CLAIMS

1. A recombinant nucleic acid, comprising:

a mitochondrial targeting sequence;

a mitochondrial protein coding sequence comprising a sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 7, 10, and 12; and

a 3'UTR nucleic acid sequence.

2. The recombinant nucleic acid of claim 1, wherein said mitochondrial targeting sequence encodes a polypeptide comprising a peptide sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 129-159.

3. The recombinant nucleic acid of claim 1, wherein said mitochondrial targeting sequence comprises a sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 2-5.

4. The recombinant nucleic acid of claim 1, wherein said mitochondrial targeting sequence comprises a sequence that encodes a polypeptide selected from the group consisting of hsCOX10, hsCOX8, scRPM2, lcSirt5, tbNDUS7, ncQCR2, hsATP5G2, hsLACTB, spilv1, gmCOX2, crATP6, hsOPA1, hsSDHD, hsADCK3, osP0644B06.24-2, Neurospora crassa ATP9 (ncATP9), hsGHITM, hsNDUFAB1, hsATP5G3, crATP6 _hsADCK3, ncATP9_ncATP9, zmLOC100282174, ncATP9_zmLOC100282174_spilv1_ncATP9, zmLOC100282174_hsADCK3_crATP6 _ hsATP5G3, zmLOC100282174_hsADCK3_hsATP5G3, ncATP9_zmLOC 100282174, hsADCK3_zmLOC100282174_crATP6 _ hsATP5G3, crATP6_hsADCK3_zmLOC100282174_hsATP5G3, hsADCK3_zmLOC100282174, hsADCK3_ zmLOC100282174_crATP6, ncATP9_zmLOC100282174_ spilv1_GNFP_ncATP9, and ncATP9_zmLOC100282174_spilv1_lcSirt5_osP0644B06.24-2_hsATP5G2_ncATP9.

5. The recombinant nucleic acid of claim 1, wherein said mitochondrial protein is selected from a group consisting of NADH dehydrogenase 4 (ND4), NADH dehydrogenase 6 (ND6), and NADH dehydrogenase 1 (ND1).

6. The recombinant nucleic acid of claim 5, wherein said mitochondrial protein comprises NADH dehydrogenase 4 (ND4).

7. The recombinant nucleic acid of claim 6, wherein said mitochondrial protein coding sequence comprises a sequence that is at least 99% identical to a sequence as set forth in SEQ ID NO: 7.

8. The recombinant nucleic acid of claim 5, wherein said mitochondrial protein comprises NADH dehydrogenase 6 (ND6).

9. The recombinant nucleic acid of claim 8, wherein said mitochondrial protein coding sequence comprises a sequence that is at least 95% identical to a sequence as set forth in SEQ ID NO: 10.

10. The recombinant nucleic acid of claim 5, wherein said mitochondrial protein comprises NADH dehydrogenase 1 (ND1).

11. The recombinant nucleic acid of claim 10, wherein said mitochondrial protein coding sequence comprises a sequence that is at least 95% identical to a sequence as set forth in SEQ ID NO: 12.

12. The recombinant nucleic acid of claim 1, wherein said 3'UTR nucleic acid sequence comprises a sequence selected from the group consisting of hsACO2, hsATP5B, hsAK2, hsALDH2, hsCOX10, hsUQCRFS1, hsNDUFV1, hsNDUFV2, hsSOD2, hsCOX6c, hsIRP1, hsMRPS12, hsATP5J2, rnSOD2, and hsOXA1L.

13. The recombinant nucleic acid of claim 1, wherein said 3'UTR nucleic acid sequence comprises a sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 111-125.

14. An adeno-associated viral (AAV) vector comprising a recombinant nucleic acid, comprising: a mitochondrial targeting sequence; a mitochondrial protein coding sequence comprising a sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 7, 10, and 12; and a 3'UTR nucleic acid sequence.

15. The AAV vector of claim 14, wherein said AAV vector is a recombinant AAV (rAAV) vector.

16. The AAV vector of claim 15, wherein said rAAV vector is rAAV2 vector.

17. A pharmaceutical composition, comprising an adeno-associated virus (AAV) comprising a recombinant nucleic acid and a pharmaceutically acceptable excipient thereof, wherein said recombinant nucleic acid comprises: a mitochondrial targeting sequence; a mitochondrial protein coding sequence comprising a sequence that is at least 95% identical to a sequence selected from the group consisting of SEQ ID NO: 7, 10, and 12; and a 3'UTR nucleic acid sequence.

18. The pharmaceutical composition of claim 17, wherein said pharmaceutically acceptable excipient comprises phosphate-buffered saline (PBS), α,α-trehalose dehydrate, L-histidine monohydrochloride monohydrate, polysorbate 20, NaCl, NaH_2PO_4, Na_2HPO_4, KH_2PO_4, K_2HPO_4, poloxamer 188, or any combination thereof.

19. The pharmaceutical composition of claim 18, wherein said pharmaceutically acceptable excipient comprises poloxamer 188.

20. The pharmaceutical composition of claim 19, wherein said pharmaceutically acceptable excipient comprises 0.0001%-0.01% poloxamer 188.

21. The pharmaceutical composition of claim 17, wherein said pharmaceutical composition has a viral titer of at least 5.0×10^{10} vg/mL.

22. The pharmaceutical composition of claim 17, when said pharmaceutical composition is subject to five freeze/thaw cycles, said pharmaceutical composition retains at least 60%, 70%, 80%, or 90% of a viral titer as compared to the viral titer prior to the five freeze/thaw cycles.