

WHAT IS CLAIMED IS:

~~1. A non-naturally occurring polynucleotide encoding a polypeptide comprising one or more immune response-inducing hepatitis B virus (HBV) polypeptides.~~ **Claims**

1.

~~2. The polynucleotide of claim 1, wherein said one or more HBV polypeptides comprises an HBV Core peptide, an HBV Surface peptide, an HBV Pol peptide, an HBV HBSP/HBx peptide, a KK linker, or any combination thereof.~~

~~3. The polynucleotide of claim 2, wherein:~~

(i) ~~— said HBV Core peptide has any one of the Core peptide sequences as shown in Table 3,~~

(ii) ~~— said HBV Surface peptide has any one of the Surface peptide sequences as shown in Table 3,~~

(iii) ~~— said HBV Pol peptide has any one of the Pol peptide sequences as shown in Table 3,~~

(iv) ~~— said HBV HBSP/HBx peptide has any one of the HBSP/HBx peptide sequences as shown in Table 3,~~

(v) ~~— said KK linker connects any one of the peptide sequences as shown in Table 3 to any other peptide sequences as shown in Table 3, or~~

(vi) ~~— any combination of (i) (v).~~

~~4. A polynucleotide comprising the polynucleotide of any one of claims 1 to 3, further comprising one or more polynucleotides encoding a gene switch system for inducible control of heterologous gene expression, wherein heterologous gene expression is regulated by said gene switch system; and, wherein said heterologous gene comprises the polynucleotide of any one of claims 1 to 3.~~

~~5. The polynucleotide of claim 4, wherein said gene switch system is an ecdysone receptor-based (EcR-based) gene switch system.~~

6. A method of regulating the expression of a heterologous gene in a cell, the method comprising:

(a) ~~introducing into said cell one or more polynucleotides that comprise~~

(i) — a repressible or inducible gene switch, and

(ii) — a heterologous immune response-inducing gene, wherein expression of said heterologous immune response-inducing gene is regulated by said gene switch, wherein said heterologous immune response-inducing gene encodes at least one of one or more HBV polypeptides; and

(b) — exposing said cell to a compound in an amount sufficient to repress or induce expression of said heterologous immune response inducing gene.

~~7. The method of claim 6, wherein said gene switch comprises a ligand binding domain derived from at least one of an ecdysone receptor (EcR), a ubiquitous receptor, an orphan receptor 1, an NER-1, a steroid hormone nuclear receptor 1, a retinoid X receptor interacting protein 15, a liver X receptor β , a steroid hormone receptor like protein, a liver X receptor, a liver X receptor α , a farnesoid X receptor, a receptor interacting protein 14, and a farnesol receptor.~~

8. A polypeptide construct, wherein said polypeptide construct comprises:

(a) — ~~an HBV HBx domain and at least one of~~ an HBV Pol domain, an HBV Core domain, and an HBV Surface domain; or (b) ~~a pre-Core domain or~~ an HBV SurfacePol domain; or

(b) — ~~a pre-Core, an HBV HBx domain, and at least one of an HBV PolSurface domain, an HBV HBx domain or an HBV Surface domain.~~

~~9. The polypeptide construct of claim 8, wherein:~~

(i) — ~~said HBV HBx domain has a sequence as shown in SEQ ID NO: 98;~~

(ii) — ~~said the HBV Pol domain comprises a deletion of at least one the amino acid as compared to a wildtype HBV Pol domain;~~

(iii) — ~~said HBV Surface domain comprises at least one of a PreS1 domain, a PreS2 domain and an S domain; or~~

(iv) — ~~any combination thereof.~~

~~10. The polypeptide construct of claim 8 or 9, wherein~~

(i) — ~~said HBV Pol domain has a sequence as shown~~ set forth in SEQ ID NO: 99;

~~2. (ii) — said HBV Surface domain has a sequence as shown in SEQ ID NO: 100.~~

(ii) — The polypeptide construct of claim 1, wherein said HBV Core domain and said HBV pre-Core domain ("Core portion") has a sequence as shown in SEQ ID NO: 101, or

(iv) — ~~any combination thereof.~~

~~11. The polypeptide construct of any one of claims 8 to 10, wherein said polypeptide construct HBx domain comprises each of SHB(Env), HBcAg, HBx, and Pol domains.~~

~~12. the amino acid sequence set forth in SEQ ID NO: 104.~~

3. The polypeptide construct of claim ~~11~~, ~~wherein: 2,~~ wherein said HBV Core domain comprises the amino acid sequence set forth in SEQ ID NO: 101.

~~4.~~ (i) ~~said SHB(Env) domain has a sequence as shown in SEQ ID NO: 102,~~

(ii) ~~said HBeAg domain has a sequence as shown in SEQ ID NO: 103,~~

(iii) ~~said HBx domain has a sequence as shown in SEQ ID NO: 104,~~

(iv) ~~said Pol domain has a sequence as shown in SEQ ID NO: 105.~~

~~13.~~ The polypeptide construct of any one of claims 8 to 12, wherein said polypeptide construct has a sequence as shown in SEQ ID NO: 106.

14. The polypeptide construct of any one of claims 8 to ~~13~~claim 1, further comprising a rigid linker.

5. ~~15.~~ The polypeptide construct of any one of claims 8 to 14, wherein said polypeptide has a sequence as shown in SEQ ID NO: 112.

