

CLAIMS

1. A method for determining if a biological sample contains antibodies that inhibit binding of a SARS-CoV-2 S glycoprotein to human angiotensin-converting enzyme 2 (hACE2), comprising:

(a) measuring binding of a SARS-CoV-2 S glycoprotein to hACE2 after exposure to a biological sample by:

- (i) providing a surface coated with the SARS-CoV-2 S glycoprotein;
- (ii) exposing the surface to the biological sample;
- (iii) exposing the surface to hACE2; and
- (iv) detecting hACE2 that is bound to the surface;

(b) measuring binding of a SARS-CoV-2 S glycoprotein to hACE2 in the absence of the biological sample of (a) by:

- (i) providing a surface coated with the SARS-CoV-2 S glycoprotein;
- (ii) exposing the surface to hACE2; and
- (iii) detecting hACE2 that is bound to the surface; and

(c) comparing binding of the SARS-CoV-2 S glycoprotein to hACE2 in (a) and (b); wherein a biological sample contains antibodies that inhibit binding of the SARS-CoV-2 S glycoprotein to hACE2 if the amount of bound hACE2 in (a) is less than the amount of bound hACE2 in (b).

2. The method of claim 1, wherein the SARS-CoV-2 S glycoprotein has at least 80 %, at least 81 %, at least 82 %, at least 83 %, at least 84 %, at least 85 %, at least 86 %, at least 87 %, at least 88 %, at least 89 %, at least 90 %, at least 91 %, at least 92 %, at least 93 %, at least 94 %, at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, or 100 % identity to a polypeptide of SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3.

3. The method of any one of claims 1-2, wherein the SARS-CoV-2 S glycoprotein has an inactive furin cleavage site.

4. The method of claim 3, wherein the SARS-CoV-2 S glycoprotein has an inactive furin cleavage site having an amino acid sequence of QQAQ (SEQ ID NO: 68).
5. The method of any one of claims 1-4, wherein amino acids 973 and 974 of the SARS-CoV-2 S glycoprotein are proline, as compared to a wild-type SARS-CoV-2 S glycoprotein having the amino acid sequence of SEQ ID NO: 2.
6. The method of any one of claims 1-3, wherein the SARS-CoV-2 S glycoprotein has at least 80 %, at least 81 %, at least 82 %, at least 83 %, at least 84 %, at least 85 %, at least 86 %, at least 87 %, at least 88 %, at least 89 %, at least 90 %, at least 91 %, at least 92 %, at least 93 %, at least 94 %, at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, or 100 % identity to a polypeptide of any one of SEQ ID NOS: 3, 5-13, 15, 17-19, 21, and 23-66.
7. The method of any one of claims 1-2 and 5, wherein the SARS-CoV-2 S glycoprotein has at least 80 %, at least 81 %, at least 82 %, at least 83 %, at least 84 %, at least 85 %, at least 86 %, at least 87 %, at least 88 %, at least 89 %, at least 90 %, at least 91 %, at least 92 %, at least 93 %, at least 94 %, at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, or 100 % identity to a polypeptide of any one of SEQ ID NOS: 3-13, 20, and 22-66.
8. The method of any one of claims 1-5, wherein the SARS-CoV-2 S glycoprotein has at least 80 %, at least 81 %, at least 82 %, at least 83 %, at least 84 %, at least 85 %, at least 86 %, at least 87 %, at least 88 %, at least 89 %, at least 90 %, at least 91 %, at least 92 %, at least 93 %, at least 94 %, at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, or 100 % identity to a polypeptide of any one of SEQ ID NOS: 3, 5-13, and 23-66.
9. The method of any one of claims 1-8, wherein the SARS-CoV-2 S glycoprotein is from a SARS-CoV-2 virus or a variant of SARS-CoV-2.
10. The method of claim 9, wherein the variant of SARS-CoV-2 is a B.1.1.7 SARS-CoV-2 strain; a B.1.351 SARS-CoV-2 strain; a P.1 SARS-CoV-2 strain; a Cal.20C SARS-CoV-2 strain; a B.1.617.2 SARS-CoV-2 strain; a B.1.525 SARS-CoV-2 strain; a B.1.526 SARS-CoV-2 strain; a B.1.617.1 SARS-CoV-2 strain; a C.37 SARS-CoV-2 strain; a B.1.621 SARS-CoV-2 strain; or a B.1.1.529 SARS-CoV-2 strain.
11. The method of any one of claims 1-10, wherein the SARS-CoV-2 S glycoprotein has at least 80 %, at least 81 %, at least 82 %, at least 83 %, at least 84 %, at least 85 %, at least

86 %, at least 87 %, at least 88 %, at least 89 %, at least 90 %, at least 91 %, at least 92 %, at least 93 %, at least 94 %, at least 95 %, at least 96 %, at least 97 %, at least 98 %, at least 99 %, or 100 % identity to a SARS-CoV-2 S glycoprotein from a SARS-CoV-2 S omicron variant selected from the group consisting of: BA.1, BA.2.12.1, BA.2, BA.3, BA.4, BA.5, XBB.1.5, XBB.2.3, and XBB.1.16.

12. The method of any one of claims 1-11, wherein the hACE2 is attached to a tag.

13. The method of claim 12, wherein the tag is a His tag.

14. The method of any one of claims 1-13, wherein the biological sample is serum, plasma, blood, saliva, a nasopharyngeal swab, or mucus.

15. The method of any one of claims 1-14, wherein the biological sample had been obtained from a patient who has previously had COVID-19 or is from a patient to whom an immunogenic composition against a SARS-CoV-2 virus or a variant thereof had previously been administered.