

We Claim:

1. An isolated antigen-binding protein that specifically binds the spike (S) protein of SARS-CoV-2, wherein the antigen-binding protein comprises a heavy chain variable domain having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6 and a light chain variable domain having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7.
2. An isolated antigen-binding protein that specifically binds the S protein of SARS-CoV-2, comprising a heavy chain variable region comprising a heavy chain complementarity determining region (CDR) 1 having the amino acid sequence of SEQ ID NO:8, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO:9, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:10, and a light chain variable region comprising a light chain CDR1 having the amino acid sequence of SEQ ID NO:11, a light chain CDR2 having the amino acid sequence of SEQ ID NO:12, and a light chain CDR3 having the amino acid sequence of SEQ ID NO:13.
3. The isolated antigen-binding protein according to claim 2, wherein the heavy chain variable domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6 and the light chain variable domain has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7.
4. The isolated antigen-binding protein according to claim 2, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:6 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:7.
5. The isolated antigen-binding protein of any one of claims 1-4, wherein the antigen-binding protein binds the S protein of SARS-CoV-2 with a dissociation constant (K_d) of 10^{-7} M or less.
6. The isolated antigen-binding protein of claim 5, wherein the antigen-binding protein binds the S protein of SARS-CoV-2 with a K_d of 10^{-8} M or less.

7. The isolated antigen-binding protein of any of claims 1-6, wherein the antigen-binding protein is an antibody or antibody fragment.
8. The isolated antigen-binding protein of any of claims 1-6, wherein the antigen-binding protein is a fully human antibody, comprises a heavy chain variable region and a light chain variable region of a fully human antibody, or comprises an antibody fragment derived from a fully human antibody.
9. The isolated antigen-binding protein of any of claims 1-8, comprising an IgG antibody, which is optionally an IgG1, IgG2, IgG3, or IgG4 antibody.
10. The isolated antigen-binding protein of claim 9, comprising an IgG1 or IgG4 antibody.
11. The isolated antigen-binding protein of claim 10, wherein the IgG1 or IgG4 antibody comprises a mutant Fc region.
12. The isolated antigen-binding protein of claim 11, wherein the Fc region comprises at least one mutation that decreases antibody-dependent-enhancement (ADE) of infection.
13. The isolated antigen-binding protein of claim 11 or 12, wherein Fc region comprises one or more mutations selected from N297A, N297Q, N297D, L234A, L235A, L235E, P329A, and P329G.
14. The isolated antigen-binding protein of claim 13, wherein Fc region comprises the mutations L234A and L235A (LALA), optionally wherein the Fc region comprises the sequence of SEQ ID NO: 14 or 16.
15. The isolated antigen-binding protein of any one of claims 11-14, wherein the Fc region comprises at least one mutation that increases antibody half-life.
16. The isolated antigen-binding protein of any one of claims 11-15, wherein Fc region comprises one or more mutations selected from M252Y, T256D, T307Q, T307W, M252Y, S254T, T256E, M428L, and N434S.

17. The isolated antigen-binding protein of claim 16, wherein Fc region comprises the mutations M252Y, S254T, and T256E (YTE), optionally wherein the Fc region comprises the sequence of SEQ ID NO: 15 or 16.
18. The isolated antigen-binding protein of any of claims 1-17, wherein the antigen-binding protein is a Fab fragment, a Fab' fragment, or a F(ab')₂ fragment.
19. The isolated antigen-binding protein of any of claims 1-17, wherein the antigen-binding protein is a single chain antibody, optionally wherein the single chain antibody is an ScFv.
20. The isolated antigen-binding protein of any one of the preceding claims, wherein the antigen-binding protein is a neutralizing antibody or antigen-binding fragment thereof that blocks binding of the SARS-CoV-2 S protein to the ACE2 protein.
21. The isolated antigen-binding protein of claim 20, wherein the IC₅₀ for blocking of binding of S to the ACE2 protein is 10 nM or less.
22. The isolated antigen-binding protein of claim 21, wherein the IC₅₀ for blocking of binding of S to the ACE2 protein is 5 nM or less.
23. The isolated antigen-binding protein of any one of the preceding claims, wherein the antigen-binding protein is a neutralizing antibody or antigen-binding fragment thereof that blocks SARS-CoV-2 infection of target cells.
24. The isolated antigen-binding protein of claim 23, wherein the IC₅₀ for blocking infection of target cells by SARS-CoV-2 is 10 nM or less.
25. The isolated antigen-binding protein of claim 24, wherein the IC₅₀ for blocking infection of target cells by SARS-CoV-2 is 5 nM or less.
26. A pharmaceutical composition, comprising the antigen-binding protein of any one of the preceding claims and a pharmaceutically-acceptable excipient.

