

ANTIGEN-BINDING PROTEIN TO SARS-CoV-2

TECHNICAL FIELD

5 The present disclosure relates broadly to antigen-binding protein capable of binding to SARS-CoV-2, and related products and methods.

BACKGROUND

10 At the end of 2019, a novel coronavirus, designated as SARS-CoV-2, emerged in Wuhan, China. Like outbreaks caused by two other pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]), SARS-CoV-2, also known as COVID-19, causes acute respiratory
15 disease that is often severe. As of March 2021, nearly 120 million individuals worldwide have been confirmed to have COVID-19 infection with more than 2 million fatalities occurred. Given the SARS-CoV outbreak in 2002 and the MERS-CoV outbreak in 2012, SARS-CoV-2 is the third coronavirus to emerge in the human population in the past two decades — an emergence that has put global
20 public health institutions on high alert.

 Although vaccine is an important tool against the virus, detecting agents and therapeutic agents (e.g., virus neutralizing antibodies) may enhance detection, and also provide immediate protection and effective treatment which are urgently needed. Thus, there is a need to provide an agent, such as an
25 antigen-binding protein, that is capable of binding and/or neutralising SARS-CoV-2, and related products and methods.

SUMMARY

30 In one aspect, there is provided an isolated antigen-binding protein that is capable of binding to and/or neutralizing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

In one embodiment, the antigen-binding protein is capable of binding to a spike protein of SARS-CoV-2, optionally a receptor-binding domain (RBD) of SARS-CoV-2.

In one embodiment, the antigen-binding protein comprises one or more of the following properties:

- an EC_{50} value of no more than about 80 nM, optionally no more than about 12 nM, further optionally no more than about 6 nM, further optionally no more than about 3 nM, further optionally no more than about 1 nM, further optionally no more than about 0.5 nM or further optionally no more than about 0.1 nM for SARS-CoV-2;
- an IC_{50} value of no more than about 360 nM, optionally no more than about 180 nM, further optionally no more than about 100 nM, further optionally no more than about 50 nM, further optionally no more than about 10 nM, further optionally no more than about 5 nM, further optionally no more than about 2 nM, further optionally no more than about 1 nM or further optionally no more than about 0.5 nM for an inhibition of binding between SARS-CoV-2 and a cell;
- an IC_{50} value of no more than about 20,000 ng/ml, optionally no more than about 10,000 ng/ml, further optionally no more than about 5000 ng/ml, further optionally no more than about 2500 ng/ml, further optionally no more than about 1000 ng/ml, further optionally no more than about 500 ng/ml, further optionally no more than about 250 ng/ml, further optionally no more than about 100 ng/ml, further optionally no more than about 50 ng/ml, further optionally no more than about 25 ng/ml or further optionally no more than about 10 ng/ml for an inhibition of SARS-CoV-2 entry into a cell; and/or
- a K_D value of no more than about 130 nM, optionally no more than about 100 nM, further optionally no more than about 50 nM, further optionally no more than about 10 nM, further optionally no more than about 2 nM, further optionally no more than about 1 nM, further optionally no more than about 0.5 nM or further optionally no more than about 1 pM for SARS-CoV-2.

In one embodiment, the antigen-binding protein does not cross-react with severe acute respiratory syndrome coronavirus (SARS-CoV).

In one embodiment, the antigen-binding protein is capable of binding to SARS-CoV.

In one embodiment, the antigen-binding protein comprises a monoclonal antigen-binding protein.

5 In one embodiment, the antigen-binding protein comprises a fully human antigen-binding protein.

In one embodiment, the antigen-binding protein comprises an IgG-like structure.

In one embodiment, the antigen-binding protein comprises a Fab fragment.

10 In one embodiment, the antigen-binding protein is capable of binding to and/or neutralizing about two or more of the following SARS-CoV-2: a SARS-CoV-2 comprising a wild-type spike protein, a SARS-CoV-2 comprising a mutated spike protein with no more than about two mutations, a SARS-CoV-2 comprising a mutated spike protein with no more than about one mutation, a SARS-CoV-2 comprising a N439K mutation, a SARS-CoV-2 comprising a V483A mutation, a
15 SARS-CoV-2 comprising a G476S mutation, a SARS-CoV-2 comprising a S494P mutation, a SARS-CoV-2 comprising a V483I mutation, a SARS-CoV-2 comprising L455I and F456V mutations and a SARS-CoV-2 comprising a D614G mutation.

20 In one embodiment, the antigen-binding protein is capable of inhibiting virus-cell fusion and/or cell-cell fusion mediated by SARS-CoV-2.

In one embodiment, the antigen-binding protein comprises:

a light-chain complementarity determining region CDR1 selected from the group consisting of: SEQ ID NO: 28-50 and conservative sequence variants thereof;
25

a light-chain CDR2 selected from the group consisting of: SEQ ID NO: 51-64 and conservative sequence variants thereof;

a light-chain CDR3 selected from the group consisting of: SEQ ID NO: 65-90 and conservative sequence variants thereof;

30 a heavy-chain CDR 1 selected from the group consisting of: SEQ ID NO: 117-132 and conservative sequence variants thereof;

a heavy-chain CDR 2 selected from the group consisting of: SEQ ID NO: 133-148 and conservative sequence variants thereof; and

a heavy-chain CDR 3 selected from the group consisting of: SEQ ID NO: 149-173 and conservative sequence variants thereof.

5 In one embodiment, the antigen-binding protein comprises the following CDR sequences:

1A5

light-chain CDR1: SGSIASHY (SEQ ID NO: 28)
10 light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYGSGFVV (SEQ ID NO: 65)
heavy-chain CDR1: GFTFSSYA (SEQ ID NO: 117)
heavy-chain CDR2: ISGSGGST (SEQ ID NO: 133)
heavy-chain CDR3: AKDYFRWL (SEQ ID NO: 149);

15

1A8

light-chain CDR1: QSVLYSSNNKNY (SEQ ID NO: 29)
light-chain CDR2: WAS (SEQ ID NO: 52)
light-chain CDR3: QQYYGTPYT (SEQ ID NO: 66)
20 heavy-chain CDR1: GVSISRSRDH (SEQ ID NO: 118)
heavy-chain CDR2: ISYSGST (SEQ ID NO: 134)
heavy-chain CDR3: ARLASLYSTFDI (SEQ ID NO: 150);

1B2

25 light-chain CDR1: GGRIATNY (SEQ ID NO: 30)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSHDTSRQAV (SEQ ID NO: 67)
heavy-chain CDR1: GYTFTSYY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
30 heavy-chain CDR3: ATGEMAGDFDY (SEQ ID NO: 151);

|

1B11

light-chain CDR1: QSLLYSNGYNY (SEQ ID NO: 31)
light-chain CDR2: LGS (SEQ ID NO: 53)
light-chain CDR3: MQALQTPYT (SEQ ID NO: 68)
5 heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPIFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ARDNPGYSSSWSPNWFDP (SEQ ID NO: 152);

1C2

10 light-chain CDR1: QSLLHSNGFTY (SEQ ID NO: 32)
light-chain CDR2: LGS (SEQ ID NO: 53)
light-chain CDR3: MQGIQTPLT (SEQ ID NO: 69)
heavy-chain CDR1: GYTFTSYY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
15 heavy-chain CDR3: ASSSAGTFYFDY (SEQ ID NO: 153);

1C3

light-chain CDR1: SGSIASYY (SEQ ID NO: 33)
light-chain CDR2: EDD (SEQ ID NO: 54)
20 light-chain CDR3: QSFDSIQHV (SEQ ID NO: 70)
heavy-chain CDR1: GYPFSTYY (SEQ ID NO: 121)
heavy-chain CDR2: IDPSGGST (SEQ ID NO: 137)
heavy-chain CDR3: ARVAEQHLDYYFDY (SEQ ID NO: 154);

1D12

25 light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDGSAAV (SEQ ID NO: 71)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
30 heavy-chain CDR2: ISAYNGNT (SEQ ID NO: 138)
heavy-chain CDR3: ARLEWLRGAFDI (SEQ ID NO: 155);

1E5

- light-chain CDR1: SGRIASNY (SEQ ID NO: 35)
light-chain CDR2: EDT (SEQ ID NO: 55)
light-chain CDR3: QSFDSGNQRRV (SEQ ID NO: 72)
5 heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPIFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ARALVGKWLLLRGFDY (SEQ ID NO: 156);

1F4

- 10 light-chain CDR1: SSNIGRNF (SEQ ID NO: 36)
light-chain CDR2: RNN (SEQ ID NO: 56)
light-chain CDR3: QSYDNSLFFV (SEQ ID NO: 73)
heavy-chain CDR1: GDSVSSNSAA (SEQ ID NO: 122)
heavy-chain CDR2: TYYRSKWYN (SEQ ID NO: 139)
15 heavy-chain CDR3: AREKGIEGPAFDP (SEQ ID NO: 157);

1H7

- light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
20 light-chain CDR3: QSYDENIRV (SEQ ID NO: 74)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARGRWLRGAFDI (SEQ ID NO: 158);

2C9

- 25 light-chain CDR1: QTVGGSY (SEQ ID NO: 37)
light-chain CDR2: GAS (SEQ ID NO: 57)
light-chain CDR3: QQYASSRT (SEQ ID NO: 75)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
30 heavy-chain CDR2: IIPILGIA (SEQ ID NO: 141)
heavy-chain CDR3: ARHGGVGATTGYYYMDV (SEQ ID NO: 159);

2C10

- light-chain CDR1: SSTIGTNY (SEQ ID NO: 38)
light-chain CDR2: DNY (SEQ ID NO: 58)
light-chain CDR3: GTWDSRLSVGV (SEQ ID NO: 76)
5 heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INYRGNT (SEQ ID NO: 142)
heavy-chain CDR3: ARWDGGNSVDH (SEQ ID NO: 160);

2C12

- 10 light-chain CDR1: QSINIY (SEQ ID NO: 39)
light-chain CDR2: AAS (SEQ ID NO: 59)
light-chain CDR3: QQSYITPQT (SEQ ID NO: 77)
heavy-chain CDR1: GFTFSSYA (SEQ ID NO: 117)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
15 heavy-chain CDR3: ARGGRFHYYYYAMDV (SEQ ID NO: 161);

2D3

- light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
20 light-chain CDR3: QSYDSSNWV (SEQ ID NO: 78)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPIFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ASSGWLRGAFDI (SEQ ID NO: 162);

2G7

- 25 light-chain CDR1: GGTIGSNY (SEQ ID NO: 40)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDSSNRV (SEQ ID NO: 79)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
30 heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARGKWLRGAFDI (SEQ ID NO: 163);

2H4

light-chain CDR1: EFIGDD (SEQ ID NO: 41)
light-chain CDR2: EAR (SEQ ID NO: 60)
light-chain CDR3: LQYDSFPLT (SEQ ID NO: 80)
5 heavy-chain CDR1: GYTFSGYY (SEQ ID NO: 124)
heavy-chain CDR2: VNPNSGGT (SEQ ID NO: 144)
heavy-chain CDR3: ARGGRPGLPAAGYIDY (SEQ ID NO: 164);

3A11

10 light-chain CDR1: SSDVGTYNY (SEQ ID NO: 42)
light-chain CDR2: DVS (SEQ ID NO: 61)
light-chain CDR3: ASFSSSSTLLV (SEQ ID NO: 81)
heavy-chain CDR1: GYTFSTYD (SEQ ID NO: 125)
heavy-chain CDR2: ISTYNGDT (SEQ ID NO: 145)
15 heavy-chain CDR3: ARGDSSVGYEYFQH (SEQ ID NO: 165);

3C5

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
20 light-chain CDR3: QSYDSSNWV (SEQ ID NO: 78)
heavy-chain CDR1: GGSLSGYY (SEQ ID NO: 126)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166);

3D2

25 light-chain CDR1: SGSIARNY (SEQ ID NO: 43)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDRTNKRIV (SEQ ID NO: 82)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
30 heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166);

3D11

- light-chain CDR1: SGNIASNY (SEQ ID NO: 44)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDNNIQV (SEQ ID NO: 83)
5 heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166);

3E9

- 10 light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDSSNLQWV (SEQ ID NO: 84)
heavy-chain CDR1: GYTFTSYG (SEQ ID NO: 127)
heavy-chain CDR2: ISAYNGNT (SEQ ID NO: 138)
15 heavy-chain CDR3: ARGITMISDY (SEQ ID NO: 167);

3F1

- light-chain CDR1: GGSIADNF (SEQ ID NO: 45)
light-chain CDR2: DYS (SEQ ID NO: 62)
20 light-chain CDR3: QSYDISNPV (SEQ ID NO: 85)
heavy-chain CDR1: GFTFSSYG (SEQ ID NO: 128)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARDGGGGMDV (SEQ ID NO: 168);

3F11

- 25 light-chain CDR1: HSDGRNY (SEQ ID NO: 46)
light-chain CDR2: DTS (SEQ ID NO: 63)
light-chain CDR3: HQFRRSVST (SEQ ID NO: 86)
heavy-chain CDR1: GYTFSSSG (SEQ ID NO: 129)
30 heavy-chain CDR2: ISTYNGNT (SEQ ID NO: 146)
heavy-chain CDR3: ATSIAGVAGIDY (SEQ ID NO: 169);

3H7

light-chain CDR1: TDSIASNY (SEQ ID NO: 47)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDGVNRGVI (SEQ ID NO: 87)
5 heavy-chain CDR1: GFTFSNYG (SEQ ID NO: 130)
heavy-chain CDR2: IWHDGTNK (SEQ ID NO: 147)
heavy-chain CDR3: VRDQGAGVWNGYSY (SEQ ID NO: 170);

3H11

10 light-chain CDR1: SGNIASYY (SEQ ID NO: 48)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDRPNHVV (SEQ ID NO: 88)
heavy-chain CDR1: GYTFTSYY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
15 heavy-chain CDR3: ASSVVPAAIYDYYYGMDV (SEQ ID NO: 171);

5A6

light-chain CDR1: QSISSY (SEQ ID NO: 49)
light-chain CDR2: AAS (SEQ ID NO: 59)
20 light-chain CDR3: QQSYNLPRT (SEQ ID NO: 89)
heavy-chain CDR1: GFTFSSYE (SEQ ID NO: 131)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172);

6F8

25 light-chain CDR1: QTINNNY (SEQ ID NO: 50)
light-chain CDR2: DAS (SEQ ID NO: 64)
light-chain CDR3: QQYGSSPRT (SEQ ID NO: 90)
heavy-chain CDR1: GFTVSSNY (SEQ ID NO: 132)
30 heavy-chain CDR2: IYSGGST (SEQ ID NO: 148)
heavy-chain CDR3: ARDYGDYYFDY (SEQ ID NO: 173); or

conservative sequence variants thereof.

In one embodiment, the antigen-binding protein comprises a light-chain variable region comprising any one of SEQ ID NO: 1-27 or a sequence sharing
5 at least about 75% sequence similarity thereto; and/or a heavy-chain variable region comprising any one of SEQ ID NO: 91-116 or a sequence sharing at least about 75% sequence similarity thereto.

In one aspect, there is provided a combination of two antigen-binding proteins, wherein a first antigen-binding protein comprises the following CDR
10 sequences:

5A6

light-chain CDR1: QSISSY (SEQ ID NO: 49)
light-chain CDR2: AAS (SEQ ID NO: 59)
15 light-chain CDR3: QQSYNLPRT (SEQ ID NO: 89)
heavy-chain CDR1: GFTFSSYE (SEQ ID NO: 131)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172)

20 and a second antigen-binding protein comprises the following CDR sequences:

3D11

light-chain CDR1: SGNIASNY (SEQ ID NO: 44)
25 light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDNNIQV (SEQ ID NO: 83)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWWLRGAFDI (SEQ ID NO: 166).

30

In one aspect, there is provided a pharmaceutical composition comprising embodiments of the antigen-binding protein or embodiments of the combination, and a pharmaceutically acceptable carrier.

In one aspect, there is provided embodiments of the antigen-binding protein, 5
embodiments of the combination or embodiments of the pharmaceutical composition, for use in therapy, or as a diagnostic agent.

In one aspect, there is provided a nucleotide sequence encoding for embodiments of the antigen-binding protein or embodiments of the combination.

In one embodiment, the nucleotide sequence comprises one of more of 10
SEQ ID NO: 174-351 or a sequence sharing at least about 75% sequence identity thereto.

In one aspect, there is provided a bacteriophage, a host cell or a non-human organism comprising embodiments of the nucleotide sequence.

In one aspect, there is provided a method of treating SARS-CoV-2 in a 15
subject, the method comprising administering to the subject embodiments of the antigen-binding protein, embodiments of the combination or embodiments of the pharmaceutical composition.

In one embodiment, where the SARS-CoV-2 comprises a V483A mutation, the method comprises administering to the subject embodiments of the 20
combination.

In one aspect, there is provided a method of detecting the presence of SARS-CoV-2 in a sample, the method comprising: contacting the sample with the 25
embodiments of the antigen-binding protein; detecting a binding event involving the antigen-binding protein; wherein the detection of a binding event is indicative of the presence of SARS-CoV-2 in the sample.

DEFINITIONS

30 The term "treating", "treat" and "therapy", and synonyms thereof as used herein refer to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) a medical

condition, which includes but is not limited to diseases (such as SARS-CoV-2 infections), symptoms and disorders. A medical condition also includes a body's response to a disease or disorder, e.g., inflammation. Those in need of such treatment include those already with a medical condition as well as those prone to getting the medical condition or those in whom a medical condition is to be prevented.

As used herein, the term "therapeutically effective amount" will be an amount of an active agent that is capable of preventing, reversing or at least slowing down (lessening) a medical condition, such as SARS-CoV-2 infections. Dosages and administration of agents, compounds, compositions and formulations of the present disclosure may be determined by one of ordinary skill in the art of clinical pharmacology or pharmacokinetics. See, for example, Mordenti and Rescigno, (1992) *Pharmaceutical Research*. 9:17-25; Morenti et al., (1991) *Pharmaceutical Research*. 8:1351-1359; and Mordenti and Chappell, "The use of interspecies scaling in toxicokinetics" in *Toxicokinetics and New Drug Development*, Yacobi et al. (eds) (Pergamon Press: NY, 1989), pp. 42-96. An effective amount of the active agent of the present disclosure to be employed therapeutically will depend, for example, upon the therapeutic objectives, the route of administration, and the condition of the subject. Accordingly, it may be necessary for the therapist to titer the dosage and modify the route of administration as required to obtain the optimal therapeutic effect.

The term "subject" as used herein includes patients and non-patients. The term "patient" refers to individuals suffering or are likely to suffer from a medical condition such as a SARS-CoV-2 infection, while "non-patients" refer to individuals not suffering and are likely to not suffer from the medical condition. "Non-patients" include healthy individuals, non-diseased individuals and/or an individual free from the medical condition. The term "subject" includes humans and animals. Animals may include, but is not limited to, mammals (for example non-human primates, canine, murine and the like), and the like. "Murine" refers to any mammal from the family Muridae, such as mouse, rat, rabbit, and the like.

