

CLAIMS

What is claimed is:

1. A vector, comprising a myocardin (MYOCD) polynucleotide encoding a MYOCD polypeptide and an Achaete-scute homolog 1 (ASCL1) polynucleotide encoding an ASCL1 polypeptide; wherein each polynucleotide is operatively linked to at least one promoter.
2. The vector of claim 1, wherein the vector further comprises a MEF2C polynucleotide encoding an MEF2C polypeptide and/or a TBX5 polynucleotide encoding a TBX5 polypeptide.
3. The vector of claim 1 or claim 2, wherein the MYOCD polynucleotide comprises an internal deletion, and encodes a functional MYOCD polypeptide comprising an internal deletion.
4. The vector of any one of claims 1 to 3, wherein the vector is a viral vector.
5. The vector of claim 4, wherein the vector is an AAV vector.
6. The vector of claim 5, wherein the AAV vector comprises an AAV5 capsid.
7. The vector of claim 4, wherein the vector is lentiviral vector.
8. The vector of any one of claims 1 to 7, wherein the ASCL1 polynucleotide and the MYOCD polynucleotide are operatively linked to the same promoter and are co-translationally expressed.
9. The vector of claim 8, wherein the MYOCD polynucleotide and ASCL1 polynucleotide are linked via a 2A sequence to form a MYOCD-2A-ASCL1 polynucleotide.
10. The vector of claim 8, wherein the MYOCD polynucleotide and ASCL1 polynucleotide are linked via a 2A sequence to form an ASCL1-2A-MYOCD polynucleotide.
11. The vector of any one of claims 1 to 7, wherein the MYOCD polynucleotide is operatively linked to a first promoter, and the ASCL1 polynucleotide is operatively linked to a second promoter.

12. The vector of any one of claims 1 to 11, wherein the MYOCD polynucleotide encodes a MYOCD polypeptide that shares at least 95% identity to SEQ ID NO: 16.
13. The vector of claim 12, wherein the MYOCD polynucleotide encodes a MYOCD polypeptide having the amino acid sequence of SEQ ID NO: 16.
14. The vector of any one of claims 1 to 13, wherein the ASCL1 polynucleotide encodes an ASCL1 polypeptide that shares at least 95% identity SEQ ID NO: 1.
15. The vector of claim 14, wherein the ASCL1 polynucleotide encodes an ASCL1 polypeptide having the amino acid sequence of SEQ ID NO: 1.
16. The vector of claim 9, wherein the MYOCD-2A-ASCL1 polynucleotide encodes a polypeptide that shares at least 95% identity with SEQ ID NO: 59.
17. The vector of claim 16, wherein the MYOCD-2A-ASCL1 polynucleotide encodes a polypeptide having the amino acid sequence of SEQ ID NO: 59.
18. The vector of any one of claims 1-17, which comprises an expression cassette comprising the MYOCD polynucleotide and the ASCL1 polynucleotide, wherein the expression cassette is flanked by two AAV inverted terminal repeats (ITRs).
19. A vector system, comprising:
 - a) a first vector encoding a MYOCD polynucleotide and a MEF6 polynucleotide, and a second vector comprising an ASCL1 polynucleotide;
 - b) a first vector comprising a MYOCD polynucleotide and a TBX5 polynucleotide, and a second vector comprising an ASCL1 polynucleotide;
 - c) a first vector comprising a MYOCD polynucleotide and a second vector comprising an ASCL1 polynucleotide and a MEF6 polynucleotide;
 - d) a first vector comprising a MYOCD polynucleotide and a second vector comprising an ASCL1 polynucleotide and a TBX5 polynucleotide; or
 - e) a first vector of any one of claims 1 to 15, and a second vector comprising a MEF6 polynucleotide and/or a TBX5 polynucleotide;wherein in any a), b), c), d) and e), the MYOCD polynucleotide comprises an internal deletion, and encodes a functional MYOCD polypeptide comprising an internal deletion.

20. A vector system comprising a first vector comprising a MYOCD polynucleotide and a second vector comprising an ASCL1 polynucleotide, when used for:

- (a) inducing a cardiomyocyte (iCM) phenotype in differentiated cells;
- (b) treating a heart condition in a subject suffering from or at risk for the heart condition, wherein the vector system is brought into contact with differentiated cells in vitro to generate iCM cells, and the iCM cells are administered to the subject; or
- (c) treating a heart condition in a subject suffering from or at risk for a heart condition, wherein the vector system is administered to the subject.

21. A pharmaceutical composition comprising the vector or vector system of any one of claims 1 to 20.

22. A method of inducing a cardiomyocyte phenotype in differentiated cells, comprising contacting the differentiated cells with the vector or the vector system of any one of claims 1-20 or the pharmaceutical composition of claim 21.

23. The method of claim 22, wherein the differentiated cells are cardiac fibroblast cells.

24. The method of claim 22 or claim 23, wherein the differentiated cells are in vitro cells during the contacting step.

25. An induced cardiomyocyte (iCM) when produced by the method of any one of claims 22 to 24.

26. A recombinant adeno-associated virus (rAAV), comprising an expression cassette, wherein the expression cassette comprises in 5' to 3' order a 5' inverted terminal repeat (ITR), a CAG promoter, an SV40 intron, a polynucleotide encoding one or more proteins, a short polyadenylation signal, and a 3' ITR, and wherein the polynucleotide encoding one or more proteins comprises in a MYOCD polynucleotide encoding a MYOCD polypeptide, a polynucleotide encoding a P2A linker, and an ASCL1 polynucleotide encoding an ASCL1 polypeptide.

27. The rAAV of claim 26, wherein the MYOCD polypeptide shares at least 95% sequence identity to SEQ ID NO:16, and the ASCL1 polypeptide shares at least 95% sequence identity to SEQ ID NO:1.

28. Use of
- a) the vector or vector system of any one of claims 1 to 20;
 - b) the pharmaceutical composition of claim 21;
 - c) the rAAV of claim 26 or claim 27; or
 - d) iCM generated by contacting differentiated cells in vitro with the vector of any one of claims 1 to 20, the pharmaceutical composition of claim 21 or the rAAV of claim 26 or claim 27; or the iCM of claim 25,
- in the manufacture of a medicament for treating a heart condition in a subject suffering from or at risk for the heart condition.
29. The use of claim 28, wherein the heart condition is selected from the group consisting of chronic myocardial infarction, acute myocardial infarction (AMI), heart failure and chronic ischemic heart failure.
30. The use of claim 28 or claim 29, wherein the medicament treats one or more symptoms, wherein the one or more symptoms comprises a decrease in ejection fraction of the heart of the subject.
31. The use of any one of claims 28 to 30, wherein the medicament is to be administered by intramyocardial injection.