

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: 151-165, 241-255, 331-357, and 547-575; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 166-180, 256-270, 358-384, and 576-604; (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 181-195, 271-285, 385-411, and 605-633; (d) an amino acid sequence of CDRL1 is as set forth in any one of SEQ ID NOs: 196-210, 286-300, 412-438, and 634-662; (e) an amino acid sequence of CDRL2 is as set forth in any one of SEQ ID NOs: 211-225, 301-315, 439-465, and 663-691; and (f) an amino acid sequence of CDRL3 is as set forth in any one of SEQ ID NOs: 226-240, 316-330, 466-492, and 692-720.
2. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 155; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 170; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 185; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 200; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 215; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 230.
3. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 152; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 167; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 182; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 197; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 212; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 227.
4. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 335; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 362; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 389; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 199; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 214; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 229.
5. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 336; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 363; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 390; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 201; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 216; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 231.
6. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 158; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 173; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 188; (d) an amino acid sequence of

CDRL1 is as set forth in SEQ ID NO: 203; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 218; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 233.

7. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 551; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 580; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 609; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 290; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 305; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 320.

8. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 549; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 578; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 607; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 292; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 307; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 322.

9. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 552; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 581; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 610; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 291; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 306; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 321.

10. The antibody or antibody fragment of claim 1, wherein (a) an amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 554; (b) an amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 583; (c) an amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 612; (d) an amino acid sequence of CDRL1 is as set forth in SEQ ID NO: 288; (e) an amino acid sequence of CDRL2 is as set forth in SEQ ID NO: 303; and (f) an amino acid sequence of CDRL3 is as set forth in SEQ ID NO: 318.

11. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment binds to a spike glycoprotein.

12. The antibody or antibody fragment of claim 1, wherein the antibody or antibody fragment binds to a receptor binding domain of the spike glycoprotein.

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

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

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

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

17. 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, 779-919, 1344-1523, and 2381-

2452; (b) an amino acid sequence of CDRH2 is as set forth in any one of SEQ ID NOs: 51-100, 920-1061, 1524-1703, and 2453-2524; and (c) an amino acid sequence of CDRH3 is as set forth in any one of SEQ ID NOs: 101-150, 1062-1202, 1704-1883, and 2525-2596.

18. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1414; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1594; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1774.

19. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1447; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1627; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1807.

20. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1474; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1654; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1834.

21. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1344; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1524; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1704.

22. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1363; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1543; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1723.

23. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 1487; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1667; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1847.

24. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 780; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 921; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1063.

25. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 782; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 923; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1065.

26. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 39; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 89; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 139.

27. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 832; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 973; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1115.

28. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 869; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1010; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1152.

29. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 889; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1030; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1172.
30. The antibody or antibody fragment of claim 17, wherein (a) the amino acid sequence of CDRH1 is as set forth in SEQ ID NO: 908; (b) the amino acid sequence of CDRH2 is as set forth in SEQ ID NO: 1049; and (c) the amino acid sequence of CDRH3 is as set forth in SEQ ID NO: 1191.
31. 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: 493-519 and 721-749, 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: 520-546 and 750-778.
32. 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: 1884-2063, 2302-2380, and 2597-2668.
33. The antibody or antibody fragment of claim 32, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 1954.
34. The antibody or antibody fragment of claim 32, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 1987.
35. The antibody or antibody fragment of claim 32, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 2014.
36. An antibody, wherein the antibody comprises a sequence comprising at least 90% sequence identity to any one of SEQ ID NOs: 1-2668; and wherein the antibody is a monoclonal antibody, a polyclonal antibody, a bi-specific antibody, a multispecific antibody, a grafted antibody, a human antibody, a humanized antibody, a synthetic antibody, a chimeric antibody, a camelized antibody, a single-chain Fvs (scFv), a single chain antibody, a Fab fragment, a F(ab')₂ fragment, a Fd fragment, a Fv fragment, a single-domain antibody, an isolated complementarity determining region (CDR), a diabody, a fragment comprised of only a single monomeric variable domain, disulfide-linked Fvs (sdFv), an intrabody, an anti-idiotypic (anti-Id) antibody, or ab antigen-binding fragments thereof.
37. 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: 493-519 and 721-749; 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: 520-546 and 750-778; and an excipient.
38. 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: 1884-2063, 2302-2380, and 2597-2668; and b) an excipient.

