CLAIMS

What is Claimed:

1. An isolated antibody or fragment thereof that binds specifically to a Dengue virus serotype 1 envelope (E) protein or fragment thereof, wherein the antibody is a human antibody with neutralizing activity that binds across two E proteins in a virus, wherein the binding across two E proteins comprises binding to DI and the hinge between DI and II on one E protein and DIII of a neighboring E protein,
wherein the antibody or fragment thereof comprises:
a heavy chain comprising three CDRs with the amino acid sequences SYGMH, VIWYDGSKTYYGDSVKG and GIAGGWAFW, and
a light chain comprising three CDRs with the amino acid sequences RASQNVYSYLG, GVTSRAT and QQYAG.

2. The antibody or fragment thereof according to claim 1, wherein the antibody or fragment thereof is selected from the group consisting of: (a) a whole immunoglobulin molecule; (b) an scFv; (c) a Fab fragment; (d) an F(ab')2; and (e) a disulfide linked Fv.

3. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a heavy chain immunoglobulin constant domain selected from the group consisting of: (a) a human IgM constant domain; (b) a human IgG1 constant domain; (c) a human IgG2 constant domain; (d) a human IgG3 constant domain; (e) a human IgG4 constant domain; and (f) a human IgA1/2 constant domain.

4. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a heavy chain with the amino acid sequence
EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLE
WVAVIWYDGSKTYYGDSVKGRFTISKDNSKKMVNLQMDSLGVEDTA
FYYCARGIAGGWAFWGIDLWGQGTLVTVSS.

5. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a heavy chain framework of IGHV1-2*02 and three of the CDRs with the amino acid sequences SYGMH, VIWYDGSKTYYGDSVKG and GIAGGWAFW.

6. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a light chain immunoglobulin constant domain selected from the group consisting of: (a) a human Ig kappa constant domain; and (b) a human Ig lambda constant domain.

7. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a light chain with the amino acid sequence

DVVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLI
FGVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAY
TFGQGTKVEIKR

or

DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLIF
GVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAYT
FGQGTKVEIKR.

8. The antibody or fragment thereof according to claim 1 or 2, wherein the antibody or fragment thereof comprises:

a light chain framework of IGKV3-20*01 and three of the CDRs with the amino acid sequences RASQNVYSYLG, GVTSRAT and QQYAG.

9. The antibody or fragment thereof according to any one of claims 1-8, wherein the antibody:

binds to a Dengue virus having the binding specificity of an antibody with the heavy chain amino acid sequence

EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLE
WVAVIWYDGSKTYYGDSVKGRFTISKDNSKKMVNLQMDSLGVEDTA
FYYCARGIAGGWAFWGIDLWGQGTLVTVSS and the light chain amino acid sequence
DVVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLI
FGVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAY
TFGQGTKVEIKR
or
DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLIF
GVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAYT
FGQGTKVEIKR.

10. The antibody or fragment thereof according to any one of claims 1-8, wherein the antibody:

is an antibody with the heavy chain amino acid sequence
EVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLE
WVAVIWYDGSKTYYGDSVKGRFTISKDNSKKMVNLQMDSLGVEDTA
FYYCARGIAGGWAFWGIDLWGQGTLVTVSS and the light chain amino acid sequence
DVVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLI
FGVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAY
TFGQGTKVEIKR
or
DIVMTQSPGTLSLSPGERATLSCRASQNVYSYLGWYQHKPGRSPRLLIF
GVTSRATGVPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSAYT
FGQGTKVEIKR.

11. The antibody or fragment thereof according to any one of claims 1-10, wherein the antibody or fragment thereof binds to an antigen with an affinity constant (K_D) of less than 1 x 10^{-8} M, and optionally binds to an antigen with an affinity constant (K_D) of less than 1 x 10^{-9} M.

12. The antibody or fragment thereof according to any one of claims 1-11, wherein the antibody is derived from a B cell of a patient who has recovered from Dengue virus infection.

13. A pharmaceutical composition comprising the antibody or fragment thereof according to any one of claims 1-12 and a pharmaceutically acceptable carrier effective to reduce or prevent Dengue virus infection in a subject.

14. The pharmaceutical composition of claim 13, further comprising a second agent.

15. An antibody or fragment thereof according to any one of claims 1-12 for use in a method of passive immunization against Dengue virus infection wherein an effective amount of the antibody or fragment thereof according to any one of claims 1-12 is to be administered to a subject.

16. An antibody or fragment thereof according to any one of claims 1-12 for use in a method of treatment of Dengue virus infection, wherein the antibody or fragment thereof according to any one of claims 1-12 is to be administered to a subject in need thereof in an amount that is effective to reduce or prevent the disease.

17. The antibody for the use according to claim 16, wherein:
the antibody is to be administered intravenously (IV), subcutaneously (SC), intramuscularly (IM), transdermally, or orally; or
the antibody is to be administered in an amount in the range of 1 to 100 milligrams per kilogram of the subject's body weight; or
said use further comprising a second agent to be administered to the subject, optionally wherein the second agent is antiviral drug or analgesic drug.

18. An isolated nucleic acid encoding the antibody or fragment thereof according to any one of claims 1-12.

19. An expression vector comprising the nucleic acid of claim 18.

20. A host cell comprising the expression vector of claim 19, optionally wherein the host cell is a bacterial cell, a eukaryotic cell, or a mammalian cell.