VARIANT NUCLEIC ACID LIBRARIES FOR CORONAVIRUS

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/115,568 filed on November 18, 2020, U.S. Provisional Patent Application No. 63/104,465 filed on October 22, 2020, U.S. Provisional Patent Application No. 63/073,362 filed on September 1, 2020, U.S. Provisional Patent Application No. 63/069,665 filed on August 24, 2020, U.S. Provisional Patent Application No. 63/034,896 filed on June 4, 2020, U.S. Provisional Patent Application No. 63/016,254 filed on April 27, 2020, each of which is incorporated by reference in its entirety.

BACKGROUND

[0002] Coronaviruses like severe acute respiratory coronavirus 2 (SARS-CoV-2) can cause severe respiratory problems. Therapies are needed for treating and preventing viral infection caused by coronaviruses like SARS-CoV-2. Antibodies possess the capability to bind with high specificity and affinity to biological targets. However, the design of therapeutic antibodies is challenging due to balancing of immunological effects with efficacy. Thus, there is a need to develop compositions and methods for the optimization of antibody properties in order to develop effective therapies for treating coronavirus infections.

INCORPORATION BY REFERENCE

[0003] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

SUMMARY

[0003a] In one aspect, provided herein is an antibody or antibody fragment comprising a variable domain, heavy chain region (VH) and a variable domain, light chain region (VL), wherein VH comprises complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein VL comprises complementarity determining regions CDRL1, CDRL2, and CDRL3, and wherein (a) an amino acid sequence of CDRH1 is as set forth in any one of SEQ ID NOs: 241-255 and 547-575; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 256-270 and 576-604; (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 271-285 and 605-633; (d) an amino acid sequence of CDRL1 is as set forth in any one of SEQ ID NOs: 286-300 and 634-662; (e) an amino acid sequence of CDRL2 is as set forth in any one of SEQ ID NOs: 301-315 and 663-691; and (f) an amino acid sequence of CDRL3 is as set forth in any one of SEQ ID NOs: 316-330 and 692-720.

[0003b] In another aspect, provided herein is an antibody or antibody fragment comprising a variable domain, heavy chain region (VH) wherein VH comprises complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein (a) an amino acid sequence of CDRH1 is as set forth in any one of SEQ ID

NOs: 1-50 and 779-919; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 51-100 and 920-1060; and (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 101-150 and 1062-1202.

[0003c] In another aspect, provided herein is an antibody or antibody fragment comprising a variable domain, heavy chain region (VH) and a variable domain, light chain region (VL), wherein the VH comprises an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 721-749, 2104-2118, and 2134-2147, and wherein the VL comprises an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 750-778, 2119-2133, and 2148-2161.

[0003d] In another aspect, provided herein is an antibody or antibody fragment comprising a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 1203-1343 and 2162-2301.

[0003e] In another aspect, provided herein is a nucleic acid composition comprising: a) a first nucleic acid encoding a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 721-749, 2104-2118, and 2134-2147; b) a second nucleic acid encoding a variable domain, light chain region (VL) comprising at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 750-778, 2119-2133, and 2148-2161; and an excipient.

[0003f] In another aspect, provided herein is a nucleic acid composition comprising: a) a first nucleic acid encoding a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 1203-1343 and 2162-2301; and b) an excipient.

[0003g] In another aspect, provided herein is a use of the antibody or antibody fragment disclosed herein in the manufacture of a medicament for the treatment of a SARS-CoV-2 infection.

[0003h] In another aspect, provided herein is the antibody or antibody fragment disclosed herein for use in therapy.