The term "micro" as used herein is to be interpreted broadly to include dimensions from about 1 micron to about 1000 microns.

The term "nano" as used herein is to be interpreted broadly to include dimensions less than about 1000 nm.

The term "particle" as used herein broadly refers to a discrete entity or a discrete body. The particle described herein can include an organic, an inorganic
5 or a biological particle. The particle used described herein may also be a macro-particle that is formed by an aggregate of a plurality of sub-particles or a fragment of a small object. The particle of the present disclosure may be spherical, substantially spherical, or non-spherical, such as irregularly shaped particles or ellipsoidally shaped particles. The term "size" when used to refer to the particle
10 broadly refers to the largest dimension of the particle. For example, when the particle is substantially spherical, the term "size" can refer to the diameter of the particle; or when the particle is substantially non-spherical, the term "size" can refer to the largest length of the particle.

The terms "coupled" or "connected" as used in this description are
15 intended to cover both directly connected or connected through one or more intermediate means, unless otherwise stated.

The term "associated with", used herein when referring to two elements refers to a broad relationship between the two elements. The relationship includes, but is not limited to a physical, a chemical or a biological relationship.
20 For example, when element A is associated with element B, elements A and B may be directly or indirectly attached to each other or element A may contain element B or vice versa.

The term "adjacent" used herein when referring to two elements refers to one element being in close proximity to another element and may be but is not
25 limited to the elements contacting each other or may further include the elements being separated by one or more further elements disposed therebetween.

The term "and/or", e.g., "X and/or Y" is understood to mean either "X and Y" or "X or Y" and should be taken to provide explicit support for both meanings or for either meaning.

30 Further, in the description herein, the word "substantially" whenever used is understood to include, but not restricted to, "entirely" or "completely" and the like. In addition, terms such as "comprising", "comprise", and the like whenever

used, are intended to be non-restricting descriptive language in that they broadly include elements/components recited after such terms, in addition to other components not explicitly recited. For example, when "comprising" is used, reference to a "one" feature is also intended to be a reference to "at least one" of that feature. Terms such as "consisting", "consist", and the like, may in the appropriate context, be considered as a subset of terms such as "comprising", "comprise", and the like. Therefore, in embodiments disclosed herein using the terms such as "comprising", "comprise", and the like, it will be appreciated that these embodiments provide teaching for corresponding embodiments using terms such as "consisting", "consist", and the like. Further, terms such as "about", "approximately" and the like whenever used, typically means a reasonable variation, for example a variation of +/- 5% of the disclosed value, or a variance of 4% of the disclosed value, or a variance of 3% of the disclosed value, a variance of 2% of the disclosed value or a variance of 1% of the disclosed value.

Furthermore, in the description herein, certain values may be disclosed in a range. The values showing the end points of a range are intended to illustrate a preferred range. Whenever a range has been described, it is intended that the range covers and teaches all possible sub-ranges as well as individual numerical values within that range. That is, the end points of a range should not be interpreted as inflexible limitations. For example, a description of a range of 1% to 5% is intended to have specifically disclosed sub-ranges 1% to 2%, 1% to 3%, 1% to 4%, 2% to 3% etc., as well as individually, values within that range such as 1%, 2%, 3%, 4% and 5%. It is to be appreciated that the individual numerical values within the range also include integers, fractions and decimals. Furthermore, whenever a range has been described, it is also intended that the range covers and teaches values of up to 2 additional decimal places or significant figures (where appropriate) from the shown numerical end points. For example, a description of a range of 1% to 5% is intended to have specifically disclosed the ranges 1.00% to 5.00% and also 1.0% to 5.0% and all their intermediate values (such as 1.01%, 1.02% ... 4.98%, 4.99%, 5.00% and 1.1%, 1.2% ... 4.8%, 4.9%, 5.0% etc.,) spanning the ranges. The intention of the above specific disclosure is applicable to any depth/breadth of a range.

Additionally, when describing some embodiments, the disclosure may have disclosed a method and/or process as a particular sequence of steps. However, unless otherwise required, it will be appreciated that the method or process should not be limited to the particular sequence of steps disclosed. Other
5 sequences of steps may be possible. The particular order of the steps disclosed herein should not be construed as undue limitations. Unless otherwise required, a method and/or process disclosed herein should not be limited to the steps being carried out in the order written. The sequence of steps may be varied and still remain within the scope of the disclosure.

10 Furthermore, it will be appreciated that while the present disclosure provides embodiments having one or more of the features/characteristics discussed herein, one or more of these features/characteristics may also be disclaimed in other alternative embodiments and the present disclosure provides support for such disclaimers and these associated alternative embodiments.

15

DESCRIPTION OF EMBODIMENTS

Exemplary, non-limiting embodiments of an agent, such as an antigen-binding molecule/protein, that is capable of recognising/interacting with/binding
20 to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and related products and methods are disclosed hereinafter.

Like two other pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]), SARS-CoV-2, also known as COVID-19,
25 can cause severe acute respiratory symptoms leading to mortality and morbidity. Common symptoms/features of a SARS-CoV-2 infection include fever, cough/dry cough, fatigue, myalgia, headache, dyspnea, sore throat, diarrhea, nausea/vomiting, loss of smell, loss of taste, abdominal pain, rhinorrhea and the like.

30 In various embodiments, there is provided an agent that is capable of recognising/interacting with/binding to SARS-CoV-2. The term "SARS-CoV-2" includes a virus having the sequence set forth in SEQ ID NO: 352, as well as

variants/mutants thereof that share at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 99.1%, at least about 99.2%, at least about 99.3%, at least about 99.4%, at least about 99.5%, at least about 99.6%, at least about 99.7%, at least about 99.8%, at least about 99.9%, at least about 99.91%, at least about 99.92%, at least about 99.93%, at least about 99.94%, at least about 99.95%, at least about 99.96%, at least about 99.97%, at least about 99.98% or at least about 99.99% sequence identity with the sequence over its entire length. Advantageously, embodiments of the agent are useful as therapeutics and detecting agents for SARS-CoV-2.

The agent may be in the form of a binding molecule, peptide (e.g., a polypeptide, an oligopeptide, a protein etc.), a peptidomimetic, an antigen binding protein, an antibody or fragments thereof (e.g., antigen binding fragments), derivatives thereof, combinations thereof, or the like. In various embodiments, a derivative of a molecule is structurally related to the molecule. For example, the derivative may share a common structural feature, fundamental structure and/or underlying chemical basis with the molecule. A derivative is not limited to one produced or obtained from the molecule although it may be one produced or obtained from the molecule. In some embodiments, the derivative is derivable, at least theoretically, from the molecule through modification of the molecule. In some embodiments, a derivative of a molecule shares or at least retains to a certain extent a function, chemical property, biological property, chemical activity and/or biological activity associated with the molecule. A skilled person will be able to identify, on a case-by-case basis and upon reading of the disclosure, the common structural feature, fundamental structure and/or underlying chemical basis of the molecule that have to be maintained in the derivative to retain the function, chemical property, biological property, chemical activity, and/or biological activity. A skilled person will also be able to identify assays that can prove the retention of the function, chemical property, biological property,

chemical activity, and/or biological activity. For example, a binding assay such as ELISA (enzyme-linked immunosorbent assay) may be carried out to determine a binding property of a derivative of a molecule.

In one embodiment, the agent comprises an antigen-binding protein. An antigen-binding protein may include any protein construct that is capable of binding to SARS-CoV-2 antigen. Examples include, but are not limited to, antibodies and fragments thereof such as antigen binding fragments. Non-limiting examples of antigen binding fragments include one or more fragments or portions of an antibody that retain the ability to specifically bind to an antigen (e.g., SARS-CoV-2), or synthetic modifications of an antibody fragments that retain the desired binding ability to the antigen. In various embodiments, antigen binding fragments include single domain antibodies, further engineered molecules (such as, but is not limited to diabodies, triabodies, tetrabodies, minibodies, and the like), Fab fragments, Fab' fragments, F(ab')₂ fragments, Fd fragments, Fv fragments, single-chain Fv (scFv) molecules, seFv molecules, scFv dimer, BsFv molecules, dsFv molecules, (dsFv)₂ molecules, dsFv-dsFv' molecules, Fv fragments, dAb fragments, bispecific antibodies, ds diabodies, nanobodies, domain antibodies, bivalent domain antibodies, and minimal recognition units consisting of the amino acid residues that mimic the hypervariable region of an antibody (e.g. an isolated complementarity determining region (CDR)). In some embodiments, antigen binding fragments may retain at least about one, at least about two, at least about three, at least about four, at least about five or at least about six of the CDR regions/sequences of the antibody.

Antigen-binding proteins may be of different formats/types, such as IgG, IgE, IgM, IgD, IgA, and IgY formats/types. They may also be of different subclasses/isotypes, such as IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2 subclasses/isotypes. In some embodiments, the antigen-binding protein comprises an IgG-like structure/format or full-length IgG-like structure/format. In some embodiments, the antigen-binding protein comprises or consists of a Fab fragment. A Fab fragment may be composed of a light chain and the variable and first constant domains of a heavy chain. A Fab fragment can be the product of papain cleavage of an antibody.

The antigen-binding protein may be recombinant, chimeric, humanised or fully human. In various embodiments, the antigen-binding protein comprises a fully human antigen-binding protein. A fully human antigen-binding protein includes an antibody in which both the CDR and framework regions comprise human sequences. Methods for producing fully human antigen-binding proteins/antibodies are known in the art. For example, fully human antigen-binding proteins/antibodies may be produced in transgenic non-human mammals, e.g., mice, that have been genetically engineered with the human immunoglobulin loci. For example, fully human antigen-binding proteins/antibodies may be produced by phage display technology.

In various embodiments, the antigen-binding protein may comprise monoclonal antigen-binding protein. The monoclonal antigen-binding protein may be part of a population of substantially homogenous antigen-binding proteins that recognise the same epitope and display substantially the same binding specificity for the same epitope. Monoclonal antigen-binding proteins are typically identical in their amino acid sequences. The preparation of monoclonal antigen-binding proteins is not limited to any particular methods, and may include the use of hybridoma, recombinant techniques, phage display techniques, combinations thereof or any other techniques that are capable of producing a substantially uniform population of antigen-binding proteins.

In some embodiments, the antigen-binding protein comprises an isolated antigen-binding protein. The term "isolated" as used herein in relation to an antigen-binding protein or other molecule refers to such molecule that has been sufficiently separated from the environment with which it would naturally be associated (e.g., tissue, body fluid, etc.). An "isolated" antigen binding protein or molecule is therefore distinguished from any such molecule that may be present *in situ* within a human or animal body or present in a sample derived from a human or animal body. The sequence of an "isolated" antigen binding protein may, however, correspond to sequences found in a human or animal body. The term "isolated" does not necessarily mean the exclusion of artificial or synthetic mixtures with other components, or the presence of impurities, for example, due to incomplete purification. In particular, isolated antigen-binding proteins or

molecules are also meant to include those that are chemically synthesised or engineered. In various embodiments, an isolated antigen-binding protein or molecule is obtained by removing or purifying it from its natural environment, by selection from an antibody source as a phage display library or a B-cell repertoire
5 or by chemical synthesis. In some embodiments, an isolated antigen-binding protein comprises a Fab fragment selected from a phage display library. In some embodiments, an isolated antigen-binding protein is obtained by cloning Fab sequences (e.g., sequences of a Fab fragment selected from a phage display library) to become an IgG format.

10 In some embodiments, the antigen-binding protein or parts thereof is naturally occurring. In some embodiments, the antigen-binding protein or parts thereof is derived or obtained from a non-immunized and/or a healthy source/donor. In some embodiments, the antigen-binding protein or parts thereof is derived from a non-infected source/donor e.g., a non-SARS-CoV-2-infected
15 source/donor. The source/donor may be a mammal, optionally a human. In some embodiments, the antigen-binding protein or parts thereof is derived or obtained from a naïve phage display library, optionally a naïve human phage display library. In some embodiments, the antigen-binding protein is derived or obtained from a Fab phage display library, optionally a human Fab phage display library,
20 further optionally a naïve human Fab phage display library. In various embodiments, a variable region of the antigen-binding protein is not further modified/engineered after being obtained from a naïve human Fab phage display library. In some embodiments, the agent is engineered, synthetic or non-naturally-occurring.

25 In various embodiments therefore, there is provided an antigen-binding protein, optionally an isolated antigen-binding protein, that is capable of binding to SARS-CoV-2 including portions thereof.

In various embodiments, the antigen-binding protein is capable of binding specifically to SARS-CoV-2. In various embodiments, the antigen-binding protein
30 is specific to SARS-CoV-2. In various examples, the antigen-binding protein is capable of binding to SARS-CoV-2 or portions thereof in a dose-dependent manner. In various embodiments, the antigen-binding protein does not

substantially bind to or cross-react with a virus of another family that is not the coronavirus family.

In various examples, the antigen-binding protein is capable of binding to pseudotyped SARS-CoV-2. In various examples, the antigen-binding protein is
5 capable of binding to live SARS-CoV-2. A “live” SARS-CoV-2 may comprise a wild-type envelope protein. In contrast, a “pseudotyped” virus may comprise a recombinant virus having a different envelope protein from the wild-type envelope protein. In some examples, the spike protein of a pseudotyped virus may contain only 1254 amino acid residues (instead of 1273 amino acid residues) without the
10 last 19 amino acid residues of the C-terminal region. In various examples, the antigen-binding protein is capable of binding to live or pseudotyped SARS-CoV-2 in solution and/or on surface.

In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to portions of SARS-CoV-2 that mediate virus
15 binding to or entry into a potential host cell. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to an envelope protein of SARS-CoV-2 or portions thereof. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to the spike protein (or spike glycoprotein) of SARS-CoV-2, e.g., a spike protein of SEQ ID
20 NO: 353, or portions thereof. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to the amino-terminal region or an amino-terminal unit of SARS-CoV-2 spike protein or portions thereof. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to the amino-terminal S1 subunit of SARS-
25 CoV-2 spike protein or portions thereof. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to the receptor binding domain (RBD) of SARS-CoV-2 spike protein, e.g., a RBD of SEQ ID NO: 354, or portions thereof. In various embodiments, the antigen-binding protein is capable of recognising/interacting with/binding to an epitope or an antigen on
30 SARS-CoV-2.

In various embodiments, the antigen-binding protein has an EC_{50} value (e.g., an average EC_{50} value) of no more than about 100 nM, no more than about

90 nM, no more than about 80 nM, no more than about 70 nM, no more than about 60 nM, no more than about 50 nM, no more than about 40 nM, no more than about 30 nM, no more than about 20 nM, no more than about 19 nM, no more than about 18 nM, no more than about 17 nM, no more than about 16 nM, no more than about 15 nM, no more than about 14 nM, no more than about 13 nM, no more than about 12 nM, no more than about 11 nM, no more than about 10 nM, no more than about 9.5 nM, no more than about 9 nM, no more than about 8.5 nM, no more than about 8 nM, no more than about 7.5 nM, no more than about 7 nM, no more than about 6.5 nM, no more than about 6 nM, no more than about 5.5 nM, no more than about 5 nM, no more than about 4.5 nM, no more than about 4 nM, no more than about 3.5 nM, no more than about 3 nM, no more than about 2.5 nM, no more than about 2 nM, no more than about 1.5 nM, no more than about 1 nM, no more than about 0.95 nM, no more than about 0.9 nM, no more than about 0.85 nM, no more than about 0.8 nM, no more than about 0.75 nM, no more than about 0.7 nM, no more than about 0.65 nM, no more than about 0.6 nM, no more than about 0.55 nM, no more than about 0.5 nM, no more than about 0.45 nM, no more than about 0.4 nM, no more than about 0.35 nM, no more than about 0.3 nM, no more than about 0.25 nM, no more than about 0.2 nM, no more than about 0.15 nM, no more than about 0.1 nM, no more than about 0.095 nM, no more than about 0.09 nM, no more than about 0.085 nM, no more than about 0.08 nM, no more than about 0.075 nM, no more than about 0.07 nM, no more than about 0.065 nM, no more than about 0.06 nM, no more than about 0.055 nM or no more than about 0.05 nM for SARS-CoV-2 e.g., a RBD of SARS-CoV-2. In various embodiments, the antigen-binding protein has an EC₅₀ value (e.g., an average EC₅₀ value) of no more than about 80 nM, optionally no more than about 12 nM, further optionally no more than about 6 nM, further optionally no more than about 3 nM, further optionally no more than about 1 nM, further optionally no more than about 0.5 nM or further optionally no more than about 0.1 nM for SARS-CoV-2 e.g., a RBD of SARS-CoV-2. In various embodiments, the antigen-binding protein has an EC₅₀ value (e.g., an average EC₅₀ value) of from about 0.05 nM to about 80 nM, from about 0.05 nM to about 12 nM, from about 0.05 nM to about 10 nM, from about 0.05 nM to about 5 nM,

from about 0.05 nM to about 2 nM, from about 0.05 nM to about 1 nM, from about 0.05 nM to about 0.5 nM, from about 0.05 nM to about 0.2 nM or from about 0.05 nM to about 0.1 nM for SARS-CoV-2 e.g., a RBD of SARS-CoV-2.

5 In various embodiments, the antigen-binding protein is capable of blocking/interfering/inhibiting/hindering/disrupting one or more of the following function(s) of SARS-CoV-2 spike protein: (i) host cell attachment; (ii) receptor binding; and (iii) mediating host cell membrane and viral membrane fusion.

In various embodiments, the antigen-binding protein is capable of blocking/interfering/inhibiting/hindering/disrupting the attachment of SARS-CoV-
10 2 to a host cell.

In various embodiments, the antigen-binding protein is capable of blocking/interfering/inhibiting/hindering/disrupting the binding of SARS-CoV-2 to a cell entry receptor. In various embodiments, the cell entry receptor comprises angiotensin converting enzyme II (ACE2). In various embodiments, the cell entry
15 receptor comprises human ACE2.

In various embodiments, the antigen-binding protein has a potent blocking/interfering/inhibiting/hindering/disrupting action against the binding of SARS-CoV-2 to the cell entry receptor. In various embodiments, the associated EC₅₀ value of the antigen-binding protein is from about 0.1 nM to about 360 nM,
20 from about 0.3 nM to about 100 nM, from about 0.3 nM to about 50 nM, from about 0.3 nM to about 25 nM, from about 0.3 nM to about 2.5 nM, from about 0.3 nM to about 2.0 nM or from about 0.3 nM to about 1.5 nM. In some embodiments, the associated EC₅₀ value of the antigen-binding protein is no more than about 2.5 nM, no more than about 2.0 nM, or no more than about 1.5 nM.

