Claims

1.

~~1.~~ A Modified Vaccinia Ankara (MVA) vector comprising 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.

2. The MVA vector of claim 1, wherein the HBV polymerase antigen comprises the amino acid sequence of SEQ ID NO: 4.

3. The MVA vector of claim 1, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 3.

4. A composition comprising the MVA vector of claim 1 and a pharmaceutically acceptable carrier.

5.

~~2.~~ The MVA vector of claim 1, wherein the HBV polymerase antigen is capable of inducing an immune response in a mammal against at least two HBV genotypes.

6. The MVA vector of claim 1, wherein~~, 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.

7. The MVA vector of claim 1, wherein~~, 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.

8.

~~3.~~ The MVA vector of claim 1~~, wherein the HBV polymerase antigen comprises the amino acid sequence of SEQ ID NO: 4.~~

~~4. The MVA vector of any one of claims 1-3~~, further comprising a polynucleotide sequence encoding a signal sequence operably linked to the HBV polymerase antigen.

9. The MVA vector of claim 8, wherein the signal sequence comprises the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 11.

10. The MVA vector of claim 8, wherein the signal sequence is encoded by the polynucleotide sequence of SEQ ID NO: 5 or SEQ ID NO: 10.

11. The MVA vector of claim

~~5. The MVA vector of any one of claims~~ 1~~-4~~, wherein the first polynucleotide sequence is at least 90% identical to SEQ ID NO: 3.

12.

~~6.~~ The MVA vector of claim ~~5, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 3.~~

~~7. The MVA vector of any one of claims~~ 1, wherein ~~6, further comprising a second polynucleotide sequence encoding a truncated HBV core antigen consisting of~~ the first~~amino acid sequence of SEQ ID NO: 2.~~

~~The MVA vector of claim 7, wherein the second~~ polynucleotide sequence is at least 90% identical to SEQ ID NO: 19.

13. The MVA vector of claim 12, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 19.

14. The MVA vector of claim 1, wherein the first polynucleotide sequence is at least 90% identical to SEQ ID NO: 20.

~~8.~~

15. ~~1.~~

~~9.~~ The MVA vector of claim 14~~8~~, wherein the first~~second~~ polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 20.

16. The ~~1.~~

~~10. A composition comprising the~~ MVA vector of claim 1, wherein the ~~any one of claims 1-9 and a pharmaceutically acceptable carrier.~~

~~11. A method of enhancing an immune response in a human subject, the method comprising:~~

~~a. administering to the human subject a first composition comprising an immunologically effective amount of an adenovirus vector comprising a non-naturally occurring nucleic acid molecule comprising a first polynucleotide sequence encoding an~~ HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity.

17. The MVA vector of claim 16, wherein the HBV polymerase comprises~~comprising~~ an amino acid sequence that is at least 99~~98~~% identical to SEQ ID NO: 4.

18. The ~~; and~~

~~b. administering to the human subject a second composition comprising an immunologically effective amount of the~~ MVA vector of claim 16, wherein~~any one of claims 1-10;~~

~~to thereby obtain an enhanced immune response against~~ the HBV polymerase comprises~~antigen in~~ the amino acid sequence of SEQ ID NO: 4.

19. ~~human subject.~~

~~12. The~~ The MVA vector~~method~~ of claim 16~~11~~, wherein the HBV polymerase antigen ~~of the first composition is capable of inducing an immune response in the human subject against at least two HBV genotypes, preferably the HBV polymerase antigen~~ is capable of inducing a T cell response in a mammal~~the human subject~~ against at least HBV genotypes B, C~~,~~ and D.

20. The MVA vector of claim 16, wherein~~, and more preferably~~ the HBV polymerase antigen

is capable of inducing a CD8 T cell response in athe human subject against at least HBV genotypes A, B, C, and D.

~~13. The method of claim 12, wherein the HBV polymerase antigen of the first composition comprises the amino acid sequence of SEQ ID NO: 4.~~

~~14. The method of any one of claims 11-13, wherein the first polynucleotide sequence of the first composition is at least 90% identical to SEQ ID NO: 19.~~

~~15. The method of claim 14, wherein the first polynucleotide sequence of the first composition comprises the polynucleotide sequence of SEQ ID NO: 19.~~

~~16. The method of any one of claims 11-15, wherein the nucleic acid molecule of the adenovirus vector in the first composition further comprises a second polynucleotide sequence encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2.~~

~~17. The method of claim 16, wherein the second polynucleotide sequence of the first composition is at least 90% identical to SEQ ID NO: 17.~~

~~18. The method of claim 17, wherein the second polynucleotide sequence of the first composition comprises the polynucleotide sequence of SEQ ID NO: 17.~~

~~19. The method of any one of claims 16-18, wherein the first and second polynucleotide sequences of the first composition encode a fusion protein comprising the truncated HBV core antigen operably linked to the HBV polymerase antigen.~~

