a viral vector; optionally wherein:

the viral vector is an adeno-associated virus vector (AAV) and/or wherein the viral vector has a packaging limit of at most about 5.5 kB;

optionally wherein the AAV vector is AAV9 or a variant thereof.

10. The vector of claim 8 or claim 9, wherein the gene product is selected from:

(i) MYBPC3, KCNH2, TRPM4, DSG2, and ATP2A2 proteins; or

(ii) CACNA1C, DMD, DMPK, EPG5, EVC, EVC2, FBN1, NF1, SCN5A, SOS1, NPR1, ERBB4, VIP, and MYH7 proteins.

11. The vector of any one of claims 8-10, wherein the gene product is a Cas9, optionally selected from SpCas9, St1Cas9, and SaCas9.

12. The vector of any one of claims 8-11, wherein the vector comprises a polynucleotide encoding second gene product; optionally wherein the second gene product is a functional RNA, optionally a microRNA or a guide RNA.

13. An isolated cell comprising the promoter of any one of claims 1-7.

14. The isolated cell of claim 13, wherein the isolated cell is an induced pluripotent stem cell or an isolated cardiomyocyte.

15. A pharmaceutical composition comprising the vector of any one of claims 8-12.

16. A cell therapy composition comprising the cell of claim 13 or claim 14.

17. A recombinant adeno-associated virus (AAV) vector genome, comprising a *MYBPC3* polynucleotide encoding a MYBPC3 protein, or a functional variant thereof, and a promoter, wherein the promoter is the modified cardiac troponin T promoter according to any one of claims 1 to 7.

18. The rAAV vector genome of claim 17, wherein the *MYBPC3* polynucleotide comprises at least about 3.5 kB, comprises about 3.8 kB, is a full-length MYBPC3, or is a truncated MYBPC3.

19. The rAAV vector genome of claim 17 or claim 18, wherein the MYBPC3 is a human MYBPC3.

20. The rAAV vector genome of any one of claims 17-19, wherein the vector expresses MYBPC3 at about the same level as, at least about 10% greater than, or at least about 20% greater than a reference AAV vector comprising a native troponin T promoter of about 600 bp.

21. A recombinant adeno-associated virus (AAV) vector genome, comprising an expression cassette comprising, in 5′ to 3′ order, a 5′ segment comprising a promoter; a polynucleotide encoding a gene product; and a 3′ segment comprising a polyA signal, the expression cassette optionally flanked by one or both of a 5′ inverted terminal repeat (ITR) and a 3′ ITR,

wherein the polynucleotide encoding the gene product comprises between 3 kb and 11kb, between 3 kb and 5kb, between 3.5 kb and 4.5kb, or between 3.7 kb and 4 kb; and

wherein:

a) the 5′ segment and the 3′ segment together comprise at most 0.8 kbp or at most 0.9 kbp;

b) the 5′ ITR, 5′ segment, the 3′ segment, and 3′ ITR together comprise or at most 1.2 kbp, at most 1.3 kbp; and/or

c) the vector genome comprises at most 4.7 kbp, at most 4.8 kbp, at most 4.9 kbp, at most 5.0 kbp, or at most 5.2 kbp.

22. The rAAV vector genome of claim 21, wherein the 5′ segment comprises at most 500 bp or at most 480 bp and/or wherein 3′ segment comprises at most 200 bp or at most 150 bp.

23. The rAAV vector genome of claim 21 or claim 22, wherein the polynucleotide encoding the gene product comprises 3.7 kbp to 3.9 kbp, optionally 3.8 kbp.

24. The rAAV vector genome of any one of claims 21-23, wherein the gene product is MYBPC3, or functional variant thereof; optionally wherein

the polynucleotide encoding MYBPC3 shares at least 90% identity to SEQ ID NO: 86, at least 95% identity to SEQ ID NO: 86, or is SEQ ID NO: 86; and /or

MYBPC shares at least 90% identity to the polypeptide sequence of SEQ ID NO: 103, at least 95% identity to the polypeptide sequence of SEQ ID NO: 103, or is the polypeptide sequence of SEQ ID NO: 103.

25. The rAAV vector genome of any one of claim 21-24, wherein the promoter is promoter is the modified cardiac troponin T promoter according to any one of claims 1 to 8.

