Claims

1. An apparatus for the controlled delivery of an HBV vaccine to a predetermined tissue site within a subject in need thereof, comprising:

a cartridge assembly comprising an outer cartridge, an inner cartridge, a reservoir containing the HBV vaccine, wherein a reservoir containment volume is contained within the outer cartridge and configured to receive the reservoir;

an applicator comprising a cartridge assembly receiving volume, a needle hub, and an insertion detector, wherein the insertion detector senses loading of the reservoir in the reservoir containment volume;

at least one interlock, wherein the interlock facilitates proper execution of the HBV vaccine administration procedure;

at least one injection orifice through which the HBV vaccine is administered;

a plurality of penetrating electrodes arranged with a predetermined spatial relationship relative to the orifice;

an electrical field generator for generating an electrical signal operatively connected to the electrodes; and

a controlled source of energy sufficient to transfer a predetermined amount of the HBV vaccine at a predetermined rate from the reservoir through the orifice to the predetermined site within the subject,

wherein the HBV vaccine comprises:

a first nucleic acid molecule comprising a first polynucleotide encoding an HBV polymerase antigen, wherein the HBV polymerase antigen comprises an amino acid sequence that is at least 98% identical to SEQ ID NO: 4 and wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNAse H activity;

a second nucleic acid molecule comprising a second polynucleotide encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2; and

a pharmaceutically acceptable carrier,

wherein the first nucleic acid molecule and the second nucleic acid molecule are present in the same nucleic acid molecule or in two different nucleic acid molecules,

preferably the electrodes are a plurality of elongate electrodes and the interlock prevents inadvertent actuation of cartridge function.

2. The apparatus of claim 1, wherein at least one interlock is selected from the group consisting of a mechanical interlock, a light emitter/collector, a cartridge breech, a force interlock, an alignment guide and a splay shield, a trigger lock, and a safety switch.

3. The apparatus of claim 1 or 2, wherein the apparatus comprises at least two sets of interlocks, wherein a first interlock is a mechanical interlock, and a second interlock is selected from the group consisting of a light emitter/collector, a cartridge breech, a force interlock, an alignment guide and a splay shield, a trigger lock, and a safety switch, preferably the mechanical interlock is a reservoir interlock further comprising (i) at least one reservoir lockout hole, or (ii) a tab extending from one or more of the cartridge surface, wherein the tab ensures that reservoir is properly inserted into the cartridge, and preferably the cartridge breech provides an optical line of sight through at least one reservoir lockout hole.

4. The apparatus of claim 3, wherein the apparatus further comprises a third interlock that is a force interlock, wherein the force interlock senses a force applied against the predetermined tissue site of the subject and prevents administration of the HBV vaccine to the subject when insufficient force is provided, preferably the force interlock further forms an electrical lock within the applicator.

5. The apparatus of any one of claims 1-4, wherein the apparatus further comprises at least one sensor, preferably selected from the group consisting of a cartridge loading sensor, a cartridge loaded sensor, a cartridge force sensor, an insertion mechanism position sensor, an insertion detector, an optical detector, and an electrical sensor.

6. The apparatus of claim 5, wherein the sensor detects a reservoir label and verifies the HBV vaccine.

7. An apparatus for the controlled delivery of an HBV vaccine to a predetermined tissue site within a subject comprising:

a cartridge assembly comprising a housing, a reservoir containing the HBV vaccine, wherein a reservoir containment volume is contained within the housing and configured to receive the reservoir;

an applicator comprising a cartridge assembly receiving volume, a needle hub, and an insertion detector, wherein the insertion detector senses loading of the reservoir in the reservoir containment volume; at least one injection orifice through which the HBV vaccine is administered;

a plurality of penetrating electrodes arranged with a predetermined spatial relationship relative to the orifice;

an electrode support structure comprising a hole and a wall, wherein the electrode support structure prevents inadvertent perpendicular motion of the electrodes;

an electrical field generator for generating an electrical signal operatively connected to the electrodes; and

a controlled source of energy sufficient to transfer a predetermined amount of the HBV vaccine at a predetermined rate from the reservoir through the orifice to the predetermined site within the subject,

wherein the HBV vaccine comprises:

a first nucleic acid molecule comprising a first polynucleotide encoding an HBV polymerase antigen, wherein the HBV polymerase antigen comprises an amino acid sequence that is at least 98% identical to SEQ ID NO: 4 and wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNAse H activity;

a second nucleic acid molecule comprising a second polynucleotide encoding a truncated HBV core antigen consisting of the amino acid sequence of SEQ ID NO: 2; and

a pharmaceutically acceptable carrier, and

wherein the first nucleic acid molecule and the second nucleic acid molecule are present in the same nucleic acid molecule or in two different nucleic acid molecules.

