What is claimed is:

1. An isolated monoclonal antibody, or an antigen-binding portion thereof, comprising a heavy chain region and a light chain region, wherein the heavy chain region comprises three complementarity determining regions (CDRs), CDR1, CDR2 and CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 29, 30 and 31, respectively, and wherein the light chain region comprises three CDRs, CDR1, CDR2 and CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 21, 22 and 23, respectively.

2. An isolated monoclonal antibody, or an antigen-binding portion thereof, that binds to *Clostridium difficile* (*C. difficile*) toxin A and comprises a heavy chain region, wherein the heavy chain region comprises three CDRs, CDR1, CDR2 and CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 29, 30 and 31, respectively.

3. An isolated monoclonal antibody, or an antigen-binding portion thereof, that binds to *C. difficile* toxin A and comprises a light chain region, wherein the light chain region comprises three CDRs, CDR1, CDR2 and CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 21, 22 and 23, respectively.

4. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody, or antigen-binding portion thereof, binds to *C. difficile* toxin A, and wherein the dissociation constant (K_D) of the antibody, or antigen-binding portion thereof, is less than about 1×10^{-11} M.

5. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion thereof is humanized or chimeric.

6. The antibody or antigen-binding portion thereof of claim 1, wherein the heavy chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 89, and wherein the light chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 91.

7. The antibody or antigen-binding portion thereof of claim 1, wherein the heavy chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 93, and wherein the light chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 95.

8. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion 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.

9. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion thereof comprises at least one constant domain selected from the group consisting of: a) an IgG constant domain; and (b) an IgA constant domain.

10. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion thereof binds to fragment 4 of *C. difficile* toxin A.

11. An isolated monoclonal antibody or an antigen-binding portion thereof, that binds to *C. difficile* toxin A and comprises a heavy chain variable region, wherein the heavy chain variable region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NOs: 12, 28, 44 or 60.

12. An isolated monoclonal antibody, or an antigen-binding portion thereof, that binds to *C. difficile* toxin A and comprises a light chain variable region, wherein the light chain variable region having an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NOs: 4, 20, 36 or 52.

13. An isolated monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody, or antigen-binding portion thereof, binds to the same epitope of *C. difficile* toxin A recognized by an antibody comprising a heavy chain variable region and a light chain variable region having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 28 and 20, respectively.

14. An antibody produced by hybridoma designated CAN20G2.

15. A hybridoma designated CAN20G2.

16. An isolated monoclonal antibody, or an antigen-binding portion thereof, wherein, in an *in vivo* toxin A challenge experiment, when the antibody, or an antigen-binding portion thereof, is administered to a mammal at a dosage ranging from about 8 mg/kg body weight to about 13 mg/kg body weight about 24 hours before the mammal is exposed to greater than about 100 ng of *C. difficile* toxin A, the chance of survival for the mammal is greater than about 80% within about 7 days.

17. The antibody or antigen-binding portion thereof of claim 17, wherein the antibody or antigen-binding portion thereof comprises a heavy chain region and a light chain region,
the heavy chain region comprising three CDRs, CDR1, CDR2, CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 29, 30 and 31, respectively,
the light chain region comprising three CDRs, CDR1, CDR2, CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 21, 22 and 23, respectively.

18. An isolated monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody, or antigen-binding portion thereof, at a concentration ranging from about 4 μM to about 17 μM, neutralizes greater than about 40% of about 150 ng/ml *C. difficile* toxin A in an *in vitro* neutralization assay.

19. The antibody or antigen-binding portion thereof of claim 18, wherein the antibody or antigen-binding portion thereof comprises a heavy chain region and a light chain region, the heavy chain region comprising three CDRs, CDR1, CDR2, CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 29, 30 and 31, respectively,
the light chain region comprising three CDRs, CDR1, CDR2, CDR3, having amino acid sequences about 80% to about 100% homologous to the amino acid sequences set forth in SEQ ID NOs: 21, 22 and 23, respectively.

20. A composition comprising the antibody or antigen-binding portion thereof of claim 1, and at least one pharmaceutically acceptable carrier.

21. Use of an effective amount of the antibody or antigen-binding portion thereof of claim 1 in the manufacture of a medicament for preventing or treating C. difficile-associated disease.

22. The use of claim 21, wherein the antibody or antigen-binding portion thereof is to be administered intravenously, subcutaneously, intramuscularly or transdermally.

23. The use of claim 21, wherein the subject is to be a second agent.

24. The use of claim 23, wherein the second agent is a different antibody or fragment thereof.

25. The use of claim 23, wherein the second agent is an antibiotic.

26. The use of claim 25, wherein the antibiotic is vancomycin, metronidazole, or fidaxomicin.

CLAIMS

1. An isolated antibody or antigen-binding portion thereof comprising a heavy chain variable region (VH) and a light chain variable region (VL),

(a) wherein the heavy chain variable region comprises three complementarity determining regions (CDRs), CDR1, CDR2, and CDR3, having the amino acid sequences set forth in SEQ ID NOs: 29, 30, and 31, respectively, or the amino acid sequences set forth in SEQ ID NOs: 29, 30, and 31 with one, two, three, or four amino acid substitutions, additions, or deletions;

(b) wherein the light chain variable region comprises three CDRs, CDR1, CDR2, and CDR3, having the amino acid sequences set forth in SEQ ID NOs: 21, 22, and 23, respectively, or the amino acid sequences set forth in SEQ ID NOs: 21, 22, and 23 with one, two, three, or four amino acid substitutions, additions, or deletions; and

(c) wherein the antibody or antigen-binding portion thereof specifically binds to *Clostridium difficile* (*C. difficile*) toxin A.

