CLAIMS

~~What is claimed is:~~

1. ~~A method of treating a disorder associated with abnormal ryanodine receptor type 2 (RYR2) function, the method comprising administering to a subject in need thereof an effective amount~~ Use of a polypeptide comprising a C-terminal domain of Cardiac Myosin binding protein C (MYBPC3) in the preparation of a medicament for treating a disorder associated with abnormal ryanodine receptor type 2 (RYR2) function in a subject.

2. ~~A method of treating a disorder associated with abnormal ryanodine receptor type 2 (RYR2) function, the method comprising administering to a subject in need thereof an effective amount~~ Use of a nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising a C-terminal domain of Cardiac Myosin binding protein C (MYBPC3) in the preparation of a medicament for treating a disorder associated with abnormal ryanodine receptor type 2 (RYR2) function in a subject.

3. The ~~method~~ use of claim 1 or claim 2, wherein the abnormal RYR2 function is caused by one or more mutations in RYR2.

4. The ~~method~~ use of claim 3, wherein the mutation in RYR2 causes excessive diastolic Ca^{2+} release in cardiomyocytes in the subject.

5. The ~~method~~ use of any one of claims 1-4, wherein the polypeptide comprises an amino acid sequence that is at least 80% identical to any one of SEQ ID NOs: 1-16 or 53-64.

6. The ~~method~~ use of claim 5, wherein the polypeptide comprises the amino acid sequence of any one of SEQ ID NOs: 1-16 or 53-64.

7. The ~~method~~ use of any one of claims 2-6, wherein the nucleotide sequence is operably linked to a promoter.

8. The ~~method~~ use of any one of claims 2-7, wherein the nucleic acid is a vector.

9. The ~~method~~ use of claim 8, wherein the vector is an expression vector.

10. The ~~method~~ use of claim 9, wherein the expression vector is a viral vector.

11. The ~~method~~ use of claim 10, wherein the viral vector is selected from a lentiviral vector, a retroviral vector, or a recombinant adeno-associated virus (rAAV) vector.

12. The ~~method~~ use of claim 11, wherein the viral vector is a rAAV vector further comprising two AAV inverted terminal repeats (ITRs) flanking the nucleotide sequence encoding the polypeptide and the promoter.

13. The ~~method~~ use of claim 11, wherein the rAAV vector is packaged in a rAAV particle.

14. The ~~method~~ use of claim 13, wherein the rAAV particle further comprises a capsid protein.

15. The ~~method~~ use of claim 14, wherein the capsid protein is of a serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV6.2, AAV7, AAV8, AAV9, AAV.rh8, AAV.rh10, AAV.rh39, AAV.43, AAV2/2-66, AAV2/2-84, and AAV2/2-125, or a variant thereof.

16. The ~~method~~ use of claim 15, wherein the capsid protein is of a serotype AAV9.

17. The ~~method~~ use of any one of claims 11-16, wherein the rAAV is a self-complementary AAV (scAAV).

18. The ~~method~~ use of any one of claims 2-12, wherein the nucleotide sequence encoding the polypeptide is codon-optimized.

19. The ~~method~~ use of any one of claims 2-6, wherein the nucleic acid is a messenger RNA (mRNA).

20. The ~~method~~ use of claim 19, wherein the mRNA is a modified mRNA.

21. The ~~method~~ use of any one of claims 1-20, wherein the polypeptide or the nucleic acid is to be delivered to a cardiomyocyte in the subject.

22. The ~~method~~ use of any one of claims 1-21, wherein the disorder is arrhythmia.

23. The ~~method~~ use of claim 22, wherein the arrhythmia is inherited or acquired.

24. The ~~method~~ use of claim 23, wherein the inherited arrhythmia is Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

25. The ~~method~~ use of claim 23, wherein the acquired arrhythmia is a ventricular arrhythmia or a supraventricular arrhythmia.

26. The ~~method~~ use of claim 25, wherein the ventricular arrhythmia is ventricular tachycardia, ventricular fibrillation, or premature ventricular contraction.

27. The ~~method~~ use of claim 25, wherein the supraventricular arrhythmia is atrial fibrillation, atrial flutter, atrial tachycardia, premature atrial contraction, or paroxysmal supraventricular tachycardia.

28. The ~~method~~ use of any one of claims 1-21, wherein the disorder is heart failure.

29. The ~~method~~ use of claim 25, wherein ~~administering~~ the polypeptide or the nucleic acid to be administered to the subject reduces the excessive diastolic Ca^{2+} release in cardiomyocytes in the subject.

30. The ~~method~~ use of any one of claims 1-29, wherein the subject is human.

31. The ~~method~~ use of any one of claims 1-30, wherein the administration~~administering~~ is via injection.

32. ~~A method of treating arrhythmia, the method comprising administering to a subject in need thereof an effective amount~~ Use of a recombinant adeno-associated virus (rAAV) in the preparation of a medicament for treating arrhythmia in a subject, wherein the rAAV comprises a capsid protein of serotype AAV9 and a nucleotide sequence encoding a polypeptide comprising a C-terminal domain of Cardiac Myosin binding protein C (MYBPC3).

33. The ~~method~~ use of claim 32 wherein the polypeptide comprises an amino acid sequence that is at least 80% identical to any one of SEQ ID NOs: 1-16 or 53-64.

34. The ~~method~~ use of claim 32 or claim 33, wherein the polypeptide comprises the amino acid sequence of any one of SEQ ID NOs: 1-16 or 53-64.

35. The ~~method~~ use of claim 32, wherein the polypeptide consists of the amino acid sequence of any one of SEQ ID NOs: 1-16 or 53-64.

36. A recombinant adeno-associated virus (rAAV) comprising a capsid protein and a nucleotide sequence encoding a polypeptide comprising a C-terminal domain of Cardiac Myosin binding protein C (MYBPC3).

37. The rAAV of claim 33, wherein the polypeptide comprises the amino acid sequence of any one of SEQ ID NOs: 1-16 or 53-64.

38. The rAAV of claim 33, wherein the polypeptide consists of the amino acid sequence of any one of SEQ ID NOs: 1-16 or 53-64.

39. Use of the rAAV of any one of claims 36-38 in the preparation of a medicament for ~~claim 33 or claim 34 in~~ treating a disorder associated with abnormal ryanodine receptor type 2 (RYR2) function.