SUMMARY OF THE INVENTION

In one aspect, there is provided a dengue virus serotype 2 vaccine composition comprising:

(i) a dengue antigen selected from the group consisting of:

(a) a live attenuated dengue virus;

(b) an inactivated dengue virus;

(c) a live attenuated or inactivated chimeric dengue virus;

(d) a dengue virus-like particle (VLP); and

(e) a combination of two or more of (a) to (d);

or

(ii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP;

wherein said dengue antigen comprises a polypeptide having at least 90% identity to SEQ ID NO: 12 and wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 308 of SEQ ID NO: 12.

~~The present invention relates to~~ Also disclosed is a dengue virus serotype 2 vaccine composition comprising:

(i) a dengue antigen selected from the group consisting of:

(a) a live attenuated dengue virus;

(b) an inactivated dengue virus;

(c) a live attenuated or inactivated chimeric dengue virus;

(d) a dengue virus-like particle (VLP); and

(e) a combination of two or more of (a) to (d);

or

(ii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP;

wherein said dengue antigen comprises a polypeptide having at least 90% identity to SEQ ID NO: 12.

~~The present invention further relates to~~ Also disclosed is a vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising a polypeptide or polypeptides as defined in the claims. In another aspect, there is provided a vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising the polypeptide or polypeptides as defined herein.

A vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence having at least 90% sequence identity to a sequence selected from the group consisting of the RNA equivalent of SEQ ID NO: 1, the RNA equivalent of SEQ ID NO: 4, the RNA equivalent of SEQ ID NO: 5, the RNA equivalent of SEQ ID NO: 6, the RNA equivalent of SEQ ID NO: 7 and SEQ ID NO: 25.

In another aspect, there is provided a vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence having at least 90% sequence identity to a sequence selected from the group consisting of the RNA equivalent of SEQ ID NO: 7.

~~The present invention further relates to~~In yet another aspect, there is provided a pharmaceutical formulation comprising a vaccine composition of the present ~~invention~~ disclosure and a pharmaceutically acceptable carrier, diluent or excipient.

~~The present invention further relates to~~ Also disclosed is a vaccine composition of the present ~~invention~~ disclosure for use in therapy.

~~The present invention further relates to~~ Also disclosed is a vaccine composition of the present ~~invention~~ disclosure for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

~~The present invention further relates to~~ Also disclosed is a vaccine composition of the present ~~invention~~ disclosure for use in a method of generating neutralising antibodies against a dengue virus of serotype 2.

In yet another aspect, there is provided a composition as defined herein for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 1, serotype 2, serotype 3 or serotype 4.

~~The present invention further relates to~~ Also disclosed is a vaccine composition of the present invention which comprises a dengue antigen of serotype 1, a dengue antigen of serotype 2, a dengue antigen of serotype 3 and a dengue antigen of serotype 4 for use in a method of generating neutralising antibodies against the four serotypes of dengue.

~~The present invention further relates to~~ Also disclosed is the use of a vaccine composition of the present invention for the manufacture of a medicament for protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

In yet another aspect there is provided a composition as claimed as described herein for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

~~The present invention further relates to~~ Also disclosed is a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2, wherein said method comprises administering to said subject an effective amount of a composition according to the present ~~invention~~disclosure.

~~The present invention further relates to~~ In yet another aspect, there is provided a kit comprising a composition according to the present ~~invention~~ disclosure and instructions for the use of said composition in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

~~The present invention relates to~~ Also disclosed is a vaccine composition for use in a method of protecting a human subject against dengue disease, wherein said composition comprises:

(i) a dengue antigen selected from the group consisting of:

(a) a live attenuated dengue virus;

(b) an inactivated dengue virus;

(c) a live attenuated or inactivated chimeric dengue virus;

(d) a dengue virus-like particle (VLP); and

(e) a combination of two or more of (a) to (d);

or

(ii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP.

~~The present invention further relates to~~ Also disclosed is the use of a vaccine composition of the present ~~invention~~ disclosure for the manufacture of a medicament for protecting a human subject against dengue disease.