8. The apparatus of claim 7 , wherein the electrode support structure provides an operative connection between a conductive contact region located on the distal region of the electrodes and the controlled source of energy when the electrodes are deployed into the predetermined tissue site within the subject, preferably the electrode support structure comprises at least one hole for passage of the electrodes and a hole for passage of an injection needle .

9. The apparatus of claim 7 or 8, wherein the electrode support structure is a planar support structure positioned perpendicularly relative to the elongate orientation of the electrodes, preferably the planar support structure comprises at least one aperture configured to allow passage of the electrode through the predetermined tissue site.

10. The apparatus of any one of claims 7 to 9, wherein the electrode support structure is an adaptive electrode support, preferably the adaptive electrode support is a compression spring made from a metal, a polymer or an elastomeric material.

11. The apparatus of any one of claims 7 to 10, wherein the electrode support structure comprises at least one of a telescoping tube, a stick shield spring, and at least one lateral support member attached to the electrodes with at least one optional hinge feature.

12. The apparatus of any one of claims 1-11, wherein the HBV vaccine is capable of inducing an immune response in a mammal against at least two HBV genotypes, preferably the HBV vaccine is capable of inducing a T cell response in a mammal against at least HBV genotypes B, C and D, and more preferably the HBV vaccine is capable of inducing a CD8 T cell response in a human subject against at least HBV genotypes A, B, C and D.

13. The apparatus of any one of claims 1-12, wherein the first non-naturally occurring nucleic acid molecule is present in a first plasmid DNA vector, and the second non-naturally occurring nucleic acid molecule is present in a second plasmid DNA vector.

14. The apparatus of claim 13, wherein the HBV vaccine comprises:

a) a first plasmid DNA vector comprising, from 3'-end to 5'-end, the promoter sequence comprising the polynucleotide sequence of SEQ ID NO: 7, the enhancer sequence comprising the polynucleotide sequence of SEQ ID NO: 8, the signal peptide coding sequence comprising the polynucleotide sequence of SEQ ID NO: 5, the first polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 3, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 11;
b) a second plasmid DNA vector comprising, from 3'-end to 5'-end, the promoter sequence comprising the polynucleotide sequence of SEQ ID NO: 7, the regulatory sequence comprising the polynucleotide sequence of SEQ ID NO: 8, the signal peptide coding sequence comprising the polynucleotide sequence of SEQ ID NO: 5, the second polynucleotide sequence comprising the polynucleotide sequence of SEQ ID NO: 1, and the polyadenylation signal sequence comprising the polynucleotide sequence of SEQ ID NO: 11; and
c) a pharmaceutically acceptable carrier,

wherein each of the first plasmid DNA vector and the second plasmid DNA vector further comprises a kanamycin resistance gene having the polynucleotide sequence of SEQ ID NO: 12, and an original of replication having the polynucleotide sequence of SEQ ID NO: 10, and wherein the first plasmid DNA vector and the second plasmid DNA vector are in the same composition or two different compositions.

~~15. The apparatus of any one of claims 1 to 14 for use in inducing an immune response against an HBV infection in a subject in need thereof, comprising delivering an HBV vaccine to a predetermined tissue site within the subject, wherein said subject is preferably a human suffering from a chronic HBV infection.~~

~~16. The apparatus of any one of claims 1 to 14 for use in treating an HBV-induced disease in a subject in need thereof, comprising delivering an HBV vaccine to a predetermined tissue site within the subject, preferably wherein said subject is a human subject and wherein the HBV-induced disease is selected from the group consisting of advanced fibrosis, cirrhosis and hepatocellular carcinoma (HCC).~~

~~17. The apparatus of claim 15 or 16, wherein the predetermined tissue site is located in a skeletal muscle of the subject.~~

~~18. The apparatus of claim 17, wherein the skeletal muscle of the subject is medial deltoid muscle or vastus lateralis muscle.~~

~~19.~~15. The apparatus of any one of claims 1-14~~ claims 15 to 18~~, wherein the electrical signal operably connected to the electrodes comprises an electrical field strength of 100 V/cm to 400 V/cm, preferably 250 V/cm; a voltage of 50 to 200 V, preferably about 150 V; and a current of 0.5 to 5 A/sec, preferably 0.6 to 4 A/sec, more preferably 0.16 A/sec.

~~20.~~16. The apparatus of any one of claims 1 to 14, ~~for use in inducing an immune response against at least two HBV genotypes, more particularly for use in the treatment of HBV-induced disease,~~ wherein said apparatus is ~~adapted for~~capable of electroporation of the HBV vaccine in a subject in need thereof, preferably in a human.