CLAIMS

What is claimed is:

1. A hepatitis B therapeutic vaccine based on inactivated whole recombinant Hansenula polymorpha cells, which expresses HBsAg and HBcAg, wherein the amino acid sequence of the HBcAg expressed by the recombinant Hansenula polymorpha cells is shown as SEQ ID NO: 4, the DNA sequence of the HBcAg expressed by the recombinant Hansenula polymorpha cells is shown as SEQ ID NO: 3, the recombinant Hansenula polymorpha cell comprises 15-21 HBcAg-specific CTL epitopes, the intracellular expression level of the HBsAg in the recombinant Hansenula polymorpha cells is 6-10 μg HBsAg per 10^8 cells, the HBsAg has 16-21 HBsAg-specific CTL epitopes, and the hepatitis B therapeutic vaccine uses the inactivated whole recombinant Hansenula polymorpha cells as an adjuvant.

2. The hepatitis B therapeutic vaccine according to claim 1, wherein the HBsAg expressed by the recombinant Hansenula polymorpha cells is adw subtype, and the DNA sequence of the HBsAg expressed by the recombinant Hansenula polymorpha cells is shown as SEQ ID NO: 1.

3. The hepatitis B therapeutic vaccine according to claim 2, wherein the amino acid sequence of the HBsAg expressed by the recombinant Hansenula polymorpha cells is shown as SEQ ID NO: 2.

4. The hepatitis B therapeutic vaccine according to claim 1, wherein the HBsAg expressed by the recombinant Hansenula polymorpha cells is a virus-like particle structure, which is formed by inserting HBsAgs into Hansenula polymorpha lipid, 9 to 12 among the 14 cysteic acids of the HBsAg

form disulfide bonds, and the HBcAg expressed by the inactivated whole recombinant Hansenula polymorpha cells is a virus-like particle structure.

5. The hepatitis B therapeutic vaccine according to any one of claim 1 to 3, wherein the HBsAg expressed by the recombinant Hansenula polymorpha cells comprises 19 CTL epitopes as follow: VLQAGFFLL, PFVQWFVGL, FLLTRILTI, WYWGPSLYSI, SLNFLGGSPV, FLGGSPVCL, LYSIVSPF, LYSIVSPFI, PFIPLLPIF, LLLCLIFLL, LLCLIFLLV, LLDYQGMLPV , LVLLDYQGML, VLLDYQGML, WLSLLVPFV, LLVPFVQWFV, GLSPTVWLSA, SIVSPFIPLL, and LLPIFFCLWV.

6. The hepatitis B therapeutic vaccine according to any one of claim 1, 4, and 5, wherein the HBcAg expressed by the recombinant Hansenula polymorpha cells comprises 19 CTL epitopes as follow: SFLPSDFF, FLPSDFFPSI, DFFPSIRDLL, FFPSIRDLL, SYVNVNMGL, SYVNVNMGLKI, YVNVNMG, YVNVNMGLK, WFHISCLTF, CLTFGRETV, VLEYLVSFGV, EYLVSFGVW, EYLVSFGVWI, AYRPPNAPI, AYRPPNAPIL, APILSTLPE, ILSTLPETTV, STLPETTVVRR, and RGRSPRRRTP.

7. The hepatitis B therapeutic vaccine according to claim 1, wherein the host Hansenula polymorpha cell line of the recombinant Hansenula polymorpha cells is HU-11, and the accession number is CGMCC No.1218, and the disrupted DNA sequence of the orphanin-5-phosphate decarboxylase gene of the host Hansenula polymorpha is shown in SEQ ID NO: 5.

8. The hepatitis B therapeutic vaccine according to claim 1, wherein the dosage form of the hepatitis B therapeutic vaccine is selected from pre-filled injection solution, injection solution, or lyophilized powder injection.

9. The hepatitis B therapeutic vaccine according to claim 1, the hepatitis B therapeutic vaccine further comprises HBsAg stock solution or aluminum adjuvant HBsAg.

10. A recombinant Hansenula polymorpha, wherein the recombinant Hansenula polymorpha comprises a DNA sequence of SEQ ID NO: 3.

11. The recombinant Hansenula polymorpha according to claim 12, wherein the DNA sequence of SEQ ID NO: 3 is integrated into the genome of the recombinant Hansenula polymorpha.