effective vaccine to protect against dengue fever and no drug treatment for the disease. Mosquito control efforts have been ineffective in preventing dengue outbreaks in endemic areas or in preventing further geographic spread of the disease. It is estimated that 3.5 billion people are threatened by infection with dengue virus. In addition, dengue virus is a leading cause of fever in travelers to endemic areas, such as Asia, Central and South America, and the Caribbean.

[0005] All four dengue virus serotypes are endemic throughout the tropical regions of the world and constitute the most significant mosquito-borne viral threat to humans in tropical regions, worldwide. Dengue viruses are transmitted to humans primarily by *Aedes aegypti* mosquitoes. Infection with one dengue virus serotype results in life-long protection from re-infection by that serotype, but does not prevent secondary infection by one of the other three dengue virus serotypes. In fact, previous infection with one dengue virus serotype leads to an increased risk of severe disease (DHF/DSS) upon secondary infection with a different serotype. The development of an effective vaccine represents an important approach to the prevention and control of this global emerging disease. Multiple immunizations make complete vaccine coverage difficult both for public health efforts in dengue virus endemic countries as well as travelers.

SUMMARY

[0006] In one aspect, the present disclosure provides a polynucleotide molecule encoding a modified live, attenuated dengue-2 virus strain PDK-53-V polypeptide molecule, wherein the polynucleotide molecule comprises: an adenine to guanine mutation at position 592 encoding a glutamic acid instead of a lysine in the polypeptide molecule at amino acid position 166 corresponding to prM-52; and an adenine to guanine mutation at position 8803 encoding a valine instead of an isoleucine in the polypeptide molecule at amino acid position 2903 corresponding to NS5-412. In another aspect, the present disclosure provides a polypeptide molecule encoded by a polynucleotide molecule. In yet another aspect, the present disclosure provides a modified live, attenuated dengue-2 strain PDK-53-V virus, comprising the polypeptide molecule as described herein, or represented by a polynucleotide molecule as described herein.

[0006a] In a further aspect, the present disclosure provides a pharmaceutical composition comprising a polynucleotide molecule as described herein, a polypeptide molecule as described herein, or a dengue-2 virus as described herein, and a pharmaceutically acceptable excipient. In a further aspect, the present disclosure provides the pharmaceutical composition as described herein for use as a medicament. In a further aspect, the present disclosure

provides a use of the pharmaceutical composition as described herein in the manufacture of a medicament for inducing an immune response in a subject.

[0006b] In a further aspect, the present disclosure provides a vector encoding a polynucleotide molecule as described herein. In a further aspect, the present disclosure provides a cell comprising the polynucleotide molecule as described herein or the vector as described herein. In a further aspect, the present disclosure provides an immunogenic composition comprising a modified live, attenuated dengue-2 strain PDK-53-V virus represented by a polynucleotide molecule as described herein and a pharmaceutically acceptable carrier. In a further aspect, the present disclosure provides a composition comprising one or more live attenuated viruses as described herein and a pharmaceutically acceptable carrier.

[0006c] ~~Embodiment~~Examples herein concern compositions, methods and uses of chimeric dengue virus constructs. In some ~~embodiment~~examples, a composition can include chimeric dengue virus constructs having an attenuated dengue virus backbone with structural genes from at least one other dengue virus serotype. Other ~~embodiment~~examples concern at least one live, attenuated virus in combination with one or more chimeric dengue viruses. Other ~~embodiment~~examples can include a composition of chimeric dengue viruses having a modified DEN-2 backbone (e.g. PDK-53 as a starting backbone in P1 (passage-1) and passage variability (after passage and growth *in vitro* on a permissive cell line) as indicated for P2, P3,…P8..P10 etc.) and one or more structural components of DEN-1, DEN-2, DEN-3 or DEN-4. In other ~~embodiment~~examples, an immunogenic composition is generated where when introduced to a subject, the composition produces an immune response to one or more dengue viruses in the subject. Therefore, constructs contemplated herein can be generated and passaged *in vitro*, and each of the passages provides an attenuated dengue virus contemplated of use in a pharmaceutically acceptable vaccine composition. In certain ~~embodiment~~examples a live, attenuated virus can be a live, attenuated dengue-2 virus alone or in combination with one or more chimeric dengue viruses.

