SUMMARY

In one aspect, the present invention refers to the use of a vaccine composition in the manufacture of a medicament for the protection of a human subject against symptomatic dengue disease caused by dengue virus of any one of serotypes 1, 3 or 4, wherein said human subject is aged 9-45 years old, is dengue immune and resides in a dengue endemic area, wherein said composition 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, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and said dengue antigen of serotype 2 is a live attenuated dengue virus which comprises a nucleic acid sequence having at least 90% sequence identity to the sequence as set forth in SEQ ID NO: 24 and wherein said medicament results in a statistically significant reduction in the incidence or likelihood of symptomatic dengue disease caused by dengue virus of any one of serotypes 1, 3 or 4. Also described herein 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 a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP.

Also disclosed is the use of a vaccine composition as described herein for the manufacture of a medicament for protecting a human subject against dengue disease.

Also disclosed is 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 as described herein.

Additionally, the present disclosure also disclose a kit comprising a composition as described herein 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

CLAIMS

1. A use of a vaccine composition in the manufacture of a medicament for the protection of a human subject against symptomatic dengue disease caused by dengue virus of any one of serotypes 1, 3 or 4, wherein said human subject is aged 9-45 years old, is dengue immune and resides in a dengue endemic area, wherein said composition 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, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and said dengue antigen of serotype 2 is a live attenuated dengue virus which comprises a nucleic acid sequence having at least 90% sequence identity to the sequence as set forth in SEQ ID NO: 24 and wherein said medicament results in a statistically significant reduction in the incidence or likelihood of symptomatic dengue disease caused by dengue virus of any one of serotypes 1, 3 or 4.

2. A use according to claim 1, wherein said human is 9-16 years of age.

3. A use according to any preceding claim, wherein said medicament reduces the incidence or likelihood of dengue disease.

4. A use according to any preceding claim, wherein said dengue disease is virologically-confirmed.

5. A use according to any preceding claim, wherein said composition is to be administered in multiple doses.

6. A use according to claim 5, wherein said composition is to be administered in three or more doses.

7. A use according to claim 5 or claim 6, wherein a first and a third dose are to be administered approximately twelve months apart.

8. A use according to any one of claims 5 to 7, wherein said composition is to be administered in a first dose, a second dose and a third dose and wherein said second

dose is to be administered about six months after said first dose and wherein said third dose is to be administered about twelve months after said first dose.

9. A use according to any preceding claim, wherein said chimeric dengue virus comprises one or more proteins from a dengue virus and one or more proteins from a different flavivirus.

10. A use according to any one of claims 1 to 9, wherein said chimeric dengue virus comprises one or more proteins from a dengue virus of one serotype and one or more proteins from a dengue virus of a different serotype.

11. A use according to claim 9, wherein the different flavivirus is a yellow fever virus.

12. A use according to claim 11, wherein the yellow fever virus is strain YF17D.

13. A use according to any one of claims 1 to 12, wherein said chimeric dengue virus comprises the prM-E sequence of a dengue virus.

14. A use according to any one of claims 1 to 9 and 11 to 13, wherein the chimeric dengue virus comprises a yellow fever virus genome whose prM-E sequence has been substituted with the prM-E sequence of a dengue virus.

15. A use according to any one of claims 1 to 14 wherein at least one serotype of said dengue virus is present in an amount of from about 10^3 to about 10^6 $CCID_{50}$.

16. A use according to claim 15, wherein said composition comprises all four serotypes of dengue virus and each of said serotypes is present in an amount of from about 10^3 to about 10^6 $CCID_{50}$.

17. A use according to claim 16, wherein said composition comprises all four serotypes of dengue virus and each of said serotypes is present in an amount of about 10^5 $CCID_{50}$.

18. A use according to any preceding claim, wherein said composition is lyophilized.

19. A use according to any preceding claim, wherein said composition is to be administered to a human subject via a subcutaneous route.

20. A use according to any preceding claim, wherein said composition comprises a pharmaceutically acceptably carrier or excipient.