

CLAIMS:

1. A recombinant adeno associated virus (AAV) vector, the vector comprising a capsid protein and a nucleic acid encapsidated by the capsid protein;
wherein the nucleic acid encodes a heterologous polypeptide or heterologous RNA sequence; and
wherein the capsid protein comprises one or more of the following substitutions, wherein the amino acids are numbered according to the amino acid sequence of SEQ ID NO:8:
 - a) a substitution of the amino acids corresponding to amino acids 455-460 with the sequence SNGRGV (SEQ ID NO:488), a substitution of the amino acids corresponding to amino acids 455-461 with the sequence VNTSING (SEQ ID NO:489), or a substitution of the amino acids corresponding to amino acids 455-461 with the sequence IRGAGAV (SEQ ID NO:490);
 - b) a substitution of the amino acids corresponding to amino acids 494-501 with the sequence YPGGNYK (SEQ ID NO:491); and/or
 - c) a substitution of the amino acids corresponding to amino acids 586-591 with the sequence KQKNVN (SEQ ID NO:492) or RMSSIK (SEQ ID NO:493).
2. The recombinant AAV vector of claim 1, wherein the one or more substitutions inhibit neutralization of infectivity of the AAV vector and/or inhibit binding of an antibody to the AAV vector, wherein the antibody binds to a capsid protein comprising the amino acid sequence of SEQ ID NO:8.
3. The recombinant AAV vector of claim 2, wherein the antibody is selected from the group consisting of HL2381, HL3283, and ADK8.
4. The recombinant AAV vector of claim 3, wherein the antibody is HL2381.
5. The recombinant AAV vector of claim 3, wherein the antibody is HL2383.
6. The recombinant AAV vector of claim 3, wherein the antibody is ADK8.

7. The recombinant AAV vector of claim 1, wherein the capsid protein further comprises a substitution at amino acid 453, 454, 502, 592, 593, 594, 595, 596, 597, 598, 599 and/or 600, in any combination.

8. The recombinant AAV vector of claim 1, wherein the capsid protein comprises a substitution of amino acids 455-460 with the sequence SNGRGV (SEQ ID NO:488).

9. The recombinant AAV vector of claim 1, wherein the capsid protein comprises a substitution of amino acids 455-460 with the sequence SNGRGV (SEQ ID NO:488) and a substitution of amino acids 494-501 with the sequence YPGGNYK (SEQ ID NO:491).

10. The recombinant AAV vector of claim 1, wherein the capsid protein comprises a substitution of amino acids 455-460 with the sequence SNGRGV (SEQ ID NO:488) and a substitution of amino acids 494-501 with the sequence KQKNVN (SEQ ID NO:492).

11. The recombinant AAV vector claim 1, wherein the heterologous polypeptide is a therapeutic polypeptide.

12. The recombinant AAV vector of claim 1, wherein the heterologous RNA is a functional RNA.

13. The recombinant AAV vector of claim 1, wherein the nucleic acid comprises terminal repeat (TR) sequences from AAV2 or AAV4.

14. A recombinant adeno-associated virus (AAV) vector, the vector comprising a capsid protein and a nucleic acid encapsidated by the capsid protein;

wherein the nucleic acid encodes a heterologous polypeptide or heterologous RNA sequence; and

wherein the capsid protein comprises one or more of the following substitutions, wherein the amino acids are numbered according to the amino acid sequence of SEQ ID NO:8:

a) a substitution of the amino acids corresponding to amino acids 455-460 with the sequence SNGRGV (SEQ ID NO:488), a substitution of the amino acids corresponding to amino acids 455-461 with the sequence VNTSING (SEQ ID NO:489), or a substitution of the amino acids corresponding to amino acids 455-461 with the sequence IRGAGAV (SEQ ID NO:490);

b) a substitution of the amino acids corresponding to amino acids 494-501 with the sequence YPGGNYK (SEQ ID NO:491); and/or

c) a substitution of the amino acids corresponding to amino acids 586-591 with the sequence KQKNVN (SEQ ID NO:492) or RMSSIK (SEQ ID NO:493), and

wherein the capsid protein with the substitutions of one or more of a)-c) is at least about 90% identical to the amino acid sequence of SEQ ID NO:8.

15. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:8.

16. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a sequence at least about 97% identical to the amino acid sequence of SEQ ID NO:8.

17. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a sequence at least about 98% identical to the amino acid sequence of SEQ ID NO:8.

18. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a sequence at least about 99% identical to the amino acid sequence of SEQ ID NO:8.

19. The recombinant AAV vector of claim 14, wherein the one or more substitutions inhibit neutralization of infectivity of the AAV vector and/or inhibit binding of an antibody to the AAV vector, wherein the antibody binds to a capsid protein comprising the amino acid sequence of SEQ ID NO:8.

20. The recombinant AAV vector of claim 19, wherein the antibody is selected from the group consisting of HL2381, HL2383, and ADK8.

21. The recombinant AAV vector of claim 20, wherein the antibody is HL2381.
22. The recombinant AAV vector of claim 20, wherein the antibody is HL2383.
23. The recombinant AAV vector of claim 20, wherein the antibody is ADK8.
24. The recombinant AAV vector of claim 14, wherein the capsid protein comprises one or more substitutions at the amino acids corresponding to amino acids 453-461 and 495-502 of SEQ ID NO:8.
25. The recombinant AAV vector of claim 14, wherein the capsid protein comprises one or more substitutions at the amino acids corresponding to amino acids 453-461 and 590-600 of SEQ ID NO:8.
26. The recombinant AAV vector of claim 14, wherein the capsid protein comprises one or more substitutions at the amino acids corresponding to amino acids 495-502 and 590-600 of SEQ ID NO:8.
27. The recombinant AAV vector of claim 14, wherein the capsid protein comprises one or more substitutions at the amino acids corresponding to amino acids 453-461, 495-502 and 590-600 of SEQ ID NO:8.
28. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a substitution of amino acids 455-460 of SEQ ID NO:8 with the sequence SNGRGV (SEQ ID NO:488).
29. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a substitution of amino acids 455-460 of SEQ ID NO:8 with the sequence SNGRGV (SEQ ID NO:488) and a substitution of amino acids 494-501 of SEQ ID NO:8 with the sequence YPGGNYK (SEQ ID NO:491).

30. The recombinant AAV vector of claim 14, wherein the capsid protein comprises a substitution of amino acids 455-460 of SEQ ID NO:8 with the sequence SNGRGV (SEQ ID NO:488) and a substitution of amino acids 494-501 of SEQ ID NO:8 with the sequence KQKNVN (SEQ ID NO:492).
31. The recombinant AAV vector claim 14, wherein the heterologous polypeptide is a therapeutic polypeptide.
32. The recombinant AAV vector of claim 14, wherein the heterologous RNA is a functional RNA.
33. The recombinant AAV vector of claim 14, wherein the nucleic acid comprises terminal repeat (TR) sequences from AAV2 or AAV4.