[0007] In certain examples, chimeric dengue virus constructs of dengue virus serotypes can include passage 7 (P7) live, attenuated viruses or chimeric viruses having nucleic acid sequences identified by SEQ ID NOS: 1, 4, 7 and 10 or polypeptide sequences indicated by SEQ ID NOS: 2, 3, 5, 6, 8, 9, 11 and 12. It is contemplated herein that any of the passages for any of the live, attenuated viruses described herein can be used in an immunogenic composition to induce immune responses to the represented dengue viruses (e.g. serotypes 1-4). In accordance with these ~~embodiment~~examples, an immunogenic composition that includes a P-8 isolated live, attenuated virus can be administered to a subject to induce an immunogenic response against one or more dengue virus serotypes depending on the construct selected. In addition, a live, attenuated virus can be combined with one or more of these chimeric viruses. This is contemplated for each of the live, attenuated viruses isolated/produced in each subsequent cell passages (*e.g.* African Green Monkey Vero cell production, hereinafter: Vero cells). It is contemplated herein that any cell line (e.g. GMP-produced cell bank, FDA or EMA-approved) capable of producing dengue viruses is of use to passage any of the viral constructs at a manufacturing scale or as appropriate contemplated herein for subsequent use in a vaccine or immunogenic composition against Dengue virus.

[0008] In other ~~embodiment~~examples, compositions contemplated herein can be combined with other immunogenic compositions against other Flaviviruses such as West Nile virus, Japanese encephalitis or any other flavivirus chimeric construct and/or live, attenuated virus. In certain ~~embodiment~~examples, a single composition can be used against multiple flaviviruses.

[0009] In certain ~~embodiment~~examples, an immunogenic composition of the present ~~invention~~summary can include chimeric dengue viruses against one or more of DEN-1, DEN-2, DEN-3 and/or DEN-4, alone or in combination with a live, attenuated dengue virus composition.

[00010] In other ~~embodiment~~examples, a construct can include a construct having adaptive mutations in the structural or non-structural regions of the virus that increase growth or production without affecting attenuation or safety of the virus when introduced to a subject. In certain ~~embodiment~~examples, any of the contemplated chimeric dengue virus constructs can include a live, attenuated DEN-2 virus having specific mutations used as a backbone where the live attenuated DEN-2 PDK virus further includes structural proteins of one or more of prM (premembrane) and E (envelope) structural proteins of the other dengue virus serotypes. In addition, a DEN-2 backbone can include additional mutations in order to increase production of or enhance the immune response to a predetermine composition in a subject upon administration (e.g. chimeric Dengue virus 2/1, 2/3 or 2/4).

[00011] In some ~~embodiment~~examples, structural protein genes can include prM and E genes of DEN-1, DEN-2, DEN-3 or DEN-4 on a DEN-2 backbone having one or two mutations that are part of a live, attenuated dengue virus. For example, a dengue construct, in certain ~~embodiment~~examples can include those constructs termed DENVax-1-A, DENVax-2-F, DENVax-3-F, and DENVax-4-F (see Example section) where the DEN-2 backbone has one or more mutations (e.g. not found in the P1 or other previous passaged virus or PDK-53) from the DEN-2 live, attenuated virus previously demonstrated to be safe and effective to induce an immune response. The DEN-2 live, attenuated virus of the instant application is an improved version of the originally used DEN-2 live, attenuated virus. A chimeric construct of the instant ~~invention~~summary can include a modified attenuated DEN-2 PDK-53 backbone, having one or more structural proteins of the second dengue virus serotype wherein the structural proteins can include additional mutations to increase an immunogenic response to the chimeric construct. In some ~~embodiment~~examples, certain mutations acquired by attenuated DEN-2 PDK-53 can produce a conservative amino acid change or not in a constructs different from the P1 construct which can result in desirable traits for production etc.

