

TITLE OF INVENTION: PROTEIN ANTIGEN-BINDING MOLECULES

REFERENCE TO RELATED APPLICATIONS

5 [0001] This application claims the priority to Singapore patent application No. 10202105095U, filed on 15 May 2021; Singapore patent application No. 10202107013P, filed on 25 June 2021; and Singapore patent application No. 10202204610V, filed on 28 April 2022, the contents of which are incorporated herein by reference.

TECHNICAL FIELD

10 [0002] The present disclosure relates generally to molecules such as protein antigen-binding molecules suitable for use in treatment or prevention of coronaviral infection particularly SARS related beta coronaviruses (sarbecovirus).

BACKGROUND

15 [0003] The following discussion of the background to the invention is intended to facilitate an understanding of the present invention only. It should be appreciated that the discussion is not an acknowledgement or admission that any of the material referred to was published, known or part of the common general knowledge of the person skilled in the art in any jurisdiction as at the priority date of the invention.

20 [0004] Emerging zoonotic viruses have become a major threat to public health and world economy in the last two decades as the world underwent three major human infectious disease pandemics caused by coronaviruses (CoVs). The three major human infectious disease pandemics caused by coronaviruses (CoVs) include SARS in 2002 - 2003 caused by SARS-CoV (Peiris *et al.* Nat Med 2004, 10:S88-97), MERS since 2012 (Zaki *et al.* N Engl J Med 2012, 367:1814-1820) and ongoing COVID-19 caused by SARS-CoV-2 (Wang *et al.* Lancet 2020, 395:470-473). All of them caused devastating economic and human losses globally. For SARS and MERS, we still don't have a licensed treatment or prevention against future infections by these viruses. For COVID-19, the unprecedented speed of vaccine development has resulted in many licensed vaccines for human use (Fauci Science 2021, 30 372:109).

[0005] There are a large number of CoVs present in wildlife reservoir animals, especially in bats. There is a high chance of future outbreaks (SARS3, SARS4, etc) caused by different, but related CoVs. The current classification of CoVs is shown in Figure 1. Four genera (alpha,

beta, delta and gamma) have been identified and the most at-risk viruses for human infection are all from genus *Betacoronavirus* (Nat Microbiol 2020, 5:536-544), particularly those from the sub-genus *Sarbecovirus*. Sarbecoviruses are the most transmissible coronaviruses in humans, possibly because they all use the human angiotensinogen converting enzyme 2 (ACE2) receptor as entry into human cells. There are hundreds of strains of SARS-related coronaviruses (SARSr-CoVs) known only to infect non-human species; bats are a major reservoir of many strains of SARS-related coronaviruses. There are two major clades of sarbecoviruses. Clade 1a includes SARS-CoV related CoVs (SC2r-CoV) and clade 1b contains SARS-CoV-2 related CoVs (SC2r-CoV). The sarbecoviruses include SARS-CoV, SC1r-CoV WIV-1, SC1r-CoV RsSHC014, SARS-CoV-2, SARS-CoV-2 B.1.1.7 (Alpha), SARS-CoV-2 B.1.351 (Beta), SARS-CoV-2 B.1.617.2 (delta), SC2r-CoV GD-1, GX-P5L and SC2r-CoV RaTG13. Studies have shown there is limited cross neutralization between SARS-CoV and SARS-CoV-2 (Yang R, et al. EBioMedicine 2020, 58:102890).

[0006] In pandemic preparedness and responses, there is a need for a multi-prong approach to combat emerging zoonotic viruses which includes vaccines, therapeutic monoclonal antibodies and small molecular drugs. For SARS-CoV-2, the first countermeasure commercial product which received FDA Emergency Use Approval (EUA) was therapeutic monoclonal antibodies (mAbs) derived from COVID-19 patients. Both antibody and T-cell immunity are important for controlling viral infections such as SARS-CoV-2 or other sarbecoviral infections. In comparison, Neutralizing antibodies (Nabs) are more important to prevent virus entry and hence initial infection whereas T-cell immunity will kick in later in the infection to reduce or control disease progression. Nabs can be induced either through infection or vaccination. Passive immunization using therapeutic mAbs remains an important part of pandemic response and containment as they can play a key role in treating severe patients, especially in the vulnerable populations (such as immunocompromised patients) or preventing onward transmission by ring-fence application in targeted high-risk populations. Unfortunately, the first generation of therapeutic mAbs for COVID-19 has proven to be less or non-effective for the newly emergent variants of concern (VOC).

[0007] The recent emergence of SARS-CoV-2 variants, the Alpha COVID-19 variant SARS-CoV-2 B.1.1.7; the Beta COVID-19 variant SARS-CoV-2 B.1.351 also known as 20H/501Y.V2, or 501Y.V2 variant; the Gamma variant P.1., the Delta SARS-CoV-2 B.1.617.2; and the Omicron variants SARS-CoV-2 B.1.1.529 BA.1 and BA.2 and the observed reduction of immune protection against new variants from vaccines based on the original virus strain raised a new challenge on the need for a broad-spectrum treatment or prevention against all known and future SARS-CoV-2 variants. Other coronaviruses are

known to be circulating in wildlife reservoirs such as the SC2r-CoV GD-1 and SC2r-CoV GX-P5L in pangolin and the SC2r-CoV RaTG13, SC1r-CoV WIV-1 and SC1r-CoV RsSHC014 in bats giving rise to a chance of future outbreaks (SARS3, SARS4, etc) caused by different, but related coronaviruses.

- 5 **[0008]** Most SARS-CoV-2 vaccines that are currently licensed for use in humans were developed against the S protein of the ancestral strain first identified in Wuhan. The emergence and dominance of VOCs have posed a significant threat and challenge as some of them, especially VOC Omicron, have evolved to escape immunity mainly through evasion of NABs in either infected or vaccinated individuals regardless of the type of vaccines and
10 even in individuals who have received booster vaccinations or hybrid immunity derived from infection and vaccination.

- [0009]** There exists a need to develop a molecule for use in treatment or prevention of human infection caused by sarbecoviruses and alleviate at least one of the aforementioned problems.

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SUMMARY

- [0010]** Protein antigen-binding molecules such as monoclonal antibodies, nucleic acid, expression vector, cell or composition suitable for broad spectrum pan-sarbecovirus for use in treatment or prevention of coronaviral infection caused by sarbecoviruses is envisaged.

- 20 **[0011]** Accordingly, an aspect of the invention refers to an antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

- 25 HC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO:1 or SEQ ID No. 111

HC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO:2 or SEQ ID No. 112

HC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:3 or SEQ ID No. 113; and

- 30 (ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID No. 114

LC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO: 5 or SEQ ID No. 115

LC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:6 or SEQ ID No. 116.

- 5 **[0012]** Another aspect of the invention refers to an antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid having formula I: $X_1-X_2-X_3-\Phi-X_4-X_{n1}-X_5-X_6$:

- 10 wherein X_1 is selected from one of G and E;

X_2 is selected from one of F, Y, N, G, D, and V;

X_3 is selected from one of P, T, S, I and F;

Φ is selected from one of F, V, L, and I;

X_4 is selected from one of S, T, R, N, G, L, and I;

- 15 X_{n1} is selected from one of S, SN, N, M, H, T, G, P, G and D;

X_5 is selected from one of Y, S, N, I and H;

X_6 is selected from one of Y, G, W, E, A, N, and T;

HC-CDR2 having the amino acid formula II: $X_7-X_8-X_9-X_{n2}-\pi-X_{n3}-X_{10}$.

wherein X_7 is selected from one of I and T;

- 20 X_8 is selected from one of Y, S, N, G, A and T;

X_9 is selected from one of S, F, P, N, H, I, Y, G, and T;

X_{n2} is selected from one of G, YN, DD, T, NG, DG, S, SS, D, ST, and NT;

π is selected from one of G, S, P, A and E;

X_{n3} is selected from one of S, I, D, G, F, N, RT, L, and RN;

- 25 X_{10} is selected from one of T, R, M, K, S, and P;

HC-CDR3 having the amino acid having formula III: $\Psi-\zeta_1-X_{n4}-X_{11}-X_{n5}-X_{12}-$

$X_{13}-X_{14}-\zeta_2-X_{15}$;

wherein Ψ is selected from one of A and V,

ζ_1 is selected from one of R, T, K and L-N

- 30 X_{n4} is selected from one of E, HLGGG, GGG, LDIII, DSI, GEAG, RVAIF, LQNG, VTYTS, ADIV, DSLA, DSL, AISQQ, DYYDN, DPL, EGIQG, and DGG;

X_{11} is selected from one of L, S, Y, T, A, N, V, and W;

X_{n5} is selected from one of R, S, LET, P, SAT, MATIWW, DGY, SY, PLPF, GS, VV, SVT, FDS, GYYY, EGAAS, V, and QLPY;

X_{12} is selected from one of H, W, G, P, T, S, N, and Y;

5 X_{13} is selected from one of Y, P, A, L, S, F, I, V, and G;

X_{14} is selected from one of F, I, N, Y, L, and M;

ζ_2 is selected from one of D, E, G, and S;

X_{15} is selected from one of Y, S, L, N, H, C, V, and F;

and

10 (ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having formula IV: $X_{16}-X_{17}-X_{18}-X_{n6}-\zeta_3-X_{19}$:

wherein X_{16} is selected from one of Q and Y;

X_{17} is selected from one of G, S, T, N, I, and A;

X_{18} is selected from one of V, I, T, F and L;

15 X_{n6} is selected from one of S, G, N, V, R, LYSSNNK, LYRSNNK, LQNNGY, VQSNGY, VHSDGN, MQLNGY and SS;

ζ_3 is selected from one of S, N, and T;

X_{19} is selected from one of W, Y, S and N;

LC-CDR2 having the amino acid having formula V: $X_{20}-X_{21}-S$:

20 wherein X_{20} is selected from one of A, W, K, T, G, L, and D;

X_{21} is selected from one of A, S, G, I, and T

LC-CDR3 having the amino acid having formula VI: $X_{22}-\zeta_4-X_{23}-X_{n7}-\zeta_5-X_{24}-X_{25}-X_{n8}-\zeta_6$:

wherein X_{22} is selected from one of Q, H, and M;

25 ζ_4 is selected from one of Q and H;

X_{23} is selected from one of Y, S, G, A, L, and T;

X_{n7} is selected from one of F, Y, N, S, L, G, T, YR, and YI;

ζ_5 is selected from one of S, T, N, Q, and D;

X_{24} is selected from one of S, Y, T, D, H, F, P, W, and I;

30 X_{25} is selected from one of P, I, and R;

X_{n8} is selected from one of F, W, K, G, Y, R, P, L, PY, EY, ED, GY, QY, and QI;

ζ_6 is selected from one of T and S.

