

(RNP) complex. The RNP is exported from the cell by the HBV envelope proteins, which are able to assemble lipoprotein vesicles that bud into the lumen of a pre-Golgi compartment before being secreted. Moreover, the HBV envelope proteins also provide a mechanism for the targeting of HDV to an uninfected cell, thereby ensuring the spread of HDV.

Complications caused by HDV include a greater likelihood of experiencing liver failure in acute infections and a rapid progression to liver cirrhosis, with an increased chance of developing liver cancer in chronic infections. In combination with hepatitis B virus, hepatitis D has the highest fatality rate of all the hepatitis infections, at 20% (Fattovich G, Giustina G, Christensen E, Pantalena M, Zagni I, Realdi G, Schalm SW. Influence of hepatitis delta virus infection on morbidity and mortality in compensated cirrhosis type B. *Gut*. 2000 Mar;46(3):420-6). The only approved therapy for chronic HDV infection is interferon-alpha. However, treatment of HDV with interferon-alpha is relatively inefficient and is not well-tolerated. Treatment with interferon-alpha results in sustained virological response six months post-treatment in one-fourth of the patients. Also, nucleos(t)ide analogs (NAs) have been widely tested in hepatitis delta, but they appear to be ineffective. Combination treatment using NAs with interferon also proved to be disappointing (Zaigham Abbas, Minaam Abbas Management of hepatitis delta: Need for novel therapeutic Options. *World J Gastroenterol* 2015 August 28; 21(32): 9461-9465). Accordingly, new therapeutic options are needed.

SUMMARY

In one aspect, the present disclosure refers to an isolated antibody that binds HBsAg comprising: (i) a heavy chain (HC) comprising the amino acid sequence according to SEQ ID NO:91; and (ii) a light chain (LC) comprising the amino acid sequence according to SEQ ID NO:93. In another aspect, the present disclosure refers to an isolated polynucleotide comprising a nucleotide sequence that encodes the antibody as described herein. In another aspect, the present disclosure refers to a vector comprising the polynucleotide as described herein. In another aspect, the present disclosure refers to a host cell comprising a heterologous polynucleotide as described herein.

In a further aspect, the present disclosure refers to a pharmaceutical composition comprising: (i) the antibody or antigen binding fragment as described herein; (ii) the polynucleotide as described herein; (iii) the vector as described herein; (iv) the host cell as described herein; or (v) any combination of (i)-(iv) and a pharmaceutically acceptable excipient, diluent or carrier. In another aspect, the present disclosure refers to a kit comprising: (a) a component selected from: (i) the antibody or antigen binding fragment as described herein; (ii) the polynucleotide as described herein; (iii) the vector as described herein; (iv) the host cell as described herein; (v) the pharmaceutical composition as described herein; or (vi) any combination of (i)-(v); and (b) instructions for using the component to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection.

In a further aspect, the present disclosure refers to a method of producing the antibody as described herein, comprising culturing the host cell as described herein under conditions and for a time sufficient to produce the antibody. In a further aspect, the present disclosure refers to the antibody as described herein; (ii) the polynucleotide as described herein; (iii) the vector as described herein; (iv) the host cell as described herein; and/or (v) the pharmaceutical composition as described herein for use in therapy. In a further aspect, the present disclosure refers to use of: (i) the antibody as described herein; (ii) the polynucleotide as described herein; (iii) the vector as described herein; (iv) the host cell as described herein; and/or (v) the pharmaceutical composition as described herein in the manufacture of a medicament to prevent, treat, attenuate, and/or diagnose a hepatitis B infection and/or a hepatitis D infection in a subject. In a further aspect, the present disclosure refers to a method for *in vitro* diagnosis of a hepatitis B infection and/or a hepatitis D infection, the method comprising: (i) contacting a sample from a subject with an antibody as described herein; and (ii) detecting a complex comprising an antigen and the antibody. In a further aspect, the present disclosure refers to a method for detecting the presence or absence of an epitope in a correct conformation in an anti-hepatitis-B vaccine and/or an anti-hepatitis-D vaccine, the method comprising: (i) contacting the vaccine with (a) an antibody as described herein; and (ii) determining whether a complex comprising an antigen and the antibody, has been formed.

BRIEF DESCRIPTION OF THE DRAWINGS

The figures provided herein are intended to illustrate subject matter included in the present disclosure in more detail. The figures are not intended to limit the disclosure in any way.

Figure 1 shows binding of HBC34-V7 and two engineered antibodies of the present disclosure ("HBC34-V34"; "HBC34-V35") at the indicated concentrations to HBsAg adw (top panel) and HBsAg adr (bottom panel), as determined in direct antigen-based ELISA assays. All antibodies were produced as IgG1 (g1m17, 1 allotype).

CLAIMS

1. An isolated antibody that binds HBsAg comprising:
 - (i) a heavy chain (HC) comprising the amino acid sequence according to SEQ ID NO:91; and
 - (ii) a light chain (LC) comprising the amino acid sequence according to SEQ ID NO:93.
2. The antibody of claim 1, wherein the antibody is capable of binding an HBsAg of a genotype selected from the HBsAg genotypes A, B, C, D, E, F, G, H, I, and J, or any combination thereof.
3. The antibody of claim 1 or claim 2, wherein the antibody is capable of reducing a serum concentration of hepatitis B virus (HBV) DNA in a mammal having an HBV infection.
4. The antibody of any one of claims 1-3, wherein the antibody is capable of reducing a serum concentration of HBsAg in a mammal having an HBV infection.
5. The antibody of any one of claims 1-4, wherein the antibody is capable of reducing a serum concentration of HBeAg in a mammal having an HBV infection.
6. The antibody any one of claims 1-5, wherein the antibody is capable of reducing a serum concentration of HBcrAg in a mammal having an HBV infection.
7. An isolated polynucleotide comprising a nucleotide sequence that encodes the antibody of any one of claims 1-6.
8. The polynucleotide of claim 7, wherein the nucleotide sequence that encodes the antibody is codon optimized for expression in a host cell.

