CLAIMS

What is claimed is:

1. A modified nucleic acid encoding frataxin (FXN), wherein said nucleic acid is expressed at a greater level compared with the level of expression of the wild type FXN nucleic acid sequence of SEQ ID NO:2 in an otherwise identical cell, and wherein the modified nucleic acid comprises the nucleic acid sequence of SEQ ID NO: 7.

2. The modified nucleic acid of claim 1, wherein the nucleic acid comprises a GC content of at least 55%, a number of CpG dinucleotides not greater than 117, and a codon adaptation index (CAI) of at least 0.86.

3. A recombinant expression vector comprising the modified nucleic acid encoding the FXN of claim 1.

4. The recombinant expression vector of claim 3, wherein said vector is a recombinant adeno-associated virus (rAAV) vector and the modified nucleic acid comprising the FXN is self-complementary.

5. The recombinant expression vector of claim 3, wherein said vector is a recombinant adeno-associated virus (rAAV) vector.

6. The rAAV vector of claim 5, wherein said rAAV vector further comprises a capsid selected from the group consisting of a capsid of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAVrh10, AAVrh74, RHM4-1, RHM15-1, RHM15-2, RHM15-3/RHM15-5, RHM15-4, RHM15-6, AAV Hu.26, AAV1.1, AAV2.5, AAV6.1, AAV6.3.1, AAV9.45, AAV2i8, AAV2G9, AAV2i8G9, AAV2-TT, AAV2-TT-S312N, AAV3B-S312N, and AAV-LK03.

7. The rAAV vector of claim 6, wherein the capsid is selected from the group consisting of a capsid of AAV2i8, AAV9, AAV-LK03 and AAV2-TT-S312N.

8. The rAAV vector of claim 4, wherein the modified nucleic acid further comprises at least one element selected from the group consisting of: at least one adeno-associated virus (AAV) terminal repeat sequence, an enhancer, a promoter, a collagen stabilizing sequence (CSS), a stop codon, and a poly-adenylation (polyA) signal sequence.

9. The rAAV vector of claim 8, said rAAV vector comprising two AAV terminal repeat sequences, a cytomegalovirus enhancer/chicken beta actin promoter (CBh) promoter, a CSS, and a bovine growth hormone poly-adenylation signal sequence (bGHpolyA).

10. The rAAV vector of claim 8, said vector comprising a nucleic acid comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) a modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS comprising the nucleic acid sequence of SEQ ID NO:25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

11. The rAAV vector of claim 10, further comprising an AAV2i8 capsid wherein the VP1 comprises the amino acid sequence of SEQ ID NO:29, said vector comprising a nucleic acid comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO26; (c) a modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS

comprising the nucleic acid sequence of SEQ ID NO: 25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

12. The rAAV vector of claim 10, further comprising an AAV2-TT-S312N capsid wherein the VP1 comprises the amino acid sequence of SEQ ID NO:33, said vector comprising a nucleic acid comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) a modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS comprising the nucleic acid sequence of SEQ ID NO:25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

13. A rAAV vector for use in the treatment of Friedreich ataxia (FRDA) in a patient in need thereof, wherein said vector comprises the modified nucleic acid encoding FXN of claim 1.

14. A pharmaceutical composition comprising the rAAV vector of claim 13, and a pharmaceutically acceptable carrier.

15. Use of the rAAV vector of claim 13 in the manufacture of a medicament for the treatment of FRDA.

16. The use of claim 15, wherein the medicament is to be administered systemically, by direct cardiac administration or by intracranial administration.

17. The use of claim 16, wherein the medicament is to be administered intracranially.

18. The use of claim 16, wherein the medicament is to be directly administered into the heart.

19. Use of the rAAV vector of claim 13 in the manufacture of a medicament for the treatment of a disease, disorder or condition mediated by a decreased level of FXN

20. An isolated host cell comprising the modified nucleic acid encoding FXN of claim 1.

21. The host cell of claim 20, wherein the cell is selected from the group consisting of VERO, WI38, MRC5, A549, HEK293 cells, B-50 HeLa, HepG2, Saos-2, HuH7, and HT1080.

22. The host cell of claim 21, wherein the cell is a HEK293 cell adapted to growth in suspension culture.

23. The host cell of claim 21, wherein the cell is a HEK293 cell having American Type Culture Collection (ATCC) No. PTA 13274.

24. The host cell of claim 20, said cell comprising at least one nucleic acid encoding at least one protein selected from the group consisting of a replication (Rep) protein, a capsid (Cap) protein, an adenovirus early region 1a (E1a) protein, a E1b protein, an E2a protein, an E4 protein and a viral associated (VA) RNA.

25. A method for increasing the level of frataxin in a cell, said method comprising transducing said cell with the recombinant expression vector of claim 1.

26. The vector of claim 8, comprising a nucleic acid comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) the modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (e) an AAV2 terminal repeat.

27. The vector of claim 26, further comprising a capsid selected from the group consisting of a capsid of AAV2i8, AAV9, AAV-LK03, and AAV2-TT-S312N.

28. The vector of claim 27, further comprising a CSS comprising the nucleic acid sequence of SEQ ID NO:25 immediately following the sequence encoding FXN.

29. The vector of claim 28, comprising a capsid of AAV2i8, and further comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) the modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS comprising the nucleic acid sequence of SEQ ID NO:25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

30. The vector of claim 28, comprising a capsid of AAV9, and further comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) the modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS comprising the nucleic acid sequence of SEQ ID NO:25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

31. The vector of claim 28, comprising a capsid of AAV-LK03, and further comprising, from 5' to 3': (a) an AAV2 terminal repeat; (b) a CBh promoter comprising the nucleic acid sequence of SEQ ID NO:26; (c) the modified nucleic acid encoding FXN comprising the nucleic acid sequence of SEQ ID NO:7; (d) a CSS comprising the nucleic acid sequence of SEQ ID NO:25; (e) a bGHpolyA signal sequence comprising the nucleic acid sequence of SEQ ID NO:27; and (f) an AAV2 terminal repeat.

32. The use of claim 16, wherein the systemic administration is intravenous administration.