The present ~~invention~~ disclosure further relates to a method of protecting a human subject against dengue disease, wherein said method comprises administering to said human subject an effective amount of a composition according to the present ~~invention~~ disclosure.

Additionally, the present ~~invention~~ disclosure relates to a kit comprising a composition according to the present ~~invention~~ disclosure and instructions for the use of said composition in a method of protecting a human subject against dengue disease.

Description of the Figure

Figure 1 illustrates the construction of the YF-VAX cDNA by RT-PCR and cloning

Definitions

The term "Dengue disease", as used herein, refers to the clinical symptoms exhibited by an individual following infection by any one of the four Dengue virus serotypes. Since 1970, clinical dengue has been classified according to World Health Organization guidelines as (i) dengue fever or (ii) dengue hemorrhagic fever (World Health Organization. Dengue hemorrhagic fever: Diagnosis, treatment, prevention and control 2nd Ed. Geneva: WHO, 1997; ISBN 92 4 154500 3). In 2009, the WHO issued new guidelines that classify clinical dengue as (i) dengue with or without warning signs or (ii)

CLAIMS

1. A dengue virus serotype 2 vaccine composition comprising:

(i) a dengue antigen selected from the group consisting of:
   (a) a live attenuated dengue virus;
   (b) an inactivated dengue virus;
   (c) a live attenuated or inactivated chimeric dengue virus;
   (d) a dengue virus-like particle (VLP); and
   (e) a combination of two or more of (a) to (d);

or

(ii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP;

wherein said dengue antigen comprises a polypeptide having at least 90% identity to SEQ ID NO: 12 and wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 308 of SEQ ID NO: 12.

2. A composition as claimed in claim 1, wherein said polypeptide comprises a valine residue at the position within the polypeptide that corresponds to position 251 of SEQ ID NO: 12.

3. A composition as claimed in any preceding claim, wherein said polypeptide comprises a isoleucine residue at the position within the polypeptide that corresponds to position 129 of SEQ ID NO: 12.

4. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 141 of SEQ ID NO: 12.

5. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 164 of SEQ ID NO: 12.

6. A composition as claimed in any preceding claim, wherein said polypeptide comprises an aspartate residue at the position within the polypeptide that corresponds to position 203 of SEQ ID NO: 12.

7. A composition as claimed in any preceding claim, wherein said polypeptide comprises a threonine residue at the position within the polypeptide that corresponds to position 226 of SEQ ID NO: 12.

8. A composition as claimed in any preceding claim, wherein said polypeptide comprises a glycine residue at the position within the polypeptide that corresponds to position 228 of SEQ ID NO: 12.

9. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 484 of SEQ ID NO: 12.

10. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 485 of SEQ ID NO: 12.

11. A composition as claimed in any preceding claim, wherein said polypeptide comprises an alanine residue at the position within the polypeptide that corresponds to position 491 of SEQ ID NO: 12.

12. A composition as claimed in any one of claims 1 to 11, wherein said polypeptide comprises: (i) the sequence as set forth in SEQ ID NO: 16 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 16.

13. A composition as claimed in claim 1, wherein said dengue antigen comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 16.

14. A composition as claimed in claim 12, wherein said dengue antigen further comprises a polypeptide comprising: (i) the sequence as set forth in SEQ ID NO:

22 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 22.

15. A composition as claimed in claim 13, wherein said dengue antigen further comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 22,.

16. A composition as claimed in claim 12, wherein said dengue antigen comprises:

i) a polypeptide having the sequence as set forth in SEQ ID NO: 16 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 16; and
a polypeptide having the sequence as set forth in SEQ ID NO: 22 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 22.

17. A composition as claimed in any preceding claim, wherein said dengue antigen is selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising a polypeptide as defined in any one of claims 1 to 16.

18. A vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising the polypeptide or polypeptides as defined in any one of claims 1 to 16.

19. A vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence having at least 90% sequence identity to a sequence selected from the group consisting of the RNA equivalent of SEQ ID NO: 7.