26. The rAAV vector genome of claim 25, wherein:

(i) the promoter comprises a sequence that shares at least 80% identity, at least 90% identity, or 100% identity to SEQ ID NO: 91; and/or

(ii) the polyA signal comprises, consists essentially of, or consists of a sequence that shares at least 90% identity to, at least 95% identity to, or is SEQ ID NO: 92.

(iii) the 5′ segment shares at least 80% identity to, at least 90% identity to, at least 95% identity to, or is SEQ ID NO: 93; and/or

(iv) the 3′ segment shares at least 80% identity, at least 90% identity to, shares at least 95% identity to, or is SEQ ID NO: 94.

27. The rAAV vector genome of any one of claims 21-26, wherein the expression cassette shares at least 80% identity to, at least 90% identity to, at least 95% identity to, or is SEQ ID NO: 95; and/or wherein the rAAV vector genome shares at least 80% identity to, at least 90% identity to, at least 95% identity to, or is SEQ ID NO: 102.

28. The AAV vector genome of any one of claims 21-27, wherein the 5′ ITR comprises a sequence that shares 95% identity to SEQ ID NO: 96 and/or the 3′ ITR comprises a sequence that shares at least 95% identity to SEQ ID NO: 97.

29. A recombinant AAV (rAAV) virion, comprising the rAAV vector genome of any one of claims 17-28, and an AAV capsid protein,

optionally wherein the rAAV virion is a serotype AAV9 virion, or a variant thereof, and/or the AAV capsid protein is an AAV9 capsid protein or variant thereof.

30. An *in vitro* or *ex vivo* method of expressing a MYBPC3 protein in a cell, comprising transducing the cell with the rAAV virion of claim 29 or the rAAV vector genome of any one of claims 17-28.

31. The method of claim 30, wherein the cell is a *MYBPC3*$^{-/-}$ cell.

32. The method of claim 30 or claim 31, wherein the cell comprises an inactivating mutation in one or both copies of the endogenous *MYBPC3* gene.

33. An rAAV virion of claim 29 or an rAAV vector genome of any one of claims 17-28, for use as a medicament.

34. An rAAV virion of claim 29 or an rAAV vector genome of any one of claims 17-28, for use in a method of treating and/or preventing a cardiomyopathy in a subject; optionally wherein the cardiomyopathy is hypertrophic cardiomyopathy.

35. An rAAV virion of claim 29 or an rAAV vector genome of any one of claims 17-28, for use in a method of treating and/or preventing a disease or disorder caused by a MYBPC3 mutation in a subject.

36. The rAAV virion or rAAV vector genome for use according to claim 34 or claim 35, wherein the method comprises expressing a MYBPC3 protein and/or increasing MYBPC3 activity and/or increasing cardiac function in the heart of the subject.

37. The rAAV virion or rAAV vector genome for use according to any one of claims 33-36, wherein administration of the rAAV virion or rAAV vector genome causes specific expression of MYBPC3 in the heart of the subject.

38. The rAAV virion or rAAV vector genome for use according to any one of claims 33-37, wherein administration of the rAAV virion or rAAV vector genome causes low or undetectable expression of MYBPC3 in the skeletal tissue, brain, and/or liver of the subject.

39. The rAAV virion or rAAV vector genome for use according to any one of claims 34-38, wherein the subject comprises a MYBPC3 mutation.

40. The rAAV virion or rAAV vector genome for use according to any one of claims 34-39, wherein the method comprises:

(i) intravenous administration of the rAAV virion or rAAV vector genome to the subject;

(ii) intracardiac administration of the rAAV virion or rAAV vector genome to the subject;

(iii) direct injection of the rAAV virion or rAAV vector genome to the subject.

41. The rAAV virion or rAAV vector genome for use according to any one of claims 34-40, wherein the subject is a mammal; optionally wherein the subject is a human.

42. The rAAV virion or rAAV vector genome for use according to any one of claims 34-41, wherein the subject is a juvenile.

43. The rAAV virion or rAAV vector genome for use according to any one of claims 34-41, wherein the subject is an adult.

44. The rAAV virion or rAAV vector genome for use according to any one of claims 33-43, wherein the rAAV virion or rAAV vector genome is administered at a dose of about 10^{11} vg/kg to about 10^{14} vg/kg.