25 In various embodiments, the antigen-binding protein is capable of neutralising or mediating (or initiating) the neutralisation of SARS-CoV-2. The neutralizing antigen-binding protein may substantially prevent, block, inhibit or hinder the binding or association of SARS-CoV-2 to a cell (e.g., the binding or association of a RBD of a SARS-CoV-2 to a cell entry receptor ACE2 of a cell),
30 thereby interrupting a biological response that would otherwise result from the interaction of SARS-CoV-2 with the cell. The neutralizing antigen-binding protein may substantially prevent, block, inhibit or hinder SARS-CoV-2 from infecting a

cell. In various examples, the antigen-binding protein is capable of substantially neutralising or mediating (or initiating) the neutralisation of SARS-CoV-2 in a dose-dependent manner. In various embodiments, the antigen-binding protein is capable of substantially neutralising or mediating the neutralisation of SARS-CoV-2 entry into cells, optionally human cells, further optionally ACE2 expressing/presenting cells. In various embodiments therefore, the antigen-binding protein comprises a SARS-CoV-2 neutralising antigen binding protein.

In various embodiments, the antigen-binding protein has a potent neutralising action against cell entry of SARS-CoV-2. In various embodiments, the associated EC_{50} value of the antigen-binding protein is from about 5 ng/ml to about 17000 ng/ml, from about 6 ng/ml to about 1000 ng/ml, from about 6 ng/ml to about 100 ng/ml, from about 6 ng/ml to about 60 ng/ml, from about 6 ng/ml to about 30 ng/ml or from about 6 ng/ml to about 12 ng/ml. In some embodiments, the associated EC_{50} value of the antigen-binding protein is no more than about 60 ng/ml, no more than about 30 ng/ml, or no more than about 12 ng/ml.

In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of no more than about 360 nM, no more than about 350 nM, no more than about 300 nM, no more than about 200 nM, no more than about 100 nM, no more than about 90 nM, no more than about 80 nM, no more than about 70 nM, no more than about 60 nM, no more than about 50 nM, no more than about 40 nM, no more than about 30 nM, no more than about 20 nM, no more than about 10 nM, no more than about 9.5 nM, no more than about 9 nM, no more than about 8.5 nM, no more than about 8 nM, no more than about 7.5 nM, no more than about 7 nM, no more than about 6.5 nM, no more than about 6 nM, no more than about 5.5 nM, no more than about 5 nM, no more than about 4.5 nM, no more than about 4 nM, no more than about 3.5 nM, no more than about 3 nM, no more than about 2.5 nM, no more than about 2 nM, no more than about 1.5 nM, no more than about 1 nM, no more than about 0.95 nM, no more than about 0.9 nM, no more than about 0.85 nM, no more than about 0.8 nM, no more than about 0.75 nM, no more than about 0.7 nM, no more than about 0.65 nM, no more than about 0.6 nM, no more than about 0.55 nM, no more than about 0.5 nM, no more than about 0.45 nM, no more than

about 0.4 nM, no more than about 0.35 nM, no more than about 0.3 nM, no more than about 0.25 nM, no more than about 0.2 nM, no more than about 0.15 nM, no more than about 0.1 nM or no more than about 0.05 nM for an inhibition of binding between SARS-CoV-2 and a cell, optionally for an inhibition of binding between a spike protein of SARS-CoV-2 and an ACE2 of a cell. In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of no more than about 360 nM, optionally no more than about 180 nM, further optionally no more than about 100 nM, further optionally no more than about 50 nM, further optionally no more than about 10 nM, further optionally no more than about 5 nM, further optionally no more than about 2 nM, further optionally no more than about 1 nM or further optionally no more than about 0.5 nM for an inhibition of binding between SARS-CoV-2 and a cell, optionally for an inhibition of binding between a spike protein of SARS-CoV-2 and an ACE2 of a cell. In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of from about 0.05 nM to about 360 nM, from about 0.05 nM to about 200 nM, from about 0.1 nM to about 100 nM, from about 0.1 nM to about 50 nM, from about 0.1 nM to about 10 nM, from about 0.1 nM to about 3 nM, from about 0.1 nM to about 1.2 nM or from about 0.1 nM to about 0.5 nM for an inhibition of binding between SARS-CoV-2 and a cell, optionally for an inhibition of binding between a spike protein of SARS-CoV-2 and an ACE2 of a cell.

In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of no more than about 20,000 ng/ml, no more than about 10,000 ng/ml, no more than about 5000 ng/ml, no more than about 4000 ng/ml, no more than about 3000 ng/ml, no more than about 2000 ng/ml, no more than about 1000 ng/ml, no more than about 900 ng/ml, no more than about 800 ng/ml, no more than about 700 ng/ml, no more than about 600 ng/ml, no more than about 500 ng/ml, no more than about 450 ng/ml, no more than about 400 ng/ml, no more than about 350 ng/ml, no more than about 300 ng/ml, no more than about 250 ng/ml, no more than about 200 ng/ml, no more than about 150 ng/ml, no more than about 100 ng/ml, no more than about 95 ng/ml, no more than about 90 ng/ml, no more than about 85 ng/ml, no more than about 80 ng/ml, no more

than about 75 ng/ml, no more than about 70 ng/ml, no more than about 65 ng/ml, no more than about 60 ng/ml, no more than about 55 ng/ml, no more than about 50 ng/ml, no more than about 45 ng/ml, no more than about 40 ng/ml, no more than about 35 ng/ml, no more than about 30 ng/ml, no more than about 25 ng/ml, no more than about 20 ng/ml, no more than about 15 ng/ml, no more than about 10 ng/ml or no more than about 5 ng/ml for an inhibition of SARS-CoV-2 entry into a cell, e.g., pseudotyped SARS-CoV-2 entry into an ACE2-expressing cell. In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of no more than about 20,000 ng/ml, optionally no more than about 10,000 ng/ml, further optionally no more than about 5000 ng/ml, further optionally no more than about 2500 ng/ml, further optionally no more than about 1000 ng/ml, further optionally no more than about 500 ng/ml, further optionally no more than about 250 ng/ml, further optionally no more than about 100 ng/ml, further optionally no more than about 50 ng/ml, further optionally no more than about 25 ng/ml or further optionally no more than about 10 ng/ml for an inhibition of SARS-CoV-2 entry into a cell, e.g., pseudotyped SARS-CoV-2 entry into an ACE2-expressing cell. In various embodiments, the antigen-binding protein has an IC_{50} value (e.g., an average IC_{50} value) of from about 5 ng/ml to about 20,000 ng/ml, from about 5 ng/ml to about 10,000 ng/ml, from about 5 ng/ml to about 1000 ng/ml, from about 5 ng/ml to about 500 ng/ml, from about 5 ng/ml to about 100 ng/ml, from about 5 ng/ml to about 50 ng/ml, from about 5 ng/ml to about 25 ng/ml or from about 5 ng/ml to about 10 ng/ml for an inhibition of SARS-CoV-2 entry into a cell, e.g., pseudotyped SARS-CoV-2 entry into an ACE2-expressing cell.

25 In various embodiments, the antigen-binding protein has a K_D value (e.g., an average K_D value) of no more than about 150 nM, no more than about 100 nM, no more than about 50 nM, no more than about 10 nM, no more than about 9 nM, no more than about 8 nM, no more than about 7 nM, no more than about 6 nM, no more than about 5 nM, no more than about 4 nM, no more than about 3 nM, no more than about 2 nM, no more than about 1 nM, no more than about 0.5 nM, no more than about 0.45 nM, no more than about 0.4 nM, no more than about 0.35 nM, no more than about 0.3 nM, no more than about 0.25 nM, no more

than about 0.2 nM, no more than about 0.15 nM, no more than about 0.1 nM, no more than about 50 pM, no more than about 10 pM, no more than about 5 pM or no more than about 1 pM for SARS-CoV-2, e.g., a RBD of SARS-CoV-2 e.g., as measured by Bio-Layer Interferometry. In various embodiments, the antigen-binding protein has a K_D value (e.g., an average K_D value) of no more than about 130 nM, optionally no more than about 100 nM, further optionally no more than about 50 nM, further optionally no more than about 10 nM, further optionally no more than about 2 nM, further optionally no more than about 1 nM, further optionally no more than about 0.5 nM or further optionally no more than about 1 pM for SARS-CoV-2, e.g., a RBD of SARS-CoV-2 e.g., as measured by Bio-Layer Interferometry. In various embodiments, the antigen-binding protein has a K_D value (e.g., an average K_D value) of less than about 1×10^{-12} M for SARS-CoV-2, e.g., a RBD of SARS-CoV-2 e.g., as measured by Bio-Layer Interferometry.

In various embodiments, the antigen-binding protein is capable of inhibiting virus-cell fusion and/or cell-cell fusion mediated by SARS-CoV-2.

In some embodiments, the antigen-binding protein does not bind to, interact with or cross-react with other human coronaviruses (other than SARS-CoV-2). In some embodiments, the antigen-binding protein does not cross-react with severe acute respiratory syndrome coronavirus (SARS-CoV). Advantageously, embodiments of the antigen-binding protein have high specificity for SARS-CoV-2.

In some embodiments, the antigen-binding protein is capable of binding to or interacting with other human coronaviruses (other than SARS-CoV-2). In some embodiments, the antigen-binding protein is capable of binding to or interacting with SARS-CoV in addition to SARS-CoV-2. Thus, embodiments of the antigen-binding protein are capable of binding to an epitope that is conserved between SARS-CoV and SARS-CoV-2. Embodiments of the antigen-binding protein may be useful for detecting, binding to or neutralising two or more human coronaviruses such as SARS-CoV and SARS-CoV-2. In some embodiments, the antigen-binding protein binds to SARS-CoV-2 more strongly than SARS-CoV. In some embodiments, the antigen-binding protein has a higher affinity for SARS-

CoV-2 than SARS-CoV. In some embodiments, the antigen-binding protein neutralises SARS-CoV-2 by a greater extent as compared to SARS-CoV.

In various embodiments the antigen-binding protein is capable of binding to and/or neutralizing SARS-CoV-2 comprising one or more mutations. In various
5 embodiments, the antigen-binding protein is capable of binding to and/or neutralizing SARS-CoV-2 comprising no more than about 50, no more than about 40, no more than about 30, no more than about 20, no more than about 10, no more than about nine, no more than about eight, no more than about seven, no more than about six, no more than about five, no more than about four, no more
10 than about three, no more than about two or no more than about one mutation(s).

In various embodiments, the antigen-binding protein is capable of binding to and/or neutralizing SARS-CoV-2 comprising a mutated spike protein, for example, a mutated spike protein comprising no more than about 10, no more than about nine, no more than about eight, no more than about seven, no more
15 than about six, no more than about five, no more than about four, no more than about three, no more than about two or no more than about one mutation(s). In various embodiments, the antigen-binding protein is capable of binding to and/or neutralizing SARS-CoV-2 comprising a mutated RBD, for example, a mutated RBD comprising no more than about 10, no more than about nine, no more than
20 about eight, no more than about seven, no more than about six, no more than about five, no more than about four, no more than about three, no more than about two or no more than about one mutation(s). In various embodiments the antigen-binding protein is capable of binding to and/or neutralizing at least about two, at least about three, at least about four, at least about five, at least about six,
25 at least about seven or more of the following SARS-CoV-2: a SARS-CoV-2 comprising a wild-type spike protein (e.g., a spike protein of SEQ ID NO: 353) or a wild-type RBD (e.g., a RBD of SEQ ID NO: 354), a SARS-CoV-2 comprising a mutated spike protein with no more than about two mutations, a SARS-CoV-2 comprising a mutated spike protein with no more than about one mutation, a
30 SARS-CoV-2 comprising a N439K mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 360), a SARS-CoV-2 comprising a V483A mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 355), a SARS-

CoV-2 comprising a G476S mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 358), a SARS-CoV-2 comprising a S494P mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 359), a SARS-CoV-2 comprising a V483I mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 356), a SARS-CoV-2 comprising L455I and F456V mutations in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 357) and a SARS-CoV-2 comprising a D614G mutation in the spike protein or RBD (e.g., a spike protein of SEQ ID NO: 361). N439K, V483A, G476S, S494P, V483I, L455I/F456V and D614G mutations are all mutations occurring in the spike protein of SARS-CoV-2, with the first six of them (i.e., N439K, V483A, G476S, S494P, V483I and L455I/F456V) occurring in the RBD and D614G occurring outside the RBD.

In various embodiments, the antigen-binding protein comprises an amino acid sequence corresponding to a sequence in Tables 1-4. In various embodiments, the antigen-binding protein comprises an amino acid sequence sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98% or at least about 99%, at least about 99.1%, at least about 99.2%, at least about 99.3%, at least about 99.4%, at least about 99.5%, at least about 99.6%, at least about 99.7%, at least about 99.8% or at least about 99.9% with a sequence in Tables 1-4. In some embodiments, the antigen-binding protein comprises an amino acid sequence that differs by about one, about two, about three, about four, about five, about six, about seven, about eight, about nine, about ten or more amino acids with a sequence in Tables 1-4.

In various embodiments, the antigen-binding protein comprises one or more amino acid region or complementarity determining region corresponding to a CDR identified in Tables 2 and 4. In various embodiments, the antigen-binding protein comprises one or more amino acid region or complementarity determining region sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at

least about 95%, at least about 96%, at least about 97%, at least about 98% or at least about 99% sequence similarity/identity with a CDR or a combination of about two, about three, about four, about five or about six CDRs identified in Tables 2 and 4. In some embodiments, the antigen-binding protein comprises an amino acid region or CDR that differs by about one, about two, about three, about four, about five, about six, about seven, about eight, about nine, about ten or more amino acids with a CDR or a combination of about two, about three, about four, about five or about six CDRs identified in Tables 2 and 4.

In various embodiments, the antigen-binding protein comprises an amino acid region, a light chain variable domain sequence and/or a heavy chain variable domain sequence corresponding to a light chain variable domain sequence and/or a heavy chain variable domain sequence identified in Tables 1 and 3. In various embodiments, the antigen-binding protein comprises an amino acid region or a light chain variable domain and/or a heavy chain variable domain sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 99.1%, at least about 99.2%, at least about 99.3%, at least about 99.4%, at least about 99.5%, at least about 99.6%, at least about 99.7%, at least about 99.8% or at least about 99.9% with a light chain variable domain and/or a heavy chain variable domain identified in Tables 1 and 3. In some embodiments, the antigen-binding protein comprises an amino acid region or a light chain variable domain and/or a heavy chain variable domain that differs by about one, about two, about three, about four, about five, about six, about seven, about eight, about nine, about ten or more amino acids with a light chain variable domain and/or a heavy chain variable domain identified in Tables 1 and 3.

In various embodiments, the antigen-binding protein comprises one of more of the following:

a light-chain CDR1 selected from the group consisting of: SEQ ID NO: 28-50 and conservative sequence variants thereof;

a light-chain CDR2 selected from the group consisting of: SEQ ID NO: 51-64 and conservative sequence variants thereof;

a light-chain CDR3 selected from the group consisting of: SEQ ID NO: 65-90 and conservative sequence variants thereof;

5 a heavy-chain CDR 1 selected from the group consisting of: SEQ ID NO: 117-132 and conservative sequence variants thereof;

a heavy-chain CDR 2 selected from the group consisting of: SEQ ID NO: 133-148 and conservative sequence variants thereof; and

a heavy-chain CDR 3 selected from the group consisting of: SEQ ID NO: 149-173 and conservative sequence variants thereof.

10 In various embodiments, the antigen-binding protein comprises the following CDR sequences:

1A5

15 light-chain CDR1: SGSIASHY (SEQ ID NO: 28)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYGSGFVV (SEQ ID NO: 65)
heavy-chain CDR1: GFTFSSYA (SEQ ID NO: 117)
heavy-chain CDR2: ISGSGGST (SEQ ID NO: 133)
20 heavy-chain CDR3: AKDYFRWL (SEQ ID NO: 149);

1A8

light-chain CDR1: QSVLYSSNNKNY (SEQ ID NO: 29)
light-chain CDR2: WAS (SEQ ID NO: 52)
25 light-chain CDR3: QQYYGTPYT (SEQ ID NO: 66)
heavy-chain CDR1: GVSISRSDH (SEQ ID NO: 118)
heavy-chain CDR2: ISYSGST (SEQ ID NO: 134)
heavy-chain CDR3: ARLASLYSTFDI (SEQ ID NO: 150);

1B11

30 light-chain CDR1: QSLLYSNGYNY (SEQ ID NO: 31)
light-chain CDR2: LGS (SEQ ID NO: 53)

light-chain CDR3: MQALQTPYT (SEQ ID NO: 68)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ARDNPGYSSSWSPNWFDP (SEQ ID NO: 152);

5

1B2

light-chain CDR1: GGRIATNY (SEQ ID NO: 30)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSHDTSRQAV (SEQ ID NO: 67)
heavy-chain CDR1: GYTFTSYY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
heavy-chain CDR3: ATGEMAGDFDY (SEQ ID NO: 151);

10

1C2

light-chain CDR1: QSLLHSNGFTY (SEQ ID NO: 32)
light-chain CDR2: LGS (SEQ ID NO: 53)
light-chain CDR3: MQGIQTPLT (SEQ ID NO: 69)
heavy-chain CDR1: GYTFTSYY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
heavy-chain CDR3: ASSSAGTFYFDY (SEQ ID NO: 153);

15

20

1C3

light-chain CDR1: SGSIASYY (SEQ ID NO: 33)
light-chain CDR2: EDD (SEQ ID NO: 54)
light-chain CDR3: QSFDSSIQHVV (SEQ ID NO: 70)
heavy-chain CDR1: GYPFSTYY (SEQ ID NO: 121)
heavy-chain CDR2: IDPSGGST (SEQ ID NO: 137)
heavy-chain CDR3: ARVAEQHLDYYFDY (SEQ ID NO: 154);

25

30

1D12

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)

light-chain CDR3: QSYDGSAWV (SEQ ID NO: 71)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: ISAYNGNT (SEQ ID NO: 138)
heavy-chain CDR3: ARLEWLRGAFDI (SEQ ID NO: 155);

5

1E5

light-chain CDR1: SGRIASNY (SEQ ID NO: 35)
light-chain CDR2: EDT (SEQ ID NO: 55)
light-chain CDR3: QSFDSGNQRVV (SEQ ID NO: 72)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPIFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ARALVGKWLLLRGFDY (SEQ ID NO: 156);

10

1F4

light-chain CDR1: SSNIGRNF (SEQ ID NO: 36)
light-chain CDR2: RNN (SEQ ID NO: 56)
light-chain CDR3: QSYDNSLFFV (SEQ ID NO: 73)
heavy-chain CDR1: GDSVSSNSAA (SEQ ID NO: 122)
heavy-chain CDR2: TYYRSKWYN (SEQ ID NO: 139)
heavy-chain CDR3: AREKGIEGPAFDP (SEQ ID NO: 157);

