

Claims

1. An isolated multispecific antibody, or an antigen binding fragment thereof, specifically binding to distinct Zika virus epitopes.
2. The antibody, or the antigen binding fragment thereof, according to claim 1, wherein the antibody, or the antigen binding fragment thereof, neutralizes Zika virus infection.
3. The antibody, or the antigen binding fragment thereof, according to claim 1 or 2, characterized in that the antibody, or antigen binding fragment thereof, does not contribute to antibody-dependent enhancement of Zika virus infection.
4. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 3, characterized in that the antibody, or antigen binding fragment thereof, comprises an Fc moiety; preferably the antibody, or antigen binding fragment thereof, comprises a mutation in the Fc moiety, said mutation reducing binding of the antibody to an Fc receptor; more preferably the antibody, or antigen binding fragment thereof, comprises a CH2 L4A mutation, a CH2 L5A mutation, or both.
5. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 4, characterized in that the antibody, or antigen binding fragment thereof, binds specifically to (at least two) distinct epitopes on Zika virus envelope protein (ZIKV E protein).
6. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 5, characterized in that the antibody, or antigen binding fragment thereof, binds to domain III of Zika virus envelope protein (EDIII).
7. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 6, characterized in that the antibody, or antigen binding fragment thereof, binds to an epitope of Zika virus envelope protein, which includes one or more amino acid residues of the lateral ridge (LR) of EDIII and/or one or more amino acid residues of the EDI-EDIII hinge region.
8. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 7, characterized in that the antibody, or the antigen binding fragment thereof, comprises CDRH1, CDRH2, and CDRH3 amino acid sequences (i) according to SEQ ID NOs: 1 – 3;

[illegible]

[illegible]

[illegible]

[illegible]

sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity.

9. The antibody, or the antigen binding fragment thereof, according to claim 8, characterized in that the antibody, or the antigen binding fragment thereof, comprises CDRH1, CDRH2, and CDRH3 amino acid sequences and CDRL1, CDRL2, and CDRL3 amino acid sequences (i) according to SEQ ID NOs: 1 - 5 and 7; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (ii) according to SEQ ID NOs: 1 - 4 and 6 - 7; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (iii) according to SEQ ID NOs: 19 - 23 and 25; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (iv) according to SEQ ID NOs: 19 - 22 and 24 - 25; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (v) according to SEQ ID NOs: 37 - 41 and 43; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (vi) according to SEQ ID NOs: 37 - 40 and 42 - 43; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (vii) according to SEQ ID NOs: 55 - 59 and 61; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (viii) according to SEQ ID NOs: 55 - 58 and 60 - 61; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (ix) according to SEQ ID NOs: 73 - 77 and 79; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least

95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; or (x) according to SEQ ID NOs: 73 – 76 and 78 – 79; or functional sequence variants thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity.

10. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 9, characterized in that the antibody, or the antigen binding fragment thereof, comprises a heavy chain variable region (VH) and, optionally, a light chain variable region (VL), wherein the heavy chain variable region (VH) comprises or consists of an amino acid sequence according to any of SEQ ID NOs: 8, 26, 44, 62, 80, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222, 226, 230, 234, 238, 242, 246, 250, 254, 258, and 262; or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity.
11. The antibody, or the antigen binding fragment thereof, according to any of claims 1 – 10, characterized in that the antibody, or the antigen binding fragment thereof, comprises (i) a heavy chain variable region (VH) amino acid sequence according to SEQ ID NO: 8 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity and/or a light chain variable region (VL) amino acid sequence according to SEQ ID NO: 9 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (ii) a heavy chain variable region (VH) amino acid sequence according to SEQ ID NO: 26 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity and/or a light chain variable region (VL) amino acid sequence according to SEQ ID NO: 27 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (iii) a heavy chain variable region (VH) amino acid sequence according

to SEQ ID NO: 44 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity and/or a light chain variable region (VL) amino acid sequence according to SEQ ID NO: 45 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; (iv) a heavy chain variable region (VH) amino acid sequence according to SEQ ID NO: 62 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity and/or a light chain variable region (VL) amino acid sequence according to SEQ ID NO: 63 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity; or (v) a heavy chain variable region (VH) amino acid sequence according to SEQ ID NO: 80 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity and/or a light chain variable region (VL) amino acid sequence according to SEQ ID NO: 81 or a functional sequence variant thereof having at least 70%, at least 75%, at least 80%, at least 85%, at least 88%, at least 90%, at least 92%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% sequence identity.

12. Use of the antibody, or the antigen binding fragment thereof, according to any one of the previous claims, in the manufacture of a medicament for the prevention and/or treatment of Zika virus infection.
13. A nucleic acid molecule comprising at least one polynucleotide encoding the antibody, or the antigen binding fragment thereof, according to any one of claims 1 – 12.
14. A vector comprising the nucleic acid molecule according to claim 13.
15. A plurality of nucleic acid molecules, each comprising at least one polynucleotide encoding a fragment of the antibody, or of the antigen binding fragment thereof, according to any

one of claims 1 – 12, wherein the plurality of nucleic acids encodes the antibody, or the antigen binding fragment thereof, according to any one of claims 1 – 12.

16. A plurality of vectors encoding the antibody, or the antigen binding fragment thereof, according to any one of claims 1 – 12.
17. A cell expressing the antibody, or the antigen binding fragment thereof, according to any of claims 1 to 12; or comprising the vector according to claim 14 or the plurality of vectors according to claim 16.
18. A pharmaceutical composition comprising the antibody, or the antigen binding fragment thereof, according to any one of claims 1 to 12, the nucleic acid molecule according to claim 13, the vector according to claim 14, the plurality of nucleic acid molecules according to claim 15, the plurality of vectors according to claim 16 and/or the cell according to claim 17.
19. Use of the antibody, or the antigen binding fragment thereof, according to any one of claims 1 to 12, the nucleic acid molecule according to claim 13, the vector according to claim 14, the plurality of nucleic acid molecules according to claim 15, the plurality of vectors according to claim 16, the cell according to claim 17, or the pharmaceutical composition according to claim 18, in the manufacture of a medicament for the prevention or treatment of Zika virus infection.
20. Use of the antibody, or the antigen binding fragment thereof, according to any of claims 1 to 12, the nucleic acid molecule according to claim 13, the vector according to claim 14, the plurality of nucleic acid molecules according to claim 15, the plurality of vectors according to claim 16, the cell according to claim 17, or the pharmaceutical composition according to claim 18 for monitoring the quality of an anti-Zika vaccine by checking that the antigen of said vaccine contains the specific epitope in the correct conformation.
21. Use of the antibody, or the antigen binding fragment thereof, according to any of claims 1 to 12, the nucleic acid molecule according to claim 13, the vector according to claim 14, the plurality of nucleic acid molecules according to claim 15, the plurality of vectors according

to claim 16, the cell according to claim 17, or the pharmaceutical composition according to claim 18 in *in vitro* diagnosis of Zika virus infection.

22. A kit of parts comprising at least one antibody, or the antigen binding fragment thereof, according to any of claims 1 to 12, at least one nucleic acid according to claim 13, at least one vector according to claim 14, the plurality of nucleic acid molecules according to claim 15, the plurality of vectors according to claim 16, at least one cell according to claim 17, or at least one pharmaceutical composition according to claim 18.