

CLAIMS

1. An isolated antigen-binding protein that is capable of binding to and/or neutralizing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
2. The antigen-binding protein according claim 1, wherein 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.
3. The antigen-binding protein according to claim 1 or claim 2, the antigen-binding protein comprising 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.
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4. The antigen-binding protein according to any one of the preceding claims, wherein the antigen-binding protein does not cross-react with severe acute respiratory syndrome coronavirus (SARS-CoV).
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5. The antigen-binding protein according to any one of claims 1-3, wherein the antigen-binding protein is capable of binding to SARS-CoV.
6. The antigen-binding protein according to any one of the preceding claims, the antigen-binding protein comprising a monoclonal antigen-binding protein.
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7. The antigen-binding protein according to any one of the preceding claims, the antigen-binding protein comprising a fully human antigen-binding protein.
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8. The antigen-binding protein according to any one of claims 1-7, wherein the antigen-binding protein comprises an IgG-like structure.
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9. The antigen-binding protein according to any one of claims 1-7, wherein the antigen-binding protein comprises a Fab fragment.
10. The antigen-binding protein according any one of the preceding claims, wherein 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
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5 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 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.

10 11. The antigen-binding protein according any one of the preceding claims, the antigen-binding protein being capable of inhibiting virus-cell fusion and/or cell-cell fusion mediated by SARS-CoV-2.

12. The antigen-binding protein according to any one of the preceding claims, comprising:

15 a light-chain complementarity determining region 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;

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

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

25 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.

30 13. The antigen-binding protein according to any one of the preceding claims, comprising the following CDR sequences:

1A5

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

1A8

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

1B2

light-chain CDR1: GGRIATNY (SEQ ID NO: 30)
light-chain CDR2: EDN (SEQ ID NO: 51)
20 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);

1B11

25 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: IIPIFGTA (SEQ ID NO: 136)

heavy-chain CDR3: ARDNPGYSSSWSPNWFDP (SEQ ID NO: 152);

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1C2

light-chain CDR1: QSLHNSNGFTY (SEQ ID NO: 32)

light-chain CDR2: LGS (SEQ ID NO: 53)

light-chain CDR3: MQGIQTPLT (SEQ ID NO: 69)

10 heavy-chain CDR1: GYTFTSY (SEQ ID NO: 119)

heavy-chain CDR2: INPSGGST (SEQ ID NO: 135)

heavy-chain CDR3: ASSSAGTFYFDY (SEQ ID NO: 153);

1C3

15 light-chain CDR1: SGSIASYY (SEQ ID NO: 33)

light-chain CDR2: EDD (SEQ ID NO: 54)

light-chain CDR3: QSFDSIQHV (SEQ ID NO: 70)

heavy-chain CDR1: GYPFSTYY (SEQ ID NO: 121)

heavy-chain CDR2: IDPSGGST (SEQ ID NO: 137)

20 heavy-chain CDR3: ARVAEQHLDYYFDY (SEQ ID NO: 154);

1D12

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

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

25 light-chain CDR3: QSYDGSWV (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);

1E5

light-chain CDR1: SGRIASNY (SEQ ID NO: 35)

light-chain CDR2: EDT (SEQ ID NO: 55)

5 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)

15 heavy-chain CDR2: TYYRSKWYN (SEQ ID NO: 139)

heavy-chain CDR3: AREKGIEGPAFDP (SEQ ID NO: 157);

1H7

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

20 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);

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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);

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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);

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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);

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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);

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

2H4

- 10 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)
15 heavy-chain CDR3: ARGGRPGLPAAGYIDY (SEQ ID NO: 164);

3A11

- light-chain CDR1: SSDVGTYNY (SEQ ID NO: 42)
light-chain CDR2: DVS (SEQ ID NO: 61)
20 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);

25 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: 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)

10 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)

15 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: ARRWLRLGAFDI (SEQ ID NO: 166);

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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)

25 heavy-chain CDR1: GYTFTSYG (SEQ ID NO: 127)

heavy-chain CDR2: ISAYNGNT (SEQ ID NO: 138)

heavy-chain CDR3: ARGITMISDY (SEQ ID NO: 167);

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)
5 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

- 10 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)
15 heavy-chain CDR3: ATSIAGAGIDY (SEQ ID NO: 169);

3H7

- light-chain CDR1: TDSIASNY (SEQ ID NO: 47)
light-chain CDR2: EDN (SEQ ID NO: 51)
20 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);

25 3H11

- 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)

heavy-chain CDR3: ASSVVPAAIYDYYYGMDV (SEQ ID NO: 171);

5 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)

10 heavy-chain CDR2: ISYDGSNK (SEQ ID NO: 143)

heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172);

6F8

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

15 light-chain CDR2: DAS (SEQ ID NO: 64)

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

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conservative sequence variants thereof.

14. The antigen-binding protein according to any one of the preceding claims,
comprising a light-chain variable region comprising any one of SEQ ID NO:
25 1-27 or a sequence sharing 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.

15.A combination of two antigen-binding proteins, wherein a first antigen-binding protein comprises the following CDR sequences:

5A6

5 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)
10 heavy-chain CDR3: ARLITMVRGEDY (SEQ ID NO: 172)

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

15 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)
heavy-chain CDR1: GGSFSGYY (SEQ ID NO: 123)
20 heavy-chain CDR2: INHSGST (SEQ ID NO: 140)
heavy-chain CDR3: ARWWLARGAFDI (SEQ ID NO: 166).

16.A pharmaceutical composition comprising the antigen-binding protein according to any one of claims 1-14 or the combination according to claim 25 15, and a pharmaceutically acceptable carrier.

17.The antigen-binding protein according to any one of claims 1-14, the combination according to claim 15 or the pharmaceutical composition according to claim 16, for use in therapy, or as a diagnostic agent.

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18. A nucleotide sequence encoding for the antigen-binding protein according to any one of claims 1-14 or the combination according to claim 15.
19. The nucleotide sequence according to claim 18, wherein the nucleotide
5 sequence comprises one of more of SEQ ID NO: 174-351 or a sequence sharing at least about 75% sequence identity thereto.
20. A bacteriophage, a host cell or a non-human organism comprising the nucleotide sequence according to claim 18 or claim 19.
- 10 21. A method of treating SARS-CoV-2 in a subject, the method comprising administering to the subject the antigen-binding protein according to any one of claims 1-14, the combination according to claim 15 or the pharmaceutical composition according to claim 16.
- 15 22. The method according to claim 21, wherein where the SARS-CoV-2 comprises a V483A mutation, the method comprises administering to the subject the combination according to claim 15.
- 20 23. A method of detecting the presence of SARS-CoV-2 in a sample, the method comprising:
contacting the sample with the antigen-binding protein according to any one of claims 1-14;
detecting a binding event involving the antigen-binding protein;
25 wherein the detection of a binding event is indicative of the presence of SARS-CoV-2 in the sample.