CLAIMS

1. An isolated nucleic acid molecule, comprising a first nucleotide sequence encoding a first protein operatively linked to a second nucleotide sequence encoding a second protein, wherein the first protein and the second protein are selected from the following combination (a) or (b):
(a) the first protein is human AADC, and the second protein is human GDNF; or
(b) the first protein is human GDNF, and the second protein is human AADC, wherein the first nucleotide sequence is at 5' upstream of the second nucleotide sequence.

2. The isolated nucleic acid molecule of claim 1, characterized in that:
(i) the polypeptide sequence of AADC comprises or is the amino acid sequence as shown in SEQ ID NO: 31; and/or
(ii) the polypeptide sequence of GDNF comprises or is the amino acid sequence as shown in SEQ ID NO: 34.

3. The isolated nucleic acid molecule of claim 1 or claim 2, when the first protein is human ADCC, the first nucleotide sequence comprises or is a nucleotide sequence selected from a group consisting of a nucleotide sequence as shown in any one of SEQ ID NOs: 1-9, 11 or 46.

4. The isolated nucleic acid molecule of any one of claims 1-3, when the second protein is human GDNF, wherein the second nucleotide sequence comprises or is a nucleotide sequence selected from a group consisting of a nucleotide sequence as shown in any one of SEQ ID NOs: 27-30.

5. The isolated nucleic acid molecule of any one of claim 1-3, wherein the nucleotide sequence encoding human GDNF is a codon-optimized coding sequence of GDNF, and the codon-optimized coding sequence differs from the wild-type coding sequence of GDNF as shown in SEQ ID NO: 30 in nucleotides not existed in the region coding for the signal peptide or pre-peptide of GDNF.

6. The isolated nucleic acid molecule of claim 5, wherein the nucleotide sequence encoding

human GDNF is a codon-optimized coding sequence of GDNF and has reduced CpG sites or has no CpG islands as compared to the wild-type coding sequence of GDNF as shown in SEQ ID NO: 30.

7. The isolated nucleic acid molecule of any one of claims 1-6, wherein the first nucleotide sequence and the second nucleotide sequence are linked in frame and are operatively linked to a promoter located at the 5' upstream to both the first and the second nucleotide sequences.

8. The isolated nucleic acid molecule of claim 7, wherein the promoter is selected from a CBh promoter, an EF1α promoter, a CAG promoter, a MBP promoter or a variant thereof.

9. The isolated nucleic acid molecule of claim 8, wherein the promoter is a truncated variant of EF1α promoter having a nucleotide sequence of any one of SEQ ID NOS: 50-56.

10. The isolated nucleic acid molecule of any one of claims 1-9, further comprising a linker sequence between the first and the second nucleotide sequences.

11. The isolated nucleic acid molecule of claim 10, wherein the linker sequence is a coding sequence of a self-cleaving peptide or an internal ribosome entry site.

12. A codon-optimized sequence of AADC, having a nucleotide sequence as shown in any one of SEQs ID NO: 1-9 or 46.

13. A codon-optimized sequence of GDNF, having a nucleotide sequence as shown in any one of SEQ ID NOs: 27-29.

14. A recombinant adeno-associated viral (rAAV) vector comprising the isolated nucleic acid molecule of any one of claims 1-11 or the codon-optimized sequence of claim 12 or claim 13.

15. A viral particle comprising the rAAV vector of claim 14.

16. The viral particle of claim 15, which comprises a capsid protein of AAV1, AAV2, AAV5, AAV8 or AAV9.

17. A pharmaceutical composition, comprising the rAAV vector of claim 14, or the viral particle of claim 15 or claim 16, and a pharmaceutically acceptable excipient.

18. Use of a therapeutically effective amount of the rAAV vector of claim 14, the viral particle of claim 15 or claim 16, or the pharmaceutical composition of claim 17 in the manufacture of a medicament for treating or preventing neurodegenerative disorders in a subject in need thereof.

19. The use of claim 18, wherein the neurodegenerative disorder is Parkinson's disease or AADC deficiency (AADCD), and the isolated nucleic acid molecule comprises the nucleotide sequence encoding human AADC.

20. The use of claim 19, wherein the isolated nucleic acid molecule further comprises the nucleotide sequence encoding GBA1, CDNF or GDNF.