20. A composition as claimed in any preceding claim, wherein said composition comprises a live attenuated chimeric dengue virus.

21. A composition as claimed in claim 20, wherein said composition comprises one or more proteins from a dengue virus and one or more proteins from a different flavivirus.

22. A composition as claimed in claim 21, wherein the different flavivirus is a yellow fever virus.

23. A composition as claimed in claim 22, wherein the yellow fever virus is YF-Vax.

24. A composition as claimed in any preceding claim, wherein the composition further comprises a dengue antigen of serotype 1, a dengue antigen of serotype 3 and a dengue antigen of serotype 4.

25. A composition as claimed in claim 24, wherein said dengue antigens of serotypes 1, 3 and 4 are each independently selected from the group consisting of a live attenuated dengue virus and a live attenuated chimeric dengue virus.

26. A composition as claimed in claim 25, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus in which the genetic backbone of a recipient flavivirus has been modified by exchanging the sequences encoding the prM and E proteins of the recipient flavivirus with the corresponding sequences of a dengue virus.

27. A composition as claimed in claim 26, wherein the recipient flavivirus is a yellow fever virus.

28. A pharmaceutical formulation comprising a composition as claimed in any preceding claim and a pharmaceutically acceptable carrier, diluent or excipient.

29. A composition as claimed in any one of claims 1 to 42 for use in therapy.

30. A composition as claimed in any one of claims 1 to 42 for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

31. A composition as claimed in any one of claims 38 to 42 for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 1, serotype 2, serotype 3 or serotype 4.

CLAIMS

1. A dengue virus serotype 2 vaccine composition comprising:

(i) a dengue antigen selected from the group consisting of:
   (a) a live attenuated dengue virus;
   (b) an inactivated dengue virus;
   (c) a live attenuated or inactivated chimeric dengue virus;
   (d) a dengue virus-like particle (VLP); and
   (e) a combination of two or more of (a) to (d);

or

(iii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP;

wherein said dengue antigen comprises a polypeptide having at least 90% identity to SEQ ID NO: 12.

2. A composition as claimed in claim 1, wherein said polypeptide comprises a valine residue at the position within the polypeptide that corresponds to position 251 of SEQ ID NO: 12.

3. A composition as claimed in claim 1 or claim 2, wherein said polypeptide comprises a methionine residue at the position within the polypeptide that corresponds to position 6 of SEQ ID NO: 12.

4. A composition as claimed in any preceding claim, wherein said polypeptide comprises a valine residue at the position within the polypeptide that corresponds to position 129 of SEQ ID NO: 12.

5. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 141 of SEQ ID NO: 12.

6. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 164 of SEQ ID NO: 12.

7. A composition as claimed in any preceding claim, wherein said polypeptide comprises an aspartate residue at the position within the polypeptide that corresponds to position 203 of SEQ ID NO: 12.

8. A composition as claimed in any preceding claim, wherein said polypeptide comprises a threonine residue at the position within the polypeptide that corresponds to position 226 of SEQ ID NO: 12.

9. A composition as claimed in any preceding claim, wherein said polypeptide comprises a glycine residue at the position within the polypeptide that corresponds to position 228 of SEQ ID NO: 12.

10. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 308 of SEQ ID NO: 12.

11. A composition as claimed in any preceding claim, wherein said polypeptide comprises a threonine residue at the position within the polypeptide that corresponds to position 478 of SEQ ID NO: 12.

12. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 484 of SEQ ID NO: 12.

13. A composition as claimed in any preceding claim, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 485 of SEQ ID NO: 12.

14. A composition as claimed in any preceding claim, wherein said polypeptide comprises an alanine residue at the position within the polypeptide that corresponds to position 491 of SEQ ID NO: 12.

15. A composition as claimed in any preceding claim, wherein said dengue antigen comprises a polypeptide having at least 90% identity to SEQ ID NO: 3.

16. A composition as claimed in any one of claims 1 to 14, wherein said polypeptide has at least 90% identity to SEQ ID NO: 3.