15

20

1H7

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDENIRV (SEQ ID NO: 74)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARGRWLRGAFDI (SEQ ID NO: 158);

25

30

2C10

light-chain CDR1: SSTIGTNY (SEQ ID NO: 38)
light-chain CDR2: DNY (SEQ ID NO: 58)

light-chain CDR3: GTWDSRLSVGV (SEQ ID NO: 76)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INYRGNT (SEQ ID NO: 142)
heavy-chain CDR3: ARWDGGNSVDH (SEQ ID NO: 160);

5

2C12

light-chain CDR1: QSINIY (SEQ ID NO: 39)
light-chain CDR2: AAS (SEQ ID NO: 59)
light-chain CDR3: QQSYITPQT (SEQ ID NO: 77)
heavy-chain CDR1: GFTFSSYA (SEQ ID NO: 117)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARGGRFHYYYYAMDV (SEQ ID NO: 161);

10

2C9

light-chain CDR1: QTVGGSY (SEQ ID NO: 37)
light-chain CDR2: GAS (SEQ ID NO: 57)
light-chain CDR3: QQYASSRT (SEQ ID NO: 75)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPILGIA (SEQ ID NO: 141)
heavy-chain CDR3: ARHGGVGATTGYYYMDV (SEQ ID NO: 159);

15

20

2D3

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDSSNWV (SEQ ID NO: 78)
heavy-chain CDR1: GGTFSSYA (SEQ ID NO: 120)
heavy-chain CDR2: IIPIFGTA (SEQ ID NO: 136)
heavy-chain CDR3: ASSGWLRGAFDI (SEQ ID NO: 162);

25

30

2G7

light-chain CDR1: GGTIGSNY (SEQ ID NO: 40)
light-chain CDR2: EDN (SEQ ID NO: 51)

light-chain CDR3: QSYDSSNRV (SEQ ID NO: 79)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARGKWLRGAFDI (SEQ ID NO: 163);

5

2H4

light-chain CDR1: EFIGDD (SEQ ID NO: 41)
light-chain CDR2: EAR (SEQ ID NO: 60)
light-chain CDR3: LQYDSFPLT (SEQ ID NO: 80)
heavy-chain CDR1: GYTFSGYY (SEQ ID NO: 124)
heavy-chain CDR2: VNPNSGGT (SEQ ID NO: 144)
heavy-chain CDR3: ARGGRPGLPAAGYIDY (SEQ ID NO: 164);

10

3A11

light-chain CDR1: SSDVGTYNY (SEQ ID NO: 42)
light-chain CDR2: DVS (SEQ ID NO: 61)
light-chain CDR3: ASFSSSSTLLV (SEQ ID NO: 81)
heavy-chain CDR1: GYTFSTYD (SEQ ID NO: 125)
heavy-chain CDR2: ISTYNGDT (SEQ ID NO: 145)
heavy-chain CDR3: ARGDSSVGYEYFQH (SEQ ID NO: 165);

15

20

3C5

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDSSNWV (SEQ ID NO: 78)
heavy-chain CDR1: GGSLSGYY (SEQ ID NO: 126)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLRGAFDI (SEQ ID NO: 166);

25

3D11

light-chain CDR1: SGNIASNY (SEQ ID NO: 44)
light-chain CDR2: EDN (SEQ ID NO: 51)

30

light-chain CDR3: QSYDNNIQV (SEQ ID NO: 83)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166);

5

3D2

light-chain CDR1: SGSIARNY (SEQ ID NO: 43)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDRTNKR (SEQ ID NO: 82)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166);

10

3E9

light-chain CDR1: SGSIASNY (SEQ ID NO: 34)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDSSNLQWV (SEQ ID NO: 84)
heavy-chain CDR1: GYTFTSYG (SEQ ID NO: 127)
heavy-chain CDR2: ISAYNGNT (SEQ ID NO: 138)
heavy-chain CDR3: ARGITMISDY (SEQ ID NO: 167);

15

20

3F1

light-chain CDR1: GGSADNF (SEQ ID NO: 45)
light-chain CDR2: DYS (SEQ ID NO: 62)
light-chain CDR3: QSYDISNPV (SEQ ID NO: 85)
heavy-chain CDR1: GFTFSSYG (SEQ ID NO: 128)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARDGGGGMDV (SEQ ID NO: 168);

25

30

3F11

light-chain CDR1: HSDGRNY (SEQ ID NO: 46)
light-chain CDR2: DTS (SEQ ID NO: 63)

light-chain CDR3: HQFRRSVST (SEQ ID NO: 86)
heavy-chain CDR1: GYTFSSSG (SEQ ID NO: 129)
heavy-chain CDR2: ISTYNGNT (SEQ ID NO: 146)
heavy-chain CDR3: ATSIAVAGIDY (SEQ ID NO: 169);

5

3H11

light-chain CDR1: SGNIASY (SEQ ID NO: 48)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDRPNHV (SEQ ID NO: 88)
heavy-chain CDR1: GYTFTSY (SEQ ID NO: 119)
heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)
heavy-chain CDR3: ASSVPAAIYDYYYGMDV (SEQ ID NO: 171);

10

3H7

light-chain CDR1: TDSIASNY (SEQ ID NO: 47)
light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDGVNRGVI (SEQ ID NO: 87)
heavy-chain CDR1: GFTFSNYG (SEQ ID NO: 130)
heavy-chain CDR2: IWHGDTNK (SEQ ID NO: 147)
heavy-chain CDR3: VRDQGAGVWNGYSY (SEQ ID NO: 170);

15

20

5A6

light-chain CDR1: QSISSY (SEQ ID NO: 49)
light-chain CDR2: AAS (SEQ ID NO: 59)
light-chain CDR3: QQSYNLPRT (SEQ ID NO: 89)
heavy-chain CDR1: GFTFSSYE (SEQ ID NO: 131)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172);

25

6F8

light-chain CDR1: QTINNNY (SEQ ID NO: 50)
light-chain CDR2: DAS (SEQ ID NO: 64)

30

light-chain CDR3: QQYGSSPRT (SEQ ID NO: 90)
heavy-chain CDR1: GFTVSSNY (SEQ ID NO: 132)
heavy-chain CDR2: IYSGGST (SEQ ID NO: 148)
heavy-chain CDR3: ARDYGDYYFDY (SEQ ID NO: 173); or

5

conservative sequence variants thereof (e.g., an antigen-binding protein comprising one CDR sequence that is a conservative sequence variant of one CDR sequence of 1A5 and five CDR sequences that are identical to the other five CDR sequences of 1A5, an antigen-binding protein comprising two CDR sequences that are conservative sequence variants of two CDR sequences of 1B2 and three CDR sequences that are identical to the other three CDR sequences of 1B2 etc.).

In various embodiments, antigen-binding protein comprises a light-chain variable region comprising any one of SEQ ID NO: 1-27 or a sequence sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 85%, at least about 95% or at least about 99% sequence similarity/identity thereto; and/or a heavy-chain variable region comprising any one of SEQ ID NO: 91-116 or a sequence sharing at least about 75%, at least about 85%, at least about 95% or at least about 99% sequence similarity/identity thereto.

In various embodiments, there is provided a combination of about two, about three, about four, about five, about six, about seven, about eight, about nine, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26 or about 27 antigen-binding proteins. In various embodiments, the antigen-binding proteins in the combination comprises the CDR sequences of one or more of the following antigen-binding proteins: 1A5, 1A8, 1B2, 1B11, 1C2, 1C3, 1D12, 1E5, 1F4, 1H7, 2C9, 2C10, 2C12, 2D3, 2G7, 2H4, 3A11, 3C5, 3D2, 3D11, 3E9, 3F1, 3F11, 3H7, 3H11, 5A6 and 6F8. In various embodiments, the antigen-binding proteins in the combination is selected from the group consisting of: 1A5, 1A8, 1B2, 1B11, 1C2, 1C3, 1D12, 1E5, 1F4, 1H7, 2C9, 2C10, 2C12,

2D3, 2G7, 2H4, 3A11, 3C5, 3D2, 3D11, 3E9, 3F1, 3F11, 3H7, 3H11, 5A6, 6F8 and combinations thereof.

In various embodiments, there is provided a combination of two antigen-binding proteins, wherein a first antigen-binding protein comprises the following
5 CDR sequences:

5A6

light-chain CDR1: QSISSY (SEQ ID NO: 49)
light-chain CDR2: AAS (SEQ ID NO: 59)
10 light-chain CDR3: QQSYNLPRT (SEQ ID NO: 89)
heavy-chain CDR1: GFTFSSYE (SEQ ID NO: 131)
heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)
heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172)

15 and a second antigen-binding protein comprises the following CDR sequences:

3D11

light-chain CDR1: SGNIASNY (SEQ ID NO: 44)
20 light-chain CDR2: EDN (SEQ ID NO: 51)
light-chain CDR3: QSYDNNIQV (SEQ ID NO: 83)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARWWLARGAFDI (SEQ ID NO: 166).

25

In various embodiments, there is provided a composition comprising the antigen-binding protein or the combination. In various embodiments, the composition comprises a therapeutically effective amount of the antigen-binding protein or the combination e.g., for use in therapy. In various embodiments, the
30 composition further comprises a suitable carrier, adjuvant, diluent and/or excipient. In various embodiments, the composition comprises a therapeutic composition.

In various embodiments, the composition comprises a pharmaceutical composition. The pharmaceutical composition may further comprise a pharmaceutically acceptable carrier and/or pharmaceutically active compound. In one embodiment, there is provided a pharmaceutical composition comprising
5 the antigen-binding protein or the combination, and a pharmaceutically acceptable carrier.

In various embodiments, there is provided the antigen-binding protein or the combination for use in therapy. In various embodiments, there is provided the antigen-binding protein or the combination when used in therapy.

10 In various embodiments, there is provided the antigen-binding protein or the combination as a detecting agent, e.g., for detecting SARS-CoV-2. In various embodiments, there is provided the antigen-binding protein or the combination as a diagnostic agent e.g., for SARS-CoV-2.

In various embodiments, there is provided the antigen-binding protein or
15 the combination for use in therapy, or as a diagnostic agent.

In various embodiments, there is provided a polynucleotide/nucleotide sequence encoding for the antigen-binding protein. The polynucleotide/nucleotide sequence may comprise DNA, cDNA and/or RNA. In various embodiments, the polynucleotide/nucleotide sequence comprises one or
20 more sequences set forth in Tables 5-8 or a sequence sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 85%, at least about 95% or at least about 99% sequence identity thereto. In various embodiments, the polynucleotide/nucleotide sequence comprises one of
25 more of SEQ ID NO: 174-351 or a sequence sharing at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 85%, at least about 95% or at least about 99% sequence identity thereto.

In various embodiments, there is provided a vector comprising the polynucleotide/nucleotide sequence. In various embodiments, the vector is selected from the group consisting of a phage, a plasmid, a viral particle, a
30 baculovirus, a yeast plasmid, a lipid based vehicle, a polymer microsphere, a liposome, and a cell based vehicle, a colloidal gold particle, lipopolysaccharide, polypeptide, polysaccharide, a viral vehicle, an adenovirus, a retrovirus, a

lentivirus, an adeno-associated viruses, a herpesvirus, a vaccinia virus, a foamy virus, a cytomegalovirus, a Semliki forest virus, a poxvirus, a pseudorabies virus, an RNA virus vector, a DNA virus vector and a vector derived from a combination of a plasmid and a phage DNA. In various embodiments, the polynucleotide/nucleotide sequence is operatively linked to an expression control sequence(s) to direct peptide synthesis. In various embodiments, the vector comprises one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells. In various embodiments, there is provided a host cell transfected with or comprising the vector. The host cell may comprise a bacterial cell, a yeast cell, an animal cell e.g., a mammalian cell and/or a plant cell.

In various embodiments, there is provided a bacteriophage, a host cell or a non-human organism comprising the polynucleotide/nucleotide sequence. In some embodiments, the non-human organism comprises a mammal. In some embodiments, the non-human organism comprises a murine.

In various embodiments, there is provided a method of treating SARS-CoV-2 infection in a subject, the method comprising administering the antigen-binding protein, the combination or the composition (e.g., pharmaceutical composition) to the subject. In various embodiments, where the SARS-CoV-2 comprises a V483A mutation, the method comprises administering the subject a combination of two antigen-binding proteins, wherein a first antigen-binding protein comprises the following CDR sequences:

5A6

25	light-chain CDR1:	QSISSY (SEQ ID NO: 49)
	light-chain CDR2:	AAS (SEQ ID NO: 59)
	light-chain CDR3:	QQSYNLPRT (SEQ ID NO: 89)
	heavy-chain CDR1:	GFTFSSYE (SEQ ID NO: 131)
	heavy-chain CDR2:	ISYDGSNK (SEQ ID NO: 143)
30	heavy-chain CDR3:	ARLITMVRGEDY (SEQ ID NO: 172)

and a second antigen-binding protein comprises the following CDR sequences:

3D11

- 5 light-chain CDR1: SGNIASNY (SEQ ID NO: 44)
 light-chain CDR2: EDN (SEQ ID NO: 51)
 light-chain CDR3: QSYDNNIQV (SEQ ID NO: 83)
 heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
 heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
10 heavy-chain CDR3: ARRWLRLGAFDI (SEQ ID NO: 166).

The method may be performed *in vitro* or *ex vivo* or *in vivo*.

15 In various embodiments, there is provided use of the antigen-binding protein, the combination or the composition (e.g., pharmaceutical composition) in the manufacture of a medicament for the treatment of SARS-CoV-2 infection in a subject.

20 In various embodiments, there is provided a method of detecting the presence of SARS-CoV-2 in a sample, the method comprising: contacting the sample with the agent, e.g., the antigen-binding protein and detecting a binding event involving the agent, e.g., the antigen-binding protein. In various embodiments, the detection of a binding event is indicative of the presence of SARS-CoV-2 in the sample. In various embodiments, no detection of any binding events involving the agent, e.g., the antigen-binding protein is indicative of the absence of SARS-CoV-2 in the sample. In various embodiments, the antigen-binding protein may be labelled e.g., coupled to a label. In one embodiment, the antigen-binding protein is labelled with horseradish peroxidase (HRP) and tetramethylbenzidine (TMB) substrate may be added for visualization. It will be appreciated that other suitable labels and substrates may also be used for detecting a binding event. In various embodiments, there is provided the antigen-binding protein when used in detecting the presence of SARS-CoV-2 in a sample.

30 The sample may be obtained from any source. For example, the sample may be a biological sample, a pharmaceutical sample, an environmental sample,

a food sample etc. In some embodiments, the sample comprises a biological sample. Examples of biological samples include, but are not limited to blood, serum, plasma, sputum, saliva, lavage fluid (e.g. bronchial lavage fluid, alveolar lavage fluid and bronchoalveolar lavage fluid), sputum, nasal
5 fluid/swab/wash/aspirate, anterior nares fluid/swab/wash/aspirate, nasal mid-turbinate fluid/swab/wash/aspirate, pharyngeal fluid/swab/wash/aspirate, nasopharyngeal fluid/swab/wash/aspirate, oropharyngeal fluid/swab/wash/aspirate, tissue biopsy e.g. lung biopsy, cerebrospinal fluid, urine, faeces, stool, anal swab, semen, sweat, tears, processed fractions thereof
10 and the like.

In various embodiments, there is provided a method of identifying an agent, optionally an antigen-binding protein, that is capable of recognising/interacting with/binding to SARS-CoV-2.

In some embodiments, the method comprises contacting a candidate
15 compound with a SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/a SARS-CoV-2 spike protein RBD domain, wherein where the candidate compound binds to the SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain, the candidate agent is identified as a potential agent. In some embodiments, the method comprises use
20 of phage display technology to identify the agent. In some embodiments, the method comprises an enzyme-linked immunosorbent assay (ELISA) method. In various embodiments, the ELISA method comprises immobilizing SARS-CoV-2 spike protein RBD domain or antigen to a surface, adding a candidate compound to the surface under conditions suitable for binding, and determining a binding
25 between the SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain or antigen and the candidate compound. In some embodiments, the SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain or antigen is tagged (e.g., with biotin).

30 In some embodiments, the method comprises determining whether a candidate compound is capable of blocking a binding between SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD

domain and ACE2 protein, wherein where the candidate compound is capable of blocking a binding between SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain and ACE2 protein, the candidate compound is identified as a potential agent. In some embodiments, the method comprises providing a candidate compound that is bound to SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain, and contacting the bound candidate compound with ACE2 protein, wherein where the bound candidate compound and/or the SARS-CoV-2/a SARS-CoV-2 spike protein (or glycoprotein)/ SARS-CoV-2 spike protein RBD domain does not bind to the ACE2 protein, the candidate compound is identified as a potential agent.

In some embodiments, the method comprises determining whether a candidate compound is capable of neutralising cell entry of SARS-CoV-2 or portions thereof, wherein where the candidate compound is capable of neutralising cell entry of SARS-CoV-2 or portions thereof, the candidate compound is identified as a potential agent. In some embodiments, the method comprises contacting SARS-CoV-2 (or a pseudotyped SARS-CoV-2) or portions thereof with ACE-expressing cells in the presence of the candidate compound, and determining an amount of entry of the SARS-CoV-2 or portions thereof into the ACE-expressing cells, wherein where the amount of entry of the SARS-CoV-2 or portions thereof into the ACE-expressing cells is substantially low/reduced, the candidate compound is identified as a potential antigen-binding protein. In various embodiments, the determining step comprises performing a luciferase assay.

In some embodiments, the candidate compound is pre-incubated with the SARS-CoV-2 or portions thereof before contact with the ACE-expressing cells.

In various embodiments, the method further comprises generating a library of sequences, optionally Fab sequences, to obtain the candidate compounds. In some embodiments, the library comprises a phase display library.

In various embodiments, there is provided a product or a method as described herein.