~~16.~~ A polypeptide construct, wherein said polypeptide construct comprises one or more HBV HBx linkers and at least one of a Core domain, a Surface domain and a Pol domain, wherein one of said Core domain, said Surface domain and said Pol domain is connected to another of said Core domain, said Surface domain and said Pol domain by said one or more HBx linkers.

17. The polypeptide construct of claim 16, wherein

(i) ~~said Surface domain comprises at least one of an HBV PreS1 domain, an HBV PreS2 domain and an HBV S domain;~~

(ii) ~~wherein said one or more HBV HBx linkers comprise a sequence as shown in any one of HBx 1, HBx 2, HBx 3, HBx 4, HBx 5 or HBx 6 of Table 3; or~~

(iii) ~~both (i) or (ii).~~

~~18.~~ The polypeptide construct of claim 16 or 17, wherein said Core domain is adjacent to said Surface domain.

~~19.~~ The polypeptide construct of any one of claims 16 to 18, wherein said Surface domain comprises a PreS1 domain, a PreS2 domain, an S domain, or any combination thereof.

~~20.~~ The polypeptide construct of any one of claims 16 to 19, wherein said polypeptide construct has a sequence as shown in SEQ ID NO: 107.

21. A polypeptide construct comprising an ankyrin-like repeat domain and one or more HBV peptides.

22. The polypeptide construct of claim 21, wherein:

(i) ~~said ankyrin-like repeat protein is a human ankyrin-like repeat protein,~~

- (ii) — said one or more HBV peptides has a sequence as shown in any one of the amino acid sequences of Table 3.
23. The polypeptide construct of claim 21 or 22, wherein said one or more HBV peptides comprises one or more of a Core peptide, a Surface peptide, a Pol peptide and an HBSP/HBx peptide.
24. The polypeptide construct of claim 23, wherein:
- (i) — said Core peptide has a sequence as shown in any one of the Core amino acid sequences of Table 3;
 - (ii) — said Surface peptide has a sequence as shown in any one of the Surface amino acid sequences of Table 3;
 - (iii) — said Pol peptide has a sequence as shown in any one of the Pol amino acid sequences of Table 3;
 - (iv) — said HBSP/HBx peptide has a sequence as shown in any one of the HBSP/HBx amino acid sequences of Table 3; or
 - (v) — any combination thereof.
25. The polypeptide construct of any one of claims 21 to 24, wherein said polypeptide construct has a sequence as shown in SEQ ID NO: 108.
26. A polypeptide construct, wherein said polypeptide construct comprises at least two HBV amino acid sequences as shown in Table 3, wherein said at least two HBV amino acid sequences are connected by a peptide linker, wherein said peptide linker is a KK linker.
27. The polypeptide construct of claim 26, wherein said at least two HBV amino acid sequences comprise at least one of a Core peptide, a Surface peptide, a Pol peptide and an HBSP/HBx peptide as shown in Table 3.
28. The polypeptide construct of claim 26 or 27, wherein said at least two HBV amino acid sequences comprise each of the amino acid sequences as shown in Table 3.
29. The polypeptide construct of any one of claims 26 to 28, wherein said polypeptide construct has a sequence as shown in SEQ ID NO: 109.
30. A polynucleotide encoding the polypeptide construct of any one of claims 8 to 29 claim 1.
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6. A vector comprising the polynucleotide of any one of claims 1 to 5 and 30 claim 5.
7. 32. The vector of claim 31, wherein said vector is an adenoviral vector.
33. The vector of claim 32, wherein said adenoviral vector is a gorilla adenoviral vector.

The polynucleotide of claim 5 for use in a vaccine.

8. The polypeptide construct of claim 3, wherein Surface domain comprises the amino acid sequence set forth in SEQ ID NO: 100.

9. The polypeptide of claim 8, further comprising a rigid linker between one or more of said HBV Pol domain, said HBV Core domain, said HBV Surface domain, and said HBV HBx domain.

10. ~~any one of claims 1 to 5 and 30, the~~ The polypeptide construct of claim 9, wherein the rigid linker comprises the amino acid sequence set forth in SEQ ID NO: 129.

11. A polypeptide construct, wherein the polypeptide construct comprises: (i) an HBV Pol domain comprising the amino acid sequence set forth in SEQ ID NO: 99; (ii) an HBV Surface domain comprising the amino acid sequence set forth in SEQ ID NO: 100; (iii) an HBV Core domain comprising the amino acid sequence set forth in SEQ ID NO: 101; and (iv) an HBV HBx domain comprising the amino acid sequence set forth in SEQ ID NO: 104.

12. ~~any~~ The polypeptide construct of claim 11, wherein one ~~of claims 8 to 29, or the vector~~ or more of the HBV domains are connected by a rigid linker.

13. ~~any~~ The polypeptide construct of claim 12, wherein one or more of the rigid linkers comprise the amino acid sequence set forth in SEQ ID NO: 129.

14. A polynucleotide encoding the polypeptide construct in any one of claims ~~31~~ 11 to 13.

15. A vector comprising the polynucleotide of claim 14.

16. ~~34.~~ The polynucleotide of claim 14 ~~33~~ for use in a vaccine.