incidence rate in 2016 was 1.0 case per 100,000 population (Centers for Disease Control and Prevention. Viral Hepatitis Surveillance—United States, 2017. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2019. Available at: www_cdc_gov/hepatitis/statistics/2017surveillance/index.htm.). In 2017 alone, a total of 3,407 cases of acute hepatitis B were reported to the Centers for Disease Control and Prevention (CDC).

[0005] Despite the availability of a prophylactic HBV vaccine, the burden of chronic HBV infection continues to be a significant unmet worldwide medical problem, due to suboptimal treatment options and sustained rates of new infections in most parts of the developing world.

SUMMARY OF THE INVENTION

[0006] Provided herein is a hepatitis B virus (HBV) Core protein comprising the amino acid sequence of SEQ ID NO: 6 or an immunogenic fragment thereof.

[0007] Also provided is an HBV polymerase N-terminal domain comprising the amino acid sequence of SEQ ID NO: 8 or an immunogenic fragment thereof.

[0008] An HBV polymerase C-terminal domain comprising the amino acid sequence of SEQ ID NO: 10 or an immunogenic fragment thereof is also disclosed.

[0009] Fusion proteins comprising: an N-terminal herpes simplex virus (HSV) glycoprotein (gD) sequence or a variant thereof; the disclosed HBV Core protein, HBV polymerase N-terminal domain, HBV polymerase C-terminal domain, or immunogenic fragments thereof; and a C-terminal HSV gD sequence or a variant thereof are also provided.

[0010] Also provided herein are fusion proteins comprising: an N-terminal herpes simplex virus (HSV) glycoprotein (gD) sequence or a variant thereof; combinations of the disclosed HBV Core protein, HBV polymerase N-terminal domain, HBV polymerase C-terminal domain, and/or immunogenic fragments thereof; and a C-terminal HSV gD sequence or a variant thereof.

[0010a] Also provided herein is a fusion protein comprising: an HBV polymerase N-terminal domain comprising the amino acid sequence of SEQ ID NO: 178, an HBV polymerase C-terminal domain comprising the amino acid sequence of SEQ ID NO: 179, and an HBV Core protein comprising the amino acid sequence of SEQ ID NO: 180.

[0011] Nucleic acid molecules encoding the disclosed proteins or fusion proteins, vectors comprising the nucleic acid molecules, and vaccines comprising the disclosed vectors are disclosed herein.

[0012] Also provided herein are methods of inducing an immune response to HBV in a subject, the method comprising providing to the subject an effective amount of any of the disclosed fusion proteins, nucleic acid molecules, vectors, or vaccines to thereby induce an immune response to HBV.

[0012a] Also provided herein is a use of the fusion protein of as described herein, the nucleic acid molecule as described herein, the vector as described herein, or the vaccine as described herein in the manufacture of a medicament for inducing an immune response to an HBV infection in a subject, wherein the fusion protein, the nucleic acid molecule, the vector, or the vaccine is to be provided to the subject.

[0012b] Also provided herein is the fusion protein as described herein, the nucleic acid molecule as described herein, the vector as described herein, or the vaccine as described herein for use in therapy.

What is claimed:

1. A fusion protein comprising:

an HBV polymerase N-terminal domain comprising the amino acid sequence of SEQ ID NO: 178, an HBV polymerase C-terminal domain comprising the amino acid sequence of SEQ ID NO: 179, and an HBV Core protein comprising the amino acid sequence of SEQ ID NO: 180.

2. The fusion protein of claim 1, comprising the amino acid sequence of SEQ ID NO: 174.

3. The fusion protein of claim 1 or 2, further comprising an N-terminal HSV gD sequence, a C-terminal HSV gD protein sequence, or both.

4. The fusion protein of claim 3, comprising:

an N-terminal HSV gD sequence,

an HBV sequence comprising an HBV polymerase N-terminal domain comprising the amino acid sequence of SEQ ID NO: 178, an HBV polymerase C-terminal domain comprising the amino acid sequence of SEQ ID NO: 179, and an HBV Core protein comprising the amino acid sequence of SEQ ID NO: 180; and

a C-terminal HSV gD protein sequence.

5. The fusion protein of claim 4, wherein the HBV sequence comprises the amino acid sequence of SEQ ID NO: 174.

6. The fusion protein of any one of claims 3-5, wherein the N-terminal HSV gD sequence comprises the amino acid sequence of SEQ ID NO: 12.

7. The fusion protein of any one of claims 3-5, wherein the N-terminal HSV gD sequence comprises amino acid residues 26-269 of SEQ ID NO: 12.

8. The fusion protein of any one of claims 3-7, wherein the C-terminal HSV gD sequence comprises the transmembrane domain of the HSV gD.

9. The fusion protein of any one of claims 3-8, wherein the C-terminal HSV gD sequence comprises the amino acid sequence of SEQ ID NO: 13.

10. The fusion protein of any one of claims 3-9, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 185.

11. A nucleic acid molecule encoding the fusion protein of any one of claims 1-10.

12. The nucleic acid molecule of claim 11, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 176.

13. The nucleic acid molecule of claim 11, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 184.

14. A vector comprising the nucleic acid molecule of any one of claims 11-13.

15. The vector of claim 14, wherein the vector is an adenoviral vector.

16. The vector of claim 15, wherein the adenoviral vector is an AdC6 vector or AdC7 vector.

17. A vaccine comprising the vector of any one of claims 14-16.

18. Use of the fusion protein of any one of claims 1-10, the nucleic acid molecule of any one of claims 11-13, the vector of any one of claims 14-16, or the vaccine of claim 17 in the manufacture of a medicament for inducing an immune response to an HBV infection in a subject, wherein the fusion protein, the nucleic acid molecule, the vector, or the vaccine is to be provided to the subject.

19. The use of claim 18, wherein the vaccine comprises an AdC6 vector comprising a fusion protein comprising the amino acid sequence of SEQ ID NO: 185.

20. The use of claim 19, wherein subsequent to provision of the vaccine comprising the AdC6 vector, a vaccine comprising an AdC7 vector comprising a fusion protein comprising the amino acid sequence of SEQ ID NO: 185 is to be further provided to the subject.

21. The use of claim 18, wherein the vaccine comprises an AdC7 vector comprising a fusion protein comprising the amino acid sequence of SEQ ID NO: 185.

22. The use of claim 21, wherein subsequent to provision of the vaccine comprising the AdC7 vector, a vaccine comprising an AdC6 vector comprising a fusion protein comprising the amino acid sequence of SEQ ID NO: 185 is to be further provided to the subject.

23. The use of any one of claims 18-22, wherein the amino acid sequence of SEQ ID NO: 185, does not contain the N-terminal 25 amino acid signal peptide.

24. The fusion protein of any one of claims 1-10, the nucleic acid molecule of any one of claims 11-13, the vector of any one of claims 14-16, or the vaccine of claim 17 for use in therapy.