

CLAIMS

What is claimed is:

1. An isolated antibody or antigen-binding fragment thereof specific for dengue virus, wherein the isolated antibody is selected from the group consisting of:

5 (i) a first antibody specific for dengue virus serotype 1 (DENV1) comprising

(a) a heavy chain variable region (V_H) which comprises a heavy chain complementary determining region (HC CDR1) of SEQ ID NO: 2, a heavy chain complementary determining region 2 (HC CDR2) of SEQ ID NO: 4, and a heavy chain complementary determining region 3 (HC CDR3) of SEQ ID NO: 6; and

10 (b) a light chain variable region (V_L) which comprises a light chain complementary determining region 1 (LC CDR1) of SEQ ID NO: 9, a light chain complementary determining region (LC CDR2) of SEQ ID NO: 11, and a light chain complementary determining region 3 (LC CDR3) of SEQ ID NO: 13;

(ii) a second antibody specific for dengue virus serotype 2 (DENV2) comprising

15 (a) a V_H which comprises a HC CDR1 of SEQ ID NO: 16, a HC CDR2 of SEQ ID NO: 18, and a HC CDR3 of SEQ ID NO: 20; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 23, a LC CDR2 of SEQ ID NO: 25, and a LC CDR3 of SEQ ID NO: 27;

(iii) a third antibody specific for dengue virus serotype 3 (DENV3) comprising

20 (a) a V_H which comprises a HC CDR1 of SEQ ID NO: 30, a HC CDR2 of SEQ ID NO: 32, and a HC CDR3 of SEQ ID NO: 34; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 37, a LC CDR2 of SEQ ID NO: 39, and a LC CDR3 of SEQ ID NO: 41;

(iv) a fourth antibody specific for dengue virus serotype 4 (DENV4) comprising

25 (a) a V_H which comprises a HC CDR1 of SEQ ID NO: 44, a HC CDR2 of SEQ ID NO: 46, and a HC CDR3 of SEQ ID NO: 48; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 51, a LC CDR2 of SEQ ID NO: 53, and a LC CDR3 of SEQ ID NO: 55; and

(v) a fifth antibody cross-reactive to DENV1, DENV2, DENV3 and DENV4

30 comprising

(a) a V_H which comprises a HC CDR1 of SEQ ID NO: 58, a HC CDR2 of SEQ ID NO: 60, and a HC CDR3 of SEQ ID NO: 62; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 65, a LC CDR2 of

SEQ ID NO: 67, and a LC CDR3 of SEQ ID NO: 69.

2. The isolated antibody or antigen-binding fragment of claim 1, wherein

5 (i) the first antibody comprises a V_H that comprises SEQ ID NO: 71 and a V_L comprising SEQ ID NO: 72;

(ii) the second antibody comprises a V_H comprising SEQ ID NO: 73 and a V_L comprising SEQ ID NO: 74;

(iii) the third antibody comprises a V_H comprising SEQ ID NO: 75 and a V_L comprising SEQ ID NO: 76;

10 (iv) the fourth antibody comprises a V_H comprising SEQ ID NO: 77 and a V_L comprising SEQ ID NO: 78; and/or

(v) the fifth antibody comprises a V_H comprising SEQ ID NO: 79 and a V_L comprising SEQ ID NO: 80.

15 3. The isolated antibody or antigen-binding fragment of claim 1, wherein the antigen-binding fragment is selected from the group consisting of scFv, (scFv)₂, Fab, Fab', and F(ab')₂ of the isolated antibody specific for dengue virus.

20 4. A composition comprising the isolated antibody or antigen-binding fragment thereof of claim 1.

5. The composition of claim 4, which is a pharmaceutical or diagnostic composition for use in treatment or diagnosis of dengue virus disease.

25 6. The composition of claim 4, which comprises a pharmaceutically acceptable carrier.

7. A method for detecting dengue virus in a sample suspected of containing said dengue virus, comprising contacting the sample with an isolated antibody or
30 antigen-binding fragment thereof specific for dengue virus, and assaying binding of the antibody with said sample, wherein the isolated antibody is selected from the group consisting of:

(i) a first antibody specific for dengue virus serotype 1 (DENV1) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 2, a HC CDR2 of SEQ ID NO: 4, and a

HC CDR3 of SEQ ID NO: 6; and a V_L comprising a LC CDR1 of SEQ ID NO: 9, a LC CDR2 of SEQ ID NO: 11, and a LC CDR3 of SEQ ID NO: 13;

(ii) a second antibody specific for dengue virus serotype 2 (DENV2) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 16, a HC CDR2 of SEQ ID NO: 18, and a HC CDR3 of SEQ ID NO: 20; and a V_L comprising a LC CDR1 of SEQ ID NO: 23, a LC CDR2 of SEQ ID NO: 25, and a LC CDR3 of SEQ ID NO: 27;

(iii) a third antibody specific for dengue virus serotype 3 (DENV3) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 30, a HC CDR2 of SEQ ID NO: 32, and a HC CDR3 of SEQ ID NO: 34; and a V_L comprising a LC CDR1 of SEQ ID NO: 37, a LC CDR2 of SEQ ID NO: 39, and a LC CDR3 of SEQ ID NO: 41;

(iv) a fourth antibody specific for dengue virus serotype 4 (DENV4) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 44, a HC CDR2 of SEQ ID NO: 46, and a HC CDR3 of SEQ ID NO: 48; and a V_L comprising a LC CDR1 of SEQ ID NO: 51, a LC CDR2 of SEQ ID NO: 53, and a LC CDR3 of SEQ ID NO: 55; and

(v) any combination of (i) the first antibody, (ii) the second antibody, (iii) the third antibody and (iv) the fourth antibody.