[0013] According to another aspect there is a nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding the antigen-binding molecule as discussed herein above.

[0014] According to another aspect there is an expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids as discussed
5 herein above.

[0015] According to another aspect there is a method for producing an antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus, comprising culturing a cell capable of expressing the antigen binding molecule as discussed herein above under conditions suitable for expression of an antigen-binding
10 molecule by the cell.

[0016] According to another aspect there is a composition comprising an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein above, an expression vector or a plurality of expression vectors as discussed herein above, and a pharmaceutically acceptable carrier, diluent, excipient or
15 adjuvant.

[0017] According to another aspect there is an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein above, an expression vector or a plurality of expression vectors as discussed herein above, or a composition as discussed herein above, for use in treatment or prevention of a disease
20 caused by infection with a sarbecovirus.

[0018] According to another aspect there is use of an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein above, an expression vector or a plurality of expression vectors as discussed herein above, or a composition as discussed herein above, in the manufacture of a medicament for use in
25 treatment or prevention of a disease caused by infection with a sarbecovirus.

[0019] According to another aspect there is a method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically effective amount of an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein
30 above, an expression vector or a plurality of expression vectors as discussed herein above, or a composition as discussed herein above.

[0020] According to another aspect there is use of an antigen-binding molecule as discussed herein above to inhibit infection of ACE2-expressing cells by a sarbecovirus.

[0021] Other aspects and features of the present invention will become apparent to those of ordinary skill in the art upon review of the following description of specific embodiments of the invention in conjunction with the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] In the figures, which illustrate, by way of non-limiting examples only, embodiments of the present invention,

[0023] **[Fig. 1]:** Family tree of four known coronavirus genera.

[0024] **[Fig. 2]: A)** Multiplex sVNT on the Luminex platform. **B)** As shown, all six RBD proteins are able to bind the hACE2 receptor molecular as expected in the following order (from high to low affinity): SARS-CoV-2 B.1.351 > SARS-CoV-2 B.1.1.7 = SC2r-CoV GX-P5L (pangolin) > SARS-CoV-2 > SARS-CoV > SC2r-CoV RaTG13 (bat).

[0025] **[Fig. 3]:** Multiplex sVNT analysis from five panels of human sera (indicated above) against ten different sarbecoviruses. All sera were used at 1:20. A cut-off of 30% was set as previously determined. A cut-off of 30% was set as previously determined.

[0026] **[Fig. 4]:** Titration of NAbS expressed in NT50 using the same serum panels and viruses as in A. Samples were tested at dilutions from 1:20 to 1:20,480 using a 4-fold serial titration. A cut-off of 1:100 was set as previously determined.

[0027] **[Fig. 5].** Converting the non-dominant cross-neutralizing antibody responses to immune dominant ones by cross-immunization with genetically distant sarbecovirus antigen(s)

[0028] **[Fig. 6]:** Inhibition of pan-sarbecovirus mAb-RBD interaction by different human serum panels. **(A)** Inhibition of RBD-ACE2 interaction by rabbit mAb 5D7B7 which has a pan-sarbecovirus RBD binding ability. **(B)** Inhibition of 5B7D7 binding to different RBDs by the five serum panels as indicated. Scatter plot shows all data points and the 0th, 25th, 50th, 75th, and 100th percentile are marked. Statistical significance was determined using Wilcoxon signed-rank test. The "SARS-Vaccinated" was set as the reference group for comparison.

[0029] [Fig. 7]. Staining of B-cells with fluorescently labeled RBDs. (A) Representative flow cytometry plots for SARS-Vaccinated group (n=5), Healthy-Vaccinated group (n=6) and COVID-19-Vaccinated group (n=5) showing frequency of SARS-CoV-1- and SARS-CoV-2-double positive cells. (B) Scatter plot on frequency of SARS-CoV-1 and SARS-CoV-2 double positive cells of all SARS-CoV-1 or SARS-CoV-2-positive cells. Scatter plot shows all data points and the 0th, 25th, 50th, 75th, and 100th percentile are marked. Statistical significance was determined using Wilcoxon signed-rank test. P value was indicated on top of each plot. n.s indicates not significant, with $P > 0.05$.

[0030] [Fig. 8]: Neutralization patterns from rabbit hyper immune sera targeting different beta coronavirus RBD proteins. A cut-off of 1:100 was set as previously determined.

[0031] [Fig. 9]: Schematic diagram to sort out double positive B-cells which produce antibodies binding to RBDs from both viruses.

[0032] [Fig. 10]: Phylogenetic analysis and sequence alignment of ACE2-binding sarbecovirus RBDs. (A) Phylogenetic tree based on receptor binding domain (RBD) sequences of sarbecoviruses which can bind human ACE2. The tree was generated using PhyML with general-time-reversible (GTR) substitution model and 1,000 bootstrap replicates. Numbers at the branches are percentage bootstrap values for the associated nodes. Scale bar represents the number of substitutions per site. Sarbecovirus RBDs involved in this study were bolded. (B) RBD amino acid sequence identity percentage among different sarbecoviruses in decreasing order for SARS-CoV-1 (right to left) and SARS-CoV-2 (left to right). (C) Alignment of amino acid sequences of sarbecovirus RBDs used in this study. Red indicates mutation/deletion. Amino acids critical for SARS-CoV-2 RBD-ACE2 interaction are indicated by the blue dots above. Viruses in the SARS-CoV-1 clade are shaded in grey.

[0033] [Fig. 11]: CD19+ B cells were sorted for those positive for binding to SARS-CoV-1 (SC1+) and SARS-CoV-2 (SC2+) RBD tetramers.

[0034] [Fig. 12]: Data for the top six monoclonal antibodies identified in the preliminary screen and four control monoclonal antibodies using multiplex sVNT platform.

[0035] [Fig. 13]: 50% inhibitory concentration (IC₅₀; ng/ml) of monoclonal antibodies in blocking RBD-ACE2 engagement using multiplex surrogate virus neutralization competition format.

[0036] [Fig. 14]: Ability of monoclonal antibodies to neutralize different sarbecoviruses against eight spike-pseudotyped reporter viruses which included SARS-CoV-2 ancestral and four VOCs (Alpha, Delta, Beta and Gamma), two zoonotic sarbecoviruses (GX-P5L and WIV-1), and SARS-CoV-1.

- 5 **[0037] [Fig. 15]:** Results of monoclonal antibody neutralisation tests against ancestral SARS-CoV-2, Omicron BA.1 and Omicron BA.2 viruses, using three different platforms **A** multiplex sVNT, **B** pseudovirus neutralization test (pVNT) and **C** plaque reduction neutralization test (PRNT).

DETAILED DESCRIPTION

- 10 **[0038]** The present disclosure provides an antigen-binding molecule(s) capable of binding to a sarbecovirus spike protein from two or more different sarbecovirus, in particular neutralising antibodies capable of inhibiting the interaction between the sarbecovirus spike protein and ACE2, thus behaving as antagonists of infection of ACE2-expressing cells by a range of sarbecovirus. Antigen-binding molecules described herein are provided with a
15 combination of advantageous properties over known SARS-CoV-2 antibodies.

[0039] Throughout this document, unless otherwise indicated to the contrary, the terms “comprising”, “consisting of”, “having” and the like, are to be construed as non-exhaustive, or in other words, as meaning “including, but not limited to”.

- [0040]** Furthermore, throughout the document, unless the context requires otherwise, the
20 word “include” or variations such as “includes” or “including” will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

- [0041]** Unless defined otherwise, all other technical and scientific terms used herein have the same meaning as is commonly understood by a skilled person to which the subject matter
25 herein belongs.

[0042] According to various embodiments there is an antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecoviruses wherein the antigen-binding molecule comprises:

- (i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO:1 or SEQ ID NO:111

HC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO:2 or SEQ ID NO:112

- 5 HC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:3 or SEQ ID NO:113; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID NO:114

- 10 LC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO: 5 or SEQ ID NO:115

LC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:6 or SEQ ID NO:116.

- 15 **[0043]** Throughout the description, it is to be appreciated that the term “**antigen-binding molecule**” and its plural form refers to one or more molecule which is capable of binding to a target antigen, and encompasses monoclonal antibodies, polyclonal antibodies, monospecific and multispecific antibodies (e.g., bispecific antibodies), and antibody fragments (e.g. Fv, scFv, Fab, scFab, F(ab')₂, Fab₂, diabodies, triabodies, scFv-Fc, minibodies, single domain antibodies (e.g. VhH), etc.), as long as they display binding to the relevant target molecule(s) and block entry into the cell via ACE2.
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- [0044]** In various embodiments, two or more different sarbecovirus may include an antigen-binding molecule being capable of binding to the spike protein of 2, or 3, or 4, or 5 or 6 or 7 or 8 or 9 or 10 or more different sarbecovirus. In various embodiments, for example, the antigen-binding molecule is capable of binding to SARS-CoV spike protein, and which is also capable of binding to SARS-CoV-2 spike protein. In various embodiments, the antigen-binding molecule is capable of binding multiple sarbecovirus spike proteins. For example, the antigen-binding molecule is capable of binding to SARS-CoV spike protein; and/or capable of binding to SARS-CoV-2 spike protein and or capable of binding to SARS-CoV-2 Alpha, and/or capable of binding to SARS-CoV-2 Beta and/or capable of binding to SARS-CoV-2 Delta and/or capable of binding to SC2r-CoV RaTG13, and/or capable of binding to SC2r-CoV GX-P5L and/or capable of binding to SC2r-CoV GD-1 and/or capable of binding
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- 30

to any other sarbecovirus spike protein such as SC2r-CoVRmYN02; RacCS203 or future unknown sarbecoviruses. A broad-spectrum antigen-binding molecule has the advantage of being able to block most sarbecoviruses effectively assisting in preventing infection of both known and unknown sarbecoviruses.

- 5 **[0045]** In various embodiments, the term capable of binding may comprise inhibition or neutralization of 30% or more binding between the sarbecovirus spike protein and ACE2. In various embodiments, inhibition or neutralization of 30% or more binding between the sarbecovirus spike protein and ACE2 may be selected from one of at least 30%, 35%, 40%, 41%, 42%, 43%, 44%, 45%, 49%, 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%,
10 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 75%, 80% or greater inhibition or neutralisation. In various embodiments the antigen-binding molecule binds to the sarbecovirus spike protein from two or more different sarbecovirus comprising inhibition or neutralization of 30% or more binding between the sarbecovirus spike protein and ACE2 (e.g. one of at least 30%, 35%, 40%, 41%, 42%, 43%, 44%, 45%, 49%, 50%, 51%, 52%,
15 53%, 54%, 55%, 56%, 57%, 58%, 59%, 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 75%, 80% or greater inhibition or neutralisation).

