demonstrated that DENV-specific Abs can enhance Zika infection [Nature. 2016;536(7614):48-53. doi: 10.1038/nature18938, Nat Immunol. 2016;17(9):1102-8.].

SUMMARY

The disclosure provides anti-DENV antibodies, polypeptides containing variant Fc regions, and methods of using the same.

In one aspect, the present disclosure refers to the use of ~~that binds to Zika virus~~ in the manufacture of a medicament for treating or preventing Zika virus infection, wherein the antibody comprises~~:~~ a VH sequence of SEQ ID NO: 6 and a VL sequence of SEQ ID NO: 7, wherein the antibody further comprises the amino acid sequence of SEQ ID NO: 59

~~(a) (i) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42), (ii) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45), and (iii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41);~~

~~(b) (i) HVR-H1 comprising the amino acid sequence SX$_1$YX$_2$H, wherein X$_1$ is N or Y, X$_2$ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41), and (iii) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42);~~

~~(c) (i) HVR-H1 comprising the amino acid sequence SX$_1$YX$_2$H, wherein X$_1$ is N or Y, X$_2$ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41), (iii) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42), (iv) HVR-L1 comprising the amino acid sequence QASQX$_1$IRX$_2$YLN, wherein X$_1$ is D or E, X$_2$ is K or Q (SEQ ID NO: 43); (v) HVR-L2 comprising the amino acid sequence DASX$_1$LKX$_2$, wherein X$_1$ is N or E, X$_2$ is T or F (SEQ ID NO: 44); and (vi) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45); or~~

~~(d) (i) HVR-L1 comprising the amino acid sequence QASQX$_1$IRX$_2$YLN, wherein X$_1$ is D or E, X$_2$ is K or Q (SEQ ID NO: 43); (ii) HVR-L2 comprising the amino acid sequence DASX$_1$LKX$_2$, wherein X$_1$ is N or E, X$_2$ is T or F (SEQ ID NO: 44); and (iii) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45),~~

~~wherein the antibody is not an antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 13, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 16, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27~~.

In another ~~aspect~~example, the present disclosure refers to the use of an antibody in the manufacture of a medicament for treating or preventing Zika virus infection, the antibody comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 2-6; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 8-10; or (c) a VH sequence of any one of SEQ ID NOs: 2-6 and a VL sequence of any one of SEQ ID NOs: 8-10.

In yet another ~~aspect~~example, the present disclosure refers to the use of an antibody that binds to Zika virus in the manufacture of a medicament for treating or preventing Zika virus infection, wherein the antibody comprises:

(a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27.

In some examples, an isolated anti-DENV antibody of the present disclosure binds to DENV E protein. In some examples, an anti-DENV antibody of the disclosure comprises:

(a) (i) HVR-H3 comprising the amino acid sequence $GGX_1ALFYDSYTTPX_2DX_3GSWWFDP$, wherein X_1 is R or E, X_2 is R or F, X_3 is G, D or L (SEQ ID NO: 42), (ii) HVR-L3 comprising the amino acid sequence $QQFX_1X_2LPIT$, wherein X_1 is D, S or E, X_2 is D or A (SEQ ID NO: 45), and (iii) HVR-H2 comprising the amino acid sequence $VINPRGGSX_1X_2SAQKFQG$, wherein X_1 is T or R, X_2 is A or R (SEQ ID NO: 41);

(b) (i) HVR-H1 comprising the amino acid sequence SX_1YX_2H, wherein X_1 is N or Y, X_2 is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence $VINPRGGSX_1X_2SAQKFQG$, wherein X_1 is T or R, X_2 is A or R (SEQ ID NO: 41), and (iii) HVR-H3 comprising the amino acid sequence $GGX_1ALFYDSYTTPX_2DX_3GSWWFDP$, wherein X_1 is R or E, X_2 is R or F, X_3 is G, D or L (SEQ ID NO: 42);

(c) (i) HVR-H1 comprising the amino acid sequence SX_1YX_2H, wherein X_1 is N or Y, X_2 is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence

WHAT IS CLAIMED IS:

1. Use of an antibody ~~that binds to Zika virus~~ in the manufacture of a medicament for treating or preventing Zika virus infection, wherein the antibody comprises~~:~~ a VH sequence of SEQ ID NO: 6 and a VL sequence of SEQ ID NO: 7, wherein the antibody further comprises the amino acid sequence of SEQ ID NO: 59

~~(a) (i) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42), (ii) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45), and (iii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41);~~

~~(b) (i) HVR-H1 comprising the amino acid sequence SX$_1$YX$_2$H, wherein X$_1$ is N or Y, X$_2$ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41), and (iii) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42);~~

