CLAIMS

1. A recombinant adeno-associated virus (AAV) vector comprising:
(a) a variant AAV2 capsid protein, wherein the variant AAV2 capsid protein comprises at least four amino acid substitutions with respect to a wild type AAV2 capsid protein; wherein the at least four amino acid substitutions are present at the following positions in an AAV2 capsid protein sequence: 457, 492, 499 and 533; and
(b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.
2. A recombinant AAV vector according to claim 1, wherein (i) the variant AAV capsid protein comprises a sequence of SEQ ID NO:2, or a sequence having at least 95% sequence identity thereto; and/or (ii) the wild type AAV capsid protein comprises a sequence of SEQ ID NO:1.
3. A recombinant AAV vector according to claim 1 or claim 2, wherein the variant AAV2 capsid protein comprises one or more of the following residues: M457, A492, D499 and Y533.
4. A recombinant AAV vector according to claim 2 or claim 3, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: Q457M, S492A, E499D and F533Y.
5. A recombinant AAV vector according to any of claims 1 to 4, wherein the variant AAV2 capsid protein further comprises one or more amino acid substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 125, 151, 162 and 205.
6. A recombinant AAV vector according to claim 5, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: I125, A151, S162 and S205.
7. A recombinant AAV vector according to claim 5 or claim 6, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: V125I, V151A, A162S and T205S.
8. A recombinant AAV vector according to any of claims 1 to 7, wherein the variant AAV2 capsid protein further comprises one or more amino acid

substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 585 and 588.

9. A recombinant AAV vector according to claim 8, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: S585 and T588.

10. A recombinant AAV vector according to claim 8 or claim 9, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: R585S and R588T.

11. A recombinant AAV vector according to any of claims 1 to 10, wherein the variant AAV2 capsid protein further comprises one or more amino acid substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 546, 548 and 593.

12. A recombinant AAV vector according to claim 11, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: D546, G548, and S593.

13. A recombinant AAV vector according to claim 11 or claim 12, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: G546D, E548G and A593S.

14. A recombinant AAV vector according to any of claims 1 to 13, wherein the variant AAV2 capsid protein comprises the residue N312.

15. A recombinant adeno-associated virus (AAV) vector comprising:
(a) a variant AAV8 capsid protein, wherein the variant AAV8 capsid protein comprises an amino acid substitution with respect to a wild type AAV8 capsid protein at position 315 in an AAV8 capsid protein sequence; and
(b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.

16. A recombinant AAV vector according to claim 15, wherein (i) the variant AAV capsid protein comprises a sequence having at least 95% sequence identity to SEQ ID NO:6; and/or (ii) the wild type AAV capsid protein comprises a sequence of SEQ ID NO:6.

17. A recombinant AAV vector according to claim 15 or claim 16, wherein the variant AAV8 capsid protein comprises the amino acid substitution S315N with respect to a wild type AAV8 capsid protein.

18. A recombinant AAV vector according to any of claims 15 to 17, further comprising one or more amino acid substitution present at one or more of the following positions in the AAV8 capsid protein sequence: 125, 151, 163, 206, 460, 495, 502, 536, 549, 551, 588, 591 and/or 596.

19. A recombinant AAV vector according to claim 18, wherein the variant AAV8 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV8 capsid protein:
    (a) V125I, Q151A, K163S, A206S, T460M, T495A, N502D, F536Y, N549D, A551G, Q588S and/or G596S; and/or
    (b) T591R.

20. A recombinant adeno-associated virus (AAV) vector comprising:
    (a) a variant AAV3B capsid protein, wherein the variant AAV3B capsid protein comprises an amino acid substitution with respect to a wild type AAV3B capsid protein at position 312 in an AAV3B capsid protein sequence; and
    (b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.

21. A recombinant AAV vector according to claim 20, wherein (i) the variant AAV3B capsid protein comprises a sequence having at least 95% sequence identity to SEQ ID NO:11; and/or (ii) the wild type AAV capsid protein comprises a sequence of SEQ ID NO:11.

22. A recombinant AAV vector according to claim 20 or claim 21, wherein the variant AAV3B capsid protein comprises the amino acid substitution S312N with respect to a wild type AAV3B capsid protein.

23. A recombinant adeno-associated virus (AAV) vector comprising:
    (a) a variant AAV-LK03 capsid protein, wherein the variant AAV-LK03 capsid protein comprises an amino acid substitution at position 312 with respect to a AAV-LK03 capsid protein sequence as defined in SEQ ID NO:12; and
    (b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.

24. A recombinant AAV vector according to claim 23, wherein the variant AAV-LK03 capsid protein comprises a sequence having at least 95% sequence identity to SEQ ID NO:12.
25. A recombinant AAV vector according to any of claims 1 to 14, wherein the recombinant AAV vector exhibits increased transduction of a neuronal or retinal tissue compared to an AAV vector comprising a corresponding wild type AAV capsid protein.
26. A recombinant AAV vector according to any of claims 15 to 24, wherein the recombinant AAV vector exhibits increased transduction of liver tissue compared to a corresponding wild type AAV capsid protein.
27. A recombinant AAV vector according to any preceding claim, wherein the gene product comprises an interfering RNA or an aptamer.
28. A recombinant AAV vector according to any of claims 1 to 27, wherein the gene product comprises a polypeptide.
29. A recombinant AAV vector according to claim 28, wherein the gene product comprises a neuroprotective polypeptide, an anti-angiogenic polypeptide, or a polypeptide that enhances function of a neuronal or retinal cell.
30. A recombinant AAV vector according to claim 29, wherein the gene product comprises glial derived neurotrophic factor, fibroblast growth factor, nerve growth factor, brain derived neurotrophic factor, rhodopsin, retinoschisin, RPE65 or peripherin.
31. A pharmaceutical composition comprising:
    (a) a recombinant AAV vector according to any preceding claim; and
    (b) a pharmaceutically acceptable excipient.
32. A method for delivering a gene product to a tissue in a subject, the method comprising administering to the subject a recombinant AAV vector or pharmaceutical composition according to any preceding claim.
33. A method according to claim 32, wherein the tissue is selected from blood, bone marrow, muscle tissue, neuronal tissue, retinal tissue, pancreatic tissue, liver tissue, kidney tissue, lung tissue, intestinal tissue or heart tissue.
34. A method according to claim 33, wherein the tissue is neuronal, retinal or liver tissue.

