CLAIMS

1. A multi-HBV immunogen viral vector vaccine comprising:

a viral vector comprising an immunogen expression cassette, wherein the expression of a protein encoded by the expression cassette is arranged to be driven by a promoter, wherein the immunogen expression cassette encodes:

a) HBV Core;

b) a modified HBV polymerase (P_{mut}), wherein the modification is a mutation to wild-type HBV polymerase to substantially remove polymerase function;

c) HBV surface antigen (HbsAg); and

d) an intergenic sequence that is arranged to cause expression of at least the HBV surface antigen (HbsAg) as a separate protein from the HBV core and the modified HBV polymerase (P_{mut}),

wherein the intergenic sequence is downstream (3') of the sequences encoding the HBV core and the modified HBV polymerase (P_{mut}) and upstream (5') of the sequence encoding the HBV surface antigen (HbsAg).

2. The multi-HBV immunogen viral vector vaccine according to claim 1, wherein the intergenic sequence comprises a cleavage domain, an IRES (Internal Ribosomal Entry Site), a splicing signal, or a secondary promoter.

3. The multi-HBV immunogen viral vector vaccine according to claim 1, wherein the intergenic sequence comprises a cleavage domain;

optionally wherein the cleavage domain comprises a ribosome skipping cleavage domain;

further optionally, wherein the cleavage domain comprises or consists of Furin-2A (F2A) peptide sequence or a functional variant thereof.

4. The multi-HBV immunogen viral vector vaccine according to claim 1, wherein the intergenic sequence comprises a secondary promoter to promote expression of at least the surface antigen (HbsAg).

5. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette further encodes HBV Pre-Core (PreC).

6. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette further encodes HBV PreS1, and/or a truncated form thereof.

7. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette further encodes HBV PreS2.

8. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette encodes HBV Pre-Core (PreC) and HBV PreS1, and a truncated form of PreS1.

9. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette is capable of expressing HBV e-Antigen.

10. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the HBV Core and modified polymerase (Pmut) are arranged to be expressed as a fusion protein.

11. The multi-HBV immunogen viral vector vaccine according to claims 5 to 10, wherein the HBV Pre-core, HBV Core and modified polymerase (Pmut) are arranged to be expressed as a fusion protein.

12. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette does not encode HBV X protein.

13. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette comprises nucleic acid comprising the sequence of:

SEQ ID NO: 46 (SIi-HBV-CPmutS) or a variant thereof;

SEQ ID NO: 47 (SIi-HBV-SCPmut) or a variant thereof;

SEQ ID NO: 48 (SIi-HBV-CPmutPreS-S(sh)) or a variant thereof;

SEQ ID NO: 49 (SIi-HBV-CPmutPreS-TPA-S(sh)) or a variant thereof; SEQ ID NO: 24 (MVA-SIi-HBV-PreS-Pmut-C-S(sh)) or a variant thereof; or

SEQ ID NO: 27 or SEQ ID NO: 58 (MVA-SIi-HBV-PreS-Pmut-C-TPA-S(sh)) or a variant thereof;

wherein the variants of SEQ ID NOs: 46, 47, 48, 49, 24, 27, or 58 comprise a sequence having at least 80% identity.

14. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the viral vector encodes the amino acid sequence of:

SEQ ID NO: 3 (SIi-HBV-CPmutS) or a variant thereof.

SEQ ID NO: 11 (SIi-HBV-SCPmut) or a variant thereof.

SEQ ID NO: 13 (SIi-HBV-CPmutPreS-S(sh)) or a variant thereof.

SEQ ID NO: 25 (SIi-HBV-CPmutPreS-TPA-S(sh)) or a variant thereof.

SEQ ID NO: 23 (MVA-SIi-HBV-PreS-Pmut-C-S(sh)) or a variant thereof.

SEQ ID NO: 26 (MVA-SIi-HBV-PreS-Pmut-C-TPA-S(sh)) or a variant thereof;

wherein the variants of SEQ ID NOs: 3, 11, 13, 25, 23, or 26 comprise a sequence having at least 80% identity.

15. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the viral vector comprises an adenovirus vector or Modified Vaccinia Ankara (MVA) vector.

16. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the viral vector may comprise a group E simian adenovirus vector.

17. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the promoter is encoded in the immunogen expression cassette, for example the promoter may be encoded at, or adjacent to, the 5' end of the immunogen expression cassette; or

wherein the promoter may be encoded as part of the viral vector nucleic acid outside of the immunogen expression cassette.

18. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the promoter promotes the expression of all the encoded protein of the immunogen expression cassette.

