

What is claimed:

1. A method of diagnosing and treating a patient having cardiac disease, comprising: identifying in a patient sample, at least one Bcl2-associated anthanogene 3 (BAG3) genetic variant as compared to a control BAG3 nucleic acid sequence, wherein detection of certain genetic variants are predictive of whether an increase in BAG3 levels is therapeutic for the patient, and, administering to the patient identified as having such a genetic variant, a therapeutically effective amount of an agent wherein the agent modulates expression or amount of BAG3 molecules, proteins or peptides thereof in a target cell or tissue, as compared to a normal control.
2. The method of claim 1, wherein detection of the variants negatively influenced the outcome of patients with non-ischemic or ischemic dilated cardiomyopathy through modulation of the function of BAG3.
3. The method of claim 2, wherein the genetic variant is a nucleotide variant (NV) in-frame insertion, in-frame-deletions, truncation, substitutions or combinations thereof.
4. The method of claim 3, wherein the in-frame insertion encodes for an amino acid.
5. The method of claim 3, wherein the in-frame insertion encodes for a nonpolar amino acid.
6. The method of claim 3, wherein the in-frame insertion comprises a 3 nucleotide insertion that adds an alanine at position 160 (p.Ala160dup, 10:121429647 A/AGCG; rs139438727).
7. The method of claim 2, wherein the genetic variant is a single nucleotide variant (SNV) in-frame insertion, in-frame-deletions, truncation, substitutions or combinations thereof.
8. The method of claim 4, wherein the SNVs comprise: p.Pro63Ala (10:121429369 C/G; rs133031999); p.His83Gln (10:151331972; rs151331972); Pro380Ser (10:121436204 C/T; rs144692954); Ala479Val (10:121436502 C/T, rs34656239) or combinations thereof.

9. The method of claim 1, wherein the agent comprises an expression vector expressing a BAG3 protein or active fragments thereof, oligonucleotides or combinations thereof.
10. The method of claim 9, wherein the expression vector comprises a viral vector, cardiotropic vector, plasmid, or a yeast vector.
11. The method of claim 10, wherein a cardiotropic vector comprises an adenovirus vector, an adeno-associated virus vector (AAV), a coxsackie virus vector, cytomegalovirus vector, Epstein-Barr virus vector, parvovirus vector, or hepatitis virus vectors.
12. The method of claim 11, wherein the expression vector is a cardiotropic pseudotyped viral vector.
13. The method of claim 1, wherein the agent comprises proteins or peptides thereof, peptidomimetics, small molecules, organic or inorganic compounds, synthetic or natural compounds.
14. The method of claim 1, wherein the cardiac disease is heart failure.
15. A method of treating a patient having cardiac disease, wherein said patient has at least one Bcl2-associated anthanogene 3 (BAG3) nucleotide variant (NV) in-frame insertion as compared to a control BAG3 nucleic acid sequence, comprising administering to said patient a therapeutically effective amount of an agent wherein the agent modulates expression or amount of BAG3 molecules, proteins or peptides thereof in a target cell or tissue.
16. The method of claim 15, wherein the in-frame insertion encodes for an amino acid.
17. The method of claim 15, wherein the in-frame insertion encodes for a nonpolar amino acid.
18. The method of claim 15, wherein the in-frame insertion comprises a 3 nucleotide insertion that adds an alanine at position 160 (p.Ala160dup, 10:121429647 A/AGCG; rs139438727).
19. A method of identifying a heart disease patient having a worse prognosis, comprising: screening a patient sample for the presence of a Bcl2-associated anthanogene 3 (BAG3)

nucleotide variant (NV) in-frame insertion as compared to a control BAG3 nucleic acid sequence, wherein detection of the BAG3 nucleotide variant (NV) in-frame insertion identifies the heart disease patient as having a worse prognosis.

20. A method of identifying a patient at risk of heart disease, comprising: screening a patient sample for the presence of a Bcl2-associated anthanogene 3 (BAG3) nucleotide variant (NV) in-frame insertion as compared to a control BAG3 nucleic acid sequence, wherein detection of the BAG3 nucleotide variant (NV) in-frame insertion identifies the patient as being at risk of heart disease.
21. The method of claim 19 or 20, wherein the in-frame insertion encodes an amino acid.
22. The method of claim 19 or 20, wherein the in-frame insertion encodes a nonpolar amino acid.
23. The method of claim 19 or 20, wherein the in-frame insertion comprises a 3 nucleotide insertion that adds an alanine at position 160 (p.Ala160dup, 10:121429647 A/AGCG; rs139438727).
24. A method of identifying a patient at risk of heart disease, comprising: screening a patient sample for the presence of a Bcl2-associated anthanogene 3 (BAG3) genetic variant, wherein the BAG3 genetic variant comprises p.Ala160dup (10:121429647 A/AGCG; rs139438727); p.Pro63Ala (10:121429369 C/G; rs133031999); p.His83Gln (10:151331972; rs151331972); Pro380Ser (10:121436204 C/T; rs144692954); Ala479Val (10:121436502 C/T, rs34656239) or combinations thereof.
25. A kit comprising one or more probes conjugated to a detectable label for identifying BCL2-associated athanogene 3 (BAG3) variants in a biological sample.
26. The kit of claim 25, wherein the BAG3 variants comprise one or more of: p.Ala160dup (10:121429647 A/AGCG; rs139438727); p.Pro63Ala (10:121429369 C/G; rs133031999); p.His83Gln (10:151331972; rs151331972); Pro380Ser (10:121436204 C/T; rs144692954); or Ala479Val (10:121436502 C/T, rs34656239).
27. The kit of claim 25, wherein detection of certain variants are predictive of whether a subject will benefit from a treatment.

28. A method of treating a subject at risk of or suffering from heart failure comprising: administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of at least one agent which modulates expression or amount of a BCL2-associated athanogene 3 (BAG3) molecule, wherein the subject has at least one BAG3 genetic variant as compared to a control BAG3 nucleic acid sequence, wherein said BAG3 genetic variant is an in-frame insertion, and wherein the agent comprises an expression vector encoding a BCL2-associated athanogene 3 (BAG3) molecule.
29. The method of claim 28, wherein the in-frame insertion encodes an amino acid.
30. The method of claim 28, wherein the in-frame insertion encodes a nonpolar amino acid.
31. The method of claim 28, wherein the in-frame insertion comprises a 3 nucleotide insertion that adds an alanine at position 160 (p.Ala160dup, 10:121429647 A/AGCG; rs139438727).
32. The method of claim 28, further comprising identifying in a biological sample, variants which are predictive of whether an increase in BAG3 levels is therapeutic for the subject, and, administering to the patient identified as having such a variant, a therapeutically effective amount of an agent wherein the agent modulates expression or amount of BAG3 molecules, proteins or peptides thereof in a target cell or tissue, as compared to a normal control.
33. The method of any of claims 1 – 8, wherein the genetic variants were not causative of disease but negatively influenced the outcome of patients with non-ischemic or ischemic dilated cardiomyopathy through modulation of the function of BAG3.