Table 1. Light chain variable domain amino acid sequences for human IgG1

Name	Light chain variable domain sequences (CDR sequences are in bold)	SEQ ID NO
1A5	NFMLTQPHSVSESPGKTVAISCTGNS SGSIASHYVQWFQQRPGSAPT TVIY EDNQRPSGVPDRFSGSIDRSSNSASLTISGLKSEDEADYYCQSYGSGFVV FGGGTK	1
1A8	EIVLTQSPDSLAVSLGERATINCKSS QSVLYSSNNKNY LAWYQQKPGQPP KLLIY WAST TRESGVPDRFSGSGSGTDFTLTISLQAEDVAVYYC QQYYGT PYTFGQGTK	2
1B2	NFMLTQPHSVSESPGKTVTISCTGSG GGRIATNYVQWYQQRPGSAPT TVIY EDNKRPSGVPDRFSGSIDASSNSASLTISGLETEDEADYYCQSHDTSRQA VFGGGTK	3
1B11	DVVMTQSPSLPVPVTPGEPASISCRSS QSLLYSNGYNY LDWYLQKPGQSPQ LLIY LGSN RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC MQALQTP YTFGQGTK	4
1C2	DVVMTQSPSLPVPVTPGEPASISCRSS QSLHNSNGFTY LDWYLQKPGQSPQ LLIY LGSN RAPGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC MQGIQTP LTFGGGTK	5
1C3	NFMLTQPHSVSESPGKTVTISCTRSS SGSIASYYVQWYQQRPGSSPT TVIY EDDQRPSGVPDRFSGSIDSSNSASLTISGLQTEDEADYYCQSFDS SIQH VVFGGGTQ	6
1D12	NFMLTQPHSVSESPGKTVTISCTGSS SGSIASNYVHWYQQRPGSAPT TVIY EDNQRPSGVPDRFSGSIDSSNSASLTISGLKTEDEADYYCQSYDGS AWV FGGGTK	7
1E5	NFMLTQPHSVSESPGKTLTISCTRSS SGRIASNYVQWYQQRPGSAPT TVIY EDTQRPSGVPDRFSGSIDSSNSASLTISGLKTEDEADYYCQSFDSGNQR VVFGGGTK	8
1F4	QSVLTQPPSVSGTPGQRTVISCSS SSNIGRNFVSWYQQLPGAAPRL LMY RNNQRPSGVPDRFSGSESATSASLAITGLQPEDEADYYCQSYDNSL FVVF GGGTK	9
1H7	NFMLTQPHSVSESPGKTVTISCTRSS SGSIASNYVQWYQQRPGSSPT TVIY EDNQRPSGVPDRFSGSVDSSNSASLTISGLKTEDEADYYCQSYDENIRV FGGGTK	10
2C9	EIVLTQSPGTLSSSPGERATLSCTAS QTVGGSY LAWYQQKRGQPPRLLIY GAST RAPGIPERFSGSGSGTDFTLTISTLEPEDFAVYFC QQYASSRT FGQ GTR	11
2C10	QSVVTQPPSASGSPGQSVTISCSS SSTIGTNYVAWYQQLPGTAPK LLIY DNYKRPSGIPDRFSGWRSATSATLVISGLQTGDEADYYCGTWDSRL SVGV FGGGTK	12
2C12	DIQMTQSPSSLSASIGDRVITITCRAS QSINIY LNWYQQKPGKAPKLLIY A ASSLQSGVPSRFSGSGSATDFTLTISLQPEDFATYYCQOSYITPQT FGQ GTK	13
2D3	NFMLTQPHSVSESPGKTVTISCTGSS SGSIASNYVQWYQQRPGSAPT TIIY EDNQRPSGVPDRFSGSVDSSNSASLTISGLKTEDEADYYCQSYDSSNWV FGGGTK	14
2G7	NFMLTQPHSVSESPGKTITISCTRSS GGTIGSNYVQWYQQRPGSSPT TVIY EDNQRPSGVPDRFSGSIDSSNSASLTISGLKTEDEADYYCQSYDSSNRV FGGGTK	15
2H4	ETTLTQSPAFVSAAPGDKVISICKAS EFIGDDVNWYQKPG EAPVFI IQE ARVPVRGIPPRFSGSGYGTDFLTIDDIQSEDSAFYFCLQYDSFPLT FGQ GTK	16

3A11	QSALTQPASVSGSPGQAITMPCTGT SSDVGTNY VSWYQHFPKGKAPKLLI YDVSHR PAGISDRFSGSKSGNTASLTISGLQAEDEADYYC CASFSSSTLL VFGGGTK	17
3C5	NFMLTQPHSVSESPGKTVTISCTGSS SGSIASNY VQWYQQRPGSAPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLKTEDEADYYC QSYDSSNWV FGGGTK	18
3D2	NFMLTQPHSVSESPGKTVTISCTGSS SGSIARNY VHWHYQQRPGSAPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLKTEDEADYYC QSYDRTNKR VFGGGTR	19
3D11	NFMLTQPHSVSASPGKTVTIPCTGSS SGNIASNY VQWYQQRPGSAPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLKTEDEADYYC QSYDNNIQV FGGGTK	20
3E9	NFMLTQPHSVSESPGKTVTISCTGSS SGSIASNY VQWYQQRPGSAPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLKTEDEADYYC QSYDSSNLQ WVFGGGTK	21
3F1	NFMLTQPHSVSESPGKTVTISCTAS GSGSIADNF VQWYQQRPGSAPTTLIY DYSRR PYGVPDRFSGSIDRSSNSASLTISGLMTEDEADYYC QSYDISNPV FGGGTK	22
3F11	ETTLTQSPGTLSSLSPGESATLSCRAS HSDGRNY IAWYQQTPGQAPRLLVY DTSNRA GVDPDRFRSGSGTDFTLTISRLEPEDFAVYF CHQFRRSVSTFG QGTK	23
3H7	NFMLTQPHSVSESPGKTVTISCTRS TDSIASNY VQWYQQRPGSAPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLKTEDEADYYC QSYDGVNRG VI FGGGTK	24
3H11	NFMLTQPHSVSESPGKTVTISCTRS SGNIASY VQWYQQRPGSSPTTVIY EDNQR PSGVPDRFSGSIDSSSNSASLTISGLQTEDEADYYC QSYDRPNHV VFGGGTR	25
5A6	DIQLTQSPSSLSASVGHVRTITCRAS QSISSY LNWYQQKPGKAPKLLIYA ASSLQ SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQSYNLPR TFGG GTK	26
6F8	EIVLTQSPGTLSSLSPGERATLSCTAS QTINNNY LAWYQQKPGQGPSLLIY DASSR ATGVDPDRFSGSGSGTDFTLTISRLEPEDFAVYYC QQYGSSPR TFG QGTK	27

Table 2. Light-chain CDR amino acid sequences for human IgG1

Name	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
1A5	SGSIASHY	28	EDN	51	QSYGSGFVV	65
1A8	QSVLYSSNNKNY	29	WAS	52	QQYYGTPYT	66
1B2	GGRIATNY	30	EDN	51	QSHDTSRQAV	67
1B11	QSLLYSNGYNY	31	LGS	53	MQALQTPYT	68
1C2	QSLLSHNGFTY	32	LGS	53	MQGIQTPLT	69
1C3	SGSIASY	33	EDD	54	QSFDSIIQHV	70
1D12	SGSIASNY	34	EDN	51	QSYDGSAAV	71
1E5	SGRIASNY	35	EDT	55	QSFDSGNQRV	72
1F4	SSNIGRNF	36	RNN	56	QSYDNSLFVV	73
1H7	SGSIASNY	34	EDN	51	QSYDENIRV	74
2C9	QTVGGSY	37	GAS	57	QQYASSRT	75

2C10	SSTIGTNY	38	DNY	58	GTWDSRLSVGV	76
2C12	QSINIY	39	AAS	59	QQSYITPQT	77
2D3	SGSIASNY	34	EDN	51	QSYDSSNWV	78
2G7	GGTIGSNY	40	EDN	51	QSYDSSNRV	79
2H4	EFIGDD	41	EAR	60	LQYDSFPLT	80
3A11	SSDVGTyny	42	DVS	61	ASFSSSSTLLV	81
3C5	SGSIASNY	34	EDN	51	QSYDSSNWV	78
3D2	SGSIARNY	43	EDN	51	QSYDRTNKRv	82
3D11	SGNIASNY	44	EDN	51	QSYDNNIQV	83
3E9	SGSIASNY	34	EDN	51	QSYDSSNLQWV	84
3F1	GGSIADNF	45	DYS	62	QSYDISNPV	85
3F11	HSDGRNY	46	DTS	63	HQFRRSVST	86
3H7	TDSIASNY	47	EDN	51	QSYDGVNRGVI	87
3H11	SGNIASYy	48	EDN	51	QSYDRPNHVv	88
5A6	QSISSY	49	AAS	59	QQSYNLPRT	89
6F8	QTINNNY	50	DAS	64	QQYGSSPRT	90

Table 3. Heavy chain variable domain amino acid sequences for human IgG1

Name	Heavy chain variable domain sequences (CDR sequences are in bold)	SEQ ID NO
1A5	QVQLQESGGGLVQPGGSLRLSCAAS GGTFSSY AMSWVRQAPGKGLEWVSA ISGSG GST YYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYC AKDYFRWL WGQGT L	91
1A8	QVQLQESGPGLVKPSSETLSLTCTVSG VSISRS SDHWGWRQPPGKGLEWIGS ISY SGST YYNPSLKS RVTISVDTSKNQLSLKLSSVTAADTAVYYC CARLASLYSTFD IW GHGTL	92
1B2	QVQLVQSGAEVKKPGASVKV SCKAS GYTF TSYYMHVVRQAPGQGLEWMGI INPSG GST SYAQKFQGRVTMTRDTSTSTVYME LSSLRSED TAVYYC ATGEMAGDFD YWGQ GTL	93
1B11	EVQLVQSGAEVKKPGSSVKV SCKAS GGTFSSY AISWVRQAPGQGLEWMGGI IPIF GT ANYAQKFQGRVTITADESTSTAYME LSSLRSED TAVYYC ARDNPGYSSSWSPN WFD PWGQGT L	94
1C2	EVQLVQSGAEVKKPGASVKV SCKAS GYTF TSYYMHVVRQAPGQGLEWMGI INPSG GST SYAQKFQGRVTMTRDTSTSTVYME LSSLRSED TAVYYC CASSAGTFYFD YWG QGTL	95
1C3	EVQLVQSGAEVKKPGASVKV SCKAS GYPF STYYIHWVRQAPGQGLEWMGI IDPSG GST SYAQKFQGRVTMTRDTSTSTVYME LRLSRSDDTAVFYC ARVAEQHLDYFD WGQGT L	96
1D12	EVQLVQSGAEVKKPGSSVKV SCKAS GGTFSSY AISWVRQAPGQGLEWMGW ISAYN GNT NYAQKLQGRVTMTTDTSTSTAYME LRLSRSED TAVYYC ARLEWLRGA FDI WG QGT T	97
1E5	EVQLVQSGAEVKKPGSSVKV SCKAS GGTFSSY AISWVRQAPGQGLEWMGGI IPIF GT ANYAQKFQGRVTITADESTSTAYME LSSLRSED TAVYYC CARALVGKWL LLRGF DY WGQGT L	98

1F4	QVQLQQSGPGLVKPSQTLSTLCAIS GDSVSSNSA AWNWRQSPSRGLEWLGR TTY RSKWYNDY AVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYC AREKGIEGPAF DPWGQGTL	99
1H7	QVQLQQWGAGLLKPSETLPLTCAVY GGSFSGYY WSWIRQPPGKGLEWIGE INHSG STN YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARGRWLRGAFDI WGQ GTM	100
2C9	QVQLVQSGAEVKKPGSSVKVSC KASGGTFSSYA ISWVRQAPGQGLEWMGR IIPIL GI ANYAQKFQGRVTITADKSTSTAYMELSSLRSED TAVYYCARHGGV GATTG YYY MDV WGKGTT	101
2C10	QVQLQQWGAGLLKPSETLSTCGVY GGSFSGYY WSWIRQSPGKGLEWIGE INYRG NTN YNPSLKSRVTISVDTSKNQFSLNVNSVTAADTAVYYC ARWDGGNSVD HWGQ TL	102
2C12	QVQLVESGGGVVQPGRSLRLSCAAS GFTFSSY AMHWVRQAPGKGLEWVAV ISYDG SNK YYADSVKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYC ARGGRFH YYYY AMD V WGQGT	103
2D3	EVQLVQSGAEVKKPGSSVKVSC KASGGTFSSYA ISWVRQAPGQGLEWMGR IIPIF GT ANYAQKFQGRVTITADESTSTAYMELSSLRSED TAVYYCASSGWL RGAFDI WG QGTM	104
2G7	QVQLQQWGAGLLKPSETLSTLCAVY GGSFSGYY WSWIRQPPGKGLEWIGE INHSG STN YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARGKWL RGAFDI WG GTM	105
2H4	QVQLVQSGAEVTKPGASVKVSC KASGYTFSGYY IHWVRQAPGQGLEWMGR VNPNS GGT KYAQKFQDRVTLTRDTSISTAYMELTSLRSDDTAMYFC ARGGRPGL PAAGY I DY WGQGT	106
3A11	EVQLVQSGAEVKKPGASVKVSC KASGYTFSTYD ISWVRQAPGQGLEWMGW ISTYN GDT NYAQKFQGRVTMTTDTSTSTIY MELRSLRSDDTAVYYCARGDSSV GYEY FQH WGQGT	107
3C5	QVQLQQWGAGLLKPSETLSTCGVY GGSLSGYY WSWIRQPPGKGLEWIGE INHSG STN YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARRWWLRGA FDI WG GTT	108
3D2, 3D11	QVQLQQWGAGLLKPSETLSTLCAVY GGSFSGYY WSWIRQPPGKGLEWIGE INHSG STN YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARRWWLRGA FDI WG GTT	109
3E9	EVQLVQSGAEVKKPGASVKVSC KASGYTFTSYG ISWVRQAPGQGLEWMGW ISAYN GNT NYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYC ARGIITMISD YWGQ GTL	110
3F1	QVQLVQSGGGVVQPGRSLRLSCAAS GFTFSSY GMHWVRQAPGKGLEWVAV ISYDG SNK YYADSVKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYC CARDGGGMDV WGQ TT	111
3F11	EVQLVQSGAEVKKPGASVKVSC KASGYTFSSSG ISWVRQAPGQGLEWMGW ISTYN GNT NYAQNFQGRVTMTTDTSTSTVY MELRGLTSDDTAVYYCATSIA VAGIDY WG GTL	112
3H7	QVQLVQSGGGVVQPGRSLRLSCAAS GFTFSSNY GMHWVRQAPGKGLEWVAV IWHDG TNK YYADSVKGRFTVSRDN SKNTLYLQMDT LRAEDTAVYYC VRDQAG VWNGYSY WGQGT	113

3H11	QVQLVQSGAEVKKPGASVKVSCKAS GYTFSSY MHWVRQAPGQGLEWMGI INPSG GST SYAQKFQGRVTMTRDTSTNTVYMESSLRSED TAVYYC ASSVVPAAIYDYYY GMDVWGQGT T	114
5A6	QVQLQESGGGLVQPGGSLRLSCAAS GFTFSSY EMNWRQAPGKGLEWVAV ISYDG SNK YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYC ARLITMVRGEDY WG QGTL	115
6F8	QVQLVESGGGLVQPGGSLRLSCAAS GFTVSSNY MSWVRQAPGKGLEWVSV IYSGG ST YYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYC ARDYGDYYFDY WGQG TL	116

Table 4. Heavy-chain CDR amino acid sequences for human IgG1

Name	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
1A5	GFTFSSYA	117	ISGSGGST	133	AKDYFRWL	149
1A8	GVSISRSDH	118	ISYSGST	134	ARLASLYSTFDI	150
1B2	GYTFSSY	119	INPSGGST	135	ATGEMAGDFDY	151
1B11	GGTFSSYA	120	IIPIFGTA	136	ARDNPGYSSSWSPNWFDP	152
1C2	GYTFSSY	119	INPSGGST	135	ASSSAGTFYFDY	153
1C3	GYPFSTYY	121	IDPSGGST	137	ARVAEQHLDYYFDY	154
1D12	GGTFSSYA	120	ISAYNGNT	138	ARLEWLRGAFDI	155
1E5	GGTFSSYA	120	IIPIFGTA	136	ARALVGKWLRLRGFDY	156
1F4	GDSVSSNSAA	122	TYRSKWYN	139	AREKGIEGPAFDP	157
1H7	GGSFSGYY	123	INHSGST	140	ARGRWLRGAFDI	158
2C9	GGTFSSYA	120	IIPILGIA	141	ARHGGVGATTGYYYMDV	159
2C10	GGSFSGYY	123	INYRGNT	142	ARWDGGNSVDH	160
2C12	GFTFSSYA	117	ISYDGSNK	143	ARGGRFHYYYAMDV	161
2D3	GGTFSSYA	120	IIPIFGTA	136	ASSGWLRGAFDI	162
2G7	GGSFSGYY	123	INHSGST	140	ARGKWLRGAFDI	163
2H4	GYTFSGYY	124	VNPNSGGT	144	ARGGRPGLPAAGYIDY	164
3A11	GYTFSTYD	125	ISTYNGDT	145	ARGDSSVGYYEFQH	165
3C5	GGSLSGYY	126	INHSGST	140	ARRWWLRGAFDI	166
3D2, 3D11	GGSFSGYY	123	INHSGST	140	ARRWWLRGAFDI	166
3E9	GYTFSSYG	127	ISAYNGNT	138	ARGIITMISDY	167
3F1	GFTFSSYG	128	ISYDGSNK	143	ARDGGGGMDV	168
3F11	GYTFSSSG	129	ISTYNGNT	146	ATSIAGIDY	169
3H7	GFTFSNYG	130	IWHDGTNK	147	VRDQGAGVWNGYSY	170
3H11	GYTFSSY	119	INPSGGST	135	ASSVVPAAIYDYYYGMDV	171
5A6	GFTFSSYE	131	ISYDGSNK	143	ARLITMVRGEDY	172
6F8	GFTVSSNY	132	IYSGGST	148	ARDYGDYYFDY	173

Table 5. Light chain variable domain nucleotide sequences for human IgG1

Name	Light chain variable domain sequences (CDR sequences are in bold)	SEQ ID NO
1A5	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAGCCATCTCCTGCACCGGCAAC AGTGGCAGCATTGCCAGCCACTATGTG CAGTGGTTCCAACAGCGCCCGGGCAGTGCCCCCACTACTGTGATCTAT GAA GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGGTGCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTTAAGAGTGAGGAC GAGGCTGACTATTACTGT CAGTCTTATGGCAGCGGCTTTGTGGTCTTTCGGC GGAGGGACCAAG	174
1A8	GAAATTGTGTTGACGCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAG AGGGCCACCATCAACTGCAAGTCCAGCC CAGAGTGTTTTATACAGCTCCAAC AATAAGAACTACTTAGCTTGGTATCAACAGAAACCAGGACAGCCTCCTAAG TTGCTCATTTAC TGGGCTTCT ACCCGGGAATCCGGGGTCCCTGACCGATTTC AGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAG GCTGAAGATGTGGCAGTTTATTACTGT CAGCAATATTATGGTACTCCGTAC ACTTTTGGCCAGGGGACCAAG	175
1B2	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACC GTAACCATCTCCTGCACCGGCAGCG GGTGGCAGGATTGCCACCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACTACTGTGATCTAT GAG GATAATAAAAGACCCTCTGGGGTCCCTCATCGGTTCTCTGGCTCCATCGAC GCCTCCTCCAATTCTGCCTCCCTCACTATCTCTGGACTGGAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTCATGATACCAGCCGTACGGCGGTTTC GGCGGCGGGACCAAG	176
1B11	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAG CCGGCCTCCATCTCCTGCAGGTCTAGT CAGAGCCTCCTGTATAGTAATGGA TACAACATATTTGGATTGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTC CTGATCTAT TTGGGTTCT AATCGGGCCTCCGGGGTCCCTGACAGGTTCACT GGCAGTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGTGGAGGCT GAGGATGTTGGGGTTTATTACTGC ATGCAAGCTCTACAAACCCCGTACACT TTTGGCCAGGGGACCAAG	177
1C2	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAG CCGGCCTCCATCTCCTGCAGGTCTAGT CAGAGCCTCCTGCATAGTAATGGA TTACACCTATTTGGATTGGTACCTGCAGAAGCCAGGGCTGTCTCCACAGCTC CTGATCTACT TTGGGTTCT AATCGGGCCCCCGGGTCCCTGACAGGTTCACT GGCAGTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGTGGAGGCT GAGGATGTTGGGGTTTATTACTGC ATGCAAGGTATACAAACCCCCCTCACT TTCGGCGGGGGACCAAG	178
1C3	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCCGCAGC AGCGGCAGCATTGCCAGCTACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTTCCCCCACTACTGTGATCTAT GAA GATGACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGTGCCTCCAACCTCAGCCTCCCTCACCATCTCTGGCCTGCAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTTTGATAGCAGCATTCAACATGTGGTCT TTCGGCGGGAGGGACCCAG	179

