

### Claims:

1. An isolated altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid for highly-effective transduction of target cells, comprising the amino acid sequence of the VP1 protein of a wild-type AAV5 capsid, encoded by the *Cap* gene, comprising one or more substitutions selected from the group comprising:

S2A and T711S,

S2A, S651A and T711S.

2. The isolated altered VP1 protein of the AAV5 capsid of Claim 1, wherein the amino acid sequence of the VP1 protein of a wild-type AAV5 capsid has the amino acid sequence represented by SEQ ID NO: 1.

3. The isolated altered VP1 protein of the AAV5 capsid of Claim 1, which comprises the S2A and T711S substitutions.

4. The isolated altered VP1 protein of the AAV5 capsid of Claim 3, which has the amino acid sequence represented by SEQ ID NO: 3.

5. The isolated altered VP1 protein of the AAV5 capsid of Claim 1, which comprises the substitutions S2A, S651A and T711S.

6. The isolated altered AAV5 VP1 capsid protein of Claim 5, which has the amino acid sequence represented by SEQ ID NO: 4.

7. An isolated nucleic acid encoding the altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid of any one of Claims 1 to 6, which is used for highly efficient transduction of target cells.

8. The isolated nucleic acid of Claim 7 encoding an altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid comprising the amino acid S2A and T711S substitutions, which is represented by the nucleic sequence of SEQ ID NO: 6 or any other sequence encoding the corresponding amino acid sequence.

9. The isolated nucleic acid of Claim 7 encoding an altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid comprising the amino acid S2A, S651A and T711S substitutions, which is represented by the nucleic sequence of SEQ ID NO: 7 or any other sequence encoding the corresponding amino acid sequence.

10. An isolated capsid for highly efficient transduction of target cells comprising the altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid of any one of Claims 1 to 6.

11. The isolated capsid of Claim 10 comprising the altered VP1 protein of adeno-associated virus serotype 5 (AAV5) capsid of any one of Claims 1 to 6, a VP2 protein of AAV5 capsid or an altered variant thereof, and a VP3 protein of AAV5 capsid or an altered variant thereof.

12. The isolated capsid of Claim 11 comprising the VP2 protein of a wild-type AAV5 capsid.

13. The isolated capsid of Claim 12, comprising the VP2 protein of a wild-type AAV5 capsid protein having the amino acid sequence represented by SEQ ID NO: 8.

14. The isolated capsid of Claim 11 comprising the altered VP2 protein of adeno-associated virus serotype 5 (AAV5) capsid.

15. The isolated capsid of Claim 14 comprising the altered VP2 protein of AAV5 capsid comprising the T575S substitution.

16. The isolated capsid of Claim 15 comprising the altered VP2 protein of AAV5 capsid comprising the T575S substitution and having the amino acid sequence represented by SEQ ID NO: 9.

17. The isolated capsid of Claim 15 comprising the altered VP2 protein of AAV5 capsid comprising the S515A and T575S substitutions.

18. The isolated capsid of Claim 17 comprising a the altered VP2 protein of AAV5 capsid comprising the S515A and T575S substitutions and having the amino acid sequence represented by SEQ ID NO: 10.

19. The isolated capsid of Claim 11 comprising the VP3 protein of a wild-type AAV5 capsid.

20. The isolated capsid of Claim 19, comprising the VP3 protein of a wild-type AAV5 capsid having the amino acid sequence represented by SEQ ID NO: 11.

21. The isolated capsid of Claim 11 comprising the altered VP3 protein of adeno-associated virus serotype 5 (AAV5) capsid.

22. The isolated capsid of Claim 21 comprising the altered VP3 protein of AAV5 capsid comprising the T519S substitution.

23. The isolated capsid of Claim 22 comprising the altered VP3 protein of AAV5 capsid comprising the T519S substitution and having the amino acid sequence represented by SEQ ID NO: 12.

24. The isolated capsid of Claim 21 comprising the altered VP3 protein of AAV5 capsid comprising the S459A and T519S substitutions.

25. The isolated capsid of Claim 24 comprising the altered VP3 protein of AAV5 capsid comprising the S459A and T519S substitutions and having the amino acid sequence represented by SEQ ID NO: 13.

26. An isolated nucleic acid encoding the capsid of any one of Claims 10 to 25, which is used for highly efficient transduction of target cells.

27. A vector based on recombinant adeno-associated virus serotype 5 (rAAV5) for delivery to a subject of a heterologous nucleic acid sequence, which comprises:

1) the capsid of any one of Claims 10 to 25, 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 target cells.

28. The vector based on rAAV5 of Claim 27, wherein the expression product of the heterologous nucleic acid sequence is a therapeutic polypeptide or a reporter polypeptide.

29. The vector based on rAAV5 of Claim 28, wherein the therapeutic polypeptide is a coagulation factor selected from the group consisting of Factor VIII, Factor IX, or a functional variant thereof.

30. The vector based on rAAV5 of Claim 29, wherein the therapeutic peptide is Factor VIII or a functional variant thereof.

31. The vector based on rAAV5 of Claim 29, wherein the therapeutic peptide is Factor IX or a functional variant thereof.

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

a) the vector based on rAAV5 of any one of Claims 27 to 31; and

b) a pharmaceutically acceptable excipient.

33. The pharmaceutical composition of Claim 32, wherein the subject is a human subject.