CLAIMS

1. An isolated flavivirus envelope (E) polypeptide comprising an ectodomain and a stem-transmembrane domain, wherein the stem-transmembrane domain is distinguished from a wild-type stem-transmembrane domain by two or more amino acid substitutions in the wild-type stem-transmembrane domain, wherein the two or more amino acid substitutions are at positions corresponding to positions 8, 11 or 15 of SEQ ID NO: 1.

2. The isolated flavivirus E polypeptide of claim 1, wherein each of the two or more amino acid substitutions is a substitution to a non-polar amino acid residue.

3. The isolated flavivirus E polypeptide of claim 2, wherein the non-polar amino acid residue is alanine (A), phenylalanine (F), isoleucine (I), leucine (L), methionine (M), proline (P), valine (V) or tryptophan (W), optionally wherein the non-polar amino acid residue is isoleucine (I), leucine (L) or phenylalanine (F).

4. The isolated flavivirus E polypeptide of any one of claims 1 to 3, wherein the ectodomain or the stem-transmembrane domain is from dengue virus (DENV), Zika virus (ZIKV), West Nile virus (WNV), yellow fever virus (YFV) or Japanese encephalitis virus (JEV), optionally wherein the ectodomain is from DENV and/or the stem-transmembrane domain is from DENV or JEV.

5. The isolated flavivirus E polypeptide of any one of claims 1 to 4, wherein the stem-transmembrane domain further comprises one or more amino acid substitutions at positions corresponding to position 1, 2, 3, 4, 5, 6, 7, 9, 10, 12, 13, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100 or 101 of SEQ ID NO: 1, optionally wherein the stem-transmembrane domain further comprises one or more amino acid substitutions at positions corresponding to position 14, 19, 26, 28, 35, 37, 39, 40, 49, 51, 52, 58, 59, 60, 61, 62 or 63 of SEQ ID NO: 1.

6. The isolated flavivirus E polypeptide of claim 5, wherein each of the one or more amino acid substitutions is a substitution to a non-polar amino acid residue, optionally wherein the non-polar amino acid residue is alanine (A), phenylalanine (F), isoleucine (I), leucine (L), methionine (M), proline (P), valine (V) or tryptophan (W), further optionally wherein the non-polar amino acid residue is isoleucine (I), leucine (L) or phenylalanine (F).

7. The isolated flavivirus E polypeptide of claim 5 or 6, wherein the polypeptide comprises an amino acid substitution at positions corresponding to one of the following sets of positions of SEQ ID NO: 1:
   (a) 8 and 15;
   (b) 8, 14 and 15;
   (c) 8, 11, 14 and 15;
   (d) 8, 15, 26 and 28;
   (e) 8, 15, 35, 37 and 39;
   (f) 8, 15, 40, 49, 51 and 52; and
   (g) 8, 15, 58, 59, 61, 62 and 63.

8. The isolated flavivirus E polypeptide of any one of claims 5 to 7, wherein the stem-transmembrane domain comprises at least two of the following:
   (a) a substitution to F, I or L at a position corresponding to position 8 of SEQ ID NO: 1;
   (b) a substitution to F, I or L at a position corresponding to position 11 of SEQ ID NO: 1;
   (c) a substitution to F, I or L at a position corresponding to position 14 of SEQ ID NO: 1;
   (d) a substitution to F, I or L at a position corresponding to position 15 of SEQ ID NO: 1;
   (e) a substitution to F, I or L at a position corresponding to position 26 of SEQ ID NO: 1;
   (f) a substitution to F, I or L at a position corresponding to position 28 of SEQ ID NO: 1;
   (g) a substitution to F, I or L at a position corresponding to position 35 of SEQ ID NO: 1;
   (h) a substitution to F, I or L at a position corresponding to position 37 of SEQ ID

NO: 1;

(i) a substitution to F, I or L at a position corresponding to position 39 of SEQ ID NO: 1;

(j) a substitution to F, I or L at a position corresponding to position 40 of SEQ ID NO: 1;

(k) a substitution to F, I or L at a position corresponding to position 49 of SEQ ID NO: 1;

(l) a substitution to F, I or L at a position corresponding to position 51 of SEQ ID NO: 1;

(m) a substitution to F, I or L at a position corresponding to position 52 of SEQ ID NO: 1;

(n) a substitution to F, I or L at a position corresponding to position 58 of SEQ ID NO: 1;

(o) a substitution to F, I or L at a position corresponding to position 59 of SEQ ID NO: 1;

(p) a substitution to F, I or L at a position corresponding to position 61 of SEQ ID NO: 1;

(q) a substitution to F, I or L at a position corresponding to position 62 of SEQ ID NO: 1; or

(r) a substitution to F, I or L at a position corresponding to position 63 of SEQ ID NO: 1;

optionally wherein the stem-transmembrane domain comprises at least two of the following:

(a) a substitution to L at a position corresponding to position 8 of SEQ ID NO: 1;

(b) a substitution to L at a position corresponding to position 11 of SEQ ID NO: 1;

(c) a substitution to L at a position corresponding to position 14 of SEQ ID NO: 1;

(d) a substitution to L at a position corresponding to position 15 of SEQ ID NO: 1;

(e) a substitution to F at a position corresponding to position 26 of SEQ ID NO: 1;

(f) a substitution to L at a position corresponding to position 28 of SEQ ID NO: 1;

(g) a substitution to L at a position corresponding to position 35 of SEQ ID NO: 1;

(h) a substitution to L at a position corresponding to position 37 of SEQ ID NO: 1;

(i) a substitution to L at a position corresponding to position 39 of SEQ ID NO: 1;

(j) a substitution to L at a position corresponding to position 40 of SEQ ID NO: 1;

(k) a substitution to L at a position corresponding to position 49 of SEQ ID NO: 1;

(l) a substitution to L at a position corresponding to position 51 of SEQ ID NO: 1;
(m) a substitution to L at a position corresponding to position 52 of SEQ ID NO: 1;
(n) a substitution to L at a position corresponding to position 58 of SEQ ID NO: 1;
(o) a substitution to L at a position corresponding to position 59 of SEQ ID NO: 1;
(p) a substitution to L at a position corresponding to position 61 of SEQ ID NO: 1;
(q) a substitution to L at a position corresponding to position 62 of SEQ ID NO: 1; or
(r) a substitution to I at a position corresponding to position 63 of SEQ ID NO: 1;

9. The isolated flavivirus E polypeptide of claim 8, wherein the stem-transmembrane domain comprises or consists of an amino acid sequence having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 7–16.

10. The isolated flavivirus E polypeptide of any one of claims 1 to 9, wherein the polypeptide is chimeric, comprising an ectodomain from a first flavivirus and a stem-transmembrane domain from a second flavivirus, optionally wherein the first and second flavivirus are different flaviviruses.

11. A virus-like particle (VLP) comprising a flavivirus E polypeptide of any one of claims 1 to 10.

12. An isolated polynucleotide comprising a nucleic acid sequence encoding a flavivirus E polypeptide of any one of claims 1 to 10.

13. A host cell comprising the isolated polynucleotide of claim 12.

14. An immunogenic composition comprising the flavivirus E polypeptide of any one of claims 1 to 10, or the VLP of claim 11.

15. Use of the immunogenic composition of claim 14 in the manufacture of a medicament for modulating an immune response in a subject, optionally wherein the immunogenic composition prevents or treats a flaviviral infection in the subject, further optionally wherein the immunogenic composition is administered in two or more doses.