[00012] In other ~~embodiment~~examples, a live, attenuated DEN-2 genome can be used to generate constructs of dengue virus serotype 1 (DEN-1) and dengue virus serotype 3 (DEN-3), dengue virus serotype 4 (DEN-4) where one or more structural protein genes of the DEN-2 viral genome can be replaced by one or more structural protein genes of DEN-1, DEN-3 or DEN-4, respectively. In some ~~embodiment~~examples, a structural protein can be the C, prM or E protein of a second dengue virus. In certain ~~embodiment~~examples, structural protein genes include the prM and E genes of DEN-1, DEN-3 or DEN-4. These hybrid viruses express the surface antigens of DEN-1, DEN-3 or DEN-4 while retaining the attenuation phenotypes of the parent attenuated DEN-2.

[00013] Constructs disclosed herein can include chimeric constructs of DEN-4, DEN-2, DEN-1, and DEN-3 expressing surface antigens of DEN-1, DEN-3 and DEN-4 using attenuated DEN-2 virus as a backbone.

[00014] In certain ~~embodiment~~examples, compositions of the instant ~~invention~~summary can include a composition that comprises a single chimeric dengue virus construct disclosed herein and a pharmaceutically acceptable carrier or excipient. Alternatively, compositions of the instant ~~invention~~summary can include a composition that comprises two or more, or three or more chimeric dengue virus constructs disclosed herein, and a pharmaceutically acceptable carrier or excipient. In accordance with these ~~embodiment~~examples, a one or more dengue virus chimeric constructs contemplated herein can be combined with one or more, live attenuated dengue

viruses. In certain ~~embodiment~~examples, a live, attenuated virus can be a live, attenuated DEN-2 virus wherein additional mutations in the NCR, NS1 regions or other regions increase the immune response, increase viral growth or other improvement for an improved live, attenuated dengue virus.

[00015] In certain ~~embodiment~~examples, the attenuation loci, nucleotide 5'NCR-57-T, NS1-53-Asp, and NS3-250-Val, of the DENV-2 vaccine have been previously determined, and all of these changes are shared by the common PDK-53 virus-specific genetic background of the four DENVax viruses. The genetic sequence of the three attenuation loci as well as the previously established *in vitro* and *in vivo* attenuation phenotypes of these vaccine candidates were carefully monitored for the cGMP-manufactured DENVax seeds. This report describes strategies used to generate master virus seeds (MVS) as well as their genetic and phenotypic characterization of use in the manufacture of dengue virus vaccine compositions. These MVS can be used for manufacture of clinical materials and ultimately commercial vaccine supplies.

Brief Description of the Drawings

[00016] The following drawings form part of the present specification and are included to further demonstrate certain embodiments. Some embodiments may be better understood by reference to one or more of these drawings alone or in combination with the detailed description of specific embodiments presented.

[00017] **Fig. 1** represents an exemplary chart reflecting an exemplary chimeric construct of the instant invention, DEN-2/DEN-4 compared to previously generated constructs and wild type dengue viruses.

[00018] **Fig. 2** represents an exemplary histogram plot comparing various responses using a live, attenuated DEN-2 backbone (with additional mutations) and a second dengue virus serotype as structural components substituted for the dengue-2 structural components (e.g. DENVax-1 MVS). This plot illustrates plaque sizes of the DENVax MVS. Wild-type Dengue viruses and previously published research-grade vaccine candidate viruses were included for control and comparison. This plot illustrates improved production of the dengue virus constructs compared to control dengue virus chimeric constructs.

[00019] **Fig. 3** represents an exemplary histogram plot that represents temperature sensitivities of DENVax MVS (Master Virus Seed). Wild type dengue viruses and previously published research-grade vaccine candidate viruses were included for comparison with the MVS grade.