- [0046]** In various embodiments, the antigen-binding molecule comprises polyclonal antibodies isolated from a patient that has had SARS and recovered. In various embodiments, the antigen-binding molecule comprises polyclonal antibodies isolated from a
20 patient that has had SARS and recovered and has been vaccinated with a COVID-19 vaccination. For example, the polyclonal antigen-binding molecule is capable of binding to SARS-CoV spike protein, and which is also capable of binding to SARS-CoV-2 spike protein. In various embodiments, the polyclonal antigen-binding molecule is capable of binding multiple sarbecovirus spike proteins. For example, the polyclonal antigen-binding molecule
25 is capable of binding to SARS-CoV spike protein; and/or capable of binding to SARS-CoV-2 spike protein and or capable of binding to SARS-CoV-2 Alpha, and/or capable of binding to SARS-CoV-2 Beta and/or capable of binding to SARS-CoV-2 Delta and/or capable of binding to SC2r-CoV RaTG13, and/or capable of binding to SC2r-CoV GX-P5L and/or capable of binding to SC2r-CoV GD-1 and/or capable of binding to any other sarbecovirus spike protein
30 such as SC2r-CoVRmYN02; RacCS203 or future unknown sarbecoviruses. A broad-spectrum antigen-binding molecule has the advantage of being able to block most sarbecoviruses effectively assisting in preventing infection of both known and unknown sarbecoviruses.

[0047] In various embodiments, the antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

5 HC-CDR1 having the amino acid having formula I: $X_1-X_2-X_3-\Phi-X_4-X_{n1}-X_5-X_6$:

wherein X_1 is selected from one of amino acids G and E; X_2 is selected from one of amino acids F, Y, N, G, D, and V; X_3 is selected from one of amino acids P, T, S, I and F; Φ is selected from one of hydrophobic amino acids F, V, L, or I; X_4 is selected from one of amino acids S, T, R, N, G, L, and I; X_{n1} is selected from one of amino acid sequence S, SN, N, M, H, T, G, P, G and D; X_5 is selected from one of amino acids Y, S, N, I and H; X_6 is selected from one of amino acids Y, G, W, E, A, N, and T;

HC-CDR2 having the amino acid formula II: $X_7-X_8-X_9-X_{n2}-\pi-X_{n3}-X_{10}$:

wherein X_7 is selected from one of amino acids I and T; X_8 is selected from one of amino acids Y, S, N, G, A and T; X_9 is selected from one of amino acids S, F, P, N, H, I, Y, G, and T; X_{n2} is selected from one of amino acid sequence G, YN, DD, T, NG, DG, S, SS, D, ST, and NT; π is selected from one of small amino acids G, S, P, A and E; X_{n3} is selected from one of amino acid sequence S, I, D, G, F, N, RT, L, and RN; X_{10} is selected from one of amino acids T, R, M, K, S, and P;

20 HC-CDR3 having the amino acid having formula III: $\Psi-\zeta_1-X_{n4}-X_{11}-X_{n5}-X_{12}-X_{13}-X_{14}-\zeta_2-X_{15}$;

wherein Ψ is selected from one of aliphatic amino acids A and V, ζ_1 is selected from one of hydrophilic amino acids R, T, K and L-N; X_{n4} is selected from one of amino acid sequence E, HLGGG, GGG, LDIII, DSI, GEAG, RVAIF, LQNG, VTYTS, ADIV, DSLA, DSL, AISQQ, DYYDN, DPL, EGIQG, and DGG; X_{11} is selected from one of amino acids L, S, Y, T, A, N, V, and W; X_{n5} is selected from one of amino acid sequence R, S, LET, P, SAT, MATIWW, DGY, SY, PLPF, GS, VV, SVT, FDS, GYYY, EGAAS, V, and QLPY; X_{12} is selected from one of amino acids H, W, G, P, T, S, N, and Y; X_{13} is selected from one of amino acids Y, P, A, L, S, F, I, V, and G; X_{14} is selected from one of amino acids F, I, N, Y, L, and M; ζ_2 is selected from one of hydrophilic amino acids D, E, G, and S; X_{15} is selected from one of amino acids Y, S, L, N, H, C, V, and F; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having formula IV: $X_{16}-X_{17}-X_{18}-X_{n6}-\zeta_3-X_{19}$:

wherein X_{16} is selected from one of amino acids Q and Y; X_{17} is selected from one of amino acids G, S, T, N, I, and A; X_{18} is selected from one of amino acids V, I, T, F and L; X_{n6} is selected from one of amino acid sequence S, G, N, V, R, LYSSNNK, LYRSNNK, LQNNGY, VQSNGY, VHSDGN, MQLNGY and SS; ζ_3 is selected from one of hydrophilic amino acids S, N, and T; X_{19} is selected from one of amino acids W, Y, S and N;

LC-CDR2 having the amino acid having formula V: X_{20} - X_{21} -S:

wherein X_{20} is selected from one of amino acids A, W, K, T, G, L, and D; X_{21} is selected from one of amino acids A, S, G, I, and T

LC-CDR3 having the amino acid having formula VI: X_{22} - ζ_4 - X_{23} - X_{n7} - ζ_5 - X_{24} - X_{25} -

X_{n8} - ζ_6 :

wherein X_{22} is selected from one of amino acids Q, H, and M; ζ_4 is selected from one of hydrophilic amino acids Q and H; X_{23} is selected from one of amino acids Y, S, G, A, L, and T; X_{n7} is selected from one of amino acid sequence F, Y, N, S, L, G, T, YR, and YI; ζ_5 is selected from one of hydrophilic S, T, N, Q, and D; X_{24} is selected from one of amino acids S, Y, T, D, H, F, P, W, and I; X_{25} is selected from one of amino acids P, I, and R; X_{n8} is selected from one of amino acid sequence F, W, K, G, Y, R, P, L, PY, EY, ED, GY, QY, and QI; ζ_6 is selected from one of hydrophilic amino acids T and S.

[0048] The antigen-binding molecule with CDRs falling within these formulas demonstrated neutralizing across several sarbecovirus including SARS-CoV-2. Antibodies 1 (SS6V1-B5) to 20 (SS6V20-F5) are examples of antigen-binding molecules with CDRs falling within these formulas. These are some of best cross-clade Neutralising antibodies reported to date.

[0049] In various embodiments, the formulas are the same as those listed above with the exception that Φ of formula I is selected from one of hydrophobic amino acids F, L, or I; X_5 of formula I is selected from one of Y, S, I and H; X_6 of formula I is selected from one of Y, W, E, A, N, and T; X_8 of formula II is I; X_{n2} of formula II is selected from one of DD, T, NG, DG, S, SS, D, ST, and NT; ζ_1 of formula III is selected from one of hydrophilic amino acids R, T, and K; X_{n4} of formula III is selected from one of HLGGG, GGG, LDIII, DSI, GEAG, LQNG, VTYTS, ADIV, DSLA, DSL, AISQQ, DYYDN, DPL, EGIQG, and DGG; X_{11} of formula III is selected from one of S, Y, T, A, V, and W; X_{n5} of formula III is selected from one of S, LET, P, SAT, MATIWW, SY, PLPF, GS, VV, SVT, FDS, GYYY, EGAAS, V, and QLPY; X_{12} of formula III is selected from one of W, G, P, T, S, N, and Y; X_{n6} of formula IV is selected from one of S, G, N, V, R, LYRSNNK, LQNNGY, VQSNGY, VHSDGN, MQLNGY and SS;

X_{23} of formula VI is selected from one of Y, S, G, A, and T; X_{n8} of formula VI is selected from one of F, W, K, G, Y, R, P, L, EY, ED, GY, QY, and QI. The antigen-binding molecule with CDRs falling within these formulas demonstrated pan-sarbecovirus neutralizing across a large breadth of sarbecovirus including SARS-CoV-1 and SARS-CoV-2. Antigen-binding molecule with CDRs falling within these formulas were double positive for staining by both SARS-CoV-1 and SARS-CoV-2 RBD proteins. Antibody 1 (SS6V1-B5) and antibodies 4 to 20 (SS6V4-A1, SS6V5-C3.... to SS6V20-F5) are examples of antigen-binding molecules with CDRs falling within these formulas.

[0050] In various embodiments, wherein X_1 is G; X_2 is selected from one of G, F, Y and V; X_3 is selected from one of S, I, T and F; Φ is selected from one of F, L and I; X_4 is selected from one of R, S, G, L, T and I; X_{n1} is selected from one of P, N, T, D and G; X_5 is selected from one of Y, S and H; X_6 is selected from one of E, N and Y; X_7 is I; X_8 is selected from one of G, S, N and Y; X_9 is selected from one of I, N, S, T and F; X_{n2} is selected from one of T, S, SS and NT; π is selected from one of G, E, S and A; X_{n3} is selected from one of G, S, F, I and N; X_{10} is selected from one of T, M and P; Ψ is A; ζ_1 is R; X_{n4} is selected from one of VTYTS, GGG, DYYDN, and DGG; X_{11} is selected from one of S, Y and W; X_{n5} is selected from one of PLPF, LET, GYYY and QLPY; X_{12} is selected from one of W, Y and G; X_{13} is selected from one of F, P, G, and Y; X_{14} is selected from one of F, M and L; ζ_2 is selected from one of D and E; X_{15} is selected from one of Y, L, V, F and S; X_{16} is selected from one of Q and Y; X_{17} is selected from one of G and S; X_{18} is selected from one of I, F and L; X_{n6} is selected from one of G, LQNNGY, R, VQSNGY, S and MQLNGY; ζ_3 is selected from one of N, S and T; X_{19} is selected from one of Y or S; X_{20} is selected from one of A, L and G; X_{21} is selected from one of A, S, T and G; X_{22} is selected from one of Q, M and L; ζ_4 is Q; X_{23} is selected from one of T, S, Y and G; X_{n7} is selected from one of YR, L, and Y; ζ_5 is selected from one of T, Q, and S; X_{24} is selected from one of P, I, W and T; X_{25} is P; X_{n8} is selected from one of ED, G, QI and L; ζ_6 is selected from one of S and T. That is in various embodiments formula I comprises $GX_2X_3\Phi X_4X_5X_6X_7$ wherein X_2 is selected from one of G, F, Y and V; X_3 is selected from one of S, I, T and F; Φ is selected from one of F, L and I; X_4 is selected from one of R, S, G, L, T and I; X_5 is selected from one of P, N, T, D and G; X_6 is selected from one of Y, S and H; X_7 is selected from one of E, N and Y; Formula II comprises $IX_9X_{10}X_{n1}\pi X_{n2}X_{11}$ wherein X_9 is selected from one of G, S, N and Y; X_{10} is selected from one of I, N, S, T and F; X_{n1} is selected from one of S, SS and NT; π is selected from one of G, E, S and A; X_{n2} is selected from one of G, S, F, I and N; X_{11} is selected from one of T, M and P; formula III comprises $ARX_{n3}X_{12}X_{n4}X_{13}X_{14}X_{15}\zeta_2X_{16}$ wherein X_{n3} is selected from one of VTYTS, GGG, DYYDN, and DGG; X_{12} is selected from one of S, Y and W; X_{n4} is selected