9. The polynucleotide of claim 7 or 8, comprising a nucleotide sequence having at least 80% identity to the nucleotide sequence according to any one of SEQ ID NO:103 and SEQ ID NO:105.
10. The polynucleotide of claim 9, comprising a V_H-encoding nucleotide sequence according to SEQ ID NO:103, and a V_L-encoding nucleotide sequence according to SEQ ID NO:105.
11. A vector comprising the polynucleotide of any one of claims 7-10.
12. The vector of claim 11, wherein the vector comprises a lentiviral vector or a retroviral vector.
13. A host cell comprising a heterologous polynucleotide of any one of claims 7-10.
14. A pharmaceutical composition comprising:
 - (i) the antibody or antigen binding fragment of any one of claims 1-6;
 - (ii) the polynucleotide according to any one of claims 7-10;
 - (iii) the vector according to claim 11 or 12;
 - (iv) the host cell of claim 13; or
 - (v) any combination of (i)-(iv) and a pharmaceutically acceptable excipient, diluent or carrier.
15. A kit comprising:
 - (a) a component selected from:
 - (i) the antibody or antigen binding fragment of any one of claims 1-6;
 - (ii) the polynucleotide according to any one of claims 7-10;
 - (iii) the vector according to claim 11 or 12;
 - (iv) the host cell of claim 13;
 - (v) the pharmaceutical composition of claim 14; or
 - (vi) any combination of (i)-(v); and

- (b) instructions for using the component to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection.
16. The composition of claim 14, or the kit of claim 15, further comprising:
- (i) a polymerase inhibitor, wherein the polymerase inhibitor optionally comprises Lamivudine, Adefovir, Entecavir, Telbivudine, Tenofovir, or any combination thereof;
 - (ii) an interferon, wherein the interferon optionally comprises IFNbeta and/or IFNalpha; (iii) a checkpoint inhibitor, wherein the checkpoint inhibitor optionally comprises an anti-PD-1 antibody or antigen binding fragment thereof, an anti-PD-L1 antibody or antigen binding fragment thereof, and/or an anti-CTLA4 antibody or antigen binding fragment thereof;
 - (iv) an agonist of a stimulatory immune checkpoint molecule; or
 - (v) any combination of (i)-(iv).
17. The composition or kit of claim 16, wherein the polymerase inhibitor comprises lamivudine.
18. A method of producing the antibody of any one of claims 1-6, comprising culturing the host cell of claim 13 under conditions and for a time sufficient to produce the antibody.
19. The antibody of any one of claims 1-6; (ii) the polynucleotide of any one of claims 7-10; (iii) the vector of claim 11 or 12; (iv) the host cell of claim 13; and/or (v) the pharmaceutical composition of claim 14 for use in therapy.
20. Use of: (i) the antibody of any one of claims 1-6; (ii) the polynucleotide of any one of claims 7-10; (iii) the vector of claim 11 or 12; (iv) the host cell of claim 13; and/or (v) the pharmaceutical composition of claim 14, in the manufacture of a medicament to prevent, treat, attenuate, and/or diagnose a hepatitis B infection and/or a hepatitis D infection in a subject.

21. The use of claim 20, further comprising that one or more of:
- (vi) a polymerase inhibitor, wherein the polymerase inhibitor optionally comprises Lamivudine, Adefovir, Entecavir, Telbivudine, Tenofovir, or any combination thereof;
 - (vii) an interferon, wherein the interferon optionally comprises IFNbeta and/or IFNalpha;
 - (viii) a checkpoint inhibitor, wherein the checkpoint inhibitor optionally comprises an anti-PD-1 antibody or antigen binding fragment thereof, an anti-PD-L1 antibody or antigen binding fragment thereof, and/or an anti-CTLA4 antibody or antigen binding fragment thereof; (ix) an agonist of a stimulatory immune checkpoint molecule; or
 - (x) any combination of (vi)-(ix) is to be administered to the subject.
22. The use of claim 20 or 21, wherein the hepatitis B virus infection is a chronic hepatitis B virus infection.
23. The use of any one of claims 20-22, wherein the subject has received a liver transplant, is non-immunized against hepatitis B virus, is a newborn, is undergoing or has undergone hemodialysis, or any combination thereof.
24. A method for *in vitro* diagnosis of a hepatitis B infection and/or a hepatitis D infection, the method comprising:
- (i) contacting a sample from a subject with an antibody of any one of claims 1-6; and
 - (ii) detecting a complex comprising an antigen and the antibody.
25. The method of claim 24, wherein the sample comprises blood isolated from the subject.
26. A method for detecting the presence or absence of an epitope in a correct conformation in an anti-hepatitis-B vaccine and/or an anti-hepatitis-D vaccine, the method comprising:
- (i) contacting the vaccine with
 - (a) an antibody of any one of claims 1-6; and
 - (ii) determining whether a complex comprising an antigen and the antibody, has been formed.