What is claimed:

1. A nucleic acid chimera comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK-53, and a second nucleotide sequence encoding at least one structural protein from dengue-1, wherein the live, attenuated dengue-2 virus further comprises at least one additional mutation that includes a mutation at nucleic acid position 3823 wherein amino acid position 116 of NS2A gene is a leucine instead of isoleucine.
2. The nucleic acid chimera of claim 1, wherein the live, attenuated dengue-2 virus further includes a mutation at position 4407 wherein amino acid position 92 of NS2B is aspartic acid instead of glutamic acid.
3. The nucleic acid chimera of claim 1, wherein the live, attenuated dengue-2 virus further includes a mutation at position 7148 wherein amino acid position 108 of NS4B is isoleucine instead of threonine.
4. The nucleic acid chimera of claim 1, wherein the live, attenuated dengue-2 virus further includes a mutation in position 7311.
5. The nucleic acid chimera of claim 1, wherein the second nucleotide sequence encodes the E protein from dengue-1 which further comprises a mutation at position 2384 wherein amino acid position 483 of the E protein is alanine instead of glycine.
6. A pharmaceutical composition comprising a nucleic acid chimera of according to any one of claims 1-5, and a pharmaceutically acceptable excipient.
7. A pharmaceutical composition comprising a polypeptide encoded by a nucleic acid chimera according to any one of claims 1-5, and a pharmaceutically acceptable excipient.
8. A method for inducing an immune response in a subject comprising administering a pharmaceutically acceptable amount of any of the compositions of claims 6 and 7, wherein the composition induces an immune response to dengue virus in the subject.
9. A vector encoding a nucleic acid sequence of any one of claims 1-5.
10. 1. A polynucleotide molecule nucleic acid sequence comprising a nucleic acid sequence encoding a modified live, attenuated dengue-2 virus strain PDK-53 V polypeptide molecule, wherein the polynucleotide molecule live, attenuated dengue-2 virus further comprises: at least one additional mutation that includes a mutation at nucleic acid position 6481 wherein amino acid position 36 of NS4A gene is a proline instead of alanine.

an adenine to guanine mutation at position 592 encoding a glutamic acid instead of a lysine in the polypeptide molecule at amino acid position 166 corresponding to prM-52; and

~~11. The nucleic acid sequence of claim 10, wherein the live, attenuated dengue-2 virus further includes a mutation at position 7156 wherein amino acid position 111 of NS4B is phenylalanine instead of leucine .~~

~~12.~~ ~~The nucleic acid sequence of claim 10, wherein the live, attenuated dengue-2 virus further includes a~~ an adenine to guanine mutation at position 8803 ~~wherein amino acid position 412 of NS5 is~~ valine instead of an isoleucine in the polypeptide molecule at amino acid position 2903 corresponding to NS5-412.

~~13.~~ ~~The nucleic acid sequence of claim 1, wherein the live, attenuated dengue-2 virus further includes a mutation at position 592 wherein amino acid position 52 of prM is glutamic acid instead of lysine.~~

2. The polynucleotide molecule according to claim 1 comprising the polynucleotide represented by SEQ ID NO: 14.

3. The polynucleotide molecule according to claim 1 or 2 encoding a modified, live attenuated dengue-2 virus strain PDK-53-V polypeptide molecule, wherein the polypeptide molecule is represented by SEQ ID NO: 6.

4. A polypeptide molecule encoded by a polynucleotide molecule according to any one of claims 1-3.

5. A modified live, attenuated dengue-2 strain PDK-53-V virus, comprising the polypeptide molecule according to claim 4, or represented by a polynucleotide molecule according to any one of claims 1-3.