from one of PLPF,LET, GYYY and QLPY; X_{13} is selected from one of W, Y and G; X_{14} is selected from one of F, P, G, and Y; X_{15} is selected from one of F, M and L; ζ_2 is selected from one of D and E; X_{16} is selected from one of Y, L, V, F and S; formula IV comprises $X_{17}X_{18}X_{19}X_{n5}\zeta_3\Omega$ wherein X_{17} is selected from one of aromatic amino acids Q and Y; X_{18} is selected from one of G and S; X_{19} is selected from one of I, F and L; X_{n5} is selected from one of G, LQNNGY, R, VQSNGY, S and MQLNGY; ζ_3 is selected from one of N, S and T; Ω is selected from one of Y or S; formula V comprises $X_{20}X_{21}S$ wherein X_{20} is selected from one of A, L and G; X_{21} is selected from one of A, S, T and G;; and formula VI comprises $X_{22}QX_{23}X_{n6}\zeta_5X_{25}PX_{n7}\zeta_6$ wherein X_{22} is selected from one of Q, L, M and L; X_{23} is selected from one of T, S, Y and G; X_{n6} is selected from one of YR, L, and Y; ζ_5 is selected from one of T, Q, and S; X_{25} is selected from one of P, I, W and T; X_{n7} is selected from one of ED, G, QI and L; ζ_6 is selected from one of S and T. The antigen-binding molecule with CDRs falling within these formulas demonstrated pan-sarbecovirus neutralizing potency and breadth across most of the sarbecovirus including SARS-CoV-1 and SARS-CoV-2. Antibody 1 (SS6V1-B5), antibody 11 (SS6V11-E7), antibody 12 (SS6V12-E11), antibody 13 (SS6V13-F1), antibody 19 (SS6V19-F4) and antibody 20 (SS6V20-F5) are examples of antigen-binding molecules with CDRs falling within these formulas.

[0051] In various embodiments, the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 selected from one of amino acid sequences GFILRNYE, GGFIFPHY, GFTFSTYN, GVSILGSY, GYTFTDYN and GGSIIIGYY; HC-CDR2 selected from one of amino acid sequences IGNTGGT, IYISGST, ISSSSSFM, IYFSENT, INTNTGIP and IYFSANT; HC-CDR3 selected from one of amino acid sequences ARVTYTSSPLPFWFLDL, ARGGGYLETGPFY, ARDYDNSGYYYYGMDV, ARGGGYLETGPFDS, ARDGGWQLPYWYFDL and ARGGGYLETGPLDF; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 selected from one of amino acid sequences QSIGNY, QSLQNNGYNY, QSIRTY, QGLVQSNGYNY, YSFSSS and QSLMQLNGYNY; LC-CDR2 selected from one of amino acid sequences AAS, LSS, GTS and LGS; LC-CDR3 selected from one of amino acid sequences QQTYRTPEDS, MQSLQIPGT, LQTYSTPQIT, MQGLQTPGT, QQYYSWPLT and MQGLQIPGT.

[0052] In various embodiments, wherein X_1 is G; X_2 is selected from one of G and V; X_3 is selected from one of S, and F; Φ is I; X_4 is selected from one of G, L and I; X_{n1} is selected from one of P and G; X_5 is selected from one of Y, S and H; X_6 is Y; X_7 is I; X_8 is Y; X_9 is selected from one of I and F; X_{n2} is S; π is selected from one of G, E and A; X_{n3} is selected from one of S and N; X_{10} is T; Ψ is A; ζ_1 is R; X_{n4} is GGG; X_{11} is Y; X_{n5} is LET; X_{12} is G; X_{13} is P; X_{14} is selected from one of F and L; ζ_2 is selected from one of D, and E; X_{15} is selected

from one of Y, F and S; X_{16} is Q; X_{17} is selected from one of G and S; X_{18} is L; X_{n6} is selected from one of LQNNGY, VQSNGY and MQLNGY; ζ_3 is N; X_{19} is Y; X_{20} is L; X_{21} is selected from one of S and G; X_{22} is M; ζ_4 is Q; X_{23} is selected from one of S and G; X_{n7} is L; ζ_5 is Q; X_{24} is selected from one of I and T; X_{25} is P; X_{n8} is G; ζ_6 is T. That is in various embodiments formula I comprises $GX_2X_3IX_4X_5X_6Y$ wherein X_2 is selected from one of G and V; X_3 is selected from one of S, and F; X_4 is selected from one of G, L and I; X_5 is selected from one of P and G; and X_6 is selected from one of Y, S and H; formula II comprises $IYX_{10}\Sigma\pi X_{n2}T$ wherein X_{10} is selected from one of I and F; π is selected from one of G, E and A; X_{n2} is selected from one of S and N; formula III comprises $ARGGGYLETGPX_{15}\zeta_2X_{16}$ wherein X_{15} is selected from one of F and L; ζ_2 is selected from one of D and E; X_{16} is selected from one of Y, F and S; formula IV comprises $QX_{18}LX_{n5}NY$ wherein X_{18} is selected from one of G and S; X_{n5} is selected from one of LQNNGY, VQSNGY and MQLNGY; formula V comprises $LX_{21}S$ wherein X_{21} is selected from one of S and G; and formula VI comprises $MQX_{23}LQX_{25}PGT$ wherein X_{23} is selected from one of S and G; X_{25} is selected from one of I and T. The antigen-binding molecule with CDRs falling within these formulas demonstrated pan-sarbecovirus neutralizing potency and breadth of all sarbecovirus tested including SARS-CoV-1 and SARS-CoV-2. Antibody 11 (SS6V11-E7), antibody 13 (SS6V13-F1) and antibody 20 (SS6V20-F5) are examples of antigen-binding molecules with CDRs falling within these formulas. These antibodies demonstrated the highest potency reported. The three monoclonal antibodies falling in this group maintained their strong neutralization capability across most SARS-CoV-2 VOCs and VOIs and Clade-1a sarbecoviruses in different virus neutralization assay platforms. All three antibodies utilized a unique combination of heavy and light chain gene classes exhibiting similarity of more than 90% in their heavy and light chain sequences. These sequences have not been previously reported for sarbecovirus-specific antibodies.

[0053] In various embodiments, the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 selected from one of amino acid sequences GGFIGHY, GVSILGSY and GGSILGYY; HC-CDR2 selected from one of amino acid sequences IYISGST, IYFSENT and IYFSANT; HC-CDR3 selected from one of amino acid sequences ARGGGYLETGPFY, ARGGGYLETGPFDS and ARGGGYLETGPLDF; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 selected from one of amino acid sequences QSLLQNNGYNY, QGLVQSNGYNY and QSLMQLNGYNY; LC-CDR2 selected from one of amino acid sequences LSS and LGS; LC-CDR3 selected from one of amino acid sequences MQLQIPGT, MQGLQTPGT and MQGLQIPGT.

[0054] In various embodiments, wherein X_1 is G; X_2 is G; X_3 is selected from one of S, and F; Φ is I; X_4 is selected from one of G, and I; X_{n1} is selected from one of P and G; X_5 is selected from one of Y and H; X_6 is Y; X_7 is I; X_8 is Y; X_9 is selected from one of I and F; X_{n2} is S; π is selected from one of G and A; X_{n3} is selected from one of S and N; X_{10} is T; Ψ is A; ζ_1 is R; X_{n4} is GGG; X_{17} is Y; X_{n5} is LET; X_{12} is G; X_{13} is P; X_{14} is selected from one of F and L; ζ_2 is selected from one of D, and E; X_{15} is selected from one of Y and F; X_{16} is Q; X_{17} is S; X_{18} is L; X_{n6} is selected from one of LQNNGY, and MQLNGY; ζ_3 is N; X_{19} is Y; X_{20} is L; X_{21} is selected from one of S and G; X_{22} is M; ζ_4 is Q; X_{23} is selected from one of S and G; X_{n7} is L; ζ_5 is Q; X_{24} is I; X_{25} is P; X_{n8} is G; ζ_6 is T. That is in various embodiments formula I comprises GGX₃IX₄X₅X₆Y wherein X_3 is selected from one of S, and F; X_4 is selected from one of G, and I; X_5 is selected from one of P and G; and X_6 is selected from one of Y and H; formula II comprises IYX₁₀ST π X_{n2}T wherein X_{10} is selected from one of I and F; π is selected from one of G and A; X_{n2} is selected from one of S and N; formula III comprises ARGGGYLETG ζ_2 PX₁₅X₁₆ wherein X_{15} is selected from one of F and L; X_{16} is selected from one of Y and F; ζ_2 is selected from one of D and E; formula IV comprises QSLX_{n5}NY wherein X_{n5} is selected from one of LQNNGY, and MQLNGY; formula V comprises LX₂₁S wherein X_{21} is selected from one of S and G; and formula VI comprises MQX₂₃LQIPGT wherein X_{23} is selected from one of S and G. The antigen-binding molecule with CDRs falling within these formulas demonstrated the best pan-sarbecovirus neutralizing potency and breadth compared to any other antibody reported to date. Epitope mapping studies of antibodies falling within these formulas indicate the antibodies have a unique contact footprint in the RBD. Antibody 11 (SS6V11-E7) and antibody 20 (SS6V20-F5) are examples of antigen-binding molecules with CDRs falling within these formulas.

[0055] In various embodiments, the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 selected from one of amino acid sequences GGFIPHY and GGSIIIGYY; HC-CDR2 selected from one of amino acid sequences IYISGST and IYFSANT; HC-CDR3 selected from one of amino acid sequences ARGGGYLETGPFY and ARGGGYLETGPLDF; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 selected from one of amino acid sequences QSLQNNNGYNY and QSLMQLNGYNY; LC-CDR2 selected from one of amino acid sequences LSS and LGS; LC-CDR3 selected from one of amino acid sequences MQSLQIPGT and MQGLQIPGT.

