Claims

1. An isolated modified capsid protein VP1 from adeno-associated virus serotype 9 (AAV9) for highly efficient production of encapsidated viral vectors based on recombinant adeno-associated virus serotype 9 (rAAV9), said isolated modified capsid protein VP1 comprising a wild-type AAV9 capsid protein VP1 amino acid sequence encoded by the *Cap* gene with one or more substitutions that are selected from the group:

F422W,

F422W and Y446F,

I601M,

wherein the wild-type AAV9 capsid protein VP1 amino acid sequence has the amino acid sequence represented by SEQ ID NO: 1.

2. The isolated modified AAV9 capsid protein VP1 according to claim 1, comprising a substitution at position F422W.

3. The isolated modified AAV9 capsid protein VP1 according to claim 2, having the amino acid sequence represented by SEQ ID NO: 2.

4. The isolated modified AAV9 capsid protein VP1 according to claim 1, comprising the substitutions F422W and Y446F.

5. The isolated modified AAV9 capsid protein VP1 according to claim 4, having the amino acid sequence represented by SEQ ID NO: 3.

6. The isolated modified AAV9 capsid protein VP1 according to claim 1, comprising the substitution I601M.

7. The isolated modified AAV9 capsid protein VP1 according to claim 6, having the amino acid sequence represented by SEQ ID NO: 4.

8. An isolated nucleic acid encoding the modified capsid protein VP1 from adeno-associated virus serotype 9 according to any one of claims 1 to 7, said capsid protein VP1 being used for highly efficient production of encapsidated viral vectors based on recombinant adeno-associated virus serotype 9.

9. The isolated nucleic acid according to claim 8 encoding a modified capsid protein VP1 from adeno-associated virus serotype 9 with the amino acid substitution F422W, said isolated nucleic acid being represented by a nucleic sequence with SEQ ID NO: 6 or by any other sequence encoding the respective amino acid sequence.

10. The isolated nucleic acid according to claim 8 encoding a modified capsid protein VP1 from adeno-associated virus serotype 9 with the amino acid substitutions F422W and Y446F, said isolated nucleic acid being represented by a nucleic sequence with SEQ ID NO: 7 or any other sequence encoding the respective amino acid sequence.

11. The isolated nucleic acid according to claim 8 encoding a modified capsid protein VP1 from adeno-associated virus serotype 9 with the amino acid substitution I601M, said isolated nucleic acid being represented by a nucleic sequence with SEQ ID NO: 8 or by any other sequence encoding the respective amino acid sequence.

12. An isolated capsid for highly efficient production of encapsidated viral vectors based on recombinant adeno-associated virus serotype 9, said isolated capsid including the modified capsid protein VP1 from adeno-associated virus serotype 9 according to any one of claims 1 to 7.

13. The isolated capsid according to claim 12 comprising the modified capsid protein VP1 from adeno-associated virus serotype 9 according to any one of claims 1 to 7, the AAV9 capsid protein VP2 or a modified variant thereof, and the AAV9 capsid protein VP3 or a modified variant thereof.

14. The isolated capsid according to claim 13 comprising the wild-type AAV9 capsid protein VP2.

15. The isolated capsid according to claim 14 comprising the wild-type AAV9 capsid protein VP2 having the amino acid sequence represented by SEQ ID NO: 9.

16. The isolated capsid according to claim 13 comprising a modified capsid protein VP2 from adeno-associated virus serotype 9.

17. The isolated capsid according to claim 16 comprising a modified AAV9 capsid protein VP2 comprising the substitution F285W.

18. The isolated capsid according to claim 17 comprising a modified AAV9 capsid protein VP2 comprising the substitution F285W and having an amino acid sequence represented by SEQ ID NO: 10.

19. The isolated capsid according to claim 16 comprising a modified AAV9 capsid protein VP2 comprising the substitutions F285W and Y309F.

20. The isolated capsid according to claim 19 comprising a modified AAV9 capsid protein VP2 comprising the substitution F285W and Y309F and having an amino acid sequence represented by SEQ ID NO: 11.

21. The isolated capsid according to claim 16 comprising a modified AAV9 capsid protein VP2 comprising the substitution I464M.

22. The isolated capsid according to claim 21 comprising a modified AAV9 capsid protein VP2 comprising the substitution I464M and having an amino acid sequence represented by SEQ ID NO: 12.

23. The isolated capsid according to claim 13 comprising the wild-type AAV9 capsid protein VP3.

24. The isolated capsid according to claim 23 comprising the wild-type AAV9 capsid protein VP3 that has an amino acid sequence represented by SEQ ID NO: 17.

25. The isolated capsid according to claim 13 comprising a modified capsid protein VP3 from adeno-associated virus serotype 9.

26. The isolated capsid according to claim 25 comprising a modified AAV9 capsid protein VP3 comprising the substitution F220W.

27. The isolated capsid according to claim 26 comprising a modified AAV9 capsid protein VP3 comprising the substitution F220W and having an amino acid sequence represented by SEQ ID NO: 18.

28. The isolated capsid according to claim 25 comprising a modified AAV9 capsid protein VP3 comprising the substitutions F220W and Y244F.

29. The isolated capsid according to claim 28 comprising a modified AAV9 capsid protein VP3 comprising the substitutions F220W and Y244F and having an amino acid sequence represented by SEQ ID NO: 19.

30. The isolated capsid according to claim 25 comprising a modified AAV9 capsid protein VP3 comprising the substitution I399M.

31. The isolated capsid according to claim 30 comprising a modified AAV9 capsid protein VP3 comprising the substitution I399M and having an amino acid sequence represented by SEQ ID NO: 20.

32. An isolated nucleic acid encoding the capsid according to any one of claims 12 to 31, said capsid being used for highly efficient production of encapsidated viral vectors based on recombinant adeno-associated virus serotype 9.

33. A vector based on recombinant adeno-associated virus serotype 9 for delivering a heterologous nucleic acid sequence to a subject, said vector comprising:

1) the modified capsid protein VP1 from adeno-associated virus serotype 9 according to any one of claims 1 to 7 or the capsid according to any one of claims 12 to 31, and

2) a heterologous nucleic acid sequence comprising regulatory sequences that promote the expression of the product encoded by the heterologous nucleic acid sequence, in the target cells.

34. The rAAV9 vector according to claim 33, wherein the product of expression of the heterologous nucleic acid sequence is a therapeutic polypeptide or reporter polypeptide.

35. A pharmaceutical composition for the delivery of a gene product to a subject in need thereof, comprising:

a) the rAAV9 vector according to any one of claims 33 to 34; and

b) a pharmaceutically acceptable excipient.

36. Use of the rAAV9 vector according to any one of claims 33 to 34 or the pharmaceutical composition according to claim 35 for treating a disease.

37. The use according to claim 36, wherein the disease is selected from the group: blood diseases; central nervous system diseases; metabolic diseases; muscle diseases; hereditary diseases.

38. A method for producing the rAAV9 vector according to any one of claims 33 to 34, comprising transfection of producer cells, respectively, with the nucleic acid comprising a sequence encoding a modified capsid protein VP1 from adeno-associated virus serotype 9 according to any one of claims 8 to 11, or with the nucleic acid encoding a capsid according to claim 32.