39. The nucleic acid composition of claim 38, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 1954.
40. The nucleic acid composition of claim 38, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 1987.
41. The nucleic acid composition of claim 38, wherein the VH comprises an amino acid sequence at least about 90% identical to SEQ ID NO: 2014.
42. A method of treating a SARS-CoV-2 infection, comprising administering the antibody or antibody fragment of any one of claims 1-36.
43. The method of claim 37, wherein the antibody is administered prior to exposure to SARS-CoV-2.
44. The method of claim 43, wherein the antibody is administered at least about 1 week prior to exposure to SARS-CoV-2.
45. The method of claim 43, wherein the antibody is administered at least about 1 month prior to exposure to SARS-CoV-2.
46. The method of claim 43, wherein the antibody is administered at least about 5 months prior to exposure to SARS-CoV-2.
47. The method of claim 37, wherein the antibody is administered after exposure to SARS-CoV-2.
48. The method of claim 47, wherein the antibody is administered at most about 24 hours after exposure to SARS-CoV-2.
49. The method of claim 47, wherein the antibody is administered at most about 1 week after exposure to SARS-CoV-2.
50. The method of claim 47, wherein the antibody is administered at most about 1 month after exposure to SARS-CoV-2.
51. A method of treating an individual with a SARS-CoV-2 infection with the antibody or antibody fragment of any one of claims 1-36 comprising:
- (a) obtaining or having obtained a sample from the individual;
 - (b) performing or having performed an expression level assay on the sample to determine expression levels of SARS-CoV-2 antibodies; and
 - (c) if the sample has an expression level of the SARS-CoV-2 antibodies then administering to the individual the antibody or antibody fragment of any one of claims 1-36, thereby treating the SARS-CoV-2 infection.
52. A method for optimizing an antibody comprising:
- (a) providing a plurality of polynucleotide sequences encoding for an antibody or antibody fragment, wherein the antibody or antibody fragment is derived from a subject having SARS-CoV-2;
 - (b) generating a nucleic acid library comprising the plurality of sequences that when translated encode for antibodies or antibody fragments that bind 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; wherein the library comprises at least 50,000 variant sequences; and

(c) synthesizing the at least 50,000 variant sequences.

53. The method of claim 52, wherein the antibody library comprises at least 100,000 sequences.
54. The method of claim 52, wherein the method further comprises enriching a subset of the variant sequences.
55. The method of claim 52, wherein the method further comprises expressing the antibody or antibody fragments corresponding to the variant sequences.
56. The method of claim 52, wherein the polynucleotide sequence is a murine, human, or chimeric antibody sequence.
57. The method of claim 52, wherein each sequence of the plurality of variant sequences comprises at least one variant in each CDR of a heavy chain or light chain, relative to the input sequence.
58. The method of claim 52, wherein each sequence of the plurality of variant sequences comprises at least two variants in each CDR of a heavy chain or light chain relative to the input sequence.
59. The method of claim 52, wherein at least one sequence when translated encodes for an antibody or antibody fragment having at least 5X higher binding affinity than a binding affinity of the input sequence.
60. The method of claim 52, wherein at least one sequence when translated encodes for an antibody or antibody fragment having at least 25X higher binding affinity than a binding affinity of the input sequence.
61. The method of claim 52, wherein at least one sequence when translated encodes for an antibody or antibody fragment having at least 50X higher binding affinity than a binding affinity of the input sequence.
62. The method of claim 52, wherein each sequence comprises at least one variant in each CDR of a heavy chain or light chain relative to a germline sequence of the input sequence.
63. The method of claim 52, wherein the nucleic acid library has a theoretical diversity of at least 10^{10} sequences.
64. The method of claim 52, wherein the nucleic acid library has a theoretical diversity of at least 10^{12} sequences.