[0056] In various embodiments, the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFILRNYE; HC-CDR2 having the amino acid sequence IGNTGGT; HC-CDR3 having the amino acid sequence ARVTYTSSPLPFWFLDL; and the light chain variable (VL) region incorporates the following

CDRs: LC-CDR1 having the amino acid sequence QSIGNY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQTYRTPPEDS. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 71 and light chain SEQ ID NO 72 of antibody 1 (SS6V1-B5). In various embodiments these CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0057] the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTVSSNY; HC-CDR2 having the amino acid sequence IYSGGST; HC-CDR3 having the amino acid sequence ARELRHYFDY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QGISSY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQLNSYPPYS. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 73 and light chain SEQ ID NO 74 of antibody 2 (SS6V2-G1). In various embodiments these CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus. This antibody was cloned from SC2+ single positive B cells and while it demonstrates reactivity to SARS-CoV-2 RBD it showed minimal reactivity to SARS-CoV-1 RBD.

[0058] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GYSFTNSG; HC-CDR2 having the amino acid sequence TNFYNGIT; HC-CDR3 having the amino acid sequence ALNRVAIFNDGYNPLGY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSVLYSSNNKNY; LC-CDR2 having the amino acid sequence WAS; LC-CDR3 having the amino acid sequence QQYFSSPFS. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 75 and light chain SEQ ID NO 76 of antibody 3 (SS6V3-G2). In various embodiments these CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus. This antibody was cloned from SC2+ single positive B cells and while it demonstrates reactivity to SARS-CoV-2 RBD it showed minimal reactivity to SARS-CoV-1 RBD.

[0059] the heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GYTFSMYW; HC-CDR2 having the amino acid sequence IYPDDSDR; HC-CDR3 having the amino acid sequence ARLQNGYSYGLLEN; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid

sequence QSTLYRSNNKNY; LC-CDR2 having the amino acid sequence WAS; LC-CDR3 having the amino acid sequence QQYYSYPWT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 77 and light chain SEQ ID NO 78 of antibody 4 (SS6V4-A1). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0060] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GYTFTHYW; HC-CDR2 having the amino acid sequence IYPDDSDT; HC-CDR3 having the amino acid sequence ATADIVVGSNFFDH; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSISTW; LC-CDR2 having the amino acid sequence KAS; LC-CDR3 having the amino acid sequence QHYNSYIKT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 79 and light chain SEQ ID NO 80 of antibody 5 (SS6V5-C3). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0061] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFNTYA; HC-CDR2 having the amino acid sequence ISSNGGIT; HC-CDR3 having the amino acid sequence VKDSLATVVTLLSY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QTISSY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQSYSTPGT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 81 and light chain SEQ ID NO 82 of antibody 6 (SS6V6-C4). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0062] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence ENIFSGYW; HC-CDR2 having the amino acid sequence IYPDDSDT; HC-CDR3 having the amino acid sequence ARHLGGGSSWPIDY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QGISNY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQYSSYPFT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 83 and light chain SEQ ID NO 84 of antibody 7 (SS6V7-C5). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed

below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0063] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFSTYA; HC-CDR2 having the amino acid sequence IASDGGIT; HC-CDR3 having the amino acid sequence VKDSLTSVTTIFDC; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QNINSY; LC-CDR2 having the amino acid sequence TAS; LC-CDR3 having the amino acid sequence QQSYTDPYT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 85 and light chain SEQ ID NO 86 of antibody 8 (SS6V8-D3). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0064] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GGSISSNIW; HC-CDR2 having the amino acid sequence IYHSGST; HC-CDR3 having the amino acid sequence ARAISQQYFDSSVLGY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSVVTN; LC-CDR2 having the amino acid sequence GAS; LC-CDR3 having the amino acid sequence QQYNNWPGYT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 87 and light chain SEQ ID NO 88 of antibody 9 (SS6V9-D11). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0065] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence EDSFTGYW; HC-CDR2 having the amino acid sequence IYPDDGDT; HC-CDR3 having the amino acid sequence ARHLGGSSWPIDS; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QGIRNY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQYNNHPFT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 89 and light chain SEQ ID NO 90 of antibody 10 (SS6V10-E1). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0066] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GGFIFPHY; HC-CDR2 having the amino acid sequence

IYISGST; HC-CDR3 having the amino acid sequence ARGGGYLETGPFY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSLLQNNGYNY; LC-CDR2 having the amino acid sequence LSS; LC-CDR3 having the amino acid sequence MQSLQIPGT. In various embodiments these are CDRs are formed in heavy chain SEQ ID NO 91 and light chain SEQ ID NO 92 of antibody 11 (SS6V11-E7). In various embodiments these CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus. The antibodies **with these CDR's** demonstrated one of the best pan-sarbecovirus neutralizing potency and breadth compared to any other antibody reported to date including being the only antibody with neutralization capacity against Omicron BA.2.

[0067] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFSTYN; HC-CDR2 having the amino acid sequence ISSSSFM; HC-CDR3 having the amino acid sequence ARDYYDNSGYYYGMDV; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSIRTY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence LQTYSTPQIT. In various embodiments these are CDRs are formed in heavy chain SEQ ID NO 93 and light chain SEQ ID NO 94 of antibody 12 (SS6V12-E11). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0068] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GVSILGSY; HC-CDR2 having the amino acid sequence IYFSENT; HC-CDR3 having the amino acid sequence ARGGGYLETGPFDS; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QGLVQSNGYNY; LC-CDR2 having the amino acid sequence LGS; LC-CDR3 having the amino acid sequence MQGLQTPGT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 95 and light chain SEQ ID NO 96 of antibody 13 (SS6V13-F1). In various embodiments these CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0069] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GGPISSYY; HC-CDR2 having the amino acid sequence IYYSGST; HC-CDR3 having the amino acid sequence ARDPLAEGAASSGFDN; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino

acid sequence QSISSY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQSYTTPRT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 97 and light chain SEQ ID NO 98 of antibody 14 (SS6V14-F2). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0070] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFSSYA; HC-CDR2 having the amino acid sequence ISYDGR TK; HC-CDR3 having the amino acid sequence ARLDIIITPPANDY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QIVSSNY; LC-CDR2 having the amino acid sequence DAS; LC-CDR3 having the amino acid sequence HQYGDSRRT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 99 and light chain SEQ ID NO 100 of antibody 15 (SS6V15-F6). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0071] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence EFTFSRYT; HC-CDR2 having the amino acid sequence IGGSTPLS; HC-CDR3 having the amino acid sequence ARDSIASATTLFDL; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QAISY; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQSYITPPEYS. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 101 and light chain SEQ ID NO 102 of antibody 16 (L8N16-C7). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0072] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFSSYA; HC-CDR2 having the amino acid sequence ISYDGRNK; HC-CDR3 having the amino acid sequence ARGEAGTMATIWSSYDY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSLVHSDGNTY; LC-CDR2 having the amino acid sequence KIS; LC-CDR3 having the amino acid sequence MQATQFPPT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 103 and light chain SEQ ID NO 104 of antibody 17 (L8N17-G3). In various embodiments these are CDRs are formed in other antigen binding

scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0073] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GFTFSSYA; HC-CDR2 having the amino acid sequence
 5 ITSNGGGT; HC-CDR3 having the amino acid sequence AREGIQGWWTYFDY; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSISTN; LC-CDR2 having the amino acid sequence AAS; LC-CDR3 having the amino acid sequence QQTYTTPQYS. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 105 and light chain SEQ ID NO 106 of antibody 18 (SS6V18-E3).
 10 In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0074] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GYTFTDYN; HC-CDR2 having the amino acid sequence
 15 INTNTGIP; HC-CDR3 having the amino acid sequence ARDGGWQLPYWYFDL; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence YSFSSS; LC-CDR2 having the amino acid sequence GTS; LC-CDR3 having the amino acid sequence QQYYSWPLT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 107 and light chain SEQ ID NO 108 of antibody 19 (SS6V19-F4).
 20 In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus.

[0075] The heavy chain variable (VH) region incorporates the following CDRs: HC-CDR1 having the amino acid sequence GGSIIIGYY; HC-CDR2 having the amino acid sequence
 25 IYFSANT; HC-CDR3 having the amino acid sequence ARGGGYLETGPLDF; and the light chain variable (VL) region incorporates the following CDRs: LC-CDR1 having the amino acid sequence QSLMQLNGYNY; LC-CDR2 having the amino acid sequence LGS; LC-CDR3 having the amino acid sequence MQGLQIPGT. In various embodiments these CDRs are formed in heavy chain SEQ ID NO 109 and light chain SEQ ID NO 110 of antibody 20 (SS6V20-F5). In various embodiments these are CDRs are formed in other antigen binding scaffolds listed below provided it is able to bind to a sarbecovirus spike protein from two or more different sarbecovirus. **The antibodies with these CDR's demonstrated one of the best pan-sarbecovirus neutralizing potency and breadth compared to any other antibody reported to date.**

[0076] In various embodiments, the antigen-binding molecule comprises a polyclonal antigen-binding molecule. In various embodiments, the antigen-binding molecule comprises at least two different antigen-binding domains (i.e. at least two antigen-binding domains, e.g. comprising non-identical VHs and VLs). The higher neutralization potencies of the disclosed antibodies will enable lower dosages of the antigen-binding molecule to be used clinically as individual antigen-binding molecule or mixed in a cocktail of two or more antigen-binding molecule or an antigen-binding molecule with two or more different antigen-binding domains.

[0077] In various embodiments, the antigen-binding molecule binds to two different sarbecovirus spike proteins, such as SARS-CoV spike protein and SARS-CoV-2 spike protein, and so is at least bispecific. The term "bispecific" means that the antigen-binding molecule is able to bind specifically to at least two distinct antigenic determinants.

[0078] In various embodiments, the bispecific antigen-binding molecule may comprise antigen-binding molecules capable of binding to the targets for which the antigen-binding molecule is specific. For example, an antigen-binding molecule which is capable of binding to SARS-CoV spike protein, and which is capable of binding to SARS-CoV-2 spike protein may comprise a component which is capable of binding to SARS-CoV spike protein, and a second component which is capable of binding to SARS-CoV-2 spike protein.

[0079] In various embodiments, the antigen-binding molecule according to the present disclosure comprises a multispecific antigen-binding molecule that may comprise antigen-binding polypeptides or antigen-binding polypeptide complexes capable of binding to the targets for which the antigen-binding molecule is specific. In some embodiments, a component antigen-binding molecule of a larger antigen-binding molecule may be referred to as an "antigen-binding domain" or "antigen-binding region" of the larger antigen-binding molecule.

[0080] In various embodiments, the multispecific antigen-binding molecule is capable of binding to multiple sarbecovirus spike proteins. For example, the multispecific antigen-binding molecule is capable of binding to SARS-CoV spike protein; and/or capable of binding to SARS-CoV-2 spike protein and/or capable of binding to SARS-CoV-2 Alpha, and/or capable of binding to SARS-CoV-2 Beta and/or capable of binding to SARS-CoV-2 Delta and/or capable of binding to SC2r-CoV RaTG13, and/or capable of binding to SC2r-CoV GX-P5L and/or capable of binding to SC2r-CoV GD-1 and/or capable of binding to any other sarbecovirus spike protein such as SC2r-CoVRmYN02; RacCS203 or future unknown sarbecoviruses. A broad-spectrum antigen-binding molecule has the advantage of being

able to block most sarbecoviruses effectively assisting in preventing infection of both known and unknown sarbecoviruses.