19. The multi-HBV immunogen viral vector vaccine according to claims 1 to 17, wherein the immunogen expression cassette comprises a secondary promoter, wherein the promoter is a primary promoter that is arranged to promote expression of at least

the HBV core and modified polymerase (Pmut), and not the HBV surface antigen (HbsAg) which is arranged to be promoted separately by the secondary promoter.

20. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the promoter comprises a CMV promoter or a pox viral promoter.

21. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the HBV Core comprises or consists of a full length wild-type HBV Core sequence.

22. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the modified HBV polymerase (P_{mut}) is not a truncated form of HBV polymerase (i.e. it is full length relative to wildtype HBV polymerase).

23. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the modified HBV polymerase (P_{mut}) comprises or consists of the sequence of SEQ ID NO: 8 or a variant thereof.

24. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the HbsAg comprises or consists of a full length wild-type HbsAg sequence, or a variant thereof.

25. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette encodes a truncated form of HBV PreS1 and the truncated PreS1 is arranged to be expressed a fusion protein with the HBV surface antigen (S / HbsAg).

26. The multi-HBV immunogen viral vector vaccine according to claim 25, further comprising a linker sequence provided between the truncated PreS1 and surface antigen (S / HbsAg).

27. The multi-HBV immunogen viral vector vaccine according to claim 25 or 26, wherein the truncated PreS1 with a fused surface antigen is encoded downstream (3') of the intergenic sequence.

28. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the expression cassette encodes a NΔPreS1 and PreS2 fusion sequence.

29. The multi-HBV immunogen viral vector vaccine according to claim 28, wherein the encoded NΔPreS1 and PreS2 fusion sequence is encoded upstream (5') of the intergenic sequence.

30. The multi-HBV immunogen viral vector vaccine according to claim 29, wherein the encoded NΔPreS1 and PreS2 fusion sequence is further fused with the modified polymerase (Pmut).

31. The multi-HBV immunogen viral vector vaccine according to claim 30, wherein a linker sequence is provided between the PreS2 and modified polymerase (Pmut).

32. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein the immunogen expression cassette further encodes a peptide adjuvant.

33. The multi-HBV immunogen viral vector vaccine according to claim 32, wherein the peptide adjuvant comprises TPA (tissue plasminogen activator) or a human or non-human invariant chain (Ii), or a fragment thereof.

34. The multi-HBV immunogen viral vector vaccine according to any preceding claim, wherein linker residues are encoded between one or more, or all, of the protein/antigen sequences that are provided in a fusion protein.

35. A nucleic acid comprising or consisting of an HBV immunogen expression cassette, wherein the immunogen expression cassette encodes:

a) HBV Core;

b) a modified HBV polymerase (P_{mut}), wherein the modification is a mutation to wild-type HBV polymerase to substantially remove polymerase function;

c) HBV surface antigen (HbsAg); and

d) an intergenic sequence that is arranged to cause expression of at least the HBV surface antigen (HbsAg) as a separate protein from the HBV core and the modified HBV polymerase (P_{mut}),

wherein the intergenic sequence is downstream (3') of the sequences encoding the HBV core and the modified HBV polymerase (P_{mut}) and upstream (5') of the sequence encoding the HBV surface antigen (HbsAg).

36. The nucleic acid according to claim 35, wherein the immunogen expression cassette further encodes a promoter.

37. The nucleic acid according to claim 35 or 36, wherein the immunogen expression cassette is isolated or provided in a non-viral vector.

38. A composition comprising the viral vector according to any of claims 1 to 34 or the nucleic acid according to any of claims 35 to 37, optionally wherein the composition is a pharmaceutically acceptable composition.

39. The composition according to any of claim 38, further comprising another therapeutically or prophylactically active ingredient and/or an adjuvant.

40. The composition according to claim 38 or 39, wherein the composition comprises a pharmaceutically acceptable carrier and/or wherein the composition is a vaccine composition.

41. The composition according to any of claims 38 to 40, the viral vector according to any of claims 1 to 34 or the nucleic acid according to any of claims 35 to 37, for use in the prophylaxis or treatment of HBV infection in a subject; optionally wherein the use is as a vaccine.

42. Use of the composition according to any of claims 38 to 40, the viral vector according to any of claims 1 to 34 or the nucleic acid according to any of claims 35 to 37, in the manufacture of a medicament for the treatment or prophylaxis of HBV infection, wherein the medicament is to be administered to a subject.

43. A prime boost vaccination kit comprising

-a prime vaccination comprising the composition according to any of claims 38 to 40, the viral vector according to any of claims 1 to 34 or the nucleic acid according to any of claims 35 to 37; and

-a boost vaccination comprising the composition according to any of claims 38 to 40, the viral vector according to any of claims 1 to 34 or the nucleic acid according to any of claims 35 to 37.

44. The prime and boost vaccination kit according to claim 43, wherein the prime and boost vaccinations comprise different viral vectors.