1D12	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCCGCAGC AGTGGCAGCATTGCCAGCAATTATGTG CATTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCAGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATGGCAGCGCTTGGGTGTT CGGC GGAGGGACCAAG	180
1E5	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG TTAACCATCTCCTGCACCCGCAGC AGTGGCAGGATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTTTATAGCGGCAATCAACGGGTGGTT TTCGGCGGAGGGACCAAA	181
1F4	CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGGGACCCCGGGCAGAGG GTCACCATCTCTTGCTCTGGAAGC AGCTCCAACATCGGACGTAATTTTGTA TCCTGGTACCAGCAGCTCCCAGGAGCGCCCCCAGACTCCTCATGTAT AGG AATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCGAGTCT GCCACCTCAGCCTCCCTGGCCATCACTGGGCTCCAGCCTGAGGATGAAGCT GATTATTACTGCC CAGTCTTATGACAACAGCCTGTTTGTGGTATTCGGCGGA GGGACCAAG	182
1H7	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCCGCAGC AGTGGCAGCATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTTCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCGTCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATGAAAACATTCGGGTGTT CGGC GGAGGGACCAAG	183
2C9	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTCGTCTCCTGGGGAG AGAGCCACCCTCTCCTGCACGGCCAGC CAGACTGTCCGGCGGCAGCTACTTA GCCTGGTACCAGCAAAAACGTGGCCAGCCTCCCAGGCTCCTCATCTAT GGT GCGTCCACTAGGGCCCCCTGGCATCCAGAGAGATTTAGTGGCAGTGGGTCT GGGACAGACTTCACTCTCACCATCAGCACCCCTGGAGCCTGAAGATTTGCA GTGTATTTCTGT CAGCAGTATGCCAGTTACGGACGTT CGGCCAAGGGACC AGG	184
2C10	CAGTCTGTCTGACGCAGCCGCCCTCCGCGTCCGGGTCTCCTGGACAGTCA GTCACCATCTCCTGTTCTGGAAGC AGCTCCACCATTGGAACATAATTATGTG GCCTGGTACCAGCAGCTCCCAGGAACAGCCCCAAACTCCTCATTTAT GAC AATTATAAGCGACCCTCGGGAATTCCTGACCGATTCTCTGGCTGGAGGTCT GGCAGCTCAGCCACCCTGGTCATCAGCGGACTCCAGACCGGGGACGAGGCC GATTATTACTGCC GGAACGTGGGATAGTAGGCTGAGTGTTGGCGTGTT CGGC GGAGGGACCAAG	185

2C12	GACATCCAGATGACCCAGTCTCCATCCCTGTCTGCATCTATAGGAGAC AGAGTCACCATCACTTGCCGGGCAAGT CAGAGCATTAACATCTATTTAAAT TGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTAT GCTGCA TCC AGTTTGCAAAGTGGGGTCCCGTCAAGGTTCAAGTGGCAGTGGATCTGCG ACAGATTTCACTCTCACCATCAGCAGTCTGCAGCCTGAAGATTTTGCAACT TACTACTGT CAACAGAGTTACATTACCCCTCAGACG TTCGGCCAAGGGACC AAG	186
2D3	AATTTTATGCTGACTCAGCCCCACTCTGTGTCTGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCGGCAGC AGTGGCAGCATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCACCACTATTATCTAT GAG GATAAC CAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCGTCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAGCAGCAATTGGGTG TTTCGGC GGAGGGACCAAG	187
2G7	AATTTTATGCTGACTCAGCCCCACTCTGTGTCTGGAGTCTCCGGGGAAGACG ATAACCATCTCCTGCACCCGCAGC GGTGGCACCATTGGCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTTCCCCACCACTGTGATCTAT GAG GATAAC CAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAGCAGCAATCGGGTG TTTCGGC GGAGGGACCAAG	188
2H4	GAAACGACACTCACGCAGTCTCCAGCATTCGTGTCTGGCGGGCTCCCGGAGAC AAAGTGTCCATCTCCTGCAAAGCCAGT GAATTCATTGGAGATGATGTGAAC TGGTACCAACAGAAACCAGGAGAGGCTCCTGTTTTATCATTTCAAG GAGGCT CGT GTTCCCGTTTCGTGGAATCCCACCCGATTCAAGTGGCAGCGGCTATGGA ACAGATTTTACCCTCACAATTGATGACATACAATCTGAGGATTCTGCATTT TACTTCTGT CTGCAATATGATTCTTTCCCTCTCACT TTTGGCCAGGGGACC AAG	189
3A11	CAATCTGCCCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGGCG ATCACCATGCCCTGCACTGGAACC AGCAGTGACGTTGGTACTTATAACTAT GTCTCCTGGTATCAACACTTCCCAGGCAAAGCCCCAAACTCTTGATTTAT GATGTCAGT CATCGGCCCCGCGGGGATTTCTGATCGCTTCTCTGGCTCCAAG TCTGGCAACACGGCCTCCCTGACCATCTCTGGCTCCAGGCTGAGGACGAA GCTGACTATTACTGCG GCTTCATTTTCATCCAGCAGCACTCTCTTAGTG TTTC GGCGGAGGGACCAAG	190
3C5	AATTTTATGCTGACTCAGCCCCACTCTGTGTCTGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCGGCAGC AGTGGCAGCATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCACCACTGTGATCTAT GAG GATAAC CAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAGCAGCAATTGGGTG TTTCGGC GGAGGGACCAAG	191

3D2	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCGGCAGC AGTGGCAGCATTGCCCGCAACTATGTG CATTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAGGACCAATAAGAGGGTTTTC GGCGGAGGGACCAGG	192
3D11	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGCGTCTCCGGGGAAGACG GTAACCATCCCCTGCACCGGCAGC AGTGGCAACATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAATAACATTTCAGGTGTTTCGGC GGAGGGACCAAG	193
3E9	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCGGCAGC AGTGGCAGCATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAG GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATAGCAGCAACCTTCAGTGGGTG TTCGGCGGAGGGACCAAG	194
3F1	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTCACCATCTCCTGCACCGCCAGC GGTGGCAGCATTGCCGACAACCTTTGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAC TATAGT CGAAGACCCTATGGGGTCCCAGATCGGTTCTCTGGCTCCATCGAC AGGTCTCTCAATTCTGCCTCCCTCACCCTCTCTGGACTGATGACTGAGGAC GAGGCTGACTACTATTGT CAGTCTTATGATATCAGCAATCCGGTGTTTCGGC GGAGGGACCAAG	195
3F11	GAAACGACACTCACGCAGTCTCCAGGCACCCTGTCTTGTCTCCAGGGGAA AGCGCCACCCTCTCCTGCAGGGCCAGT CACAGTGATGGCAGGAATTACATT GCCTGGTACCAGCAGACACCTGGCCAGGCTCCCAGGCTCCTCGTTTAT GAT ACGT CGAACAGGGCCGCTGGCGTCCCAGACAGGTTTCAGAGGCAGTGGGTCT GGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAGGATTTTGCA GTTTATTTCTGT CATCAATTTTCGGAGGTCCGTGTCCACTTTTGCCAGGGG ACCAAA	196
3H7	AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCCGCAGC ACTGACAGCATTGCCAGCAACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTGCCCCCACCCTGTGATCTAT GAA GATAACCAAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCAGCCTCCCTCACCATCTCTGGACTGAAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATGGCGTCAATCGCGGCGTGATA TTCGGCGGAGGGACCAAG	197

3H11	AATTTTATGCTGACTCAGCCCCACTCTGTGTGCGGAGTCTCCGGGGAAGACG GTAACCATCTCCTGCACCCGAGC AGTGGCAACATTGCCAGTTACTATGTG CAGTGGTACCAGCAGCGCCCGGGCAGTTCCTCCCACTGTGATCTAT GAG GATAAC CAAAGACCTTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGAC AGCTCCTCCAACCTCTGCCTCCCTCACCATCTCTGGACTGCAGACTGAGGAC GAGGCTGACTACTACTGT CAGTCTTATGATCGTCCCAATCATGTGGTGTTC GGCGGCGGGACCAGG	198
5A6	GACATCCAGTTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGACAC AGAGTCACCATCACTTGCCGGGCAAGT CAGAGCATTAGCAGCTATTTAAAT TGGTATCAGCAGAAACCAGGGAAAGCCCCCTAAGCTCCTGATTTAT GCTGCA TCCAGTTTGCAAAGTGGGGTCCCATCAAGGTT CAGCGGCAGTGGATCTGGG ACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCGACT TACTACTGT CAACAGAGTTACAATCTTCCGCGCACTT TCGGCGGAGGGACC AAG	199
6F8	GAAATTGTGCTGACTCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAA AGAGCCACCCTCTCCTGCACGGCCAGT CAGACTATTAAACAACA ACTACTTA GCCTGGTACCAGCAGAAACCTGGCCAGGGTCCAGCCTCCTCATCTAT GAT GCATCC AGCAGGGCCACTGGCGTCCCAGACAGGTT CAGTGGCAGTGGGT CG GGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCA GTGTATTACTGT CAGCAGTATGGAAGCTCGCCTCGGACGTT CGGCCAAGGG ACCAAG	200

Table 6. Light-chain CDR nucleotide sequences for human IgG1

Name	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
1A5	AGTGGCAGCATTGC CAGCCACTAT	201	GAAGATAAC	225	CAGTCTTATGGCAG CGGCTTTGTGGTC	241
1A8	CAGAGTGTTTTATA CAGCTCCAACAATA AGAACTAC	202	TGGGCTTCT	226	CAGCAATATTATGG TACTCCGTACACT	242
1B2	GGTGGCAGGATTGC CACCAACTAT	203	GAGGATAAT	227	CAGTCTCATGATAC CAGCCGTCAGGCGG TT	243
1B11	CAGAGCCTCCTGTA TAGTAATGGATACA ACTAT	204	TTGGGTTCT	228	ATGCAAGCTCTACA AACCCCGTACACT	244
1C2	CAGAGCCTCCTGCA TAGTAATGGATTCA CCTAT	205	TTGGGTTCT	228	ATGCAAGGTATACA AACCCCCCTCACT	245
1C3	AGCGGCAGCATTGC CAGCTACTAT	206	GAAGATGAC	229	CAGTCTTTTGATAG CAGCATTCAACATG TGGTC	246
1D12	AGTGGCAGCATTGC CAGCAATTAT	207	GAGGATAAC	230	CAGTCTTATGATGG CAGCGCTTGGGTG	247

1E5	AGTGGCAGGATTGC CAGCAACTAT	208	GAGGATAACC	231	CAGTCTTTTGATAG CGGCAATCAACGGG TGGTT	248
1F4	AGCTCCAACATCGG ACGTAATTTT	209	AGGAATAAT	232	CAGTCCTATGACAA CAGCCTGTTTGTGG TA	249
1H7	AGTGGCAGCATTGC CAGCAACTAT	210	GAGGATAAC	230	CAGTCTTATGATGA AAACATTTCGGGTG	250
2C9	CAGACTGTCGGCGG CAGCTAC	211	GGTGCCTCC	233	CAGCAGTATGCCAG TTCACGGACG	251
2C10	AGCTCCACCATTGG AACTAATTAT	212	GACAATTAT	234	GGAACGTGGGATAG TAGGCTGAGTGTG GCGTG	252
2C12	CAGAGCATTAACAT CTAT	213	GCTGCATCC	235	CAACAGAGTTACAT TACCCCTCAGACG	253
2D3	AGTGGCAGCATTGC CAGCAACTAT	210	GAGGATAAC	230	CAGTCTTATGATAG CAGCAATTGGGTG	254
2G7	GGTGGCACCATTGG CAGCAACTAT	214	GAGGATAAC	230	CAGTCTTATGATAG CAGCAATCGGGTG	255
2H4	GAATTCATTGGAGA TGAT	215	GAGGCTCGT	236	CTGCAATATGATTC TTCCCTCTCACT	256
3A11	AGCAGTGACGTTGG TACTTATAACTAT	216	GATGTCAGT	237	GCTTCATTTTCATC CAGCAGCACTCTCT TAGTG	257
3C5	AGTGGCAGCATTGC CAGCAACTAT	210	GAGGATAAC	230	CAGTCTTATGATAG CAGCAATTGGGTG	254
3D2	AGTGGCAGCATTGC CCGCAACTAT	217	GAGGATAAC	230	CAGTCTTATGATAG GACCAATAAGAGGG TT	258
3D11	AGTGGCAACATTGC CAGCAACTAT	218	GAGGATAAC	230	CAGTCTTATGATAA TAACATTTCAGGTG	259
3E9	AGTGGCAGCATTGC CAGCAACTAT	210	GAGGATAAC	230	CAGTCTTATGATAG CAGCAACCTTCAGT GGGTG	260
3F1	GGTGGCAGCATTGC CGACAACCTT	219	GACTATAGT	238	CAGTCTTATGATAT CAGCAATCCGGTG	261
3F11	CACAGTGATGGCAG GAATTAC	220	GATACGTCG	239	CATCAATTTCCGAG GTCCGTGTCCACT	262
3H7	ACTGACAGCATTGC CAGCAACTAT	221	GAAGATAAC	225	CAGTCTTATGATGG CGTCAATCGCGGCG TGATA	263
3H11	AGTGGCAACATTGC CAGTTACTAT	222	GAGGATAAC	230	CAGTCTTATGATCG TCCCAATCATGTGG TG	264
5A6	CAGAGCATTAGCAG CTAT	223	GCTGCATCC	235	CAACAGAGTTACAA TCTTCCGCGCACT	265

6F8	CAGACTATTAACAA CAACTAC	224	GATGCATCC	240	CAGCAGTATGGAAG CTCGCCTCGGACG	266
-----	---------------------------	-----	-----------	-----	---------------------------------	-----

Table 7. Heavy chain variable domain nucleotide sequences for human IgG1

Name	Heavy chain variable domain sequences (CDR sequences are in bold)	SEQ ID NO.
1A5	CAGGTGCAGCTGCAGGAGTCGGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCT GAGACTCTCCTGTGCAGCCTCT GGATTACCTTTAGCAGCTATGCCAT GAGCT GGGTCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCT ATTAGTGGT AGTGGTGGTAGCACATA CTACGCAGACTCCGTGAAGGGCCGGTTACCATCTC CAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCCGTATATTACTGT GCGAAAGATTACTTCAGGTGGTTAT GGGGC CAGGGAACCTG	267
1A8	CAGGTGCAGCTGCAGGAGTCGGGGCCAGGACTGGTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCACTGTCTCT GGTGTCTCCATCAGCAGTAGAAGTGACCACT GGGGCTGGGTCCGCCAGCCCCAGGGAAGGGGCTGGAGTGGATTGGAAGT ATC TCTTATAGTGGGAGCACCT ACTACAACCCGTCCCTCAAGAGCCGAGTCACCAT ATCCGTAGACACCTCCAAGAACCAACTCTCCCTGAAGCTGAGCTCTGTGACCG CCGCAGACACGGCTGTCTATTACTGT GCGAGACTCGCTTCCCTTTATTCTACT TTTGATATCT GGGGCCACGGCACCTG	268
1B2	CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTTCCTGCAAGGCATCT GGATACACCTTCACCAGCTACTATAT GCACT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATA AATCAACCCCT AGTGGTGGTAGCACA AGCTACGCACAGAAGTTCAGGGCAGAGTCACCATGAC CAGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGACTGGGGAGATGGCAGGGGATTTTGAC TACT GGGGCCAGGGCACCTG	269
1B11	GAAGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGT GAAGGTCTCCTGCAAGGCCTTCT GGAGGCACCTTCAGCAGCTATGCTAT CAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG ATCATCCCT ATCTTTGGTAGCACA AACTACGCACAGAAGTTCAGGGCAGAGTCACGATTAC CGCGGACGAATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGAGACAACCCCGGTATAGCAGCAGC TGGTCCCCCAACTGGTTCGACCCCT GGGGCCAGGGAACCTG	270
1C2	GAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCATCT GGATACACCTTCACCAGCTACTATAT GCACT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATA AATCAACCCCT AGTGGTGGTAGCACA AGCTACGCACAGAAGTTCAGGGCAGAGTCACCATGAC CAGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGCTCTTCGGCTGGTACGTTCTACTTT GACTACT GGGGCCAGGGCACCTG	271

