CLAIMS

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

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;

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; and

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

2. An isolated antibody heavy chain variable region that comprises three CDRs, CDRl, CDR2 and CDR3, having the amino acid sequences set forth in SEQ ID NOs: 29, 30 and 31, respectively,

wherein an antibody or antigen-binding portion thereof comprising the heavy chain variable region and a light chain variable region comprising the amino acid sequence SEQ ID NO: 20 can specifically bind to *C. difficile* toxin A.

3. An isolated antibody light chain variable region that comprises three CDRs, CDRl, CDR2 and CDR3, having the amino acid sequences set forth in SEQ ID NOs: 21, 22 and 23, respectively,

wherein an antibody or antigen-binding portion thereof comprising the light chain variable region and a heavy chain variable region comprising the amino acid sequence SEQ ID NO: 28 can specifically bind to *C. difficile* toxin A.

4. The antibody or antigen-binding portion thereof of claim 1 or 2, wherein the heavy chain variable region comprises the amino acid sequence SEQ ID NO: 28.

5. The antibody or antigen-binding portion thereof of claim 1 or 3, wherein the light chain variable region comprises the amino acid sequence SEQ ID NO: 20.

6. The antibody or antigen-binding portion thereof of any one of claims 1 to 3, wherein the heavy chain variable region comprises the amino acid sequence SEQ ID NO: 28 and the light chain variable region comprises the amino acid sequence SEQ ID NO: 20.

7. The antibody or antigen-binding portion thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence SEQ ID NO: 89 and wherein the light chain variable region comprises the amino acid sequence SEQ ID NO: 91.

8. The antibody or antigen-binding portion thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 93 and wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 95.

9. The antibody or antigen-binding portion thereof of any one of claims 1 to 8, 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.

10. The antibody or antigen-binding portion thereof of any one of claims 1 to 9, wherein the antibody or antigen-binding portion thereof is humanized or chimeric.

11. The antibody or antigen-binding portion thereof of any one of claims 1 to 10, wherein the antigen-binding portion thereof is a whole immunoglobulin molecule, an scFv, a Fab fragment, an F(ab′)2, or a disulfide-linked Fv.

12. The antibody or antigen-binding portion thereof of any one of claims 1 to 11, wherein the antibody or antigen-binding portion thereof comprises at least one constant domain selected from the group consisting of an IgG constant domain and an IgA constant domain.

13. The antibody or antigen-binding portion thereof of any one of claim claims 1 to 12, wherein the antibody or antigen-binding portion thereof binds to fragment 4 of *C. difficile* toxin A.

14. An antibody produced by hybridoma designated CAN20G2.

15. A hybridoma designated CAN20G2.

16. An isolated antibody or antigen-binding portion thereof that specifically binds to the same *C. difficile* toxin A epitope recognized by a reference antibody comprising a heavy chain variable region and a light chain variable region, 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.

17. An isolated antibody or antigen-binding portion thereof that competes for binding to *C. difficile* toxin A with a reference antibody comprising a heavy chain variable region and a light chain variable region, 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.

18. The antibody or antigen-binding portion thereof of any one of claims 1 to 14, wherein the antibody or antigen-binding portion thereof is functionally linked to another molecule.

19. The antibody or antigen-binding portion thereof of claim 18, 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.

20. A composition comprising the antibody or antigen-binding portion thereof of any one of claims 1 to14, and at least one pharmaceutically acceptable carrier.

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

22. The kit of claim 21, 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.

23. 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.

24. The use of claim 23, wherein a dosage of the medicament comprises an effective amount of the antibody or antigen binding portion thereof.

25. The use of claim 23 or 24, wherein the antibody or antigen-binding portion thereof is to be administered intravenously, subcutaneously, intramuscularly or transdermally.

26. The use of any one of claims 23 to 25, wherein the medicament further comprises a second agent.

27. The use of claim 26, wherein the second agent is a different antibody or antigen-binding portion thereof.

28. The use of claim 27, wherein the second agent is an antibiotic.

29. The use of claim 28, wherein the antibiotic is vancomycin, metronidazole, or fidaxomicin.

30. 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 the 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.

31. 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.

32. An isolated polynucleotide comprising a nucleic acid that encodes the heavy chain variable region or the light chain variable region of an antibody or antigen-binding portion thereof of any one of claims 1 to 14.

33. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 70.

34. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 71.

35. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 88.

36. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 90.

37. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 92.

38. The polynucleotide of claim 32, comprising the nucleic acid sequence SEQ ID NO: 94.

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.