

Claims

1. An isolated codon-optimized nucleic acid encoding the FIX (coagulation factor IX) protein having the amino acid sequence of SEQ ID NO:1, that includes a nucleotide sequence that is selected from the group comprising: SEQ ID NO: 2 or SEQ ID NO: 4.
2. An expression cassette that includes the codon-optimized nucleic acid according to claim 1.
3. The expression cassette according to claim 2, comprising the following elements in the 5'-end to 3'-end direction:
 - a left-hand (first) ITR (inverted terminal repeats);
 - TTR promoter (transthyretin promoter);
 - an intron of the hBG1 gene (an intron-bearing fragment of the human β -globin gene);
 - the codon-optimized nucleic acid according to claim 1;
 - an hGH1 polyadenylation signal (human growth hormone gene polyadenylation signal);
 - a right-hand (second) ITR.
4. The expression cassette according to claim 3, that includes a nucleotide sequence that is selected from the group comprising: SEQ ID NO: 3 or SEQ ID NO: 5.
5. An expression vector that includes the codon-optimized nucleic acid according to claim 1 or the expression cassette according to any of claims 2 to 4.
6. An isolated AAV5 (adeno-associated virus serotype 5)-based recombinant virus for increasing the FIX gene expression in target cells, which includes the codon-optimized nucleic acid according to claim 1 or the expression cassette according to any of claims 2 to 4.
7. The AAV5-based recombinant virus according to claim 6, wherein the capsid includes the AAV5 protein VP1.
8. The AAV5-based recombinant virus according to claim 7, wherein the capsid includes the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 11.
9. The AAV5-based recombinant virus according to claim 7, wherein the capsid includes the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 11 with one or more point mutations.
10. The AAV5-based recombinant virus according to claim 9, wherein the capsid includes the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 14.
11. The AAV5-based recombinant virus according to any of Claims 6 to 10, wherein the capsid includes the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 11 or the amino acid sequence of SEQ ID NO: 11 with one or more point mutations, and the expression cassette includes the following elements in the 5'-end to 3'-end direction:

a left-hand (first) ITR (inverted terminal repeats);
a TTR promoter;
an intron of the hBG1 gene (an intron-bearing fragment of the human β -globin gene);
the codon-optimized nucleic acid according to claim 1;
an hGH1 polyadenylation signal (human growth hormone gene polyadenylation signal);
a right-hand (second) ITR.

12. The AAV5-based recombinant virus according to claim 11, wherein the capsid includes the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 11 or the amino acid sequence of SEQ ID NO: 11 with one or more point mutations, and the expression cassette comprises a nucleotide sequence selected from the group comprising SEQ ID NO: 3 or SEQ ID NO: 5.

13. The AAV5-based recombinant virus according to any of claims 11 to 12, wherein the AAV5 protein VP1 having the amino acid sequence of SEQ ID NO: 11 with one or more point mutations is the amino acid sequence of SEQ ID NO: 14.

14. A pharmaceutical composition for delivering the FIX gene to target cells, comprising the AAV5-based recombinant virus according to any of claims 6 to 13 in combination with one or more pharmaceutically acceptable excipients.

15. Use of the AAV5-based recombinant virus according to claims 6 to 13 or the composition according to claim 14 for delivering the FIX gene to target cells.

16. Use of the AAV5-based recombinant virus according to any of claims 6 to 13 or the composition according to claim 14 for providing the FIX protein to a subject that has hemophilia B and/or that does not have fully functional copies of the FIX gene.

17. Use of the AAV5-based recombinant virus according to any of claims 6 to 13 or the composition according to claim 14 for treating hemophilia B in a subject that has hemophilia B.

18. An AAV5-based recombinant virus according to claims 6 to 13 or the composition according to claim 14 for use in the manufacture of a medicament for treating hemophilia B .