CLAIMS

1. A polynucleotide, comprising an expression cassette and optionally flanking adeno-associated virus (AAV) inverted terminal repeats (ITRs), wherein the polynucleotide comprises a polynucleotide sequence encoding a B-cell Lymphoma 2–Associated Anthanogene 3 (BAG3), or a functional variant thereof, operatively linked to a promoter, optionally wherein the promoter is a heterologous promoter.

2. The polynucleotide of claim 1, wherein the promoter is a cardiac-specific promoter; or

wherein the promoter is a muscle-specific promoter; or

wherein the promoter is a cardiomyocyte-specific promoter; or

wherein the promoter is a Myosin Heavy-chain Creatine Kinase 7 (MHCK7) promoter; or

wherein the promoter is a cardiac troponin T (hTNNT2) promoter; or

wherein the promoter is a human heat shock factor 70 (hHSP70) promoter; or

wherein the promoter is a ubiquitous promoter, optionally a CMV promoter or a CAG promoter or a chicken b-globin promoter or a UBC promoter (SEQ ID NO: 116).

3. The polynucleotide of claim 2, wherein the MHCK7 promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 31.

4. The polynucleotide of claim 2, wherein the hTNNT2 promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 32.

5. The polynucleotide of claim 2, wherein the hHSP70 promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 115.

6. The polynucleotide of any one of claims 1 to 5, wherein the expression cassette comprises exon 1 of the cardiac troponin T (hTNNT2) gene, wherein optionally the hTNNT2 promoter and exon 1 together share at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 32.

7. The polynucleotide of any one of claims 1 to 6, wherein the expression cassette comprises a polyA signal, optionally wherein the polyA signal is a human growth hormone (hGH) polyA; or

wherein the expression cassette comprises a Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE), optionally a mutant or modified WPRE (WPRE(x)), optionally WPRE Mut6 (SEQ ID NO:63).

8. The polynucleotide of any one of claims 1 to 7, wherein the B-cell Lymphoma 2–Associated Anthanogene 3 (BAG3) or functional fragment or variant thereof is a full length or wild-type BAG3.

9. The polynucleotide of any one of claims 1 to 7, wherein the BAG3 is a human BAG3.

10. The polynucleotide of any one of claims 1 to 9, wherein the polynucleotide sequence encoding BAG3 shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 2; or

wherein the polynucleotide sequence encoding BAG3 is a human BAG3 polynucleotide.

11. The polynucleotide of any one of claims 1 to 10, wherein the expression cassette is flanked by 5′ and 3′ inverted terminal repeats (ITRs).

12. The polynucleotide of claim 11, wherein the ITRs are AAV2 ITRs and/or the ITRs share at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with any one of SEQ ID NO: 15-21.

13. A gene therapy vector, comprising the polynucleotide of any one of claims 1 to 12.

14. The vector of claim 13, wherein the gene therapy vector is a recombinant adeno-associated virus (rAAV) vector.

15. The vector of claim 14, wherein the rAAV vector is an AAVrh74 or a functional variant thereof; or

wherein the rAAV vector comprises a capsid protein that shares 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NO: 100; or

wherein the rAAV vector is an AAV9 or a functional variant thereof; or

wherein the rAAV vector comprises a capsid protein that shares 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to any one of SEQ ID NO: 97; or

wherein the rAAV vector is an AAV6 or a functional variant thereof; or

wherein the rAAV vector comprises a capsid protein that shares 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NO: 98; or

wherein the rAAV vector is an AAVrh10 or a functional variant thereof; or

wherein the rAAV vector comprises a capsid protein that shares 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NO: 99.

16. Use of the vector of any one of claims 13-15 in the manufacture of a medicament for treating and/or preventing a disease or disorder in a subject in need thereof, wherein the vector is to be administered to the subject.

17. The use of claim 16, wherein the disease or disorder is a cardiac disorder; or

wherein the cardiac disorder is a cardiomyopathy, optionally a BAG3-related dilated cardiomyopathy.

18. The use of claim 17, wherein the cardiomyopathy is a hypertrophic cardiomyopathy (HCM) (hypertrophic); or

wherein the cardiomyopathy is a dilated cardiomyopathy (DCM); or

wherein the disease or disorder is arrhythmia, optionally atrial fibrillation or sinus node disease; or

wherein the disease or disorder is heart failure.

19. The use of any one of claims 16 to 18, wherein the subject is a mammal; or

wherein the subject is a primate; or

wherein the subject is a human; or

wherein the subject has a mutation in a *BAG3* gene and/or reduced expression of *BAG3* as compared to a healthy subject.

20. The use of any one of claims 16 to 19, wherein the vector is to be administered by intravenous injection, intracardiac injection, intracardiac infusion, and/or cardiac catheterization.

21. The use of any one of claims 16 to 20, wherein the administration increases BAG3 expression by at least about 5%; or

wherein the administration increases BAG3 expression by at least about 30%; or

wherein the administration increases BAG3 expression by at least about 70%; or

wherein the administration increases BAG3 expression by about 5% to about 10%; or

wherein the administration increases BAG3 expression by about 30% to about 50%; or

wherein the administration increases BAG3 expression by about 50% to about 70%; or

wherein the administration increases BAG3 expression by about 70% to about 100%.

22. The use of any one of claims 16 to 21, wherein the use treats and/or prevents the disease or disorder.

23. The use of claim 22, wherein the disease or disorder is related to or caused by truncation of BAG3 in the subject.

24. The use of any one of claims 16 to 23, wherein between about 1×10^{11} vector genomes and about 1×10^{13} vector genomes of the vector is to be administered to the subject, between about 1×10^{12} vector genomes and about 1×10^{14} vector genomes of the vector is to be administered to the subject, or between about 1×10^{13} vector genomes and about 1×10^{15} vector genomes of the vector is to be administered to the subject.

25. A pharmaceutical composition comprising the vector of any one of claims 13 to 15.

26. A vector according to any one of claims 13 to 15 for use in therapy.

27. A polynucleotide, comprising a polynucleotide sequences that shares at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to any one of SEQ ID NOs: 107-116.

28. Use of the vector of any one of claims 13 to 15 in the manufacture of a medicament for treating and/or preventing a cardiac disorder in a subject identified as having a mutation or truncation in BAG3, wherein the vector is to be administered to the subject.

29. The use of claim 28, wherein the disease or disorder is a cardiomyopathy, optionally a dilated cardiomyopathy (DCM); or

wherein the cardiac disorder is arrhythmia, optionally atrial fibrillation or sinus node disease, or BAG3-related dilated cardiomyopathy; or

wherein the cardiac disorder is heart failure.

30. The use of any one of claims 28 or 29, wherein the subject is a mammal.

31. The use of any one of claims 28 or 29, wherein the vector is to be administered by intravenous injection, intracardiac injection, intracardiac infusion, and/or cardiac catheterization.