1C3	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTTTCCTGCAAGGCATCT GGATACCCCTTCAGCACTTACTAT ATACACT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATA AATCGACCCCT AGTGGTGGTAGCACA AGCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGAC CAGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGGAGCCTAAGATCTG ACGACACGGCCGTGTTTTACTGT GCGAGAGTTGCCGAGCAACACCTGGACTAC TACTTTGACTACT TGGGGCCAGGGAACCCCTG	272
1D12	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGT GAAGGTCTCCTGCAAGGCTTCT GGAGGCACCTTCAGCAGCTATGCT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGG ATCAGCGCT TACAATGGTAACACA AACTATGCACAGAAGCTCCAGGGCAGAGTCACCATGAC CACAGACACATCCACGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGGCTTGAGTGGCTACGTGGTGC TTTT GATATCT TGGGGCCAAGGGACCACG	273
1E5	GAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGT GAAGGTCTCCTGCAAGGCTTCT GGAGGCACCTTCAGCAGCTATGCT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG ATCATCCCT ATCTTTGGTACAGCA AACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTAC CGCGGACGAATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGAGCGTTAGTCGAAAGTGGTTATTA CTACGGGGCTTTGACTACT TGGGGCCAGGGAACCCCTG	274
1F4	CAGGTACAGCTGCAGCAGTCAAGTCCAGGACTGGTGAAGCCCTCGCAGACCCCT CTCACTCACCTGTGCCATCTCC GGGGACAGTGCTCTCTAGCAACAGTGCTGCTT GGAACTGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTGGCTGGGAAG ACACA TACTACAGGTCCAAGTGGTATAAT GATTATGCAGTATCTGTGAAAAGTCGAAT AACCATCAACCCAGACACATCCAAGAACCAGTTCTCCCTGCAGCTGAACTCTG TGACTCCCGAGGACACGGCTGTGTATTACTGT GCAAGAGAAAAGGGCATCGAA GGGCCTGCGTTCGACCCCT TGGGGCCAGGGAACCCCTG	275
1H7	CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCCT GCCCCCTCACCTGCGCTGTCTAT GGTGGGTCCTTCAGTGGTTACTACT TGGAGCT GGATCCGCCAGCCCCCAGGGAAGGGCTTGAGTGGATTGGGGAA ATCAATCAT AGTGGAAAGCACCA ACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGT AGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGG ACACGGCTGTGTATTACTGT GCGAGAGGGAGGTGGCTGCGGGGTGCTTTTGAT ATCT TGGGGCCAAGGGACAATG	276
2C9	CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGT GAAGGTCTCCTGCAAGGCTTCT GGAGGCACCTTCAGCAGCTATGCT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAAGG ATCATCCCT ATCCTTGGTATAGCA AACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTAC CGCGGACAAATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGACATGGGGGGGTGGGAGCTACTACG GGTTACTACTACATGGACGCT TGGGGCAAAGGGACCACG	277

2C10	CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCGGTGTCTAT GGTGGGTCCCTTCAGTGGTTACTACT GGAGCT GGATCCGCCAGTCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA ATCAATTAT AGAGGAAACACCA ACTACAACCCGTCTCTCAAGAGTCGAGTCACCATATCGGT AGACACGTCCAAAAACAGTTCTCCCTAAACGTGAACCTCTGTGACCGCCGCGG ACACGGCTGTGTATTATTGT GCGAGATGGGACGGTGGTA ACTCCGTGGACCAC TGGGGCCAGGGAACCCTG	278
2C12	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCT GAGACTCTCCTGTGCAGCCTCT GGATTACCTTCAGTAGCTATGCT ATGCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT ATATCATAT GATGGAAGTAATAA ATACTATGCAGACTCCGTGAAGGGCCGATTACCATCTC CAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTG AGGACACGGCTGTGTATTACTGT GCGAGAGGGGGACGAT TC CACTACTACTAC TATGCCATGGACGCT TGGGGCCAAGGGACCACG	279
2D3	GAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGT GAAGGTCTCCTGCAAGGCTTCT GGAGGCACCTTCAGCAGCTATGCT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG ATCATCCCT ATCTTTGGTACAGCA AACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTAC CGCGGACGAATCCACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGCAGTGGCTGGTTAAGGGGTGCTTTT GATATCT TGGGGCCAAGGGACAATG	280
2G7	CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCGGTGTCTAT GGTGGGTCCCTTCAGTGGTTACTACT GGAGCT GGATCCGCCAGCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA ATCAATCAT AGTGGAAAGCACCA ACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGT AGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGG ACACGGCTGTGTATTACTGT GCGAGAGGGAAATGGTTACGGGGTGCTTTTGAT ATCT TGGGGCCAAGGGACAATG	281
2H4	CAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGACGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCTTCT GGATACACCTTCAGCGGC TACTATATACACT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGGCGGG TCAACCCT AATAGTGGTGGCACAA AGTATGCACAGAAGTTTCAGGACAGGGTCACGTTGAC CAGGGACACGTCCATCAGTACTGCCTACATGGAATTGACCAGTCTGAGATCTG ACGACACGGCCATGTATTTCTGT GCGAGAGGTGGCAGGCCCGGTTTACCTGCA GCTGGCTATATTGACTACT TGGGGCCAGGGCACCCCTG	282
3A11	GAGGTCCAGCTGGTACAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCTTCT GGTTACACGTTTAGCACCTATGAT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGG ATCAGCACT TACAATGGTGACACA AACTATGCACAGAAGTTCCAGGGCAGAGTCACCATGAC CACAGACACGTCCACGAGCACAACTACATGGAGCTGAGGAGCCTGAGATCTG ACGACACGGCCGTCTATTACTGT GCGAGGGGAGATAGCAGTGT CGGGT TACGAA TACTTCCAACACT TGGGGCCAGGGAACCCTG	283

3C5	CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCGGTGTCTAT GGTGGGTCCTTAAGTGGTTACTACT GGAGCT GGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA ATCAATCAT AGTGGAAGCACCA ACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGT AGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGG ACACGGCTGTGTATTACTGT GCGAGACGGTGGTGGCTACGAGGTGCTTTTGAT ATCT GGGGCCAAGGGACCACG	284
3D2, 3D11	CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCT GTCCCTCACCTGCGGTGTCTAT GGTGGGTCCTTCAGTGGTTACTACT GGAGCT GGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA ATCAATCAT AGTGGAAGCACCA ACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGT AGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGG ACACGGCTGTGTATTACTGT GCGAGACGGTGGTGGCTACGAGGTGCTTTTGAT ATCT GGGGCCAAGGGACCACG	285
3E9	GAAGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCTTCT GGTTACACCTTTACCAGCTATGGT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGG ATCAGCGCT TACAATGGTAACACA AACTATGCACAGAAGCTCCAGGGCAGAGTCACCATGAC CACAGACACATCCACGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCTG ACGACACGGCCGTGTATTACTGT GCGAGAGGCATTATTACTATGATATCGGAC TACT GGGGCCAGGGAACCCCTG	286
3F1	CAGGTGCAGCTGGTGCAATCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCT GAGACTCTCCTGTGCAGCCTCT GGATTACCTTCAGTAGCTATGGC ATGCACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTTGAGTGGGTGGCAGTT ATATCATAT GATGGAAGTAATAAA TACTATGCAGACTCCGTGAAGGGCCGATTACCATCTC CAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTG AGGACACGGCTGTGTATTACTGT GCGAGAGACGGTGGGGGAGGTATGGACGTC TGGGGCCAAGGGACCACG	287
3F11	GAGGTCCAGCTGGTACAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTCTCCTGCAAGGCTTCT GGTTACACCTTTAGCAGCTCTGGT ATCAGCT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGG ATCAGCACT TACAATGGTAACACA AACTATGCACAGAATTTCCAGGGCAGAGTCACCATGAC CACAGACACGTCCACGAGCACAGTCTACATGGAGTTGAGGGGCCTGACATCTG ACGACACGGCCGTGTATTACTGT GCTACGAGTATAGCGGTGGCTGGTATTGAC TACT GGGGCCAGGGCACCCCTG	288
3H7	CAGGTGCAGCTGGTGCAATCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCT GAGACTGTCTGTGCAGCGTCT GGATTACCTTCAGTAAC TATGGCATGCACT GGGTCCGCCAGGCTCCGGGCAAGGGGCTTGAGTGGGTGGCAGTT ATATGGCAT GATGGAACCAATAAA TACTATGCAGACTCCGTGAAGGGCCGATTACCGTCTC CAGAGACAATTGAAGAACACTCTGTATTTGCAAATGGACACTCTGAGAGCCG AGGACACGGCTGTGTATTACTGT GTGAGAGATCAGGGGGCCGGTGT TTTGAAT GGTTATTCTTACT GGGGCCAGGGAACCCCTG	289

3H11	CAGGTGCAGCTGGTGCAATCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGT GAAGGTTTCCTGCAAGGCATCT GGATACACCTTCACCAGCTACTAT ATGCACT GGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATA AATCAACCCT AGTGGTGGTAGCACA AGCTACGCACAGAAGTTCCAGGGCAGAGTCACCATGAC CAGGGACACGTCCACGAACACAGTCTACATGGAGCTGAGCAGCCTGAGATCTG AGGACACGGCCGTGTATTACTGT GCGAGCTCAGTAGTACCAGCTGCTATTTAC GACTACTACTACGGTATGGACGTCT GGGGCCAAGGGACCACG	290
5A6	CAGGTGCAGCTGCAGGAGTCGGGGGGAGGCTTGGTACAGCCTGGAGGGTCCCT GAGACTCTCCTGTGCAGCCTCT GGATTACCTTCAGTAGTTATGAA ATGAACT GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT TATATCATAT GATGGAAGCAATAAA TACTACGCAGACTCCGTGAAGGGCCGATTACCATCTC CAGAGACAATGCCAAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCG AGGACACGGCTGTGTATTACTGT GCGAGACTGATTACTATGGTT CGGGGAGAG GACTACT TGGGGCCAGGGCACCCCTG	291
6F8	CAGGTGCAGCTGGTGGAGTCCGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCT GAGACTCTCCTGTGCAGCCTCT GGGTTACCGTCAGTAGCAACTTAC ATGAGCT GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGTT ATTTATAGC GGTGGTAGCACATA TACTACGCAGACTCCGTGAAGGGCCGATTACCATCTCCAG AGACAATTCCAAGAACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGG ACACGGCCGTGTATTACTGT GCGAGAGACTACGGTGACTATTACTTTGACTAC TGGGGCCAGGGCACCCCTG	292

Table 8. Heavy-chain CDR nucleotide sequences for human IgG1

Name	CDR1	SEQ ID NO.	CDR2	SEQ ID NO.	CDR3	SEQ ID NO.
1A5	GGATTACCTTTAG CAGCTATGCC	293	ATTAGTGGTAG TGGTGGTAGCA CA	310	GCGAAAGATTAC TTCAGGTGGTTA	327
1A8	GGTGTCTCCATCAG CAGTAGAAGTGACC AC	294	ATCTCTTATAG TGGGAGCACC	311	GCGAGACTCGCT TCCCTTTATTCT ACTTTTGATATC	328
1B2	GGATACACCTTCAC CAGCTACTAT	295	ATCAACCCTAG TGGTGGTAGCA CA	312	GCGACTGGGGAG ATGGCAGGGGAT TTTGACTAC	329
1B11	GGAGGCACCTTCAG CAGCTATGCT	296	ATCATCCCTAT CTTTGGTACAG CA	313	GCGAGAGACAAC CCCGGTATAGC AGCAGCTGGTCC CCCAACTGGTTC GACCCC	330
1C2	GGATACACCTTCAC CAGCTACTAT	295	ATCAACCCTAG TGGTGGTAGCA CA	312	GCGAGCTCTTCG GCTGGTACGTTC TACTTTGACTAC	331
1C3	GGATACCCCTTCAG CACTTACTAT	297	ATCGACCCTAG TGGTGGTAGCA CA	314	GCGAGAGTTGCC GAGCAACACCTG	332

					GACTACTACTTT GACTAC	
1D12	GGAGGCACCTTCAG CAGCTATGCT	296	ATCAGCGCTTA CAATGGTAACA CA	315	GCGAGGCTTGAG TGGCTACGTGGT GCTTTTGATATC	333
1E5	GGAGGCACCTTCAG CAGCTATGCT	296	ATCATCCCTAT CTTTGGTACAG CA	313	GCGAGAGCGTTA GTCGGAAAGTGG TTATTACTACGG GGCTTTGACTAC	334
1F4	GGGGACAGTGTCTC TAGCAACAGTGCTG CT	298	ACATACTACAG GTCCAAGTGGT ATAAT	316	GCAAGAGAAAAG GGCATCGAAGGG CCTGCGTTCGAC CCC	335
1H7	GGTGGGTCCTTCAG TGGTTACTAC	299	ATCAATCATAG TGGAAGCACC	317	GCGAGAGGGAGG TGGCTGCGGGGT GCTTTTGATATC	336
2C9	GGAGGCACCTTCAG CAGCTATGCT	296	ATCATCCCTAT CCTTGGTATAG CA	318	GCGAGACATGGG GGGGTGGGAGCT ACTACGGGTAC TACTACATGGAC GTC	337
2C10	GGTGGGTCCTTCAG TGGTTACTAC	299	ATCAATTATAG AGGAAACACC	319	GCGAGATGGGAC GGTGGTAACCTC GTGGACCAC	338
2C12	GGATTACCTTCAG TAGCTATGCT	300	ATATCATATGA TGGAAGTAATA AA	320	GCGAGAGGGGGA CGATTCCACTAC TACTACTATGCC ATGGACGTC	339
2D3	GGAGGCACCTTCAG CAGCTATGCT	296	ATCATCCCTAT CTTTGGTACAG CA	313	GCGAGCAGTGGC TGGTTAAGGGGT GCTTTTGATATC	340
2G7	GGTGGGTCCTTCAG TGGTTACTAC	299	ATCAATCATAG TGGAAGCACC	317	GCGAGAGGGAAA TGGTTACGGGGT GCTTTTGATATC	341
2H4	GGATACACCTTCAG CGGCTACTAT	301	GTCAACCCTAA TAGTGGTGGCA CA	321	GCGAGAGGTGGC AGGCCCGGTTTA CCTGCAGCTGGC TATATTGACTAC	342
3A11	GGTTACACGTTTAG CACCTATGAT	302	ATCAGCACTTA CAATGGTGACA CA	322	GCGAGGGGAGAT AGCAGTGTCGGG TACGAATACTTC CAACAC	343
3C5	GGTGGGTCCTTAAG TGGTTACTAC	303	ATCAATCATAG TGGAAGCACC	317	GCGAGACGGTGG TGGCTACGAGGT GCTTTTGATATC	344
3D2, 3D11	GGTGGGTCCTTCAG TGGTTACTAC	299	ATCAATCATAG TGGAAGCACC	317	GCGAGACGGTGG TGGCTACGAGGT GCTTTTGATATC	344

3E9	GGTTACACCTTTAC CAGCTATGGT	304	ATCAGCGCTTA CAATGGTAACA CA	315	GCGAGAGGCATT ATTACTATGATA TCGGACTAC	345
3F1	GGATTACCTTCAG TAGCTATGGC	305	ATATCATATGA TGGAAGTAATA AA	320	GCGAGAGACGGT GGGGGAGGTATG GACGTC	346
3F11	GGTTACACCTTTAG CAGCTCTGGT	306	ATCAGCACTTA CAATGGTAACA CA	323	GCTACGAGTATA GCGGTGGCTGGT ATTGACTAC	347
3H7	GGATTACCTTCAG TAACTATGGC	307	ATATGGCATGA TGGAACCAATA AA	324	GTGAGAGATCAG GGGGCCGGTGTT TGGAATGGTTAT TCCTAC	348
3H11	GGATACACCTTCAC CAGCTACTAT	295	ATCAACCCTAG TGGTGGTAGCA CA	312	GCGAGCTCAGTA GTACCAGCTGCT ATTTACGACTAC TACTACGGTATG GACGTC	349
5A6	GGATTACCTTCAG TAGTTATGAA	308	ATATCATATGA TGGAAGCAATA AA	325	GCGAGACTGATT ACTATGGTTTCGG GGAGAGGACTAC	350
6F8	GGGTTACCGTCAG TAGCAACTAC	309	ATTTATAGCGG TGGTAGCACA	326	GCGAGAGACTAC GGTGACTATTAC TTTGACTAC	351

It will be appreciated by a person skilled in the art that other variations and/or modifications may be made to the embodiments disclosed herein without departing from the spirit or scope of the disclosure as broadly described. For example, in the description herein, features of different exemplary embodiments may be mixed, combined, interchanged, incorporated, adopted, modified, included etc. or the like across different exemplary embodiments. The present embodiments are, therefore, to be considered in all respects to be illustrative and not restrictive.

10

DETAILED DESCRIPTION OF FIGURES

Example embodiments of the disclosure will be better understood and readily apparent to one of ordinary skill in the art from the following discussions and if applicable, in conjunction with the figures. It should be appreciated that other modifications within the purview of the skilled person in the art may be made

15

without deviating from the scope of the invention. Example embodiments are not necessarily mutually exclusive as some may be combined with one or more embodiments to form new exemplary embodiments. The example embodiments should not be construed as limiting the scope of the disclosure.

5 FIG. 1 shows binding ELISA of supernatants of 27 Fab clones to the antigen protein of biotinylated RBD-mFc. The 27 Fab clones were tested in a binding ELISA assay to assess their antigen binding to biotinylated RBD with a mouse Fc tag and detected by goat-anti-human Fab-HRP. In this assay, the clones were tested with 70 μ l of 0.2 μ g/ml Biotinylated SARS-CoV-2 RBD_mFc,
10 total 14 ng per well.

 FIG. 2 shows blocking of spike RBD protein binding to ACE2-His by supernatants of 27 Fab clones. The 27 Fab clones were tested in an ELISA assay to assess their potency in blocking spike protein binding to the recombinant ACE2 protein (ACE2 with His tag), with an irrelevant Fab clones used as a negative
15 control. In this assay, the clones were tested with 100 μ l of 0.5 nM Biotinylated SARS-CoV-2 RBD_mFc, total 0.05 pmol per well.

 FIG. 3 shows binding ELISA of 19 IgGs to the antigen protein of biotinylated RBD-mFc. The 19 antibody clones were tested in a binding ELISA assay to assess their antigen binding to biotinylated RBD with a mouse Fc tag,
20 and detected by anti-human Fc-HRP, with an irrelevant IgG1 used as a negative control antibody. In this assay, the clones were tested with 70 μ l of 0.2 μ g/ml Biotinylated SARS-CoV-2 RBD_mFc, total 14 ng per well.

 FIG. 4 shows blocking of spike RBD protein binding to ACE2-Fc by 19 IgGs. The 19 antibody clones were tested in an ELISA assay to assess their
25 potency in blocking spike protein binding to the recombinant ACE2 protein (ACE2 with human Fc tag), with an irrelevant IgG used as a negative control antibody. In this assay, the clones were tested with 100 μ l of 0.5 nM Biotinylated SARS-CoV-2 RBD_mFc, total 0.05 pmol per well.

 FIG. 5 shows competition of RBD-binding between ACE2 and six IgGs by
30 Bio-Layer Interferometry assay. A weak blocking IgG clone 1C3 (black line) was included as a negative control.

FIG. 6 shows binding avidity of six IgGs to the RBD by Bio-Layer Interferometry assay. A range of IgG concentration from 12.5 nM to 0.39 nM (in 2-fold dilutions) are shown for each IgG. The sensorgrams are in grey lines and curve fittings are in black. Results shown are a representative of two independent experiments.