[0081] Throughout the description, it is to be appreciated that the term 'Sarbecovirus' and its plural form include any beta coronavirus that uses angiotensinogen converting enzyme 2 (ACE2) receptor as entry into cells. In various embodiments, the sarbecovirus comprises any beta coronavirus that uses ACE2 receptor as entry into cells. In various embodiments, the sarbecovirus comprises any beta coronavirus that uses human ACE2 receptor as entry into human cells. In various embodiments, the sarbecovirus comprises any known or new sarbecovirus. In various embodiments, the sarbecovirus is selected from the group comprising or consisting of SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV LYRa11, SC1r-CoV WIV-1, SARS-CoV, SC2r-CoV WIV-1, SC1r-CoV RsSHC014, SARS-CoV-2 Alpha, SARS-CoV-2 Beta, SARS-CoV-2 Delta, SC2r-CoV RaTG13, SC2r-CoV GD-1 and SC2r-CoV GX-P5L.

[0082] Throughout the description, it is to be appreciated that the term 'SARS-CoV' refers to the SARSr-CoV having the nucleotide sequence of GenBank: NC_004718.3 ("Severe acute respiratory syndrome coronavirus isolate, complete genome"), and encompasses variants thereof having a nucleotide sequence with at least 85% sequence identity (e.g. one of at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or greater sequence identity) to the nucleotide sequence of GenBank: NC_004718.3 set forth in SEQ ID NO: 7.

[0083] Throughout the description, it is to be appreciated that the term 'SARS-CoV-2' refers to the SARSr-CoV having the nucleotide sequence of GenBank: NC_045512.2 ("Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu 1, complete genome"), reported in Zhou et al., Nature (2020) 579: 270–273, and encompasses variants thereof having a nucleotide sequence with at least 85% sequence identity (e.g. one of at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or greater sequence identity) to the nucleotide sequence of GenBank: NC_045512.2 set forth in SEQ ID NO: 8.

[0084] Sarbecoviruses like all coronaviruses have a genome which encodes four major structural proteins: the spike (S) protein, the envelope (E) protein, the membrane (M) protein,

and the nucleocapsid (N) protein. Generally, the spike protein has a section that incorporates the receptor binding domain (RBD).

[0085] In various embodiments, the sarbecovirus spike protein may be characterised by any one of the consensus amino acid sequences set forth in SEQ ID NOS: 18 to 25 (SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO: 20; SEQ ID NO: 21; SEQ ID NO: 22; SEQ ID NO: 23; SEQ ID NO: 24; or SEQ ID NO: 25).

[0086] Fragments of sarbecovirus spike protein may have a minimum length of one of 25, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1,000, 1,100 or 1,200 amino acids, and may have a maximum length of one of 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1,000, 1,100 or 1,200 amino acids.

[0087] In various embodiments, the spike protein of SARS-CoV has the amino acid sequence shown in SEQ ID NO:9. SARS-CoV spike protein comprises S1 (SEQ ID NO:11) and S2 subunits. The S1 subunit comprises a receptor-binding domain (RBD) comprising; SEQ ID NO:12 or SEQ ID NO: 17, through which the SARS-CoV binds to ACE2 expressed by the host cells.

[0088] In various embodiments, the spike protein of SARS-CoV-2 has the amino acid sequence shown in SEQ ID NO:10. SARS-CoV-2 spike protein comprises S1 (SEQ ID NO:13 or SEQ ID NO:16) and S2 subunits. The S1 subunit comprises a receptor-binding domain (RBD) comprising of SEQ ID NO:14 or SEQ ID NO:15 through which the SARS-CoV-2 binds to ACE2 expressed by host cells.

[0089] In various embodiments, the RBD of sarbecovirus spike protein refers to a polypeptide having the amino acid sequence shown in any one of SEQ ID NOS:12, 14, 15, 17, or 26-30, or polypeptide having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or greater amino acid sequence identity to any one of SEQ ID NOS:12, 14, 15, 17, or 26-30. Such polypeptides may include e.g., isoforms, fragments, variants of the RBD of the spike protein encoded by SARS-CoV-2, and the corresponding region of spike protein homologues from other SARS-CoV or other known sarbecoviruses.

[0090] In various embodiments, fragments of the RBD of sarbecovirus spike protein may have a minimum length of one of 10, 20, 30, 40, 50, 100, 150, 200 amino acids, and may have a maximum length of one of 20, 10, 20, 30, 40, 50, 100, 150, 200 amino acids.

[0091] In various embodiments, isoforms, fragments, variants or homologues may optionally be functional isoforms, fragments, variants or homologues, e.g., having a functional property/activity of the reference protein, as determined by analysis by a suitable assay for the functional property/activity where it binds and or enters a host cell via ACE2.

5 For example, an isoform, fragment, variant or homologue of the spike protein of sarbecovirus may display association with ACE2.

[0092] In various embodiments, the sarbecovirus spike protein comprises a spike protein comprising or consisting of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to any one of consensus sarbecovirus spike protein SEQ ID NOS: 18-25 (SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO: 20; SEQ ID NO: 21; SEQ ID NO: 22; SEQ ID NO: 23; SEQ ID NO: 24; or SEQ ID NO: 25). In various embodiments, the sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to any one of SEQ ID NOS: 9, 10, or 18-25.

[0093] In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NOS:13-16. In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NOS:12, 14, 15, 17, or 26-30. In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NO:26. In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NO:27. In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NO:28. In various embodiments, a fragment of sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NO: 29. In various embodiments, a fragment of

sarbecovirus spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NO: 30.

5 **[0094]** In some embodiments, a fragment of the RBD of SARS-CoV-2 spike protein comprises, or consists of, an amino acid sequence having at least 75%, including one of 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity to SEQ ID NOS:12, 14, 15, 17, or 26-30.

[0095] In various embodiments, the antigen-binding molecule comprises two antigen-binding molecules which binds to a sarbecovirus spike protein.

10 **[0096]** In various embodiments, the antigen-binding molecule binds to the receptor binding domain (RBD) of the Sarbecovirus spike protein.

[0097] In various embodiments, the antigen-binding molecule inhibits interaction between the sarbecovirus spike protein and Angiotensinogen converting enzyme 2 (ACE2).

15 **[0098]** In various embodiments, the antigen-binding molecule inhibits infection of ACE2-expressing cells by the sarbecovirus.

[0099] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

25 **[00100]** In various embodiments, the sarbecovirus SARS-CoV refers to the SARSr-CoV having the nucleotide sequence of GenBank: NC_004718.3, reported in He et al., Biochem. Biophys. Res. Commun. 316 (2), 476-483 (2004), and encompasses variants thereof having a nucleotide sequence with at least 85% sequence identity (e.g. one of at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or greater sequence identity) to the nucleotide sequence of GenBank: NC_004718.3.

30 **[00101]** In various embodiments, the sarbecovirus SARS-CoV-2 refers to the SARSr-CoV having the nucleotide sequence of GenBank: NC_045512.2, reported in Wu et al., Nature 579 (7798), 265-269 (2020), and encompasses variants thereof having a nucleotide

sequence with at least 85% sequence identity (e.g. one of at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or greater sequence identity) to the nucleotide sequence of GenBank: NC_045512.2. In various embodiments, the sarbecovirus SARS-CoV-2 variants comprise UK COVID-19 variant SARS-CoV-2 B.1.1.7, the South African COVID-19 variant SARS-CoV-2 B.1.351 also known as 20H/501Y.V2, or 501Y.V2 variant, Indian variant B.1.617, and the Brazil variant P.1.

[00102] The antigen-binding molecules of the present disclosure may be designed and prepared using the sequences of monoclonal antibodies (mAbs) capable of binding to sarbecovirus spike protein. Antigen-binding regions of antibodies, such as single chain variable fragment (scFv), Fab and F(ab')₂ fragments may also be used/provided. An "antigen-binding region" is any fragment of an antibody which is capable of binding to the target for which the given antibody is specific. A mAbs is one of the most efficient and powerful tools for rapid development and deployment in fighting future emerging zoonotic viruses, and sarbecoviruses in particular.

[00103] Antibodies generally comprise six complementarity-determining regions (CDRs); three in the heavy chain variable (VH) region: HC-CDR1, HC-CDR2 and HC-CDR3, and three in the light chain variable (VL) region: LC-CDR1, LC-CDR2, and LC-CDR3. The six CDRs together define the paratope of the antibody, which is the part of the antibody which binds to the target antigen.

[00104] The VH region and VL region comprise framework regions (FRs) either side of each CDR, which provide a scaffold for the CDRs. From N-terminus to C-terminus, VH regions comprise the following structure: N term-[HC-FR1]-[HC-CDR1]-[HC-FR2]-[HC-CDR2]-[HC-FR3]-[HC-CDR3]-[HC-FR4]-C term; and VL regions comprise the following structure: N term-[LC-FR1]-[LC-CDR1]-[LC-FR2]-[LC-CDR2]-[LC-FR3]-[LC-CDR3]-[LC-FR4]-C term. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.31 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 32. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.33 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 34. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.35 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 36. In various embodiments, the VH region comprises the amino acid encoded

[illegible]

the nucleic acid sequence set forth in SEQ ID NO. 64. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.65 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 66. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.67 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 68. In various embodiments, the VH region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO.69 and VL region comprises the amino acid encoded by the nucleic acid sequence set forth in SEQ ID NO. 70.

10 **[00105]** In various embodiments, the antigen-binding molecule comprises the CDRs of an antibody capable of binding to sarbecovirus spike protein described herein or comprises CDRs which are derived from an antibody capable of binding to sarbecovirus spike protein described herein. In some embodiments, the antigen-binding molecule comprises the FRs of an antibody capable of binding to sarbecovirus spike protein described herein or
15 comprises FRs which are derived from an antibody capable of binding to sarbecovirus spike protein described herein. In some embodiments, the antigen-binding molecule comprises the CDRs and the FRs of an antibody capable of binding to sarbecovirus spike protein described herein or comprises CDRs and FRs which are derived from an antibody capable of binding to sarbecovirus spike protein described herein. That is, in some embodiments the antigen-binding molecule comprises the VH region and the VL region of an antibody capable of binding to sarbecovirus spike protein described herein or comprises VH and VL regions which are derived from an antibody capable of binding to sarbecovirus spike protein described herein.

