Claims

1.

~~1.~~ A composition comprising: (a)

~~(a)~~ a first non-naturally occurring nucleic acid molecule comprising a first polynucleotide encoding a HBV polymerase antigen comprising the~~having an~~ amino acid sequence of~~that is at least 90% identical to~~ SEQ ID NO: 4, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity; (b)

~~(b)~~ a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide encoding a truncated HBV core antigen consisting of the~~an~~ amino acid sequence of~~that is at least 95% identical to~~ SEQ ID NO: 2 or SEQ ID NO: 14; and (c)

~~(c)~~ a pharmaceutically acceptable carrier,

wherein the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule are present in the same non-naturally occurring nucleic acid molecule or in two different non-naturally occurring nucleic acid molecules.

~~2. A kit comprising:~~

~~(a) a first non-naturally occurring nucleic acid molecule comprising a first polynucleotide encoding a HBV polymerase antigen having an amino acid sequence that is at least 90% identical to SEQ ID NO: 4, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity;~~

~~(b) a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide encoding a truncated HBV core antigen consisting of an amino acid sequence that is at least 90% identical to SEQ ID NO: 2 or SEQ ID NO: 14; and~~

~~(c) a pharmaceutically acceptable carrier,~~

~~wherein the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule are present in the same non-naturally occurring nucleic acid molecule or in two different non-naturally occurring nucleic acid molecules.~~

2. The composition of claim 1

~~3. The composition or kit of claim 1 or claim 2, wherein the first polynucleotide encodes an HBV polymerase antigen comprising an amino acid sequence that is at least 98%~~

~~identical to SEQ ID NO: 4, and the second polynucleotide encodes an HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 14.~~

~~4. The composition or kit of claim 1 or claim 2, wherein the first polynucleotide encodes an HBV polymerase antigen comprising the amino acid sequence of SEQ ID NO: 4.~~

~~5. The composition or kit of any one of claims 1 to 4~~, wherein at least one of the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule further comprises a polynucleotide sequence encoding a signal sequence operably linked to at least one of the HBV polymerase antigen and the truncated HBV core antigen.

3.

~~6.~~ The composition ~~or kit~~ of claim 2, wherein the first non-naturally occurring nucleic acid molecule further comprises a polynucleotide sequence encoding a ~~5, wherein the~~ signal sequence having ~~independently comprises~~ the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 19.

4. ~~, preferably the signal sequence is encoded by the polynucleotide sequence of SEQ ID NO: 5 or SEQ ID NO: 18.~~

~~7.~~ The composition ~~or kit of any one of claims 1 to 6, wherein the first polynucleotide sequence is at least 90% identical to SEQ ID NO: 3 or SEQ ID NO: 16.~~

~~8. The composition or kit~~ of claim 1~~7~~, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 16.

5.

9. The composition or kit of any one of claims 1 to 8, wherein the second polynucleotide sequence is at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 15.

10. The composition or kit of claim 19, wherein the second polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 15.

6.

11. The composition or kit of claimany one of claims 1 to 10, wherein the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule are present in the same vector.

7.

12. The composition or kit of claim 611, wherein the vector encodes a fusion protein comprising the truncated HBV core antigen operably linked to the HBV polymerase antigen, optionally via a linker.

8.

13. The composition or kit of claim 712, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 20.

9.

14. The composition or kit of claim 712 or claim 13, wherein the vector contains, from 5'5' end to 3'3' end, a promoter sequence, an enhancer sequence, a signal peptide coding sequence, the second polynucleotide sequence, a linker coding sequence, the first polynucleotide sequence, and a polyadenylation signal sequence.

10.

15. The composition or kit of claim 914, wherein the vector is an adenoviral vector.

11. , preferably an Ad26 or Ad35 vector.

~~16.~~ The composition ~~or kit~~ of claim 10~~15~~, wherein the adenoviral vector contains the promoter sequence comprising the polynucleotide sequence of SEQ ID NO: 17, the regulatory sequence comprising the polynucleotide sequence of SEQ ID NO: 23, the signal peptide coding sequence comprising the polynucleotide sequence of SEQ ID NO: 18, the second polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 15, the linker coding sequence comprising the polynucleotide sequence of SEQ ID NO: 22, the first polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 16, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 24.

12.

~~17.~~ The composition ~~or kit~~ of claim~~any one of claims~~ 1~~ to 10~~, wherein the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule are present in two different vectors.

13.

~~18.~~ The composition ~~or kit~~ of claim 12~~17~~, wherein the first non-naturally occurring nucleic acid molecule is present in a first plasmid DNA vector, and the second non-naturally occurring nucleic acid molecule is present in a second plasmid DNA vector.

14.

~~19.~~ The composition ~~or kit~~ of claim 13~~18~~, wherein each of the first and second plasmid DNA vectors comprises an origin of replication, an antibiotic resistance gene, and from 5'~~5’~~ end to 3'~~3’~~ end, a promoter sequence, a regulatory sequence, a signal peptide coding sequence, the first polynucleotide sequence or the second polynucleotide sequence, and a polyadenylation signal sequence.

15.

~~20.~~ The composition ~~or kit~~ of claim 14~~19~~, wherein the antibiotic resistance gene is a kanamycin resistance gene having a polynucleotide sequence at least 90% identical to SEQ ID NO: 12.

16. , preferably 100% identical to SEQ ID NO: 12.