~~14. A pharmaceutical composition comprising a nucleic acid chimera of according to any one of claims 10-13, and a pharmaceutically acceptable excipient.~~

~~15.~~ 6. A pharmaceutical composition comprising a polynucleotide molecule according to any one of claims 1-3, a polypeptide molecule according to claim 4~~encoded by a nucleic acid sequence according to any one of claims 10-13~~, or a dengue-2 virus according to claim 5, and a pharmaceutically acceptable excipient.

7. The pharmaceutical composition according to claim 6 for use as a medicament.

8. Use of the pharmaceutical composition according to claim 6 in the manufacture of a medicament for inducing an immune response in a subject.

9. A vector encoding a polynucleotide molecule according to any one of claims 1-3.

10. A cell comprising the polynucleotide molecule according to any one of claims 1-3 or the vector according to claim 9.

~~16. A method for inducing an immune response in a subject comprising administering a pharmaceutically acceptable amount of any of the compositions of claims 14 and 15, wherein the composition induces an immune response to dengue virus in the subject.~~

~~17. A vector encoding a nucleic acid sequence of any one of claims 10-13.~~

~~18. A nucleic acid chimera comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK-53, and a second nucleotide sequence encoding at least one structural protein from dengue-3, wherein the live, attenuated dengue-2 virus further comprises at least one additional mutation that includes a mutation at nucleic acid position 6436 wherein amino acid position 23 of N42A gene is asparagine instead of aspartic acid.~~

~~19. The nucleic acid chimera of claim 16, wherein the live, attenuated dengue-2 virus further includes a mutation at position 7620.~~

~~20. The nucleic acid chimera of claim 16, wherein the second nucleotide sequence encodes the E protein from dengue-3 which further comprises a mutation at position 1603 wherein amino acid position 223 of the E protein is serine instead of threonine.~~

~~21. A pharmaceutical composition comprising a nucleic acid chimera of according to any one of claims 18-20, and a pharmaceutically acceptable excipient.~~

~~22. A pharmaceutical composition comprising a polypeptide encoded by a nucleic acid chimera according to any one of claims 18-20, and a pharmaceutically acceptable excipient.~~

~~23. A method for inducing an immune response in a subject comprising administering a pharmaceutically acceptable amount of any of the compositions of claims 21 and 22, wherein the composition induces an immune response to dengue virus in the subject.~~

~~24. A vector encoding a nucleic acid sequence of any one of claims 18-20.~~

~~25. A nucleic acid chimera comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK-~~

~~53, and a second nucleotide sequence encoding at least one structural protein from dengue-4, wherein the live, attenuated dengue-2 virus further comprises at least one additional mutation that includes a mutation at nucleic acid position 3674 wherein amino acid position 66 of NS2A gene is an glycine instead of aspartic acid.~~

~~26. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 3773 wherein amino acid position 99 of NS2A is arginine instead of lysine .~~

~~27. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 5391.~~

~~28. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 6437 wherein amino acid position 21 of NS4A is valine instead of alanine.~~

~~29. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 7026.~~

~~30. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 7538 wherein amino acid position 238 of NS4B is phenylalanine instead of serine.~~

~~31. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 9750.~~

~~32. The nucleic acid chimera of claim 22, wherein the live, attenuated dengue-2 virus further includes a mutation at position 225.~~

~~33. A pharmaceutical composition comprising a nucleic acid chimera of according to any one of claims 25-32, and a pharmaceutically acceptable excipient.~~

~~34. A pharmaceutical composition comprising a polypeptide encoded by a nucleic acid chimera according to any one of claims 25-32, and a pharmaceutically acceptable excipient.~~

~~35. A method for inducing an immune response in a subject comprising administering a pharmaceutically acceptable amount of any of the compositions of claims 33 and 34, wherein the composition induces an immune response to dengue virus in the subject.~~

~~36. A vector encoding a nucleic acid sequence of any one of claims 25-32.~~

~~37. A nucleic acid sequence comprising one or more nucleic acid sequences identified by SEQ ID NOS. 1, 7, and 10.~~

~~38. The nucleic acid according to claim 33, wherein the nucleic acid chimera encodes a polypeptide represented by SEQ ID NOS. 2, 3, 8, 9, 11 or 12.~~

~~39.~~ 11. An immunogenic composition comprising a modified live, attenuated dengue-2 strain PDK-53-V virus represented by a polynucleotide molecule according to any of

claims 1-3 ~~one or more nucleic acid sequences of claim 37 or polypeptides of claim 38,~~ and a pharmaceutically acceptable carrier.

