CLAIMS

1. A composition comprising:

(1) a fusion molecule or a nucleic acid sequence encoding the fusion molecule, wherein the fusion molecule comprises at least one DNA binding protein and at least one gene expression modulator, and

(2) at least one single guide RNA (sgRNA), or a nucleic acid sequence encoding the sgRNA,

wherein the sgRNA is complementary to a target DNA sequence in the vicinity of a hepatitis B virus (HBV) gene and/or within a HBV gene regulatory element, the HBV gene is a type B HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 1, a type C HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 2, or a type D HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 3, the HBV gene regulatory element comprises a transcription initiation site, a core promoter, a promoter, an enhancer, a silencer, an insulator element, a boundary element, and/or a locus control region, and the target DNA sequence is located between nucleotide at position 1056 and nucleotide at position 2354, between nucleotide at position 2639 and nucleotide at position 2658, between nucleotide at position 2863 and nucleotide at position 2930, and/or between nucleotide at position 3048 and nucleotide at position 3067 of the HBV gene.

2. The composition according to claim 1, wherein the target DNA sequence is located in one or more of following regions of the type B HBV gene: between nucleotide at position 1149 and nucleotide at position 1190, between nucleotide at

position 1210 and nucleotide at position 1310, between nucleotide at position 1350 and nucleotide at position 1400, between nucleotide at position 1420 and nucleotide at position 1450, and between nucleotide at position 1470 and nucleotide at position 1592, the target DNA sequence is located in one or more of following regions of the type C HBV gene: between nucleotide at position 1150 and nucleotide at position 1180, between nucleotide at position 1200 and nucleotide at position 1310, between nucleotide at position 1350 and nucleotide at position 1390, between nucleotide at position 1420 and nucleotide at position 1460, and between nucleotide at position 1480 and nucleotide at position 1593 or the target DNA sequence is located in one or more of following regions of the type D HBV gene: between nucleotide at position 1056 and nucleotide at position 1079, between nucleotide at position 1101 and nucleotide at position 1900, between nucleotide at position 1972 and nucleotide at position 2082, between nucleotide at position 2134 and nucleotide at position 2264, between nucleotide at position 2335 and nucleotide at position 2354, between nucleotide at position 2639 and nucleotide at position 2658, between nucleotide at position 2863 and nucleotide at position 2882, between nucleotide at position 2911 and nucleotide at position 2930, and between nucleotide at position 3048 and nucleotide at position 3067.

3. The composition according to any one of claims 1-2, wherein the target DNA sequence is located in one or more of following regions of the type D HBV gene: between nucleotide at position 1060 and nucleotide at position 1079, between nucleotide at position 1160 and nucleotide at position 1310, between nucleotide at position 1253 and nucleotide at position 1284, between nucleotide at position 1370 and

nucleotide at position 1470, between nucleotide at position 1490 and nucleotide at position 1612, between nucleotide at position 1693 and nucleotide at position 1852, and between nucleotide at position 2863 and nucleotide at position 2882.

4. The composition according to any one of claims 1-3, wherein the sgRNA comprises a nucleotide sequence as set forth in any one of SEQ ID NOs: 4-1165 or the sgRNA comprises a partial sequence of the nucleotide sequence as set forth in any one of SEQ ID NOs: 4-1165, and the partial sequence has a length of 15-20 base pairs.

5. The composition according to any one of claims 1-4, wherein the at least one DNA binding protein is a CRISPR enzyme, a zinc finger nuclease (ZNF), a transcription activator-like effector nuclease (TALEN), a homing endonuclease, a dCas9-FokI nuclease, or a MegaTal nuclease.

6. The composition according to any one of claims 1-5, wherein the at least one DNA binding protein is dCas9.

7. The composition according to claim 6, wherein the dCas9 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1170-1187.

8. The composition according to any one of claims 1-7, wherein the at least one gene expression modulator comprises one or more selected from a DNA methyltransferase, a DNA hydroxymethylase, a DNA demethylase, a histone methyltransferase, a histone demethylase, a histone acetyltransferase, a histone deacetylase, a phosphatase, a kinase, a transcriptional activator, a transcriptional repressor, a portion of the above, and any combination of the above, and the DNA methyltransferase is DNMT3A, DNMT3B, DNMT3L, DNMT1 or DNMT2.

9. The composition according to any one of claims 1-8, wherein the at least one gene expression modulator comprises one or more selected from a DNA methyltransferase (DNMT), a zinc finger protein-based transcription factor, a portion of the above, and any combination of the above, and the DNA methyltransferase is selected from DNMT3A and DNMT3L and a combination thereof, and the zinc finger protein-based transcription factor is KRAB or ZIM3 KRAB.

10. The composition according to claim 9, wherein the DNMT3A comprises an amino acid sequence as set forth in SEQ ID NO: 1166, the DNMT3L comprises an amino acid sequence as set forth in SEQ ID NO: 1167 or 1195, and the zinc finger protein-based transcription factor comprises an amino acid sequence as set forth in SEQ ID NO: 1168 or 1196.

