

CLAIMS

1. An isolated recombinant monoclonal antibody that specifically binds to ZIKA virus (ZIKV) and/or a ZIKV envelope glycoprotein (E), wherein the antibody neutralizes ZIKV *in vitro* with an IC_{50} less than or equal to about $10^{-9}M$ and wherein the antibody comprises three complementarity determining regions (CDRs) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 114, and three CDRs of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 122, and a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357 or SEQ ID NO: 358.
2. The isolated monoclonal antibody of claim 1, wherein the three CDRs of the HCVR (HCDR1, HCDR2, and HCDR3) comprise the amino acid sequences of SEQ ID NOs: 116, 118, and 120, respectively, and the three CDRs of the LCVR (LCDR1, LCDR2, and LCDR3) comprise the amino acid sequences of SEQ ID NOs: 124, 126, and 128, respectively.
3. The isolated monoclonal antibody of claim 1, comprising a HCVR comprising the amino acid sequence of SEQ ID NO: 114, and a LCVR comprising the amino acid sequence of SEQ ID NO: 122.
4. The isolated monoclonal antibody of any one of claims 1-3, whereby the antibody comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357.
5. The isolated monoclonal antibody of any one of claims 1-3, whereby the antibody comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 358.
6. Use of one or more anti-ZIKV antibodies of any one of claims 1-5 in the manufacture of a medicament for neutralizing infectious ZIKV by enhancing protection of the cell from virus infection, or from cell death.

7. Use of one or more anti-ZIKV antibodies of any one of claims 1-5 in the manufacture of a medicament for use in combinatorial therapy for, neutralizing infectious ZIKV by enhancing protection of the cell from virus infection, or from cell death, wherein said medicament is to be administered in combination with one or more additional therapeutic agents or anti-ZIKV treatment modalities, wherein the one or more additional therapeutic agents is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), one or more different anti-ZIKV antibodies, a vaccine for ZIKV, an immunomodulator and an interferon.

8. Use of one or more anti-ZIKV antibodies of any one of claims 1-5 in the manufacture of a medicament for use in combinatorial therapy for, neutralizing infectious ZIKV by enhancing protection of the cell from virus infection, or from cell death, wherein said medicament is to be administered in combination with one or more different anti-ZIKV antibodies or antigen-binding fragments thereof, wherein the one or more different anti-ZIKV antibodies or antigen-binding fragments thereof comprise a heavy chain variable region (HCVR) and a light chain variable region (LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, ~~114/122~~, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330 and 338/346.

9. A pharmaceutical composition comprising the isolated monoclonal antibody of any one of claims 1-3, and a pharmaceutically acceptable carrier or diluent.

10. The pharmaceutical composition of claim 9, further comprising one or more additional isolated monoclonal antibodies or antigen-binding fragments thereof that bind specifically to ZIKV, and comprise three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) contained within a HCVR comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 18, 34, 50, 66, 82, 98, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322 and 338; and three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) contained within a LCVR comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 26, 42, 58, 74, 90, 106, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330 and 346.

11. The pharmaceutical composition of claim 10, wherein the one or more additional isolated monoclonal antibodies or antigen-binding fragments that bind specifically to ZIKV comprise an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330 and 338/346.

12. The pharmaceutical composition of claim 11, wherein the one or more additional isolated antibodies comprise a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357 or SEQ ID NO: 358.

13. The pharmaceutical composition of claim 11, wherein the one or more additional isolated monoclonal antibodies or antigen-binding fragments that bind specifically to ZIKV comprise an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 66/74, and 258/266.

14. The pharmaceutical composition of claim 9, further comprising an additional isolated monoclonal antibody or antigen-binding fragment that binds specifically to ZIKV and comprises three heavy chain complementarity determining regions, HCDR1, HCDR2, and HCDR3, comprising the amino acid sequences of SEQ ID NOs: 260, 262, and 264, respectively, and three light chain complementarity determining regions, LCDR1, LCDR2, and LCDR3, comprising the amino acid sequences of SEQ ID NOs: 268, 270, and 272, respectively.

15. The pharmaceutical composition of claim 9, further comprising an additional isolated monoclonal antibody or antigen-binding fragment that binds specifically to ZIKV and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 258, and a LCVR comprising the amino acid sequence of SEQ ID NO: 266.

16. The pharmaceutical composition of claim 9, further comprising an additional isolated monoclonal antibody that binds specifically to ZIKV and comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 258, a LCVR comprising the amino acid sequence of SEQ ID NO: 266, and a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357 or 358.