~~40. The composition of claim 39, further comprising a live, attenuated dengue-2 virus.~~

12. The immunogenic composition according to claim 11, further comprising a dengue-1/dengue-2 chimera represented by a polynucleotide molecule encoding a dengue-1/dengue-2 polypeptide chimera, the polynucleotide molecule comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK 53-V, and a second nucleotide sequence encoding at least one structural protein from dengue-1, wherein the polynucleotide molecule comprises:

an adenine to a cytosine mutation at position 3823 encoding a leucine instead of an isoleucine in the dengue-1/dengue-2 polypeptide chimera at amino acid position 1243 corresponding to NS2A-116;

an adenine to thymine mutation at position 4407 encoding an aspartic acid instead of a glutamic acid in the dengue-1/dengue-2 polypeptide chimera at amino acid position 1437 corresponding to NS2B-92; and

an adenine to guanine mutation at position 7311.

13. The immunogenic composition according to claim 12, wherein the polynucleotide molecule encoding the dengue-1/dengue-2 polypeptide chimera further comprises:

a cytosine to thymine mutation at position 7148 encoding an isoleucine instead of a threonine in the dengue-1/dengue-2 polypeptide chimera at amino acid position 2351 corresponding to NS4B-108; and

a guanine to cytosine mutation at position 2384 encoding an alanine instead of glycine in the dengue-1/dengue-2 polypeptide chimera at amino acid position 763 corresponding to E-483.

14. The immunogenic composition according to claim 12, wherein the polynucleotide molecule encoding the dengue-1/dengue-2 polypeptide chimera comprises the polynucleotide represented by SEQ ID NO: 13.

15. The immunogenic composition according to claim 12 or 14, wherein the polynucleotide molecule encodes the dengue-1/dengue-2 polypeptide chimera represented by SEQ ID NO: 3.

16. The immunogenic composition according to claim 11, further comprising a dengue-3/dengue-2 chimera represented by a polynucleotide molecule encoding a dengue-3/dengue-2 polypeptide chimera, the polynucleotide molecule comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK-53-V, and a second nucleotide sequence encoding at least one structural protein from dengue-3,

wherein the polynucleotide molecule comprises:

an adenine to thymine mutation at position 1603 encoding a serine instead of a threonine in the dengue-3/dengue-2 polypeptide chimera at amino acid position 503 corresponding to E-223; and

an adenine to guanine mutation at position 7620.

17. The immunogenic composition according to claim 16, wherein the polynucleotide molecule encoding the dengue-3/dengue-2 polypeptide chimera further comprises a guanine to adenine mutation at position 6436 encoding an asparagine instead of an aspartic acid in the dengue-3/dengue-2 polypeptide chimera at amino acid position 2114 corresponding to NS4A-23.

18. The immunogenic composition according to claim 16, wherein the polynucleotide molecule encoding the dengue-3/dengue-2 polypeptide chimera comprises the polynucleotide represented by SEQ ID NO: 15.

19. The immunogenic composition according to claim 16 or 18, wherein the polynucleotide molecule encodes the dengue-3/dengue-2 polypeptide chimera represented by SEQ ID NO: 9.