8. The method of claim 7, wherein each of the first antibody, the second antibody, the third antibody and the fourth antibody, is paired with a partner antibody.

9. The method of claim 8, wherein the partner antibody is a serotype cross-reactive antibody to dengue virus which comprises

(a) a V_H which comprises a HC CDR1 of SEQ ID NO: 58, a HC CDR2 of SEQ ID NO: 60, and a HC CDR3 of SEQ ID NO: 62; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 65, a LC CDR2 of SEQ ID NO: 67, and a LC CDR3 of SEQ ID NO: 69.

10. The method of claim 7, wherein

(i) binding of the first antibody with the sample is an indicative of the presence of DENV1 in the sample;

(ii) binding of the second antibody to the dengue virus is an indicative of the presence of DENV2 in the sample;

(iii) binding of the third antibody to the dengue virus is an indicative of the presence of DENV3 in the sample; and/or

(iv) binding of the fourth antibody to the dengue virus is an indicative of the presence of DENV4 in the sample.

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11. A kit for detecting the presence of dengue virus in a sample, wherein the kit comprises one or more antibodies specific to dengue virus, selected from the group consisting of:

10 (i) a first antibody specific for dengue virus serotype 1 (DENV1) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 2, a HC CDR2 of SEQ ID NO: 4, and a HC CDR3 of SEQ ID NO: 6; and a V_L comprising a LC CDR1 of SEQ ID NO: 9, a LC CDR2 of SEQ ID NO: 11, and a LC CDR3 of SEQ ID NO: 13;

15 (ii) a second antibody specific for dengue virus serotype 2 (DENV2) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 16, a HC CDR2 of SEQ ID NO: 18, and a HC CDR3 of SEQ ID NO: 20; and a V_L comprising a LC CDR1 of SEQ ID NO: 23, a LC CDR2 of SEQ ID NO: 25, and a LC CDR3 of SEQ ID NO: 27;

20 (iii) a third antibody specific for dengue virus serotype 3 (DENV3) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 30, a HC CDR2 of SEQ ID NO: 32, and a HC CDR3 of SEQ ID NO: 34; and a V_L comprising a LC CDR1 of SEQ ID NO: 37, a LC CDR2 of SEQ ID NO: 39, and a LC CDR3 of SEQ ID NO: 41;

(iv) a fourth antibody specific for dengue virus serotype 4 (DENV4) that comprises a V_H comprising a HC CDR1 of SEQ ID NO: 44, a HC CDR2 of SEQ ID NO: 46, and a HC CDR3 of SEQ ID NO: 48; and a V_L comprising a LC CDR1 of SEQ ID NO: 51, a LC CDR2 of SEQ ID NO: 53, and a LC CDR3 of SEQ ID NO: 55;

25 (v) any combination of (i) the first antibody, (ii) the second antibody, (iii) the third antibody and (iv) the fourth antibody; and

(vi) an optional partner antibody.

30 12. The kit of claim 11, wherein the partner antibody is a serotype cross-reactive antibody to dengue virus which comprises

(a) a V_H which comprises a HC CDR1 of SEQ ID NO: 58, a HC CDR2 of SEQ ID NO: 60, and a HC CDR3 of SEQ ID NO: 62; and

(b) a V_L which comprises a LC CDR1 of SEQ ID NO: 65, a LC CDR2 of SEQ ID NO: 67, and a LC CDR3 of SEQ ID NO: 69.

13. The kit of claim 11, wherein at least one of the serotype-specific antibodies or the partner antibody comprises a detectable label.

5 14. The kit of claim 11, wherein the detectable label is selected from the group consisting of an enzymatic label, a fluorescent label, a metal label and a radio label.

15 15. The kit of claim 13, wherein the detectable label is selected from the group consisting of gold nanoparticles, colored latex beads, magnetic particles, carbon
10 nanoparticles, selenium nanoparticles.

16. The kit of claim 11, wherein the kit is an immunoassay kit.

15 17. The kit of claim 16, wherein the immunoassay is selected from the group consisting of ELISA (enzyme-linked immunosorbent assay), RIA (radioimmunoassay), FIA (fluorescence immunoassay), LIA (luminescence immunoassay), or ILMA immunoluminometric assay.

20 18. The kit of claim 16, wherein the immunoassay is in a lateral flow assay format.

19. The kit of claim 16, wherein the immunoassay is a sandwich assay.

25 20. A nucleic acid comprising a nucleotide sequence encoding a heavy chain variable region (V_H), a light chain variable region (V_L) or both, wherein the V_H and V_L are as set forth in claim 1.

21. An isolated host cell comprising the nucleic acid of claim 20.

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