

CLAIMS

What is claimed is:

1. A hepatitis B vaccine comprising a recombinant *Hansenula* polymorpha, comprising and expressing hepatitis B surface antigen (HBsAg) of SEQ ID NO: 1, wherein a host *Hansenula* polymorpha cell line of the recombinant *Hansenula* polymorpha is HU-11, and the accession number of the host *Hansenula* polymorpha cell line is CGMCC No.1218, and a disrupted DNA sequence of an orotidine-5-phosphate decarboxylase gene of the host *Hansenula* polymorpha is SEQ ID NO: 3, wherein the dose of the HBsAg in the hepatitis B vaccine is 40 pg/dose for adults and 20 pg/dose for children, and wherein the pure stock solution yield of the hepatitis B vaccine is 300 mg/L fermentation liquid to 400 mg/L fermentation liquid.
2. The hepatitis B vaccine comprising a recombinant *Hansenula* polymorpha according to claim 1, wherein the amino acid sequence of the HBsAg expressed by the recombinant *Hansenula* polymorpha is shown in SEQ ID NO: 2.
3. The hepatitis B vaccine comprising a recombinant *Hansenula* polymorpha according to claim 1, wherein the HBsAg expressed by the recombinant *Hansenula* polymorpha is a virus-like particle structure, which is formed by inserting HBsAg into *Hansenula* polymorpha lipid, and wherein 9 to 12 among the 14 cysteic acids of the HBsAg form disulfide bonds.
4. The hepatitis B vaccine comprising a recombinant *Hansenula* polymorpha according to claim 1, wherein the hepatitis B vaccine further comprises an adjuvant; the adjuvant is aluminum adjuvant prepared by in-situ coprecipitation or the direct adsorption; the aluminum adjuvant is preferably prepared by in-situ coprecipitation.
5. The hepatitis B vaccine comprising a recombinant *Hansenula* polymorpha according to claim 1, wherein the immunization procedure of the high dosage of hepatitis B vaccine is one injection respectively in 0, 1, 2 to 12 months for three needles; the preferably immunization procedure is one injection respectively in 0, 1, and 6 months for three needles.

6. The hepatitis B vaccine comprising a recombinant *Hansenula polymorpha* according to claim 1, wherein the dosage form of the hepatitis B vaccine is selected from prefilled injection solution, injection solution or lyophilized powder injection; the dosage form is preferably the prefilled injection solution.
7. The hepatitis B vaccine comprising a recombinant *Hansenula polymorpha* according to claim 1, wherein the hepatitis B surface antigen is adw subtype.
8. A recombinant *Hansenula polymorpha*, wherein the recombinant *Hansenula polymorpha* comprises the nucleotide sequence of SEQ ID NO: 1, and the nucleotide sequence of SEQ ID NO: 1 is integrated into the genome of the recombinant *Hansenula polymorpha*, wherein a host *Hansenula polymorpha* cell line of the recombinant *Hansenula polymorpha* is HU-11, and the accession number of the host *Hansenula polymorpha* cell line is CGMCC No.1218, and a disrupted DNA sequence of an orotidine-5-phosphate decarboxylase gene of the host *Hansenula polymorpha* is SEQ ID NO: 3.
9. The hepatitis B vaccine comprising a recombinant *Hansenula polymorpha* according to claim 3, wherein the HBsAg expressed by the recombinant *Hansenula polymorpha* is a virus-like particle structure, which is formed by inserting HBsAg into *Hansenula polymorpha* lipid, and wherein 9 to 12 among the 14 cysteine acids of the HBsAg form disulfide bonds.
10. The hepatitis B vaccine comprising a recombinant *Hansenula polymorpha* according to claim 3, wherein the hepatitis B vaccine further comprises an adjuvant; the adjuvant is aluminum adjuvant prepared by in-situ coprecipitation or the direct adsorption; the aluminum adjuvant is preferably prepared by in-situ coprecipitation.
11. The hepatitis B vaccine comprising a recombinant *Hansenula polymorpha* according to claim 4, wherein the hepatitis B vaccine further comprises an adjuvant; the adjuvant is aluminum adjuvant prepared by in-situ coprecipitation or the direct adsorption; the aluminum adjuvant is preferably prepared by in-situ coprecipitation.