20. The immunogenic composition according to claim 11, further comprising a dengue-4/dengue-2 chimera represented by a polynucleotide molecule encoding a dengue-4/dengue-2 polypeptide chimera, the polynucleotide molecule comprising a first nucleotide sequence encoding nonstructural proteins from a modified live, attenuated dengue-2 virus strain PDK-53-V, and a second nucleotide sequence encoding at least one structural protein from dengue-4, wherein the polynucleotide molecule comprises:

an adenine to thymine mutation at position 225;

an adenine to guanine mutation at position 3674 encoding a glycine instead of an aspartic acid in the dengue-4/dengue-2 polypeptide chimera at amino acid position 1193 corresponding to NS2A-66;

a cytosine to thymine mutation at position 5391;

a cytosine to thymine mutation at position 6437 encoding a valine instead of an alanine in the dengue-4/dengue-2 polypeptide chimera at amino acid position 2114 corresponding to NS4A-21,

an adenine to cytosine mutation at position 9750, and

optionally a thymine to cytosine mutation at position 7026, and optionally an adenine to guanine mutation at position 3773 encoding an arginine instead of a lysine in the dengue-4/dengue-2 polypeptide chimera at amino acid position 1226 corresponding to NS2A-99.

21. The immunogenic composition according to claim 20, wherein the polynucleotide

molecule encoding the dengue-4/dengue-2 polypeptide chimera further comprises a cytosine to thymine mutation at position 7538 encoding a phenylalanine instead of a serine in the dengue-4/dengue-2 polypeptide chimera at amino acid position 2481 corresponding to NS4B-238.

22. The immunogenic composition according to claim 20, wherein the polynucleotide molecule encoding the dengue-4/dengue-2 polypeptide chimera comprises the polynucleotide represented by SEQ ID NO: 16.

23. The immunogenic composition according to any one of claims 20 or 22, wherein the polynucleotide molecule encodes the dengue-4/dengue-2 polypeptide chimera represented by SEQ ID NO: 12.

~~41. The composition of claim 40, wherein the live, attenuated dengue-2 virus is represented by the nucleic acid sequence of SEQ ID NO.4 or the amino acid sequence of one or more of SEQ ID NOS. 5 and 6.~~

~~42.~~ 24. The immunogenic composition according to any of claims ~~40~~11 to 23, wherein the composition contains all four dengue virus serotypes, which is a tetravalent composition.

~~43.~~ 25. The immunogenic composition according to any of claims ~~39~~11 to 24, further comprising an immunogenic composition against other ~~for a f~~Flaviviruses such as ~~selected from the group consisting of yellow fever virus, tick-borne encephalitis virus,~~ West Nile virus, Japanese encephalitis ~~virus, West Nile virus, hepatitis C virus, and a combination of two or more thereof~~.

~~44. A kit comprising at least one nucleic acid sequence according to any of claims 1-5, 10-13, 18-20 or 25-32; or at least one composition according to any of claims 6, 7, 14, 15, 21, 22, 33 or 34 and a container.~~

~~45. A live, attenuated virus comprising one or more nucleic acid sequences according to any of 1-5, 10-13, 18-20 or 25-32.~~

~~46. A nucleic acid sequence or polypeptide encoded by one or more nucleic acid sequences comprising the nucleic acid sequences of Table 3.~~

~~47. A nucleic acid sequence or polypeptide encoded by one or more nucleic acid sequences comprising one or more of DENVax-1-A, DENVax-2-F, DENVax-3-F, and DENVax-4-F.~~

~~48. A composition comprising one or more nucleic acid sequences or polypeptides encoded by the nucleic acid sequences of claim 47, and a pharmaceutically acceptable carrier or excipient.~~

~~49. The composition of claim 48, further comprising a pharmaceutically acceptable adjuvant.~~

~~50.~~ 26. A composition comprising one or more live attenuated viruses ~~of~~ according to claim ~~4~~5, and a pharmaceutically acceptable carrier.

~~51~~27. The composition according to~~of~~ claim ~~50~~26, wherein the composition comprises a tetravalent dengue virus composition capable of inducing an immune response in a subject against all four dengue virus serotypes.

28. The vector according to claim 9, wherein the vector is a plasmid vector.

29. The vector according to claim 9, wherein the vector is a cDNA infectious clone.