[0004] Provided herein are nucleic acid libraries comprising: a plurality of sequences that when translated encode for antibodies or antibody fragments that bind to SARS-CoV-2 or ACE2 protein, wherein each of the sequences comprises a predetermined number of variants within a CDR relative to an input sequence that encodes an antibody, and wherein the library comprises at least 50,000 variant sequences. Further provided herein are nucleic acid libraries, wherein the antibodies or antibody fragments bind to a spike glycoprotein, a membrane protein, an envelope protein, a nucleocapsid protein, or combinations thereof of the SARS-CoV-2. Further provided herein are nucleic acid libraries, wherein the antibodies or antibody fragments bind to a spike glycoprotein. Further provided herein are nucleic acid libraries, wherein the antibodies or antibody fragment bind to a receptor binding domain of the spike glycoprotein. Further provided herein are nucleic acid libraries, wherein the library comprises at least 100,000 variant sequences. Further provided herein are nucleic acid libraries, wherein at least some of the sequences encode for an

antibody light chain. Further provided herein are nucleic acid libraries, wherein at least some of the sequences encode for an antibody heavy chain. Further provided herein are nucleic acid libraries, wherein

CLAIMS

WHAT IS CLAIMED IS:

1. An antibody or antibody fragment comprising a variable domain, heavy chain region (VH) and a variable domain, light chain region (VL), wherein VH comprises complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein VL comprises complementarity determining regions CDRL1, CDRL2, and CDRL3, and wherein (a) an amino acid sequence of CDRH1 is as set forth in any one of SEQ ID NOs: 241-255 and 547-575; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 256-270 and 576-604; (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 271-285 and 605-633; (d) an amino acid sequence of CDRL1 is as set forth in any one of SEQ ID NOs: 286-300 and 634-662; (e) an amino acid sequence of CDRL2 is as set forth in any one of SEQ ID NOs: 301-315 and 663-691; and (f) an amino acid sequence of CDRL3 is as set forth in any one of SEQ ID NOs: 316-330 and 692-720.

2. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment binds to ACE2.

3. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment binds to an extracellular domain of ACE2.

4. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment comprises a K_D of less than 50 nM.

5. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment comprises a K_D of less than 25 nM.

6. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment comprises a K_D of less than 10 nM.

7. An antibody or antibody fragment comprising a variable domain, heavy chain region (VH) wherein VH comprises complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein (a) an amino acid sequence of CDRH1 is as set forth in any one of SEQ ID NOs: 1-50 and 779-919; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 51-100 and 920-1060; and (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 101-150 and 1062-1202.

8. An antibody or antibody fragment comprising a variable domain, heavy chain region (VH) and a variable domain, light chain region (VL), wherein the VH comprises an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 721-749, 2104-2118, and 2134-2147, and wherein the VL comprises an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 750-778, 2119-2133, and 2148-2161.

9. An antibody or antibody fragment comprising a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 1203-1343 and 2162-2301.

10. A nucleic acid composition comprising: a) a first nucleic acid encoding a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth

in any one of SEQ ID NOs: 721-749, 2104-2118, and 2134-2147; b) a second nucleic acid encoding a variable domain, light chain region (VL) comprising at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 750-778, 2119-2133, and 2148-2161; and an excipient.

11. A nucleic acid composition comprising: a) a first nucleic acid encoding a variable domain, heavy chain region (VH) comprising an amino acid sequence at least about 90% identical to a sequence as set forth in any one of SEQ ID NOs: 1203-1343 and 2162-2301; and b) an excipient.

12. Use of the antibody or antibody fragment of any one of claims 1-9 in the manufacture of a medicament for the treatment of a SARS-CoV-2 infection.

13. The use of claim 12, wherein the antibody or antibody fragment is to be administered prior to exposure to SARS-CoV-2.

14. The use of claim 13, wherein the antibody or antibody fragment is to be administered at least about 1 week prior to exposure to SARS-CoV-2.

15. The use of claim 13, wherein the antibody or antibody fragment is to be administered at least about 1 month prior to exposure to SARS-CoV-2.

16. The use of claim 13, wherein the antibody or antibody fragment is to be administered at least about 5 months prior to exposure to SARS-CoV-2.

17. The use of claim 12, wherein the antibody or antibody fragment is to be administered after exposure to SARS-CoV-2.

18. The use of claim 17, wherein the antibody or antibody fragment is to be administered at most about 24 hours after exposure to SARS-CoV-2.

19. The use of claim 17, wherein the antibody or antibody fragment is to be administered at most about 1 week after exposure to SARS-CoV-2.

20. The use of claim 17, wherein the antibody or antibody fragment is to be administered at most about 1 month after exposure to SARS-CoV-2.

21. The antibody or antibody fragment of any of claims 1-9 for use in therapy.