

CLAIMS

WHAT IS CLAIMED IS:

1. A polypeptide comprising the amino acid sequence as set forth in SEQ ID NOs:1-11 or SEQ ID NOs:14-36.
2. A polypeptide comprising two or more amino acid sequences as set forth in SEQ ID NOs:16-36.
3. The polypeptide of claim 2, wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:19 or 29, the amino acid sequence as set forth in SEQ ID NO:16, 21, 27, 28, or 34, and the amino acid sequence as set forth in SEQ ID NO:20, 22, 23, 30, 31, 35, or 36.
4. The polypeptide of claim 2, wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:3 and the amino acid sequence as set forth in SEQ ID NO:4.
5. The polypeptide of claim 2, wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:5 and the amino acid sequence as set forth in SEQ ID NO:6.
6. The polypeptide of claim 2, wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:7 and the amino acid sequence as set forth in SEQ ID NO:8.
7. The polypeptide of claim 2, wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:9, the amino acid sequence as set forth in SEQ ID NO:10, and the amino acid sequence as set forth in SEQ ID NO:11.

8. The polypeptide of claim 3, further comprising one or more amino acid sequences as set forth in SEQ ID NOs:17 and 18.
9. A cytomegalovirus (CMV) vector comprising a polynucleotide comprising the sequence encoding one or more amino acid sequences as set forth in SEQ ID NOs:1-36.
10. The CMV vector of claim 9, wherein the CMV vector is a human CMV (HCMV) vector or a rhesus CMV (RhCMV) vector.
11. The CMV vector of claim 9 or claim 10, wherein the CMV vector lacks the UL82 gene.
12. The CMV vector of any one of claims 9-11, wherein the CMV vector lacks the UL128-UL130 gene region and lacks the UL146-UL147 gene region.
13. The CMV vector of any one of claims 9-11, wherein the CMV vector has an intact UL128-UL130 gene region and an intact UL146-UL147 gene region.
14. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise one or more of SEQ ID NOs:1-11, SEQ ID NOs:14-15, and SEQ ID NOs:24-26.
15. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise one or more of SEQ ID NOs:16-23 and SEQ ID NOs: 27-36.

16. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise two or more of SEQ ID NOs:16-23 and SEQ ID NOs: 27-36.

17. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise:

- a) the sequence as set forth in SEQ ID NO:19 or 29;
- b) the sequence as set forth in any one of SEQ ID NOs:16, 21, 27, 28, or 34; and
- c) the sequence as set forth in any one of SEQ ID NOs:20, 22, 23, 30, 31, 33, 35, or 36.

18. The CMV vector of claim 17, wherein the one or more amino acid sequences further comprise one or more of SEQ ID NOs:17 and 18.

19. The CMV vector of any one of claims 15-18, wherein the sequences encoded by the polynucleotide are ordered for improved expression.

20. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise:

- a) the sequence as set forth in SEQ ID NO:3; and
- b) the sequence as set forth in SEQ ID NO:4.

21. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise:

- a) the sequence as set forth in SEQ ID NO:5; and
- b) the sequence as set forth in SEQ ID NO:6.

22. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise:

- a) the sequence as set forth in SEQ ID NO:7; and
- b) the sequence as set forth in SEQ ID NO:8.

23. The CMV vector of any one of claims 9-13, wherein the one or more amino acid sequences comprise:

- a) the sequence as set forth in SEQ ID NO:9;
- b) the sequence as set forth in SEQ ID NO:10; and
- c) the sequence as set forth in SEQ ID NO:11.

24. A composition comprising two or more CMV vectors according to any of claims 9-23.

25. A hepatitis B virus (HBV) vaccine comprising one or more polypeptides according to any of claims 1-8.

26. A hepatitis B virus (HBV) vaccine comprising a CMV vector and a polynucleotide encoding one or more HBV episensus antigens.

27. The vaccine of claim 26, wherein the CMV vector is a human CMV (HCMV) vector or a rhesus CMV (RhCMV) vector.

28. The vaccine of claim 26 or 27, wherein the CMV vector lacks the UL82 gene.

29. The vaccine of claim 28, wherein the polynucleotide encoding the one or more HBV episensus antigens replaces the UL82 gene.

30. The vaccine of any one of claims 26-29, wherein the CMV vector lacks the UL128-UL130 gene region and lacks the UL146-UL147 gene region.

31. The vaccine of any one of claims 26-29, wherein the CMV vector has an intact UL128-UL130 gene region and an intact UL146-UL147 gene region.

32. The vaccine of any one of claims 26-31, wherein the polynucleotide encodes two or more HBV episensus antigens.

33. The vaccine of any one of claims 26-31, wherein the one or more episensus antigens comprise an amino acid sequence selected from the group consisting of SEQ ID NOs:1-36.

34. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:1.

35. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:2.

36. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:3.

37. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:4.

38. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:5.

39. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:6.

40. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:7.

41. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:8.

42. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:9.

43. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:10.

44. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:11.

45. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:14.

46. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:15.

47. The vaccine of claim 33, wherein the episensus antigen comprises one or more amino acid sequences selected from the group consisting of SEQ ID NOs: 16-23 and SEQ ID NOs: 27-36.

48. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:24.

49. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:25.

50. The vaccine of claim 33, wherein the episensus antigen comprises the amino acid sequence of SEQ ID NO:26.

51. The vaccine of any one of claims 26-50, wherein the episensus antigen comprises one or more episensus sequences derived from one or more of the C protein, the S protein, or the P protein.

52. The vaccine of claim 51, wherein the episensus antigen comprises episensus sequences derived from the C protein, the S protein, and a conserved region of the P protein.

53. The vaccine of claim 51 or 52, wherein the episensus sequences derived from the C protein, S protein, and P protein are ordered for improved expression.

54. The vaccine of any one of claims 51-52, wherein the episensus antigen further comprises episensus sequences derived from one or more of the PreS1 domain, the PreS2 domain, and a non-conserved region of the P protein.

55. The vaccine of any one of claims 26-54, wherein at least one protein sequence from which the episensus antigen is derived contains one or more mutations.

56. The vaccine of claim 55, wherein the mutation is a deletion or substitution.

57. The vaccine of claim 55, wherein the mutation is a P protein mutation set forth in Table 1.

58. The vaccine of any one of claims 26-57, wherein the episensus antigen comprises two or more episensus sequences.

59. The vaccine of claim 58, wherein the episensus antigen comprises two episensus sequences developed using HBV sequences from China.

60. The vaccine of claim 59, wherein the episensus antigen comprises the amino acid sequences of SEQ ID NO:3 and SEQ ID NO:4.

61. The vaccine of claim 58, wherein the episensus antigen comprises an episensus sequence developed using HBV sequences from China and an episensus sequence developed using HBV sequences from a Global set.

62. The vaccine of claim 61, wherein the episensus antigen comprises the amino acid sequences of SEQ ID NO:5 and SEQ ID NO:6.

63. The vaccine of claim 61, wherein the episensus antigen comprises the amino acid sequences of SEQ ID NO:7 and SEQ ID NO:8.

64. The vaccine of claim 58, wherein the episensus antigen comprises three episensus sequences developed using HBV sequences from a Global set.

65. The vaccine of claim 64, wherein the episensus antigen comprises the amino acid sequences of SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

66. An HBV vaccine comprising:
- a) one or more HBV episensus antigens;

- b) one or more polynucleotides encoding one or more HBV episensus antigens; or
- c) one or more vectors comprising one or more polynucleotides, wherein the one or more polynucleotides encode one or more HBV episensus antigens.

67. The vaccine of claim 66, wherein the vaccine comprises:

- a) two or more HBV episensus antigens;
- b) two or more polynucleotides encoding one or more HBV episensus antigens; or
- c) two or more vectors comprising one or more polynucleotides, wherein the one or more polynucleotides encode one or more HBV episensus antigens.

68. A composition comprising two or more HBV vaccines according to any of claims 26-67.

69. The composition of claim 68, wherein a first HBV vaccine encodes or comprises a first episensus antigen developed using HBV samples from China and a second HBV vaccine encodes or comprises a second episensus antigen developed using HBV samples from China.

70. The composition of claim 69, wherein the first episensus antigen comprises the amino acid sequence of SEQ ID NO:3 and the second episensus antigen comprises the amino acid sequence of SEQ ID NO:4.

71. The composition of claim 68, wherein a first HBV vaccine encodes or comprises a first episensus antigen developed using HBV sequences from China and a second HBV vaccine encodes or comprises a second episensus antigen developed using HBV sequences from a Global set.

72. The composition of claim 71, wherein the first episensus antigen comprises the amino acid sequence of SEQ ID NO:5 and the second episensus antigen comprises the amino acid sequence of SEQ ID NO:6.

73. The composition of claim 71, wherein the first episensus antigen comprises the amino acid sequence of SEQ ID NO:7 and the second episensus antigen comprises the amino acid sequence of SEQ ID NO:8.

74. The composition of claim 68, wherein a first HBV vaccine encodes or comprises a first episensus antigen developed using HBV sequences from a Global set, a second HBV vaccine encodes or comprises a second episensus antigen developed using HBV sequences from a Global set, and a third HBV vaccine encodes or comprises a third episensus antigen developed using HBV sequences from a Global set.

75. The composition of claim 74, wherein the first episensus antigen comprises the amino acid sequence of SEQ ID NO:9, the second episensus antigen comprises the amino acid sequence of SEQ ID NO:10, and the third episensus antigen comprises the amino acid sequence of SEQ ID NO:11.

76. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV sequences from Asia.

77. The vaccine or composition of claim 76, wherein the at least one episensus antigen is central to HBV sequences from China.

78. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV sequences from the United States.

79. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV sequences from Europe.

80. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV sequences from the United States and Europe.

81. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to a Global set of HBV sequences.

82. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype A epidemic.

83. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype B epidemic.

84. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype C epidemic.

85. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype CB epidemic.

86. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype D epidemic.

87. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype DC epidemic.

88. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype DE epidemic.

89. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype E epidemic.

90. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to HBV genotype F epidemic.

91. The vaccine of any one of claims 26-67 or the composition of any one of claims 68-75, wherein at least one episensus antigen is central to a HBV genotype other than genotype A, B, C, CB, D, DC, DE, E, and F.

92. The vaccine of any one of claims 26-67 and 76-91 or the composition of any one of claims 68-75, wherein the vaccine is a prophylactic vaccine.

93. The vaccine of any one of claims 26-67 and 76-91 or the composition of any one of claims 68-75, wherein the vaccine is a therapeutic vaccine.

94. The vaccine of any one of claims 26-67 and 76-91 or the composition of any one of claims 68-75, further comprising a pharmaceutically acceptable carrier.

95. A method of treating HBV in a subject comprising administering an effective amount of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of any one of claims 24 or 68-75 to the subject in need thereof.

96. A method of protecting a subject from an HBV infection comprising administering an effective amount of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of any one of claims 24 or 68-75 to the subject in need thereof.

97. A method of generating or inducing an immune response to HBV in a subject comprising administering an effective amount of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of any one of claims 24 or 68-75 to the subject in need thereof.

98. The polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of any one of claims 24 or 68-75 for use in treating HBV.

99. The polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of any one of claims 24 or 68-75 for use in protecting a subject from an HBV infection.

100. The polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 or 76-94, or the composition of

any one of claims 24 or 68-75 for use in generating or inducing an immune response to HBV in a subject.

101. The use of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 and 76-94, or the composition of any one of claims 24 or 68-75 for the manufacture of a medicament for use in treatment of HBV.

102. The use of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 and 76-94, or the composition of any one of claims 24 or 68-75 for the manufacture of a medicament for use in protecting a subject from an HBV infection.

103. The use of the polypeptide of any one of claims 1-8, the vector of any one of claims 9-23, the vaccine of any one of claims 25-67 and 76-94, or the composition of any one of claims 24 or 68-75 for the manufacture of a medicament for use in generating or inducing an immune response to HBV in a subject.

104. A method of designing and producing an HBV vaccine for a subject in a geographic area comprising:

- (a) designing one or more episensus antigens that efficiently cover the HBV genotype diversity within the geographic area; and
- (b) producing one of:
 - an HBV vaccine comprising a CMV backbone and a nucleic acid encoding the episensus antigens; or
 - an HBV vaccine comprising the episensus antigens.

105. A method of designing and producing an HBV vaccine for a subject comprising:
- (a) determining the amino acid sequence of HBV viruses in the subject;
 - (b) designing one or more episensus antigens to efficiently cover the HBV genotype diversity within the viruses present in the subject; and
 - (c) producing one of:
 - an HBV vaccine comprising a CMV backbone and a nucleic acid encoding the episensus antigens; or
 - an HBV vaccine comprising the episensus antigens.
106. A method of inducing an effector memory T cell response comprising:
- (a) designing one or more episensus antigens;
 - (b) producing a vaccine comprising a CMV backbone and a nucleic acid encoding the one or more episensus antigens; and
 - (c) administering the vaccine to a subject in need thereof.
107. A method of treating an HBV infection in a subject comprising:
- (a) producing an immunogenic composition comprising a CMV backbone and a nucleic acid encoding one or more episensus antigens; and
 - (b) administering an effective amount of the immunogenic composition to the subject.
108. A method of preventing an HBV infection in a subject comprising:
- (a) producing an immunogenic composition comprising a CMV backbone and a nucleic acid encoding one or more episensus antigens; and
 - (b) administering an effective amount of the immunogenic composition to the subject.

109. A method of inducing an immune response to HBV in a subject comprising:

- (a) producing an immunogenic composition comprising a CMV backbone and a nucleic acid encoding one or more episensus antigens; and
- (b) administering an effective amount of the immunogenic composition to the subject.

110. A method of inducing an effector memory T cell response in a subject comprising:

- (a) producing an immunogenic composition comprising a CMV backbone and a nucleic acid encoding one or more episensus antigens; and
- (b) administering an effective amount of the immunogenic composition to the subject.

111. The method of any one of claims 104-110, wherein the one or more episensus antigens comprise one or more of the amino acid sequences selected from the group consisting of SEQ ID NOs:1-11, SEQ ID NOs:14-36.