~~20. The method of claim 19, wherein the fusion protein of the first composition comprises the truncated HBV core antigen operably linked to the HBV polymerase antigen via a linker.~~

~~21. The method of claim 20, wherein the linker of the first composition comprises the amino acid sequence of (AlaGly)n, and n is an integer of 2 to 5, preferably the linker is encoded by a polynucleotide sequence comprising SEQ ID NO: 14.~~

~~22. The method of claim 21, wherein the fusion protein of the first composition comprises the amino acid sequence of SEQ ID NO: 12.~~

~~23. The method of any one of claims 11-22, wherein the enhanced immune response comprises an enhanced antibody response against the HBV antigen in the human subject.~~

~~24. The method of claim 23, wherein the enhanced immune response comprises an enhanced CD8+ T cell response against the HBV antigen in the human subject.~~

~~25. The method of claim 23 or 24, wherein the enhanced immune response comprises an enhanced CD4+ T cell response against the HBV antigen in the human subject.~~

~~26. The method of any one of claims 11-25, wherein the adenovirus vector is an rAd26 or rAd35 vector.~~

~~27. The method of any one of claims 11-26, wherein step (b) is conducted 1-12 weeks after step (a).~~

~~28. The method of any one of claims 11-26, wherein step (b) is conducted 2-12 weeks after step (a).~~

~~29. The method of any one of claims 11-26, wherein step (b) is conducted at least 1 week after step (a).~~

~~30. The method of any one of claims 11-26, wherein step (b) is conducted at least 2 weeks after step (a).~~

~~31. A method of enhancing an immune response in a human subject, the method comprising:~~

~~a. administering to the human subject a first composition comprising an immunologically effective amount of a first plasmid comprising a first 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 and a second plasmid comprising a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide sequence encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2; and~~

~~b. administering to the human subject a second composition comprising an immunologically effective amount of the MVA vector of any one of claims 1-10;~~

~~to thereby obtain an enhanced immune response against the HBV antigen in the human subject.~~

32. The method of claim 31, wherein the HBV polymerase antigen of the first composition does not have reverse transcriptase activity and RNase H activity.

33. The method of claim 31 or 32, wherein the first composition is for priming the immune response and the second composition is for boosting the immune response.

34. The method of any one of claims 31-33, wherein the HBV polymerase antigen of the first composition is capable of inducing an immune response in the human subject against at least two HBV genotypes, preferably the HBV polymerase antigen is capable of inducing a T cell response in the human subject 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 the human subject against at least HBV genotypes A, B, C, and D.

35. The method of any one of claims 31-34, wherein the HBV polymerase antigen of the first composition comprises the amino acid sequence of SEQ ID NO: 4.

36. The method of any one of claims 31-35, further comprising a polynucleotide sequence encoding a signal sequence operably linked to the HBV polymerase antigen of the first composition.

37. The method of claim 36, wherein the signal sequence comprises the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 11, preferably the signal sequence is encoded by the polynucleotide sequence of SEQ ID NO: 5 or SEQ ID NO: 10.

38. The method of any one of claims 31-37, wherein the first polynucleotide sequence of the first composition is at least 90% identical to SEQ ID NO: 20.

39. The method of claim 38, wherein the first polynucleotide sequence of the first composition comprises the polynucleotide sequence of SEQ ID NO: 20.

40. The method of any one of claims 31-39, wherein the second polynucleotide sequence of the first composition is at least 90% identical to SEQ ID NO: 18.

41. The method of claim 40, wherein the second polynucleotide sequence of the first composition comprises the polynucleotide sequence of SEQ ID NO: 18.

42. The method of any one of claims 31-41, wherein the first and second polynucleotide sequences of the first composition further comprise a promoter sequence, optionally one or more additional regulatory sequences, preferably the promoter sequence comprises the

~~polynucleotide sequence of SEQ ID NO:7, and the additional regulatory sequence is selected from the group consisting of an enhancer sequence of SEQ ID NO: 8 or SEQ ID NO: 15, and a polyadenylation signal sequence of SEQ ID NO: 16.~~

~~43. The method of any one of claims 31-42, wherein the enhanced immune response comprises an enhanced antibody response against the HBV antigen in the human subject.~~

~~44. The method of claim 43, wherein the enhanced immune response comprises an enhanced CD8+ T cell response against the HBV antigen in the human subject.~~

~~45. The method of claim 43 or 44, wherein the enhanced immune response comprises an enhanced CD4+ T cell response against the HBV antigen in the human subject.~~

~~46. The method of any one of claims 31-45, wherein step (b) is conducted 1-12 weeks after step (a).~~

~~47. The method of any one of claims 31-45, wherein step (b) is conducted 2-12 weeks after step (a).~~

~~48. The method of any one of claims 31-45, wherein step (b) is conducted at least 1 week after step (a).~~

~~49. The method of any one of claims 31-45, wherein step (b) is conducted at least 2 weeks after step (a).~~