[00106] In some embodiments the antigen-binding molecule comprises the CDRs, FRs and/or the VH and/or VL regions of an antibody capable of binding to sarbecovirus spike protein selected from any one of sarbecovirus spike protein of SARS-CoV, SC2r-CoV WIV-1, SC1r-CoV RsSHC014, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta, SARS-CoV-2 Delta, SC2r-CoV RaTG13, SC2r-CoV GD-1 and SC2r-CoV GX-P5L.

[00107] In various embodiments, the antigen-binding molecule comprises:
30 (i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:1

HC-CDR2 having the amino acid sequence of SEQ ID NO:2

HC-CDR3 having the amino acid sequence of SEQ ID NO:3; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO: 4

LC-CDR2 having the amino acid sequence of SEQ ID NO: 5

LC-CDR3 having the amino acid sequence of SEQ ID NO: 6.

5 **[00108]** In various embodiments, the antigen-binding molecule comprises: a VH region comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 2, 3 or 4; and a VL region comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 5, 6 or 7.

10 **[00109]** In various embodiments the antigen-binding molecule comprises a VH region comprising an amino acid sequence having at least 75% sequence identity, including one of at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO:1.

15 **[00110]** In various embodiments the antigen-binding molecule comprises a VH region comprising an amino acid sequence having at least 75% sequence identity, including one of at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO: 2.

20 **[00111]** In various embodiments the antigen-binding molecule comprises a VH region comprising an amino acid sequence having at least 75% sequence identity, including one of at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO:3.

[00112] In various embodiments the antigen-binding molecule comprises a VL region comprising an amino acid sequence having at least 75% sequence identity, including one of at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO: 4.

25 **[00113]** In various embodiments the antigen-binding molecule comprises a VL region comprising an amino acid sequence having at least 75% sequence identity, including one of at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO:5.

30 **[00114]** In various embodiments the antigen-binding molecule comprises a VL region comprising an amino acid sequence having at least 75% sequence identity, including one of

at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to the amino acid sequence of SEQ ID NO:6.

[00115] In embodiments in accordance with the present disclosure in which one or more amino acids are substituted with another amino acid, the substitutions may be conservative substitutions, for example an aliphatic amino acid is replaced with another aliphatic amino acid such as a non-polar amino acid G, or A, or P, or I, or L, or V is replaced with a different non-polar amino acid; such as a polar uncharged amino acid C, or S, or T, or M, or N, or Q is replaced with a different polar uncharged amino acid such as a polar charged amino acid D, or E, or K, or R is replaced with a different polar charged amino acid or an aromatic amino acid is replaced with another aromatic amino acid such as H, or F, or W, or Y, is replaced with a different aromatic amino acid.

[00116] In variable embodiments, substitution(s) may be functionally conservative. That is, in some embodiments the substitution may not affect (or may not substantially affect) one or more functional properties (e.g., target binding) of the antigen-binding molecule comprising the substitution as compared to the equivalent unsubstituted molecule.

[00117] The VH and VL region of an antigen-binding region of an antibody together constitute the Fv region. In some embodiments, the antigen-binding molecule according to the present disclosure comprises, or consists of, an Fv region which binds to sarbecovirus spike protein. In various embodiments, the VH and VL regions of the Fv may be provided as single polypeptide joined by a linker region, i.e., a single chain Fv (scFv).

[00118] The VL and light chain constant (CL) region, and the VH region and heavy chain constant 1 (CH1) region of an antigen-binding region of an antibody together constitute the Fab region. In some embodiments the antigen-binding molecule comprises a Fab region comprising a VH, a CH1, a VL and a CL (e.g., **C_κ** or **C_λ**). In various embodiments, the Fab region comprises a polypeptide comprising a VH and a CH1 (e.g., a VH-CH1 fusion polypeptide), and a polypeptide comprising a VL and a CL (e.g., a VL-CL fusion polypeptide). In various embodiments, the Fab region comprises a polypeptide comprising a VH and a CL (e.g., a VH-CL fusion polypeptide) and a polypeptide comprising a VL and a CH (e.g., a VL-CH1 fusion polypeptide); that is, in some embodiments the Fab region is a CrossFab region. In various embodiments, the VH, CH1, VL and CL regions of the Fab or CrossFab are provided as single polypeptide joined by linker regions, i.e., as a single chain Fab (scFab) or a single chain CrossFab (scCrossFab).

[00119] In various embodiments, the antigen-binding molecule of the present disclosure comprises, or consists of, a Fab region which binds to sarbecovirus spike protein.

[00120] In various embodiments, the antigen-binding molecule described herein comprises, or consists of, a whole antibody which binds to sarbecovirus spike protein. As used herein, **“whole antibody”** refers to an antibody having a structure which is substantially similar to the structure of an immunoglobulin (Ig).

[00121] Immunoglobulins of type G (i.e., IgG) are ~150 kDa glycoproteins comprising two heavy chains and two light chains. From N- to C-terminus, the heavy chains comprise a VH followed by a heavy chain constant region comprising three constant domains (CH1, CH2, and CH3), and similarly the light chain comprise a VL followed by a CL. Depending on the heavy chain, immunoglobulins may be classed as IgG (e.g., IgG1, IgG2, IgG3, IgG4), IgA (e.g., IgA1, IgA2), IgD, IgE, or IgM. The light chain may be kappa (κ) or lambda (λ).

[00122] In some embodiments, the antigen-binding molecule described herein comprises, or consists of, an IgG (e.g., IgG1, IgG2, IgG3, IgG4), IgA (e.g. IgA1, IgA2), IgD, IgE, or IgM which binds to sarbecovirus spike protein.

[00123] In some embodiments the antigen-binding molecule of the present disclosure comprises one or more regions (e.g., CH1, CH2, CH3, etc.) of an immunoglobulin heavy chain constant sequence. In some embodiments the immunoglobulin heavy chain constant sequence is, or is derived from, the heavy chain constant sequence of an IgG (e.g., IgG1, IgG2, IgG3, IgG4), IgA (e.g., IgA1, IgA2), IgD, IgE or IgM, e.g. a human IgG (e.g. hIgG1, hIgG2, hIgG3, hIgG4), hIgA (e.g. hIgA1, hIgA2), hIgD, hIgE or hIgM. In some the immunoglobulin heavy chain constant sequence is, or is derived from, the heavy chain constant sequence of a human IgG1 allotype (e.g., G1m1, G1m2, G1m3 or G1m17).

[00124] According to various embodiments there is an antigen-binding molecule as discussed herein above, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[00125] In various embodiments, the antigen-binding molecule as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

[00126] In various embodiments, the antigen-binding molecule as discussed herein above, is suitable for use in individuals that are infection or vaccination naive to any

sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, or SARS-CoV-2 Beta, SARS-CoV-2 Delta.

[00127] In various embodiments, the antigen-binding molecule as discussed herein above, is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00128] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[00129] According to various embodiments there is use of an antigen-binding molecule as discussed herein above, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[00130] In various embodiments, the use of the antigen-binding molecule as discussed herein above in the manufacture of a medicament is suitable for use in treatment or prevention in individuals that have had SARS-CoV-2 vaccination or infection.

[00131] In various embodiments, the use of an antigen-binding molecule as discussed herein above, is suitable for use in treatment or prevention in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alphas, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00132] In various embodiments, the use of the antigen-binding molecule as discussed herein above in the manufacture of a medicament is suitable for treatment in individuals that have been diagnosed with a sarbecovirus infection.

[00133] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[00134] According to various embodiments there is a method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically effective amount of an antigen-binding molecule as discussed herein above.

5 **[00135]** In various embodiments, the subject is an individual that has had SARS-CoV-2 vaccination or infection.

[00136] In various embodiments, the subject is an individual that has been diagnosed with a sarbecovirus infection

10 **[00137]** In various embodiments, the subject is an individual that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00138] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, 15 SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[00139] According to various embodiments there is a nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding an antigen-binding molecule as discussed herein above.

20 **[00140]** According to various embodiments there is an expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids as discussed herein above.

25 **[00141]** According to various embodiments there is a nucleic acid or a plurality of nucleic acids as discussed herein above, or an expression vector, or a plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

30 **[00142]** In various embodiments, the nucleic acid or the plurality of nucleic acids as discussed herein above, or the expression vector, or the plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-

binding molecule as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

5 **[00143]** In various embodiments, the nucleic acid or the plurality of nucleic acids as discussed herein above, or the expression vector, or the plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, is suitable for use in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, or SARS-CoV-2 B.1.351.

10 **[00144]** In various embodiments, the nucleic acid or the plurality of nucleic acids as discussed herein above, or the expression vector, or the plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

15 **[00145]** In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

20 **[00146]** According to various embodiments there is a nucleic acid or a plurality of nucleic acids as discussed herein above, or an expression vector or a plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

25 **[00147]** In various embodiments, use of the nucleic acid or the plurality of nucleic acids as discussed herein above, the expression vector or the plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, in the manufacture of a medicament is suitable for use in treatment or prevention in individuals that have had SARS-CoV-2 vaccination or
30 infection.

[00148] In various embodiments, use of the nucleic acid or the plurality of nucleic acids as discussed herein above, the expression vector or the plurality of expression vectors

comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, in the manufacture of a medicament is suitable for use in treatment or prevention in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00149] In various embodiments, use of the nucleic acid or the plurality of nucleic acids as discussed herein above, the expression vector or the plurality of expression vectors comprising the nucleic acid or the plurality of nucleic acids, capable of expressing an antigen-binding molecule as discussed herein above, in the manufacture of a medicament is suitable for use in treatment in individuals have been diagnosed with a sarbecovirus infection.

[00150] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, SARS-CoV.

[00151] According to various embodiments there is a method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically effective amount of an antigen-binding molecule wherein the antigen-binding molecule is expressed by a nucleic acid or a plurality of nucleic acids as discussed herein above, or expressed in an expression vector or a plurality of expression vectors as discussed herein above.

[00152] In various embodiments, the subject is an individual that has had SARS-CoV-2 vaccination or infection.

[00153] In various embodiments, the subject is an individual that is infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00154] In various embodiments, the subject is an individual that has been diagnosed with a sarbecovirus infection.

[00155] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2

B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

5 **[00156]** According to various embodiments there is a cell comprising an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein above, or an expression vector or a plurality of expression vectors as discussed herein above.

10 **[00157]** According to various embodiments there is a method for producing an antigen-binding molecule which binds to a sarbecovirus spike protein, comprising culturing a cell as discussed herein above under conditions suitable for expression of an antigen-binding molecule by the cell.

[00158] According to various embodiments there is a cell as discussed herein above, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

15 **[00159]** In various embodiments, the cell as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

[00160] In various embodiments, the cell as discussed herein above, is suitable for use in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

20 **[00161]** In various embodiments, the cell as discussed herein above, is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00162] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

25 **[00163]** According to various embodiments there is use of a cell as discussed herein above, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

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[00164] In various embodiments, use of the cell as discussed herein above, in the manufacture of a medicament is suitable for use in individuals that have had SARS-CoV-2 vaccination or infection.