FIG. 7 shows binding avidity of six IgG antibodies to SARS-CoV-2 (circle) and SARS-CoV (triangle) spike RBD proteins tested by ELISA. The 6 antibody IgG clones 1F4, 2H4, 3D11, 3F11, 5A6 and 6F8 were tested in a binding ELISA assay to assess their antigen binding to biotinylated SARS-CoV-2 RBD with a mouse Fc tag as well as biotinylated SARS-CoV RBD with a His tag and detected by anti-human Fc-HRP. In this assay, the antibodies were tested with 70 µl of 0.2 µg/ml Biotinylated SARS-CoV-2 RBD_mFC, total 14 ng per well or 70 µl of 0.2 µg/ml Biotinylated SARS-CoV RBD_His, total 14 ng per well.

FIG. 8 shows epitope binding of 5A6 by Bio-Layer Interferometry (BLI) analysis. Buffer alone, an irrelevant antibody (AB) and 5A6 IgG were included as controls.

FIG. 9 shows binding affinity of five Fab clones to SARS-CoV-2 Spike RBD protein measured by Bio-Layer Interferometry. Fab binding to immobilized Fc-RBD was tested using a range of Fab concentrations from 100 nM to 3.125 nM (in 2-fold dilution). A representative set of measurements is shown with sensorgrams in grey and curve fittings in black.

FIG. 10 shows binding of the 6 IgG antibodies (solid lines) and 5A6 Fab (dashed line,) to the purified SARS-CoV-2 pseudovirus. In this assay, the antibodies were tested with 70 µl of 1 µg/ml of pseudoviral particles, total 70 ng per well.

FIG. 11 shows SARS-CoV-2 pseudotyped virus neutralization assay by 19 IgGs. The 19 antibody clones were tested in a pseudotyped virus neutralization assay to assess their potency in neutralizing pseudotyped virus entry to ACE2 expression cells.

FIG. 12 shows neutralization of the SARS-CoV-2 and SARS-CoV pseudotyped viruses by anti-SARS-CoV-2 spike RBD IgG and Fab antibodies. (A) Infection of CHO-ACE2 cells by SARS-CoV-2 pseudovirus were determined

in the presence of 1F4, 2H4, 3D11, 3F11, 5A6 and 6F8 IgG antibodies. (B) Infection of CHO-ACE2 cells by SARS-CoV pseudovirus were determined in the presence of 1F4, 2H4, 3D11, 3F11, 5A6 and 6F8 IgG antibodies. (C) Infection of CHO-ACE2 cells by SARS-CoV-2 pseudovirus were determined in the presence of 1F4, 2H4, 3D11, 3F11, and 5A6 Fab antibodies. (D) Infection of CHO-ACE2 cells by SARS-CoV pseudovirus were determined in the presence of 1F4, 2H4, 3D11, 3F11, and 5A6 Fab antibodies. Luciferase activities in the CHO-ACE2 cells were measured, and the percent neutralization was calculated. Data are presented as means $\pm$ SEM in triplicates and are representative of two independent experiments. The IC₅₀ values shown in (A) and (C) were calculated by a variable slope four parameter non-linear regression model without or with top and bottom constraints set at 100% and 0% respectively.

FIG. 13 shows binding avidity of 5A6 IgG (A) and 3D11 IgG (B) to the wildtype RBD and RBD mutants measured by biolayer interferometry. A range of 5A6 and 3D11 IgG concentrations from 12.5 nM to 0.39 nM (in 2-fold dilutions) are measured for each experiment. The sensorgrams are in grey lines and curve fittings are in black.

FIG. 14 shows neutralization of the SARS-CoV-2 pseudovirus with either wildtype (WT) or RBD mutations by 5A6 (A) and 3D11 (B) IgGs. Data are presented as means $\pm$ SEM in triplicates and are representative of two independent experiments.

FIG. 15 shows anti-SARS-CoV-2 Spike RBD IgG antibodies affect trypsin induced cell syncytia formation. Vero E6 cells were transfected with furin recognition mutation of SARS-CoV-2 S-protein (R682RAR to A682AAR)-GFP. After 48 hours, the cell culture medium was changed to DMEM (no serum) and treated with or without antibodies and incubated for 1 hour at 37°C. The cells were then treated with or without trypsin 15 μ g/ml for 2 hours at 37°C. Cells were fixed with 4%PFA and stained with DAPI. (A) 5A6 IgG (20 μ g/ml), 5A6 Fab (20 μ g/ml), 3D11 IgG (20 μ g/ml) and 2H4 IgG (10 μ g/ml) treated S-protein expressing Vero E6 cell images in 10x, 20x and 40x objective view. Images were taken by Olympus confocal microscope. (B) Dosage response of 5A6 IgG, 5A6 Fab, 3D11 IgG and 2H4 IgG. S-protein expressing Vero E6 were treated with 0, 0.1, 0.5, 2,

10 µg/ml of each antibody. 2×10^5 cells/sample were used for transfection of 5A6 IgG dosage response. 1.6×10^5 cells/sample were used for transfection of 5A6 Fab, 2H4 IgG and 3D11 IgG. Data quantification were calculated on syncytia numbers and nuclei number presented in each syncytium.

5 FIG. 16 shows the amino acid sequences of the antibodies as described herein. CDRs are shaded and identified consecutively as CDR1 (first shaded region), CDR2 (second shaded region), and CDR3 (third shaded region).

 FIG. 17 shows the nucleotide sequences of the antibodies as described herein. CDRs are shaded and identified consecutively as CDR1 (first shaded
10 region), CDR2 (second shaded region), and CDR3 (third shaded region).

EXPERIMENTAL SECTION

 A newly identified novel coronavirus (SARS-CoV-2) is causing
15 pneumonia-associated respiratory syndrome across the world. Epidemiology, genomics, and pathogenesis of the SARS-CoV-2 show high homology with that of SARS-CoV. Current efforts are focusing on development of therapeutic agents for the treatment of coronavirus disease 2019 (COVID-19).

 Like SARS-CoV, SARS-CoV-2 also uses the angiotensin converting
20 enzyme II (ACE2) as the cell entry receptor. During infection, the spike glycoprotein on coronavirus envelope is responsible for host cell attachment, receptor binding, and for mediating host cell membrane and viral membrane fusion. The spike protein contains an amino-terminal S1 unit and a carboxyl-terminal S2 subunit. The receptor binding domain (RBD) within the S1 subunit of
25 SARS-CoV-2, which mediates the virus binding to ACE2, is believed to be critical in mediating virus entry into the infected cells. Hence, there is a need to develop therapeutic neutralizing antibodies which can potently bind to RBD of SARS-CoV-2 spike protein and therefore, to prevent infection by blocking the live viral particles from entering the susceptible cells expressing ACE2.

30 Nucleotide and amino acid sequences for 27 fully human monoclonal antibodies, derivatives thereof, or antigen-binding portions thereof disclosed herein, are able to specifically target/bind SARS-CoV-2 spike protein RBD and

mediate neutralization of virus entry into cells and hence block viral infections. Namely, the antibodies are 1A5, 1A8, 1B2, 1B11, 1C2, 1C3, 1D12, 1E5, 1F4, 1H7, 2C9, 2C10, 2C12, 2D3, 2G7, 2H4, 3A11, 3C5, 3D2, 3D11, 3E9, 3F1, 3F11, 3H7, 3H11, 5A6, and 6F8. The antibodies, derivatives thereof, or antigen-binding
5 portions thereof disclosed herein are able to specifically target/bind SARS-CoV-2 spike protein RBD both in solution and on the surface of the pseudotyped virus.

Materials and Methods for converting Fab sequences to IgG antibodies and production of IgG antibodies

10 Fabs were reformatted into human IgG in the pTT5 vector (National Research Council of Canada) by using In-Fusion HD Cloning kit (Takara Bio) and the IgG antibodies were expressed using ExpiCHO expression system (Thermo Fisher Scientific) by transient co-transfection of plasmids expressing the heavy and light chain of each antibody clone. Eight days after transfection, ExpiCHO-S
15 cell suspension was centrifuged for 10 min at 2000 rpm and filtered with 0.22 µm filter to remove the cells and debris. Antibodies were then purified from the culture supernatant using Protein G Agarose (Merck Millipore, Cat#16-266) following the manufacturer's instructions. After elution, the purified antibodies were dialyzed at 4°C for 4-20 hours against 1x PBS, for 3 times and concentrated to 1-2 mg/ml
20 using 10MWCO Vivaspin 20 (Sartorius, Cat#VS2001).

Antibodies characterisation and tests

Recombinant SARS-CoV-2 spike protein RBD domain with a mouse Fc tag (RBD-mFc) was used to isolate binders from a library of Fab sequences
25 constructed by SIgN, using phage display technology. Out of 570 clones screened, 48 clones showing the positive Fab supernatant binding signals to RBD-mFc and potent antigen-receptor (RBD-ACE2) blocking were sequenced and 27 unique sequences were identified: 1A5, 1A8, 1B2, 1B11, 1C2, 1C3, 1D12, 1E5, 1F4, 1H7, 2C9, 2C10, 2C12, 2D3, 2G7, 2H4, 3A11, 3C5, 3D2, 3D11, 3E9,
30 3F1, 3F11, 3H7, 3H11, 5A6, and 6F8 (FIG. 16, FIG. 17). The results of binding ELISA and antigen-receptor blocking ELISA using Fab supernatants for the 27 unique clones were shown in FIG. 1 and FIG. 2, respectively.

Out of 27 unique clones, 19 clones were selected and cloned into IgG1 format for further characterisation: 1A8, 1B11, 1C2, 1C3, 1E5, 1F4, 2C12, 2H4, 3A11, 3C5, 3D2, 3D11, 3E9, 3F1, 3F11, 3H7, 3H11, 5A6, and 6F8.

The 19 antibody clones were tested in ELISA against biotinylated recombinant SARS-CoV-2 spike protein RBD-mFc to assess binding avidity for the target, with an irrelevant IgG1 used as a negative control antibody. In brief, neutravidin was coated at 5µg/ml onto the 96-well ELISA plates in coating buffer overnight at 4°C. After blocking with casein for 2 hours, biotinylated antigen of spike protein RBD-mFc at 0.2 µg/ml was added to the plates and captured by neutravidin during 1-hour incubation at room temperature. After washing with 0.05% PBST for 5 times, 19 antibody IgGs were added at different concentrations with 3 times dilutions and incubated for 1 hour. The wells were then washed again with PBST, followed by addition of HRP conjugated anti-human Fc (1:3000). The results showed dose dependent antigen binding of all 19 IgG clones (FIG. 3).

Next, the 19 antibody clones were tested in an ELISA to assess their abilities in blocking spike protein RBD binding to human ACE2 protein. In brief, the recombinant human ACE2 protein with human Fc tag (ACE2-Fc) was coated onto the 96-well ELISA plates in coating buffer overnight at 4°C and blocked in casein. Then different concentrations of IgGs with 3 times dilutions were pre-incubated with 0.5nM biotinylated spike protein RBD-mFc for 1 hour at room temperature before they were added to the ELISA plates coated with ACE2-Fc. After 1-hour incubation, the wells were washed with 0.05% PBST for 5 times and HRP conjugated goat-anti-mouse antibody was added at a dilution of 1:3000. The results in FIG. 4 showed dose dependent blocking of antigen-receptor binding by most IgG1 clones except for 1C3. Out of 18 clones showing capacities of blocking, 5A6 stands out as the most potent clones with a IC50 of 0.3 nM.

Out of the 19 IgGs, 6 antibody clones 1F4, 2H4, 3D11, 3F11, 5A6 and 6F8 also showed potent blocking (FIG. 5) and strong binding avidity (FIG. 6) as measured by the Bio-Layer Interferometry (BLI) assay, and hence were chosen for further detailed characterizations.

To test if any of these six antibody clones cross-react with SARS-CoV RBD, an avidity binding ELISA was performed for both SARS-CoV-2 and SARS-

CoV RBD proteins. Interestingly, only 3D11 was able to cross react with SARS-CoV spike RBD, although the binding was much weaker (FIG. 7). The data suggested that 3D11 recognized a distinct epitope that is different from the other 5 antibodies and is conserved between SARS-CoV-2 and SARS-CoV. Indeed, stepwise binding assay by BLI confirmed that 5A6 and 3D11 had non-overlapping footprints on the RBD while 5A6 shared overlapping epitopes with the other 4 antibodies (FIG. 8).

The present inventors also produced Fab antibodies for clone 1F4, 2H4, 3D11, 3F11 and 5A6 and measured their binding affinity to SARS-CoV-2 spike RBD protein by BLI (FIG. 9). A comparison of K_D of Fab binding (affinity) and apparent K_D of IgG binding (avidity) was also compared and shown in Table 9.

Table 9. K_D of Fab and apparent K_D of IgG measured by Bio-Layer Interferometry (BLI).

Clone ID	K_D (M) of Fab	Apparent K_D (M) of IgG
1F4	$8.02 \pm 1.09 \times 10^{-8}$	$<1 \times 10^{-12}$
2H4	$4.72 \pm 0.91 \times 10^{-8}$	$1.39 \pm 0.09 \times 10^{-10}$
3D11	$1.64 \pm 0.06 \times 10^{-9}$	$<1 \times 10^{-12}$
3F11	$1.20 \pm 0.07 \times 10^{-7}$	$2.73 \pm 2.21 \times 10^{-10}$
5A6	$7.61 \pm 0.07 \times 10^{-9}$	$1.73 \pm 0.47 \times 10^{-10}$
6F8	Not measured	$4.76 \pm 0.89 \times 10^{-10}$

K_D of Fab based on 1:1 Langmuir fitting and apparent K_D of IgG based on 1:2 bivalent analyte fitting of BLI sensorgrams for immobilized Fc-RBD. Values are the Mean $\pm$ SD of two independent experiments

Next, the SARS-CoV-2 pseudotyped virus was purified by gradient centrifugation and immobilized the viral particles on the ELISA plates to test if the antibodies as disclosed herein also bind efficiently to the natural RBD displayed on the viral surface. Concentration-dependent binding curves of the 5 IgG clones (1F4, 2H4, 3D11, 3F11, and 5A6) revealed that 5A6 was packed on the viral surface at a much higher density than the other 4 antibodies and 5A6 Fab antibody, as shown by the higher optical signal (FIG. 10).

SARS-CoV-2 pseudotyped virus neutralization assay

The present disclosure tested the function of the 19 IgG antibody clones in neutralizing a pseudotyped virus particles expressing the spike protein of SARS-CoV-2. Briefly, serially diluted IgG antibodies were pre-incubated with an equal volume of pseudotyped virus (12 ng equivalent of p24) for 1 hour before the mixture was added to the monolayer of pre-seeded CHO-ACE2 cells. After 1 hour of pseudotyped virus infection, culture medium was topped up for further incubation of cells for another 48 hours. Then the cells were washed with PBS and lysed in Passive Lysis Buffer and the luciferase assay was performed using the Luciferase Assay System (Promega). The luciferase reading corresponds to the amount of entry of pseudotyped virus particles into the susceptible cells. The results showed that clone 1F4, 5A6, 3F11, 2H4 could potentially neutralize the cell entry of pseudotyped virus (FIG. 11). Next, a neutralization assay using both SARS-CoV-2 and SARS-CoV pseudotyped virus was performed with the 6 IgG clones 1F4, 2H4, 3D11, 3F11, 5A6 and 6F8. All 6 antibodies showed dose-response neutralization (FIG. 12A). 5A6 strongly neutralized the SARS-CoV-2 pseudovirus with an IC_{50} of 75.5 ng/ml, followed by 1F4 (108 ng/ml), 2H4 (109 ng/ml), 6F8 (428.3 ng/ml), and 3F11 (930.4 ng/ml). Interestingly, while 3D11 neutralized SARS-CoV-2 pseudovirus, the neutralization did not follow the typical sigmoidal dose response, suggesting a unique mechanism of inhibition. Consistent with the binding results, none of these antibodies showed significant neutralization to the SARS-CoV pseudotyped virus (FIG. 12B), suggesting high specificity of the antibodies as disclosed herein to the SARS-CoV-2. Interestingly, although 3D11 was able to bind weakly to the SARS-CoV RBD (FIG. 7), it was unable to neutralize the SARS-CoV pseudotyped virus to a significant extent. In addition, neutralization potency of both SARS-CoV-2 and SARS-CoV pseudotyped virus was also performed in the presence of 5 Fab clones 1F4, 2H4, 3D11, 3F11 and 5A6 (FIG. 12C and 12D).

Sensitivity of 5A6 and 3D11 to RBD mutations

Of more than 40,000 SARS-CoV-2 genomes sequenced, mutations that resulted in amino acid changes in 6 positions at or near the ACE2 interface have

been isolated. These include **N439K** in 246 samples (244 Scottish, 1 England, 1 Romania), **V483A** in 30 samples (26 USA/WA, 2 USA/UN, 1 USA/CT, 1 England), **G476S** in 18 samples (13 USA/WA, 2 USA/OR, 1 USA/ID, 1 USA/CT, 1 Belgium), **S494P** in 7 samples (3 USA/MI, 1 England, 1 Spain, 1 India, 1 Sweden), **V483I** in 2 English samples, and **L455I together with F456V** in one Brazilian sample.

To determine if any of these mutant viruses could escape neutralization by 5A6 or 3D11, the recombinant mutant RBD proteins were produced to determine changes in binding avidity. 5A6 IgG had a 4-fold reduction in binding avidity to the V483A mutation while insensitive to the other 5 mutations (FIG. 13A). Consistent with the binding results, 5A6 significantly lost neutralizing capacity against the V483A mutant pseudovirus. However, 5A6 largely retains activity against the other variants, including the D614G mutation that has spread at an alarming rate and become the dominant pandemic strain with a global frequency of 70.5% (GISAID), since its first identification in Europe in March 2020 (FIG. 14A). Interestingly, 3D11 binding was not affected by any of these mutations (FIG. 13B), but its neutralizing potency against the D614G mutant was partially reduced (FIG. 14B). The difference between the activity profiles of 5A6 and 3D11 could be explained by the different epitopes recognized by each antibody (FIG. 8). Hence, 3D11 could potentially rescue the loss of potency by 5A6 in neutralizing mutant virus strain bearing V483A mutation, when these two antibodies are used as a combination.

5A6 IgG blocks cell-cell fusion

Using a trypsin-triggered cell-cell fusion assay, the impact of the anti-SARS-CoV-2 spike RBD antibodies on syncytia formation was assayed. The 5A6 IgG has an inhibitory effect on syncytia in a dose dependent manner (FIG. 15B), by contrast 2H4 IgG has no significant effect. Surprisingly, 3D11 potentiates cell-cell fusion. Furthermore, 5A6 Fabs also enhanced syncytial fusion, albeit weakly (FIG. 15A). Thus, it was concluded that 5A6 IgG directly inhibits Spike-mediated fusion, while other receptor blocking antibodies fail to inhibit or even accelerate this process. This observation also suggests that the 5A6 epitope and its binding mode combine efficient receptor blockade and cooperative, avid binding with

conformational trapping of the pre-fusion state, prohibiting the post-fusion transition and preventing both targeted viral fusion and cell-cell fusion mediated by spike protein.