(i) a heavy chain with three Complementarity Determining Regions (CDRs) comprising a CDR1 comprising an amino acid sequence of GYSTH (SEQ ID NO:21), a CDR2 comprising an amino acid sequence of WDNPSSGDTTYAENFRG (SEQ ID NO:22), and a CDR3 comprising an amino acid sequence of GGDDYSFDH (SEQ ID NO:23);
(ii) a light chain with three CDRs comprising a CDR1 comprising an amino acid sequence of RGDSLRSYYAS (SEQ ID NO:24), a CDR2 comprising an amino acid sequence of GENNRPS (SEQ ID NO:25), and a CDR3 comprising an amino acid sequence of NSRDSSDHLLL (SEQ ID NO:26);
(iii) a modified Fc region having mutations at amino acid positions 234 and 235, such that the Fc region does not bind to an Fcγ receptor, wherein
a) the mutations are L234A and L235A wherein positions 234 and 235 determined according to the EU numbering index, correspond to positions 240 and 241 of the heavy chain amino acid sequence of the isolated humanized monoclonal antibody (SEQ ID NO:20), respectively, and
b) the antibody binds and neutralizes a flavivirus.

[0010] The present disclosure further provides an isolated humanized monoclonal antibody that neutralizes a flavivirus.

[0011] The present disclosure also provides antibodies with a modified Fc region such that the Fc region does not bind to the Fcγ receptor. The modified Fc region contains mutations at amino acid positions 234 and 235. In one embodiment, the mutations are L234A and L235A. In one embodiment, the modified Fc region comprises a CH2 region wherein the amino acids at positions 4 and 5 of the CH2 region are mutated. For example, the leucine amino acids at positions 4 and 5 are mutated to a different amino acid, preferably, an alanine. In other embodiments, the modified Fc region comprises an Fc region where the amino acids at positions 108 and 109 are mutated. For example, the leucines at positions 108 and 109 of the Fc region are mutated to a different amino acid, preferably, an alanine. In another embodiment, the modified Fc region comprises the amino acid sequence of SEQ ID NO: 7. The modified Fc region binds to the neonatal Fc receptor (FcRn).

[0012] According to the present disclosure, the antibody does not contribute to an antibody-dependent enhancement of a flavivirus infection.

[0013] According to the present disclosure, the antibody is linked to a therapeutic agent. The therapeutic agent is a toxin, a radiolabel, a siRNA, a small molecule, or a cytokine. For example, the cytokine is TGF-beta.

[0014] The present disclosure further provides a cell producing a huFV antibody. The cell may be a mammalian cell (*i.e.*, a mouse, rabbit, goat, or sheep), or a plant cell (*i.e.* tobacco plant).

[0014a] In one aspect, the present disclosure provides an isolated cell that produces the antibody disclosed herein.

[0014b] In another aspect, the present disclosure provides a use of an antibody disclosed herein in the manufacture of a medicament for reducing antibody-dependent enhancement of a flavivirus infection in a subject.

[0014c] In another aspect, the present disclosure provides a use of an antibody disclosed herein in the manufacture of a medicament for preventing, treating or alleviating a symptom of a flavivirus infection in a subject.

anti-viral agent are administered sequentially or concurrently. The anti-viral agent is an antibody, an antibody linked to a therapeutic agent, or a small molecule.

[0018] The flavivirus is West Nile virus, Dengue virus (serotypes 1-4), St. Louis encephalitis virus, yellow fever virus, Japanese encephalitis virus, and Murray Valley encephalitis virus.

[0019] The present disclosure also provides a nucleic acid sequence containing a nucleic acid sequence of SEQ ID NO: 2, 4 and 8.

[0020] The present disclosure further provides a nucleic acid sequence encoding a polypeptide of SEQ ID NO: 1 and 3. The present disclosure further provides a polypeptide containing the amino acid sequence of SEQ ID NO: 1, 3 and 7.

[0021] The present disclosure further provides a vector containing the nucleic acid sequence containing SEQ ID NO: 2, 4 and 8, or encoding a polypeptide of SEQ ID NO: 1, 3 and 7.

