

## CLAIMS

We claim:

- 5           1. A composition 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;
- 10           (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 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-
- 15           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
- 20           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
- 25           (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.
3. The composition or kit of claim 1 or claim 2, wherein the first polynucleotide encodes an
- 30           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.
6. The composition or kit of claim 5, wherein the signal sequence independently comprises the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 19, 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 7, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 16.
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 9, wherein the second polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 15.
11. The composition or kit of 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 the same vector.
12. The composition or kit of claim 11, wherein the vector encodes a fusion protein comprising the truncated HBV core antigen operably linked to the HBV polymerase antigen, optionally via a linker.
13. The composition or kit of claim 12, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 20.
14. The composition or kit of claim 12 or claim 13, wherein the vector contains, from 5' end to 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.

15. The composition or kit of claim 14, wherein the vector is an adenoviral vector, preferably an Ad26 or Ad35 vector.
- 5 16. The composition or kit of claim 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
- 10 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.
17. The composition or kit of 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.
- 15 18. The composition or kit of claim 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.
- 20 19. The composition or kit of claim 18, wherein each of the first and second plasmid DNA vectors comprises an origin of replication, an antibiotic resistance gene, and from 5' end to 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.
- 25 20. The composition or kit of claim 19, wherein the antibiotic resistance gene is a kanamycin resistance gene having a polynucleotide sequence at least 90% identical to SEQ ID NO: 12, preferably 100% identical to SEQ ID NO: 12.
21. The composition or kit of claim 20, comprising,
- 30 (a) a first plasmid DNA vector comprising, from 3'-end to 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;
- 5 (b) a second plasmid DNA vector comprising, from 3'-end to 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
- 10 ID NO: 1, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 11; and
- (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
- 15 SEQ ID NO: 12, and an origin 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.
22. The composition or kit of any one of claims 1 to 21 for use in inducing an immune
- 20 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
- 25 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
- 30 antigen is capable of inducing an immune response in a mammal against at least two HBV genotypes, 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  
5 encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 14.

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

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