11. The composition according to any one of claims 1-10, wherein the fusion molecule comprises the at least one gene expression modulator fused to the C-terminus, the N-terminus or both termini of the at least one DNA binding protein, and the at least one gene expression modulator is directly fused to the at least one DNA binding protein or the at least one gene expression modulator is indirectly fused to the at least one DNA binding protein via a non-regulatory agent, a second modulator or a linker.

12. The composition according to any one of claims 1-11, wherein the fusion molecule comprises domains DNMT3A-DNMT3L-dCas9-KRAB or domains DNMT3A-DNMT3L-ZIM3 KRAB-dCas9, wherein "-" means that the individual domains of the fusion molecule are directly and/or indirectly linked, and the individual domains are linked in order from N-terminus to C-terminus.

13. The composition according to any one of claims 1-12, wherein the fusion molecule comprises an amino acid sequence as set forth in SEQ ID NO: 1169 or 1194.

14. The composition according to any one of claims 1-13, wherein the fusion molecule is packaged in liposomes, lipid nanoparticles or AAV vectors.

15. The composition according to any one of claims 1-14, wherein the fusion molecule and the sgRNA are packaged in liposomes, lipid nanoparticles or AAV vectors, and the fusion molecule and the sgRNA are packaged in the same liposome, lipid nanoparticle or AAV vector, or in different liposomes, lipid nanoparticles or AAV vectors.

16. A single guide RNA (sgRNA), wherein the sgRNA comprises a sequence complementary to a target DNA sequence, and the target DNA sequence is located in the vicinity of a hepatitis B virus (HBV) gene and/or within an HBV gene regulatory element; the HBV gene is a type B HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 1, a type C HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 2, or a type D HBV gene comprising a nucleotide sequence as set forth in SEQ ID NO: 3; the HBV gene regulatory element comprises a transcription initiation site, a core promoter, a promoter, an enhancer, a silencer, an insulator element, a boundary element, and/or a locus control region, and the target DNA sequence is located between nucleotide at position 1056 and nucleotide at position 2354, between nucleotide at position 2639 and nucleotide at position 2658, between nucleotide at position 2863 and nucleotide at position 2930, and/or between nucleotide at position 3048 and nucleotide at position 3067 of the HBV gene.

17. The sgRNA according to claim 16, wherein the target DNA sequence is located in one or more of following regions of the type B HBV gene: between nucleotide at position 1149 and nucleotide at position 1190, between nucleotide at position 1210 and nucleotide at position 1310, between nucleotide at position 1350 and nucleotide at position 1400, between nucleotide at position 1420 and nucleotide at position 1450, and between nucleotide at position 1470 and nucleotide at position 1592, the target DNA sequence is located in one or more of following regions of the type C HBV gene: between nucleotide at position 1150 and nucleotide at position 1180, between nucleotide at position 1200 and nucleotide at position 1310, between nucleotide at position 1350 and nucleotide at position 1390, between nucleotide at position 1420 and nucleotide at position 1460, and between nucleotide at position 1480 and nucleotide at position 1593 or the target DNA sequence is located in one or more of following regions of the type D HBV gene: between nucleotide at position 1056 and nucleotide at position 1079, between nucleotide at position 1101 and nucleotide at position 1900, between nucleotide at position 1972 and nucleotide at position 2085, between nucleotide at position 2134 and nucleotide at position 2264, between nucleotide at position 2335 and nucleotide at position 2354, between nucleotide at position 2639 and nucleotide at position 2658, between nucleotide at position 2863 and nucleotide at position 2882, between nucleotide at position 2911 and nucleotide at position 2930, and between nucleotide at position 3048 and nucleotide at position 3067.

18. The sgRNA according to any one of claims 16-17, wherein the target DNA sequence is located in one or more of following regions of the type D HBV gene:

between nucleotide at position 1060 and nucleotide at position 1079, between nucleotide at position 1160 and nucleotide at position 1310, between nucleotide at position 1253 and nucleotide at position 1284, between nucleotide at position 1370 and nucleotide at position 1470, between nucleotide at position 1490 and nucleotide at position 1612, between nucleotide at position 1693 and nucleotide at position 1852, and between nucleotide at position 2863 and nucleotide at position 2882.

19. The sgRNA according to any one of claims 16-18, wherein the sgRNA comprises a nucleotide sequence as set forth in any one of SEQ ID NOs: 4-1165 or the sgRNA comprises a partial sequence of a nucleotide sequence as set forth in any one of SEQ ID NOs: 4-1165, and the partial sequence has a length of 15 to 20 base pairs.

20. The composition according to any one of claims 1-15 for use in the manufacture of a medicament for treating a hepatitis B virus (HBV) infection-related disease in a subject or alleviating a symptom of a HBV infection-related disease in a subject.