

CLAIMS:

1. A recombinant adeno-associated virus (rAAV) useful as a liver-directed therapeutic for hemophilia A, said rAAV comprising an AAV capsid, and a vector genome packaged therein, said vector genome comprising:

- (a) an AAV 5' inverted terminal repeat (ITR) sequence;
- (b) a transthyretin enhancer (enTTR);
- (c) a transthyretin (TTR) promoter;
- (d) a coding sequence encoding a human Factor VIII having coagulation function; and
- (e) an AAV 3' ITR sequence;

wherein the coding sequence comprises a nucleotide sequence that is at least 95% identical to the nucleotide sequence as set forth in SEQ ID NO: 2.

2. The rAAV according to claim 1, wherein the coding sequence comprises the nucleotide sequence as set forth in SEQ ID NO: 2.

3. The rAAV according to claim 1 or claim 2, wherein the transthyretin (TTR) promoter comprises the nucleotide sequence as set forth in SEQ ID NO: 7.

4. The rAAV according to any one of claims 1 to 3, wherein the rAAV capsid is a hu37 capsid.

5. The rAAV according to any one of claims 1 to 4, wherein the AAV 5' ITR and/or the AAV 3' ITR is from AAV2.

6. The rAAV according to claim 1 or claim 2, wherein the enTTR comprises the nucleotide sequence as set forth in SEQ ID NO: 5.

7. The rAAV according to any one of claims 1 to 6, wherein the vector genome further comprises a polyA sequence.

8. The rAAV according to claim 7, wherein the polyA sequence comprises the nucleotide sequence as set forth in SEQ ID NO: 10.

9. The rAAV according to any one of claims 1 to 8, wherein the vector genome is about 5 kilobases to about 5.5 kilobases in size.

10. The rAAV according to any one of claims 1 to 9, wherein the vector genome comprises nucleotides 1-5110 of the nucleotide sequence as set forth in SEQ ID NO: 13.

11. An aqueous suspension suitable for administration to a hemophilia A patient, said suspension comprising an aqueous suspending liquid and about 1×10^{12} GC/mL to about 1×10^{14} GC/mL of the rAAV according to any one of claims 1 to 10.

12. The aqueous suspension according to claim 11, wherein the suspension is suitable for intravenous injection.

13. The aqueous suspension according to claim 11 or claim 12, wherein the suspension further comprises a surfactant, preservative, and/or buffer dissolved in the aqueous suspending liquid.

14. The rAAV according to any one claims 1 to 10 for use in treating a patient having hemophilia A.

15. Use of the rAAV virus according to any one of claims 1 to 10 in the preparation of a medicament for treating a patient having hemophilia A.

16. Use according to claim 15, wherein the rAAV is to be delivered at 1×10^{12} to 1×10^{14} genome copies (GC/kg) in an aqueous suspension

17. Use according to claim 16, wherein the rAAV is to be administered at first time point and a later time point.