17. A composition as claimed in claim 15 or 16, wherein said polypeptide comprises a glycine residue at the position within the polypeptide that corresponds to position 15 of SEQ ID NO: 3.

18. A composition as claimed in any one of claims 15 to 17, wherein said polypeptide comprises a leucine residue at the position within the polypeptide that corresponds to position 24 of SEQ ID NO: 3.

19. A composition as claimed in any one of claims 15 to 18, wherein said polypeptide comprises an isoleucine residue at the position within the polypeptide that corresponds to position 39 of SEQ ID NO: 3.

20. A composition as claimed in any one of claims 15 to 19, wherein said polypeptide comprises a valine residue at the position within the polypeptide that corresponds to position 120 of SEQ ID NO: 3.

21. A composition as claimed in any one of claims 15 to 20, wherein said polypeptide comprises a threonine residue at the position within the polypeptide that corresponds to position 125 of SEQ ID NO: 3.

22. A composition as claimed in any one of claims 1 to 21, wherein said polypeptide comprises: (i) the sequence as set forth in SEQ ID NO: 13 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 13; (ii) the sequence as set forth in SEQ ID NO: 14 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 14; (iii) the sequence as set forth in SEQ ID NO: 15 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 15; (iv) the sequence as set forth in SEQ ID NO: 16 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 16; (v) the sequence as set forth in SEQ ID NO: 18 or a sequence

having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 18 or (vi) the sequence as set forth in SEQ ID NO: 26 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 26.

23. A composition as claimed in claim 1, wherein said dengue antigen comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 13; SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 18 and SEQ ID NO: 26.

24. A composition as claimed in claim 23, wherein said dengue antigen comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 13 and SEQ ID NO: 16.

25. A composition as claimed in claim 22, wherein said dengue antigen further comprises a polypeptide comprising: (i) the sequence as set forth in SEQ ID NO: 19 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 19; (ii) the sequence as set forth in SEQ ID NO: 20 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 20; (iii) the sequence as set forth in SEQ ID NO: 21 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 21; (iv) the sequence as set forth in SEQ ID NO: 22 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 22; (v) the sequence as set forth in SEQ ID NO: 23 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 23; (vi) the sequence as set forth in SEQ ID NO: 27 or a sequence having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 27.

26. A composition as claimed in claim 23, wherein said dengue antigen further comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 19; SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23 and SEQ ID NO: 27.

27. A composition as claimed in claim 22, wherein said dengue antigen comprises:

i) a polypeptide having the sequence as set forth in SEQ ID NO: 13 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 13; and
a polypeptide having the sequence as set forth in SEQ ID NO: 19 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 19;

ii) a polypeptide having the sequence as set forth in SEQ ID NO: 14 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 14; and
a polypeptide having the sequence as set forth in SEQ ID NO: 20 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 20;

iii) a polypeptide having the sequence as set forth in SEQ ID NO: 15 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 15; and
a polypeptide having the sequence as set forth in SEQ ID NO: 21 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 21;

iv) a polypeptide having the sequence as set forth in SEQ ID NO: 16 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 16; and
a polypeptide having the sequence as set forth in SEQ ID NO: 22 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 22;

v) a polypeptide having the sequence as set forth in SEQ ID NO: 18 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 18; and
a polypeptide having the sequence as set forth in SEQ ID NO: 23 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 23; or

vi) a polypeptide having the sequence as set forth in SEQ ID NO: 26 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 26; and

a polypeptide having the sequence as set forth in SEQ ID NO: 27 or a polypeptide having at least 1 and no more than 5 amino acid substitutions with respect to the sequence as set forth in SEQ ID NO: 27.

