- the amino acid sequence set forth in SEQ ID NO:22(p697-706),

or

k) the amino acid sequence set forth in SEQ ID NO:23(p723-731),

or

l) at least 10 consecutive amino acids of the region from position 755 to position 765 of HBV polymerase, comprising:

- the amino acid sequence set forth in SEQ ID NO:24(p755-764), and/or
- the amino acid sequence set forth in SEQ ID NO:25(p756-765),

or

m) the amino acid sequence set forth in SEQ ID NO:26(p829-837).

In further examples, the disclosure relates to polynucleotides comprising a nucleotide sequence encoding a peptide according to the disclosure, to immunogenic compositions comprising immunogenic peptides or polynucleotides of the disclosure and to uses of peptides, polynucleotides, recombinant viruses or immunogenic compositions of the disclosure in the treatment of HBV related diseases.

In one aspect, the disclosure relates to an immunogenic peptide consisting of the amino acid sequence set forth in SEQ ID NO:31.

In another aspect, the disclosure relates to an immunogenic composition comprising:
- a peptide according to the disclosure, and
- a pharmaceutically-acceptable carrier,

optionally further comprising an adjuvant.

In another aspect, the disclosure relates to the peptide according to the disclosure or an immunogenic composition according to the disclosure for use in therapy.

In another aspect, the disclosure relates to a use of the peptide according to the disclosure or an immunogenic composition according to the disclosure in the manufacture of a medicament for treating or preventing an HBV-related disease in a human subject.

In another aspect, the disclosure relates to a method of ex vivo stimulation of antigen-loaded activated antigen-presenting cells or expanded antigen-specific T cells, wherein the method comprises that the peptide according to the disclosure is contacted with the antigen-loaded activated antigen-presenting cells or expanded antigen-specific T cells.

In another aspect, the disclosure relates to a use of the peptide according to the disclosure, or an immunogenic composition according to the disclosure in the manufacture of a medicament for treating an HBV-related disease in a human subject, wherein:

(i) antiviral treatment is to be given to an HBV infected patient to reduce viral load,

(ii) when the viral load is significantly reduced, the immunogenic peptide or immunogenic composition is to be administered, and

(iii) when sufficient time has passed for an initial T cell response in the patient to have occurred, antiviral treatment is to be interrupted or discontinued.

BRIEF DESCRIPTION OF FIGURES

Figure 1. Alignment of validated HLA-I epitopes and predicted HLA-binding peptide sequences to protein conservation and function for HBx. A centered bar diagram depicts the length of the consensus sequence of the HBx protein (methods) in which the conservation score across viral genotypes is indicated by a grey scale code (legend) for each amino acid. Reported validated epitope sequences obtained from the Hepitopes database are aligned to this consensus protein sequence and shown on top. Below this, potential novel binders predicted by NetMHCpan (9-11 amino acids), are depicted for each HLA-supertype representative. Below the aligned binders we plotted the frequency distribution of each amino acid within all predicted binders (8-14 amino acids in length) over the protein sequence. The conservation score (legend) of each amino acid is shown as a horizontal grey scale-coded bar diagram. Essential amino acids of which mutation leads to loss of viral persistence are indicated by arrows matching the color of the conservation score. Functional domains are depicted at the bottom according to the nomenclature of HBVdb.

Figure 2. Alignment of validated HLA-I epitopes and predicted HLA-binding peptide sequences to protein conservation and function for Polymerase. Depicted are the first 200 amino acids (A, E), amino acids 201-474 (B, F), 475-631 (C, G) and amino acids 632-843 (D, H). Reported validated epitope sequences obtained from the Hepitopes database are shown on top. Below this, potential novel

Claims

1. An immunogenic peptide consisting of the amino acid sequence set forth in SEQ ID NO:31.

2. An immunogenic composition comprising:
- a peptide according to claim 1, and
- a pharmaceutically-acceptable carrier,
optionally further comprising an adjuvant.

3. The peptide according to claim 1 or an immunogenic composition according to claim 2 for use in therapy.

4. Use of the peptide according to claim 1 or an immunogenic composition according to claim 2 in the manufacture of a medicament for treating or preventing an HBV-related disease in a human subject.

5. A method of ex vivo stimulation of antigen-loaded activated antigen-presenting cells or expanded antigen-specific T cells, wherein the method comprises that the peptide according to claim 1 is contacted with the antigen-loaded activated antigen-presenting cells or expanded antigen-specific T cells.

6. Use of the peptide according to claim 1 or an immunogenic composition according to claim 2 in the manufacture of a medicament for treating an HBV-related disease in a human subject, wherein:
(i) antiviral treatment is to be given to an HBV infected patient to reduce viral load,
(ii) when the viral load is significantly reduced, the immunogenic peptide or immunogenic composition is to be administered, and
(iii) when sufficient time has passed for an initial T cell response in the patient to have occurred, antiviral treatment is to be interrupted or discontinued.