[0022] Additionally, the present disclosure provides a cell containing a vector containing the nucleic acid sequence containing SEQ ID NO: 2, 4 and 8, or encoding a polypeptide of SEQ ID NO: 1, 3 and 7.

[0023] Other features and advantages of the present disclosure will be apparent from and are encompassed by the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] **Figure 1** shows a schematic of an expression vector containing wild-type mAb-11.

[0025] **Figure 2** shows a schematic of an expression vector containing engineered mAb-11-LALA.

What is claimed is:

1. An isolated humanized monoclonal antibody comprising:

(i) a heavy chain with three Complementarity Determining Regions (CDRs) comprising a CDR1 comprising an amino acid sequence of GYSTH (SEQ ID NO:21), a CDR2 comprising an amino acid sequence of WDNPSSGDTTYAENFRG (SEQ ID NO:22), and a CDR3 comprising an amino acid sequence of GGDDYSFDH (SEQ ID NO:23);

(ii) a light chain with three CDRs comprising a CDR1 comprising an amino acid sequence of RGDSLRSYYAS (SEQ ID NO:24), a CDR2 comprising an amino acid sequence of GENNRPS (SEQ ID NO:25), and a CDR3 comprising an amino acid sequence of NSRDSSDHLLL (SEQ ID NO:26);

(iii) a modified Fc region having mutations at amino acid positions 234 and 235, such that the Fc region does not bind to an Fcγ receptor, wherein

a) the mutations are L234A and L235A wherein positions 234 and 235 determined according to the EU numbering index, correspond to positions 240 and 241 of the heavy chain amino acid sequence of the isolated humanized monoclonal antibody (SEQ ID NO:20), respectively, and

b) the antibody binds and neutralizes a flavivirus.

2. The antibody of claim 1, wherein said antibody does not contribute to an antibody-dependent enhancement of a flavivirus infection.

3. The antibody of claim 1, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 7 or SEQ ID NO: 13.

4. The antibody of claim 1, wherein the modified Fc region binds to the neonatal Fc receptor.

5. The antibody of claim 1, wherein the flavivirus is West Nile virus, Dengue virus (serotypes 1-4), St. Louis encephalitis virus, yellow fever virus, Japanese encephalitis virus, or Murray Valley encephalitis virus.

6. The antibody of claim 1, wherein said humanized monoclonal antibody is produced in a plant.

7. The antibody of claim 1, linked to a therapeutic agent.

8. The antibody of claim 7, wherein said therapeutic agent is a toxin, a radiolabel, a siRNA, a small molecule, or a cytokine.

9. The antibody of claim 8, wherein said cytokine is TGF-beta.

10. An isolated cell that produces the antibody of claim 1.

11. Use of an antibody of any one of claims 1-9 in the manufacture of a medicament for reducing antibody-dependent enhancement of a flavivirus infection in a subject.

12. The use of claim 11, wherein said antibody is to be administered to said subject after a first infection by a flavivirus.

13. Use of an antibody according to any one of claims 1-9 in the manufacture of a medicament for preventing, treating or alleviating a symptom of a flavivirus infection in a subject.

14. Use of an antibody according to any one of claims 1-9 in the manufacture of a medicament for delaying the onset of one or more symptoms of a flavivirus infection in a subject.

15. The use of claim 13 or 14, wherein an anti-viral agent is to be further administered to said subject.

16. The use of claim 15, wherein the anti-viral agent is an antibody, an antibody linked to a therapeutic agent, or a small molecule.

17. The use of claim 15, wherein said antibody and the anti-viral agent are to be administered sequentially or concurrently.

18. The use of any one of claims 13-17, wherein said one or more symptom comprises weight loss, paralysis, fever, headache, nausea, vomiting, skin rash, and body aches.

19. The use of any one of claims 13-18, wherein said flavivirus is West Nile virus, Dengue virus (serotypes 1-4), St. Louis encephalitis virus, yellow fever virus, Japanese encephalitis virus, or Murray Valley encephalitis virus.

20. The isolated cell of claim 10, wherein said isolated cell is a plant cell.