28. A composition as claimed in claim 26, wherein said dengue antigen comprises: i) a polypeptide of SEQ ID NO: 13 and a polypeptide of SEQ ID NO: 19; ii) a polypeptide of SEQ ID NO: 14 and a polypeptide of SEQ ID NO: 20; iii) a polypeptide of SEQ ID NO: 15 and a polypeptide of SEQ ID NO: 21; iv) a polypeptide of SEQ ID NO: 16 and a polypeptide of SEQ ID NO: 22; v) a polypeptide of SEQ ID NO: 18 and a polypeptide of SEQ ID NO: 23 or vi) a polypeptide of SEQ ID NO: 26 and a polypeptide of SEQ ID NO: 27.

29. A composition as claimed in claim 15 or claim 16, wherein said dengue antigen comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 8; SEQ ID NO: 9, SEQ ID NO: 10 and SEQ ID NO: 11.

30. A composition as claimed in claim 29, wherein said dengue antigen comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 8; and SEQ ID NO: 11.

31. A composition as claimed in any preceding claim, wherein said dengue antigen is selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising a polypeptide as defined in any one of claims 1 to 30.

32. A vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence encoding a protein comprising the polypeptide or polypeptides as defined in any one of claims 1 to 30.

33. A vaccine composition comprising a dengue antigen of serotype 2 selected from the group consisting of: (a) a live attenuated dengue virus; (b) an inactivated dengue virus; (c) a live attenuated or inactivated chimeric dengue virus; or (d) a

combination of two or more of (a) to (c); wherein said dengue antigen comprises a nucleotide sequence having at least 90% sequence identity to a sequence selected from the group consisting of the RNA equivalent of SEQ ID NO: 1, the RNA equivalent of SEQ ID NO: 4, the RNA equivalent of SEQ ID NO: 5, the RNA equivalent of SEQ ID NO: 6, the RNA equivalent of SEQ ID NO: 7 and SEQ ID NO: 25.

34. A composition as claimed in any preceding claim, wherein said composition comprises a live attenuated chimeric dengue virus.

35. A composition as claimed in claim 34, wherein said composition comprises one or more proteins from a dengue virus and one or more proteins from a different flavivirus.

36. A composition as claimed in claim 35, wherein the different flavivirus is a yellow fever virus.

37. A composition as claimed in claim 36, wherein the yellow fever virus is YF-Vax.

38. A composition as claimed in any preceding claim, wherein the composition further comprises a dengue antigen of serotype 1, a dengue antigen of serotype 3 and a dengue antigen of serotype 4.

39. A composition as claimed in claim 38, wherein said dengue antigens of serotypes 1, 3 and 4 are each independently selected from the group consisting of a live attenuated dengue virus and a live attenuated chimeric dengue virus.

40. A composition as claimed in claim 39, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus in which the genetic backbone of a recipient flavivirus has been modified by exchanging the sequences encoding the prM and E proteins of the recipient flavivirus with the corresponding sequences of a dengue virus.

41. A composition as claimed in claim 40, wherein the recipient flavivirus is a yellow fever virus.

42. A composition as claimed in any one of claims 38 to 41, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and the dengue antigen of serotype 2 is a live attenuated dengue virus of serotype 2 which comprises a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 24.

43. A pharmaceutical formulation comprising a composition as claimed in any preceding claim and a pharmaceutically acceptable carrier, diluent or excipient.

44. A composition as claimed in any one of claims 1 to 42 for use in therapy.

45. A composition as claimed in any one of claims 1 to 42 for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

46. A composition as claimed in any one of claims 38 to 42 for use in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 1, serotype 2, serotype 3 or serotype 4.

47. A method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2, wherein said method comprises administering to said subject an effective amount of a composition according to any one of claims 1 to 42.

48. A method of protecting a human subject against dengue disease caused by a dengue virus of serotype 1, serotype 2, serotype 3 or serotype 4, wherein said method comprises administering to said subject an effective amount of a composition according to any one of claims 38 to 42.

49. A kit comprising a composition according to any one of claims 1 to 42 and instructions for use of said composition in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 2.

50. A kit comprising a composition according to any one of claims 38 to 42 and instructions for use of said composition in a method of protecting a human subject against dengue disease caused by a dengue virus of serotype 1, serotype 2, serotype 3 or serotype 4.