2. An isolated antibody or antigen-binding portion thereof comprising a heavy chain region and a light chain region, wherein the heavy chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 89 or SEQ ID NO: 93, wherein the light chain region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NO: 91 or SEQ ID NO: 95, and wherein the antibody or antigen-binding portion thereof specifically binds to *C. difficile* toxin A.

3. The antibody or antigen-binding portion thereof of claim 2, wherein the heavy chain region comprises the amino acid sequence set forth in SEQ ID NO: 89, and wherein the light chain region comprises the amino acid sequence set forth in SEQ ID NO: 91.

4. The antibody or antigen-binding portion thereof of claim 2, wherein the heavy chain region comprises the amino acid sequence set forth in SEQ ID NO: 93, and wherein the light chain region comprises the amino acid sequence set forth in SEQ ID NO: 95.

5. The antibody or antigen-binding portion thereof of claim 1, wherein the dissociate constant (K_D) of the antibody or antigen-binding portion thereof binding to *C. difficile* toxin A is less than about 8×10^{-10} M.

6. The antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion thereof comprises an IgG constant region or an IgA constant region.

7. An isolated antibody or antigen-binding fragment thereof that specifically binds to the same *C. difficile* toxin A epitope recognized by a reference antibody comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the heavy chain variable region of the reference antibody comprises the amino acid sequence SEQ ID NO:89; and the light chain variable region of the reference antibody comprises the amino acid sequence SEQ ID NO: 91.

8. An isolated antibody or antigen-binding fragment thereof that competes for binding to *C. difficile* toxin A with a reference antibody comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the heavy chain variable region of the reference antibody comprises the amino acid sequence SEQ ID NO:89; and the light chain variable region of the reference antibody comprises the amino acid sequence SEQ ID NO: 91.

9. The antibody or antigen-binding portion thereof of any one of claims 1 to 8, wherein the antibody or antigen-binding portion thereof is functionally linked to another molecule.

10. The antibody or antigen-binding portion thereof of claim 9, wherein the molecule is an antibody, detectable agent, a cytotoxic agent, a pharmaceutical agent, a protein or peptide that mediates association with another molecule, an amino acid linker, a signal sequence, or an immunogenic carrier.

11. The antibody or antigen-binding portion thereof of any one of claims 1 to 10, wherein the antibody or antigen-binding portion thereof is humanized or chimeric.

12. The antibody or antigen-binding portion thereof of any one of claims 1 to 11, wherein the antigen-binding portion thereof is an scFv, a Fab fragment, an F(ab′)2, or a disulfide-linked Fv.

13. The antibody or antigen-binding portion thereof of any one of claims 1 to 12, wherein the antibody or antigen-binding portion thereof is IgG, IgA, IgD, or IgE.

14. An isolated monoclonal antibody or an antigen-binding portion thereof, which comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NOs: 12, 28, 44 or 60, wherein the light chain variable region having an amino acid sequence about 80% to about 100% homologous to the amino acid sequence set forth in SEQ ID NOs: 4, 20, 36 or 52, and the antibody or antigen-binding portion thereof specifically binds to *C. difficile* toxin A.

15. A composition comprising the antibody or antigen-binding portion thereof of any one of claims 1 to 14, and at least one pharmaceutically acceptable carrier.

16. A kit comprising the antibody or antigen-binding portion thereof of any one of claims 1 to 14.

17. The kit of claim 16, further comprising: instructions for use; a therapeutic agent; a coupling agent; one or more of *C. difficile* whole toxin A, toxoid A, toxin A fragment 4, whole toxin B, toxoid B, toxin B fragment 4; or a pharmaceutically acceptable carrier.

18. Use of an effective amount of the antibody or antigen-binding portion thereof of any one of claims 1 to 14 in the manufacture of a medicament for preventing or treating *C. difficile*-associated disease (CDAD).

19. The use of claim 18, wherein the antibody or antigen-binding portion thereof is to be administered intravenously, subcutaneously, intramuscularly or transdermally.

20. The use of claim 18, wherein the medicament comprises a second agent.

21. The use of claim 20, wherein the second agent is a different antibody or antigen-binding portion thereof.

22. The use of claim 20, wherein the second agent is an antibiotic.

23. The use of claim 22, wherein the antibiotic is vancomycin, metronidazole, or fidaxomicin.

24. A method of detecting *Clostridium difficile* (*C. difficile*) toxin A, comprising the steps of contacting a sample suspected or known to contain *C. difficile* toxin A with an antibody or antigen-binding portion thereof of any one of claims 1 to 14 and detecting binding of the antibody or antigen-binding portion thereof to *C. difficile* toxin A.

25. A method of isolating *Clostridium difficile* (*C. difficile*) toxin A from a sample, which comprises contacting a sample comprising or suspected of comprising *C. difficile* toxin A with the antibody or antigen-binding portion thereof of any one of claims 1 to 14.