27. The pharmaceutical composition of claim 26, wherein the antigen-binding protein is an IgG antibody, a Fab, Fab' or F(ab')₂ fragment, or a single chain antibody.
28. The pharmaceutical composition of claim 27, wherein the antigen-binding protein is an IgG antibody.
29. The pharmaceutical composition of claim 28, wherein the antigen-binding protein is an IgG antibody having an Fc region comprising L234A and L235A mutations.
30. A nucleic acid molecule that comprises a nucleic acid sequence encoding a polypeptide comprising a heavy chain variable region having at least 95% identity to SEQ ID NO:6.
31. The nucleic acid molecule of claim 30, wherein the nucleic acid molecule comprises a vector, wherein the vector comprises a promoter operably linked to the nucleic acid sequence encoding a polypeptide comprising the heavy chain variable region.
32. A nucleic acid molecule that comprises a nucleic acid sequence encoding a polypeptide comprising a light chain variable region having at least 95% identity to SEQ ID NO:7.
33. The nucleic acid molecule of claim 32, wherein the nucleic acid molecule comprises a vector, wherein the vector comprises a promoter operably linked to the nucleic acid sequence encoding a polypeptide comprising the light chain variable region.
34. A vector comprising a nucleic acid sequence encoding a heavy chain variable region having at least 95% identity to SEQ ID NO:6 and a nucleic acid sequence encoding a light chain variable region having at least 95% identity to SEQ ID NO:7.
35. One or more nucleic acid molecules encoding the antigen-binding protein of any one of claims 1-25.
36. One or more vectors comprising the one or more nucleic acid molecules of claim 35.

37. A host cell harboring the nucleic acid molecule or vector of any one of claims 30-36.
38. A pharmaceutical composition comprising the one or more nucleic acid molecules of claim 35.
39. A method for preparing a neutralizing antibody or a heavy or light chain thereof, the method comprising: culturing a population of the host cell of claim 37 under conditions suitable for expressing the heavy chain variable region and/or the light chain variable region or the antigen-binding protein.
40. The method of claim 39, further comprising: recovering from the host cells the expressed heavy chain variable region and/or the light chain variable region or the antigen-binding protein.
41. A method for treating a subject having or suspected of having a coronavirus infection, the method comprising: administering to the subject an effective amount of the antigen-binding protein of any one of claims 1-25 or the pharmaceutical composition of any one of claims 26-29.
42. A method for treating a subject having or suspected of having a coronavirus infection, comprising: administering a pharmaceutical composition of any one of claims 26-29 to the subject, wherein said administration is by pulmonary delivery by inhalation.
43. The method of claim 42, wherein said pulmonary delivery is by a nebulizer.
44. A method for treating a subject having or suspected of having a coronavirus infection, comprising: administering a pharmaceutical composition of any one of claims 26-29 to the subject, wherein said administration is by intranasal delivery.

45. The method of any of claims 41-44, further comprising administering to the subject an anti-viral agent.
46. The method of any one of claims 39-45, wherein the subject has a coronavirus infection.
47. The method of any one of claims 39-45, wherein the coronavirus infection is a SARS-CoV-2 infection.
48. A method for detecting the presence of a coronavirus in a sample, comprising:
 - a) contacting the sample with the antigen-binding protein of any one of claims 1-25 under conditions suitable to form an antibody-antigen complex, wherein the sample contains a target antigen; and
 - b) detecting the presence of the antibody-antigen complex.
49. The method of claim 48, wherein the sample comprises phlegm, saliva, blood, cheek scraping, tissue biopsy, hair or semen.
50. The method of claim 48 or 49, wherein the antibody-antigen complex is detected using a radioactive, colorimetric, antigenic, enzymatic, a detectable bead (such as a magnetic or electrodense (e.g., gold) bead), biotin, streptavidin or protein A-based mode of detection.
51. A method for diagnosing a subject suspected of having a coronavirus infection using the method of any one of claims 48-50.
52. The antigen-binding protein of any one of claims 1-25 for use in the method of any one of claims 42-51.
53. Use of the antigen-binding protein of any one of claims 1-25 for the manufacture of a medicament for treating, detecting, or diagnosing according to the method of any one of claims 42-51.