Claims

1. A virus-like particle capable of eliciting immune response in a mammal comprising a modified form of M and E structural proteins of flavivirus,
   wherein the modified form comprises an amino acids sequence corresponding to an M and E sequence setting forth in SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3 or SEQ ID NO. 4,
   wherein conserved amino acid His at positions M7, E261, E282, and E317 of dengue virus sequence, are replaced by amino acid Ala at positions 7, 336, 357 and 392 in SEQ ID NO. 1-3, or conserved amino acid His at positions M7, E259, E280 and E315 of dengue virus sequence are replaced by amino acid Ala at positions 7, 334, 355 and 390 in SEQ ID NO. 4.

2. The virus-like particle of claim 1, wherein the flavivirus is from dengue virus, Japanese encephalitis virus, Yellow fever virus, West Nile virus or Zika virus.

3. The virus-like particle of claim 1, wherein the modified form further comprises replacement of conserved amino acid His at positions E27, E149 and E209 of dengue virus sequence with amino acid Asn at positions 102, 224 and 284 in SEQ ID NO. 1-3 or replacement of conserved amino acid His at positions E27, E149 and E207 of dengue virus sequence with amino acid Asn at positions 102, 224 and 282 in SEQ ID NO. 4.

4. The virus-like particle of claim 1, wherein the modified form further comprises any one or combination of replacement of amino acids Ser or Glu at position E186 of dengue virus sequence or amino acid Ser at position E184 of dengue virus sequence with amino acid Phe at position 261 in SEQ ID NO. 1-3 or at position 259 in SEQ ID NO. 4, respectively, or replacement of amino acid Arg at position E188 of dengue virus sequence or position E186 of dengue virus sequence with amino acid Leu at position 263 in SEQ ID NO. 1-3 or at position 261 in SEQ ID NO. 4, respectively, or replacement of amino acid Asn or Val at position E242 of dengue virus sequence or amino acid Asn at position E240 of dengue virus sequence with amino acid Ser at position 317 in SEQ ID NO. 2 -3 or position 315 in SEQ ID NO. 4, or replacement of amino acid Arg or Lys at position E323 of dengue virus sequence or amino acid Lys at position E321 of dengue virus sequence with amino acid Gln at position 398 of SEQ ID NO. 2-3 or position 396 of SEQ ID NO. 4.

5. An isolated polynucleotide encoding a virus-like particle or polypeptide capable of eliciting immune response in a subject upon administrating the virus-like particle or polypeptide to the subject at a pharmaceutically effective dosage, the virus-like particle or polypeptide comprising a modified form of M and E structural proteins of flavivirus, wherein a nucleotide sequence of the modified form is corresponding to a sequence setting forth in SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7 or SEQ ID NO. 8, or an amino acid sequence of the modified form is corresponding to a sequence setting forth in SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3 or SEQ ID NO. 4, wherein conserved amino acid His at positions M7, E261, E282 and E317 of dengue virus sequence are replaced with amino acid Ala at positions 7, 336, 357, and 392 in SEQ ID NO. 1-3 or conserved amino acid His at positions M7, E259, E280 and E315 of dengue virus sequence are replaced with amino acid Ala at positions 7, 334, 355 and 390 in SEQ ID NO. 4.

6. The isolated polynucleotide of claim 5, wherein the modified form further comprises replacement of conserved amino acid His at positions E27, E149 and E209 of dengue virus sequence with amino acid Asn at positions 102, 224 and 284 in SEQ ID NO. 1-3 or replacement of conserved amino acid His at positions E27, E149 and E207 of dengue virus sequence with amino acid Asn at positions 102, 224 and 282 in SEQ ID NO. 4.

7. The isolated polynucleotide of claim 5, wherein the modified form further comprises any one or combination of replacement of amino acid Ser or Glu at position E186 of dengue virus sequence or amino acid Ser at position E184 of dengue virus sequence with amino acid Phe at position 261 of SEQ ID NO. 1-3 or at position 259 of SEQ ID NO. 4, respectively, or replacement of amino acid Arg at position E188 of dengue virus sequence or position E186 of dengue virus sequence with amino acid Leu at position 263 in SEQ ID NO. 1-3, or at position 261 in SEQ ID NO. 4, respectively, or replacement of amino acid Asn or Val at position E242 of dengue virus sequence or amino acid Asn at position E240 of dengue virus sequence with amino acid Ser at position 317 in SEQ ID NO. 2 -3 or position 315 in SEQ ID NO. 4, or replacement of amino acid Arg or Lys at position E323 of dengue virus sequence or amino acid Lys at position E321 of dengue virus sequence with amino acid Gln at position 398 of SEQ ID NO. 2-3 or position 396 of SEQ ID NO. 4.

8. A vaccine composition comprising: pharmaceutically acceptable adjuvant; and polypeptides or virus-like particles, which are immunologically active upon administrating

to a subject, having an amino acids sequence corresponding to a sequence setting forth in SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3 or SEQ ID NO. 4, wherein the amino acids sequence comprises a modified form of dengue virus sequence, wherein conserved amino acid His at positions M7, E261, E282, and E317 of dengue virus sequence, are replaced by amino acid Ala at positions 7, 336, 357 and 392 in SEQ ID NO. 1-3, or conserved amino acid His at positions M7, E259, E280 and E315 of dengue virus sequence are replaced by amino acid Ala at positions 7, 334, 355 and 390 in SEQ ID NO. 4.

9. The vaccine composition of claim 8, wherein the modification further comprises replacement of conserved amino acid His at positions E27, E149 and E209 of dengue virus sequence with amino acid Asn at positions 102, 224 and 284 in SEQ ID NO. 1-3 or replacement of conserved amino acid His at positions E27, E149 and E207 of dengue virus sequence with amino acid Asn at positions 102, 224 and 282 in SEQ ID NO. 4.

10. The vaccine composition of claim 8, wherein the modifications further comprises any one or combination of replacement of amino acids Ser or Glu at position E186 of dengue virus sequence or amino acid Ser at position E184 of dengue virus sequence with amino acid Phe at position 261 in SEQ ID NO. 1-3 or at position 259 in SEQ ID NO. 4, respectively, or replacement of amino acid Arg at position E188 of dengue virus sequence or position E186 of dengue virus sequence with amino acid Leu at position 263 in SEQ ID NO. 1-3 or at position 261 in SEQ ID NO. 4, respectively, or replacement of amino acid Asn or Val at position E242 of dengue virus sequence or amino acid Asn at position E240 of dengue virus sequence with amino acid Ser at position 317 in SEQ ID NO. 2 -3 or position 315 in SEQ ID NO. 4, or replacement of amino acid Arg or Lys at position E323 of dengue virus sequence or amino acid Lys position E321 of dengue virus sequence with amino acid Gln at position 398 of SEQ ID NO. 2-3 or position 396 of SEQ ID NO. 4.

11. A vaccine composition comprising pharmaceutically acceptable adjuvant; and a nucleotide sequence setting forth in SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7 or SEQ ID NO. 8 respectively corresponding to amino acids sequence SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3 and SEQ ID NO. 4.