CLAIMS

What is claimed is:

1. A multimeric polypeptide that inhibits CaMKII.

2. The multimeric polypeptide of claim 1, wherein the multimeric polypeptide comprises from about 2 to about 20 repeats of an AIP peptide.

3. The multimeric polypeptide of claim 2, wherein the AIP repeats are contiguous and/or separated by linkers.

4. The multimeric polypeptide of claim 1, wherein the multimeric polypeptide comprises a sequence having at least 85% amino acid sequence identity to:

AIPx3

YKKALHRQEAVDALYKKALHRQEAVDALYKKALHRQEAVDAL; or

AIPx5

YKKALHRQEAVDALYKKALHRQEAVDALYKKALHRQEAVDALYKKALHRQEAVDALYKKALHRQEAVDAL.

5. The multimeric polypeptide of claim 1, wherein the multimeric polypeptide is fused to a 12.6-kDa FK506-binding protein (FKBP12.6) polypeptide.

6. The multimeric polypeptide of claim 1, wherein the EC50 for inhibition of CaMKII by the multimeric polypeptide is less than 10% of the EC50 for AIP.

7. An expression vector comprising a polynucleotide encoding the multimeric polypeptide of any one of claims 1 - 6.

8. The expression vector of claim 7, wherein the multimeric polypeptide is operably linked to a promoter suitable for driving expression of the multimeric polypeptide in a mammalian cardiac cell.

9. A pharmaceutical composition comprising an effective amount of the multimeric polypeptide of any one of claims 1 - 6.

10. A pharmaceutical composition comprising an effective amount of the expression vector of claim 7 or 8.

11. A cell comprising the expression vector of claim 7 or 8.

12. Use of the multimeric polypeptide of any one of claims 1 - 6, or a polynucleotide encoding the multimeric polypeptide of any one of claims 1 – 6, in the manufacture of a medicament for modulating a cardiac arrhythmia in a subject.

13. Use of the multimeric polypeptide of any one of claims 1 to 6, or a polynucleotide encoding the multimeric polypeptide of any one of claims 1 to 6, in the manufacture of a medicament for inhibiting phosphorylation of a ryanodine channel (RYR2) polypeptide in a subject.

14. Use of the multimeric polypeptide of any one of claims 1 to 6, or a polynucleotide encoding the multimeric polypeptide of any one of claims 1 to 6, in the manufacture of a medicament for treating a subject comprising a mutation associated with a cardiac arrhythmia.

15. The use of claim 14, wherein the mutation is in a cardiac ryanodine channel (RYR2).

16. The use of claim 14 or claim 15, wherein the mutation is $RYR2^{R4651I}$.

17. Use of a multimeric AIP polypeptide or a polynucleotide encoding said multimeric AIP polypeptide in the manufacture of a medicament for treating a cardiac disease, condition, or disorder characterized by a cardiac arrhythmia in a subject.

18. Use of an adeno-associated viral vector comprising a polynucleotide encoding a multimeric AIP polypeptide in the manufacture of a medicament for treating a cardiac disease, condition, or disorder characterized by a cardiac arrhythmia in a subject, wherein an effective amount of the adeno-associated viral vector is to be administered to the subject.

19. The use of claim 18, wherein the effective amount is between about $1x10^{10}$ viral genomes/kg and about $1x10^{14}$ viral genomes/kg.

20. Use of a multimeric AIP polypeptide or a polynucleotide encoding said multimeric AIP polypeptide in the manufacture of a medicament for reducing cardiac variability in a subject having atrial fibrillation.

21. The multimeric polypeptide of any one of claims 1 to 6, or a polynucleotide encoding the multimeric polypeptide of any one of claims 1 – 6, for use as a medicament.