17. The pharmaceutical composition of claim 16, whereby the additional antibody comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357.

18. The pharmaceutical composition of claim 16, whereby the additional antibody comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 358.

19. A pharmaceutical composition comprising:

a) an isolated first monoclonal antibody, or antigen-binding fragment thereof that binds specifically to ZIKV, comprising a HCDR1 having the amino acid sequence of SEQ ID NO: 116, a HCDR2 having the amino acid sequence of SEQ ID NO: 118, a HCDR3 having the amino acid sequence of SEQ ID NO: 120, a LCDR1 having the amino acid sequence of SEQ ID NO: 124, a LCDR2 having the amino acid sequence of SEQ ID NO: 126, a LCDR3 having the amino acid sequence of SEQ ID NO: 128;

b) an isolated second monoclonal antibody, or antigen-binding fragment thereof that binds specifically to ZIKV, comprising a HCDR1 having the amino acid sequence of SEQ ID NO: 260, a HCDR2 having the amino acid sequence of SEQ ID NO: 262, a HCDR3 having the amino acid sequence of SEQ ID NO: 264, a LCDR1 having the amino acid sequence of SEQ ID NO: 268, a LCDR2 having the amino acid sequence of SEQ ID NO: 270, a LCDR3 having the amino acid sequence of SEQ ID NO: 272; and

c) a pharmaceutically acceptable carrier or diluent.

20. The pharmaceutical composition of claim 19, wherein the first monoclonal antibody or antigen-binding fragment thereof comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 114 and a LCVR comprising the amino acid sequence of SEQ ID NO: 122, and the second monoclonal antibody or antigen-binding fragment thereof comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 258 and a LCVR comprising the amino acid sequence of SEQ ID NO: 266.

21. The pharmaceutical composition of claim 19 or 20, wherein the one or more anti-ZIKV antibodies neutralize one or more ZIKV strains selected from the group consisting of MR766 (Uganda 1947), PRVABC59 (Puerto Rico 2015) and FLR (Colombia 2015) strains.

22. An isolated nucleic acid molecule encoding a monoclonal antibody-that binds specifically to ZIKV according to any one of claims 1-3.

23. A vector comprising the nucleic acid molecule of claim 33.

24. An isolated cell expressing the vector of claim 34.

25. Use of an isolated monoclonal antibody of any one of claims 1-3 in the manufacture of a medicament for preventing, treating or ameliorating at least one symptom of ZIKV infection, or of decreasing the frequency or severity of at least one symptom of ZIKV infection in a subject in need thereof.

26. The use of claim 25, wherein the medicament is for use in combinatorial therapy for preventing, treating or ameliorating at least one symptom of ZIKV infection, or of decreasing the frequency or severity of at least one symptom of ZIKV infection, wherein said medicament is to be administered in combination with one or more additional isolated monoclonal antibodies that bind specifically to ZIKV and comprise an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330 and 338/346.

27. The use of claim 26, wherein the one or more additional isolated antibodies comprises an HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 258/266.

28. The use of claim 26 or 27, wherein the one or more additional isolated antibodies comprise a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 357 or SEQ ID NO: 358.

29. The use of claims 25-28, wherein the at least one symptom is selected from the group consisting of fever, headache, arthralgia, myalgia and a maculopapular rash.

30. The use of claim 25, wherein the medicament is for administration prophylactically or therapeutically to the subject in need thereof.

31. The use of claim 25, wherein the subject in need thereof is at risk for exposure to, or for acquiring a ZIKV infection and wherein the subject is selected from the group consisting of a pregnant woman who has been exposed to ZIKV, or who has been bitten by a mosquito suspected of harboring the ZIKV, a woman who lives in an area that has a ZIKV outbreak, or is visiting an area that has a ZIKV outbreak and who is considering conceiving a child, an immunocompromised individual, a person who is suspected of having been exposed to a person harboring the ZIKV, a person who comes into physical contact or close physical proximity with an infected individual, a hospital employee, a pharmaceutical researcher, maintenance personnel responsible for cleaning a hospital facility or institution where a ZIKV patient has been treated, individuals who have visited or are planning to visit an area or country known to have or suspected to have an outbreak of ZIKV, or a country known to have mosquitoes harboring the ZIKV.

32. The use of claim 25, wherein the medicament is for use in combinatorial therapy for preventing, treating or ameliorating at least one symptom of ZIKV infection, or of decreasing the frequency or severity of at least one symptom of ZIKV infection, wherein said medicament is to be administered in combination with a second therapeutic agent, wherein the second therapeutic agent is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), a different antibody to ZIKV, a vaccine for ZIKV, an immunomodulator and an interferon.