35. A method for treating a disorder in a subject, the method comprising administering to the subject a recombinant AAV vector or pharmaceutical composition according to any preceding claim.
36. A recombinant AAV vector or pharmaceutical composition according to any of claims 1 to 31, for use in treating a disorder in a subject.
37. A method, recombinant AAV vector or pharmaceutical composition for use according to claim 35 or claim 36, wherein the disorder is a neurological, ocular or hepatic disorder.
38. A method, recombinant AAV vector or pharmaceutical composition for use according to claim 37, wherein the neurological disorder is a neurodegenerative disease.
39. A method, recombinant AAV vector or pharmaceutical composition for use according to claim 37, wherein the ocular disorder is glaucoma, retinitis pigmentosa, macular degeneration, retinoschisis or diabetic retinopathy.

CLAIMS

1. A recombinant adeno-associated virus (AAV) vector comprising:
   (a) a variant AAV2 capsid protein, wherein the variant AAV2 capsid protein comprises at least four amino acid substitutions with respect to a wild type AAV2 capsid protein; wherein the at least four amino acid substitutions are present at the following positions in an AAV2 capsid protein sequence: 457, 492, 499 and 533; and
   (b) a heterologous nucleic acid comprising a nucleotide sequence encoding a gene product.
2. A recombinant AAV vector according to claim 1, wherein (i) the variant AAV capsid protein comprises a sequence of SEQ ID NO:2, or a sequence having at least 95% sequence identity thereto; and/or (ii) the wild type AAV capsid protein comprises a sequence of SEQ ID NO:1.
3. A recombinant AAV vector according to claim 1 or claim 2, wherein the variant AAV2 capsid protein comprises one or more of the following residues: M457, A492, D499 and Y533.
4. A recombinant AAV vector according to claim 2 or claim 3, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: Q457M, S492A, E499D and F533Y.
5. A recombinant AAV vector according to any of claims 1 to 4, wherein the variant AAV2 capsid protein further comprises one or more amino acid substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 125, 151, 162 and 205.
6. A recombinant AAV vector according to claim 5, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: I125, A151, S162 and S205.
7. A recombinant AAV vector according to claim 5 or claim 6, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: V125I, V151A, A162S and T205S.
8. A recombinant AAV vector according to any of claims 1 to 7, wherein the variant AAV2 capsid protein further comprises one or more amino acid substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 585 and 588.

9. A recombinant AAV vector according to claim 8, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: S585 and T588.
10. A recombinant AAV vector according to claim 8 or claim 9, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: R585S and R588T.
11. A recombinant AAV vector according to any of claims 1 to 10, wherein the variant AAV2 capsid protein further comprises one or more amino acid substitutions with respect to the wild type AAV capsid protein at the following positions in the AAV2 capsid protein sequence: 546, 548 and 593.
12. A recombinant AAV vector according to claim 11, wherein the variant AAV2 capsid protein comprises one or more of one or more of the following residues: D546, G548, and S593.
13. A recombinant AAV vector according to claim 11 or claim 12, wherein the variant AAV2 capsid protein comprises one or more of the following amino acid substitutions with respect to a wild type AAV2 capsid protein: G546D, E548G and A593S.
14. A recombinant AAV vector according to any of claims 1 to 13, wherein the variant AAV2 capsid protein comprises the residue N312.
15. A recombinant AAV vector according to any of claims 1 to 14, wherein the recombinant AAV vector exhibits increased transduction of a neuronal or retinal tissue compared to an AAV vector comprising a corresponding wild type AAV capsid protein.
16. A recombinant AAV vector according to any preceding claim, wherein the gene product comprises an interfering RNA or an aptamer.
17. A recombinant AAV vector according to any of claims 1 to 16, wherein the gene product comprises a polypeptide.
18. A recombinant AAV vector according to claim 17, wherein the gene product comprises a neuroprotective polypeptide, an anti-angiogenic polypeptide, or a polypeptide that enhances function of a neuronal or retinal cell.
19. A recombinant AAV vector according to claim 18, wherein the gene product comprises glial derived neurotrophic factor, fibroblast growth factor, nerve growth factor, brain derived neurotrophic factor, rhodopsin, retinoschisin, RPE65 or peripherin.
20. A pharmaceutical composition comprising:
    (a) a recombinant AAV vector according to any preceding claim; and

(b) a pharmaceutically acceptable excipient.

21. A recombinant AAV vector or pharmaceutical composition according to any of claims 1 to 20, for use in the treatment of a disorder in a subject.

22. The use of a recombinant AAV vector or pharmaceutical composition according to any of claims 1 to 20, in the manufacture of a medicament for the treatment of a neurological disorder or hepatic disorder wherein the neurological disorder is a neurodegenerative disease.

23. The use of a recombinant AAV vector or pharmaceutical composition according to any of claims 1 to 20, in the manufacture of a medicament for the treatment of an ocular disorder wherein the ocular disorder is glaucoma, retinitis pigmentosa, macular degeneration, retinoschisis or diabetic retinopathy.