~~(c) (i) HVR-H1 comprising the amino acid sequence SX$_1$YX$_2$H, wherein X$_1$ is N or Y, X$_2$ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence VINPRGGSX$_1$X$_2$SAQKFQG, wherein X$_1$ is T or R, X$_2$ is A or R (SEQ ID NO: 41), (iii) HVR-H3 comprising the amino acid sequence GGX$_1$ALFYDSYTTPX$_2$DX$_3$GSWWFDP, wherein X$_1$ is R or E, X$_2$ is R or F, X$_3$ is G, D or L (SEQ ID NO: 42), (iv) HVR-L1 comprising the amino acid sequence QASQX$_1$IRX$_2$YLN, wherein X$_1$ is D or E, X$_2$ is K or Q (SEQ ID NO: 43); (v) HVR-L2 comprising the amino acid sequence DASX$_1$LKX$_2$, wherein X$_1$ is N or E, X$_2$ is T or F (SEQ ID NO: 44); and (vi) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45); or~~

~~(d) (i) HVR-L1 comprising the amino acid sequence QASQX$_1$IRX$_2$YLN, wherein X$_1$ is D or E, X$_2$ is K or Q (SEQ ID NO: 43); (ii) HVR-L2 comprising the amino acid sequence DASX$_1$LKX$_2$, wherein X$_1$ is N or E, X$_2$ is T or F (SEQ ID NO: 44); and (iii) HVR-L3 comprising the amino acid sequence QQFX$_1$X$_2$LPIT, wherein X$_1$ is D, S or E, X$_2$ is D or A (SEQ ID NO: 45),~~

~~wherein the antibody is not an antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 13, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 16, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27~~.

~~2. The use of claim 1 (b), wherein the antibody further comprises a heavy chain variable domain framework FR1 comprising the amino acid sequence of SEQ ID NO: 31, FR2 comprising the amino acid sequence of SEQ ID NO: 32, FR3 comprising the amino acid sequence of SEQ ID NO: 33 or 34, FR4 comprising the amino acid sequence of SEQ ID NO: 35.~~

~~3. The use of claim 1 (d), wherein the antibody further comprises a light chain variable domain framework FR1 comprising the amino acid sequence of SEQ ID NO: 36, FR2 comprising the amino acid sequence of SEQ ID NO: 37, FR3 comprising the amino acid sequence of SEQ ID NO: 38, FR4 comprising the amino acid sequence of SEQ ID NO: 39.~~

~~4. Use of an antibody in the manufacture of a medicament for treating or preventing Zika virus infection, the antibody comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 2-6; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 8-10; or (c) a VH sequence of any one of SEQ ID NOs: 2-6 and a VL sequence of any one of SEQ ID NOs: 8-10.~~

~~5. Use of an antibody that binds to Zika virus in the manufacture of a medicament for treating or preventing Zika virus infection, wherein the antibody comprises:~~

~~(a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27.~~

~~6. The use of any one of claims 1 to 5, wherein the antibody further comprises a polypeptide, wherein the polypeptide comprising a variant Fc region comprising at least one amino acid alteration in a parent Fc region, wherein the variant Fc region has a substantially decreased Fc γ R-binding activity and does not have a substantially decreased C1q-binding activity when compared to the parent Fc region.~~

~~7. The use of claim 6, wherein the variant Fc region comprises Ala at position 234, Ala at position 235 and further amino acid alterations of any one of the following (a)-(c):~~

~~(a) positions 267, 268, and 324;~~

~~(b) positions 236, 267, 268, 324, and 332; and~~

~~(c) positions 326 and 333;~~

~~according to EU numbering.~~

~~8. The use of claim 7, wherein the variant Fc region comprises amino acids selected from the group consisting of:~~

~~(a) Glu at position 267;~~

~~(b) Phe at position 268;~~

~~(c) Thr at position 324;~~

~~(d) Ala at position 236;~~

~~(e) Glu at position 332;~~

~~(f) Ala, Asp, Glu, Met, or Trp at position 326; and~~

~~(g) Ser at position 333;~~

~~according to EU numbering.~~

~~9. The use of any one of claims 6 to 8, wherein the variant Fc region further comprises amino acids selected from the group consisting of:~~

~~(a) Ala at position 434;~~

~~(b) Ala at position 434, Thr at position 436, Arg at position 438, and Glu at position 440;~~

~~(c) Leu at position 428, Ala at position 434, Thr at position 436, Arg at position 438, and Glu at position 440; and~~

~~(d) Leu at position 428, Ala at position 434, Arg at position 438, and Glu at position 440;~~

~~according to EU numbering.~~

~~10. The use of any one of claims 6 to 9, wherein the polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: 51-59.~~

~~11~~2. The use of ~~any one of~~ claim~~s~~ 1 ~~to 10~~, wherein the antibody comprises a VH ~~variant~~ sequence as shown in ~~selected from the group consisting of: 3CH1047 (~~SEQ ID NO: 6~~)~~, ~~and 3CH1049 (SEQ ID NO: 95)~~ with a human IgG1 CH sequence as shown in ~~selected from the group consisting of: SG182 (SEQ ID NO: 46), SG1095 (SEQ ID NO: 54) and SG1106 (~~SEQ ID NO: 59~~);~~ and a VL ~~variant~~ sequence as shown in ~~selected from the group consisting of 3CL (~~SEQ ID NO: 7 ~~) and 3CL633 (SEQ ID NO: 98),~~ with a human CL sequence as shown in ~~SK1 (~~SEQ ID NO: 60~~)~~.