33. The use of claim 25, wherein the medicament is for administration subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.

34. Use of an isolated monoclonal antibody of any one of claims 1-3 in the manufacture of a medicament for decreasing the likelihood of transmitting ZIKV to the fetus of a pregnant female or prevention of transmission to the male reproductive organs.

35. The use of claim 34, wherein the medicament is for combinatorial therapy for decreasing the likelihood of transmitting ZIKV to the fetus of a pregnant female or prevention of transmission to the male reproductive organs, wherein said medicament is to be administered in combination with an isolated monoclonal antibody comprising a HCVR comprising the amino

acid sequence of SEQ ID NO: 258 and a LCVR comprising the amino acid sequence of SEQ ID NO: 266.

36. The use of claim 34, wherein the medicament is for administration prophylactically or therapeutically to a subject in need thereof.

37. The use of claim 34, wherein the medicament is for use in combinatorial therapy for decreasing the likelihood of transmitting ZIKV to the fetus of a pregnant female or prevention of transmission to the male reproductive organs, wherein said medicament is to be administered in combination with a second therapeutic agent, wherein the second therapeutic agent is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), a different antibody to ZIKV, a vaccine for ZIKV, an immunomodulator, and an interferon.

38. The use of claim 37, wherein the medicament is for administration subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.

39. The antibody of any one of claims 1-3 for use in neutralizing infectious ZIKV by enhancing protection of the cell from virus infection, or from cell death.

40. The antibody for use of claim 39, wherein the enhanced protection is observed when the antibody is used alone, or when it is used in combination with one or more additional therapeutic agents or anti-ZIKV treatment modalities, wherein the one or more additional therapeutic agents is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), one or more different anti-ZIKV antibodies, a vaccine for ZIKV, an immunomodulator and an interferon.

41. The antibody of any one of claims 1-3 for use in preventing, treating or ameliorating at least one symptom of ZIKV infection, or of decreasing the frequency or severity of at least one symptom of ZIKV infection in a subject in need thereof.

42. The antibody for use of claim 41, wherein the at least one symptom is selected from the group consisting of fever, headache, arthralgia, myalgia and a maculopapular rash.

43. The antibody for use of claim 41 that is for administration prophylactically or therapeutically to the subject in need thereof.

44. The antibody for use of claim 41, wherein the subject in need thereof is at risk for exposure to, or for acquiring a ZIKV infection and wherein the subject is selected from the group consisting of a pregnant woman who has been exposed to ZIKV, or who has been bitten by a mosquito suspected of harboring the ZIKV, a woman who lives in an area that has a ZIKV outbreak, or is visiting an area that has a ZIKV outbreak and who is considering conceiving a child, an immunocompromised individual, a person who is suspected of having been exposed to a person harboring the ZIKV, a person who comes into physical contact or close physical proximity with an infected individual, a hospital employee, a pharmaceutical researcher, maintenance personnel responsible for cleaning a hospital facility or institution where a ZIKV patient has been treated, individuals who have visited or are planning to visit an area or country known to have or suspected to have an outbreak of ZIKV, or a country known to have mosquitoes harboring the ZIKV.

45. The antibody for use of claim 41 and a second therapeutic agent for use as a medicament in combinatorial therapy, wherein the second therapeutic agent is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), a different antibody to ZIKV, a vaccine for ZIKV, an immunomodulator and an interferon.

46. The antibody for use of claim 41 that is for administration subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.

47. The antibody of any one of claims 1-3 for use in decreasing the likelihood of transmitting ZIKV to the fetus of a pregnant female or preventing transmission to the male reproductive organs.

48. The antibody for use of claim 47, wherein the use comprises a mixture further comprising an anti-ZIKV antibody comprising a HCVR comprising the amino acid sequence of SEQ ID NO: 258 and a LCVR comprising the amino acid sequence of SEQ ID NO: 266.

49. The antibody for use of claim 47 that is for administration prophylactically or therapeutically to a subject in need thereof.

50. The antibody for use of claim 47 and a second therapeutic agent for use as a medicament in combinatorial therapy, wherein the second therapeutic agent is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug (*e.g.* corticosteroids and non-steroidal anti-inflammatory drugs), a different antibody to ZIKV, a vaccine for ZIKV, an immunomodulator, and an interferon.

51. The antibody for use of claim 50 that is for administration subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.