21. The composition or kit of claim 1520, comprising, (a)

(a) a first plasmid DNA vector comprising, from 3'3'-end to 5'5'-end, the promoter sequence comprising the polynucleotide sequence of SEQ ID NO: 7, the regulatory sequence comprising the polynucleotide sequence of SEQ ID NO: 8, the signal peptide coding sequence comprising the polynucleotide sequence of SEQ ID NO: 5, the first polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 3, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 11; (b)

(b) a second plasmid DNA vector comprising, from 3'3'-end to 5'5'-end, the promoter sequence comprising the polynucleotide sequence of SEQ ID NO: 7, the regulatory sequence comprising the polynucleotide sequence of SEQ ID NO: 8, the signal peptide coding sequence comprising the polynucleotide sequence of SEQ ID NO: 5, the second polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 1, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 11; and (c)

(c) a pharmaceutically acceptable carrier,

wherein each of the first plasmid DNA vector and the second plasmid DNA vector further comprises a kanamycin resistance gene having the polynucleotide sequence of SEQ ID NO: 12, and an originoriginal of replication having the polynucleotide sequence of SEQ ID NO: 10, and

wherein the first plasmid DNA vector and the second plasmid DNA vector are in the same composition or two different compositions.

17.

22. The composition or kit of any one of claims 1 to 21 for use in inducing an immune response against a hepatitis B virus in a subject in need thereof, preferably the subject has chronic HBV infection.

23. The composition or kit of any one of claims 1 to 21 for use in treating a hepatitis B virus (HBV) induced disease in a subject in need thereof, preferably the subject has

chronic HBV infection, and the HBV-induced disease is selected from the group consisting of advanced fibrosis, cirrhosis and hepatocellular carcinoma (HCC).

24. A non-naturally occurring nucleic acid molecule comprising a first polynucleotide sequence encoding an HBV polymerase antigen comprising an amino acid sequence that is at least 98% identical to SEQ ID NO: 4, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H- activity, wherein the HBV polymerase antigen is capable of inducing an immune response in a mammal against at least two HBV genotypes, and preferably the HBV polymerase antigen is capable of inducing a T cell response in a mammal against at least HBV genotypes B, C and D, and more preferably the HBV polymerase antigen is capable of inducing a CD8 T cell response in a human subject against at least HBV genotypes A, B, C and D, optionally, the non-naturally occurring nucleic acid molecule further comprises a second polynucleotide sequence encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 14.

18.

25. The non-naturally occurring nucleic acid molecule of claim 17 24, encoding a fusion protein comprising the truncated HBV core antigen operably linked to the HBV polymerase antigen, optionally via a linker.

19. The composition of claim 1 for use in a method of inducing an immune response against a hepatitis B virus, wherein an effective amount of the composition is to be administered to the subject in need thereof. A method of inducing an immune response against a hepatitis B virus in a subject in need thereof, the method comprising administering to the subject the composition of claim 1.

20. The composition of claim 1 for use in the treatment of a hepatitis B virus (HBV)-induced disease selected from the group consisting of advanced fibrosis, cirrhosis and hepatocellular carcinoma (HCC), wherein an effective amount of the composition is to be administered to the subject in need thereof. A method of treating a hepatitis B virus (HBV)-induced disease selected from the group consisting of advanced fibrosis, cirrhosis and hepatocellular carcinoma (HCC) in a subject in need thereof, the method

~~comprising administering to the subject the composition of claim 1.~~

21. The composition of claim 2, wherein the second non-naturally occurring nucleic acid molecule further comprises a polynucleotide sequence encoding a signal sequence having the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 19.

22. A composition comprising: (a) a first non-naturally occurring nucleic acid molecule comprising a first polynucleotide encoding a HBV polymerase antigen comprising the amino acid sequence that is at least 98% identical to SEQ ID NO: 4, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity; (b) a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide encoding a truncated HBV core antigen consisting of the amino acid sequence that is at least 95% identical to SEQ ID NO: 2 or SEQ ID NO: 14; and (c)

~~-~~a pharmaceutically acceptable carrier, wherein the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule are present in the same non-naturally occurring nucleic acid molecule or in two different non-naturally occurring nucleic acid molecules.

23. The composition of claim 22, wherein the first polynucleotide and the second polynucleotide are present in a vector or in two separate vectors, and the vector is an RNA vector, a DNA plasmid, a cosmid, an artificial chromosome, or a viral vector selected from the group consisting of an adenoviral vector, adeno-associated virus vector, pox virus vector, enteric virus vector, Tobacco Mosaic Virus vector, lentiviral vector and arenavirus viral vector.

24. A non-naturally occurring nucleic acid molecule comprising a first polynucleotide sequence encoding an HBV polymerase antigen comprising an amino acid sequence that is at least 98% identical to SEQ ID NO: 4, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity, wherein the HBV polymerase antigen is capable of inducing an immune response in a mammal against at least two HBV genotypes, and the non-naturally occurring nucleic acid molecule further comprises a second polynucleotide sequence encoding a truncated HBV core antigen consisting of the amino acid sequence that is at least 97% identical to SEQ ID NO: 2 or SEQ ID NO: 14.

25. The composition of claim 24, wherein the non-naturally occurring nucleic acid molecule is an RNA vector.

26. The composition of claim 24, wherein the non-naturally occurring nucleic acid molecule is a DNA plasmid, a cosmid, or an artificial chromosome.

27. The composition of claim 24, wherein the non-naturally occurring nucleic acid molecule is a viral vector selected from the group consisting of an adenoviral vector, adeno-associated virus vector, pox virus vector, enteric virus vector, Tobacco Mosaic Virus vector, lentiviral vector and arenavirus viral vector.