[00165] In various embodiments, use of the cell as discussed herein above, in the manufacture of a medicament is suitable for use in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00166] In various embodiments, use of the cell as discussed herein above, in the manufacture of a medicament is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00167] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[00168] According to various embodiments there is a method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically effective amount of an antigen-binding molecule as discussed herein above, wherein the antigen-binding molecule is expressed in a cell as discussed herein above.

[00169] In various embodiments, the subject is an individual that have had SARS-CoV-2 vaccination.

[00170] In various embodiments, the subject is an individual that is infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, or SARS-CoV-2 Delta.

[00171] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1,

SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

5 **[00172]** According to various embodiments there is a composition comprising an antigen-binding molecule as discussed herein above, a nucleic acid or a plurality of nucleic acids as discussed herein above, an expression vector or a plurality of expression vectors as discussed herein above, or a cell as discussed herein above, and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

10 **[00173]** According to various embodiments there is a composition as discussed herein above, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[00174] In various embodiments, the composition as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

15 **[00175]** In various embodiments, the composition as discussed herein above, is suitable for use in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00176] In various embodiments, the composition as discussed herein above, is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

20 **[00177]** In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

25 **[00178]** According to various embodiments there is use of a composition as discussed herein above, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

30 **[00179]** In various embodiments, use of the composition as discussed herein above, in the manufacture of a medicament is suitable for use in individuals that have had SARS-CoV-2 vaccination.

[00180] In various embodiments, use of the composition as discussed herein above, in the manufacture of a medicament is suitable for use in individuals that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

- 5 **[00181]** In various embodiments, use of the composition as discussed herein above, in the manufacture of a medicament is suitable for use in treatment of individuals that have been diagnosed with a sarbecovirus infection.

- [00182]** In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.
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- [00183]** According to various embodiments there is a method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically effective amount of a composition as discussed herein above.
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[00184] In various embodiments, the subject is an individual that have had SARS-CoV-2 vaccination or infection.

- 20 **[00185]** In various embodiments, the subject is an individual that are infection or vaccination naive to any sarbecovirus including SARS-CoV, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta or SARS-CoV-2 Delta.

[00186] In various embodiments, the subject is an individual that has been diagnosed with a sarbecovirus infection.

- 25 **[00187]** In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SC2r-CoV WIV-1, SC1r-CoV RsSHC014, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta, SARS-CoV-2 Delta, SC2r-CoV RaTG13, SC2r-CoV GD-1 and SC2r-CoV GX-P5L.

- [00188]** According to various embodiments there is use of an antigen-binding molecule as discussed herein above to inhibit infection of ACE2-expressing cells by a sarbecovirus.
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[00189] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SC2r-CoV WIV-1, SC1r-CoV RsSHC014, SARS-CoV-2, SARS-CoV-2 Alpha, SARS-CoV-2 Beta, SARS-CoV-2 Delta, SC2r-CoV RaTG13, SC2r-CoV GD-1 and SC2r-CoV GX-P5L

5 **[00190]** Sequences

SEQ ID NO:	DESCRIPTION	SEQUENCE
1	Heavy chain variable region HC-CDR1	GFTFSXYX
2	Heavy chain variable region HC-CDR2	IYXXGXT
3	Heavy chain variable region HC-CDR3	ARXXXXFDY
4	light chain variable region LC-CDR1	QSIXTY
5	Light chain variable region LC-CDR2	XAS
6	Light chain variable region LC-CDR3	QQSXXTPXT
7	SARS-CoV (GenBank: NC_004718.3)	ATATTAGGTTTTACCTACCCAGGAAAAGCCAACCAACCTCGATCTCTTGTAGATCTG TTCTCTAAACGAACTTTAAATCTGTGTAGCTGTCGCTCGGCTGCATGCCTAGTGCAC CTACGCAGTATAAAACAATAATAATTTTACTGTCGTTGACAAGAAACGAGTAACCTGT CCTCTTTCTGCAGACTGCTTACGGTTTCGTCCGTGTTGCAGTCGATCATCAGCATAAC CTAGGTTTTCGTCCGGGTGTGACCGAAAGGTAAGATGGAGAGCCTTGTCTTGGTGTG AACGAGAAAACACACGTCCTCACTCAGTTTGCCTGTCCTTCAGGTTAGAGACGTGCTA GTGCGTGGCTTCGGGGACTCTGTGGAAGAGGCCCTATCGGAGGCACGTGAACACCT CAAAAATGGCACTTGTGGTCTAGTAGAGCTGGAAAAAGGCGTACTGCCCCAGCTTGA ACAGCCCTATGTGTTCAATTAACGTTCTGATGCCTTAAGCACCAATCACGGCCACAA GGTCGTTGAGCTGGTTGACGAAATGGACGGCATTGAGTACGGTCGTAGCGGTATAA CACTGGGAGTACTCGTGCCACATGTGGGCGAAACCCCAATTGCATACCGCAATGTTT TTCTTCGTAAGAACGGTAATAAGGGAGCCGGTGGTCACTAGCTATGGCATCGATCTAA AGTCTTATGACTTAGGTGACGAGCTTGGCACTGATCCCATTAAGATTATGAACAAAA CTGGAACACTAAGCATGGCAGTGGTGCCTGCACTCACTCGTGAGCTCAATG GAGGTGCAGTCACTCGCTATGTGCAACAATAATTTCTGTGGCCAGATGGGTACCCCTC TTGATTGCATCAAAGATTTTCTGCGACGCGCGGGCAAGTCAATGTGCACTCTTTCCG AACAACCTTGATTACATCGAGTGAAGAGAGGTGTCTACTGCTGCCGTGACCATGAGC ATGAAATTGCCTGGTTCACTGAGCGCTCTGATAAGAGCTACGAGCACCAGACACCCT TCGAAATTAAGAGTGCCAAGAAATTTGACACTTTCAAAGGGGAATGCCCAAAGTTTGT GTTTCCTCTTAACCAAAAGTCAAAGTCAATCAACCACGTGTTGAAAAGAAAAAGACT GAGGGTTTCATGGGGCGTATACGCTCTGTGTACCCTGTTGCATCTCCACAGGAGTGT AACAATATGCACCTGTCTACCTTGATGAAATGTAATCATTGCGATGAAGTTTCATGGC AGACGTGCGACTTTCTGAAAGCCACTTGTGAACATTGTGGCACTGAAAAATTTAGTTAT TGAAGGACCTACTACATGTGGGTACCTACCTACTAATGCTGTAGTGAATGCCATGT CCTGCCGTGCAAGACCCAGAGATTGGACCTGAGCATAGTGTGAGCATTATCACAACT CACTCAAACATTGAAACTCGACTCCGCAAGGGAGGTAGGACTAGATGTTTTGGAGGC TGTGTGTTTGCCTATGTTGGCTGCTATAATAAGCGTGCCTACTGGGTTCCCTCGTGCTA GTGCTGATATTGGCTCAGGCCATACTGGCATTACTGGTGACAATGTGGAGACCTTGA ATGAGGATCTCCTTGAGATACTGAGTCGTGAACGTGTTAACATTAACTGTTGGCGA TTTTCATTTGAATGAAGAGGTTGCCATCATTTTGGCATCTTTCTCTGCTTCTACAAGTG CCTTTATTGACACTATAAAGAGTCTTGATTACAAGTCTTTCAAACCAATTGTTGAGTCC TGCGGTAACATAAAGTTACCAAGGGAAAGCCCGTAAAGGTGCTTGGAACTTGGGA CAACAGAGATCAGTTTAAACCACTGTGTGGTTTTCCCTCACAGGCTGCTGGTGTTA TCAGATCAATTTTTCGCGCACACTTGATGCAGCAAACTCAATTCCTGATTGCA AAGAGCAGCTGTACCATACCTTGATGGTATTTCTGAACAGTCATTACGCTTGTGCGAC

		GCCATGGTTTATACTTCAGACCTGCTCACCAACAGTGTCTATTATTATGGCATATGTAA CTGGTGGTCTTGACAAACAGACTTCTCAGTGGTTGTCTAATCTTTTGGGCACTACTGT TGAAAACTCAGGCCTATCTTTGAATGGATTGAGGCGAAACTTAGTGACAGGAGTTGA ATTTCTCAAGGATGCTTGGGAGATTCTCAAATTTCTCATTACAGGTGTTTTGACATC GTCAAGGGTCAAATACAGGTTGCTTCAGATAACATCAAGGATTGTGTAAAAATGCTTCA TTGATGTTGTTAAACAAGGCACCTCGAAATGTGCATTGATCAAGTCACTATCGCTGGCG CAAAGTTGCGATCACTCAACTTAGGTGAAGTCTTCATCGCTCAAAGCAAGGGACTTTA CCGTCAAGTGATACGTGGCAAGGAGCAGCTGCAACTACTCATGCCCTTTAAGGCACC AAAAGAAGTAACCTTTCTTGAAGGTGATTACATGACACAGTACTTACCTCTGAGGAG GTTGTTCTCAAGAACGGTGAAGTCTGAAGCACTCGAGACGCCCGTTGATAGCTTCACA AATGGAGCTATCGTTGGCACACCAGTCTGTGTAAATGGCCTCATGCTCTTAGAGATT AAGGACAAAGAACAATACTGCGCATTGTCTCTGGTTTACTGGCTACAAACAATGTCT TTCGCTTAAAAAGGGGGTGACCAATTAAGGTGTAACCTTTGGAGAAGATACTGTTT GGGAAGTTCAAGGTTACAAGAATGTGAGAATCACATTTGAGCTTGATGAACGTGTTG ACAAAGTGCTTAATGAAAAGTGCTCTGTCTACACTGTTGAATCCGGTACCGAAGTTAC TGAGTTTGATGTTGTAGCAGAGGCTGTTGTGAAGACTTTACAACCAAGTTTCTGAT CTCCTTACCAACATGGGTATTGATCTTGATGAGTGAGTGAGTACATTCTACTTAT TTGATGATGCTGGTGAAGAAAACTTTTCATCAGTATGATTGTTCTTTTACCCTCCA GATGAGGAAGAAGAGGACGATGCAGAGTGTGAGGAAGAAGAAATTGATGAAACCTG TGAACATGAGTACGGTACAGAGGATGATTATCAAGGTCTCCCTCTGGAATTTGGTGC CTCAGCTGAAACAGTTTCGAGTTGAGGAAGAAGAAGAGGAAGACTGGCTGGATGATA CTACTGAGCAATCAGAGATTGAGCCAGAACCAGAACCCTACACCTGAAGAACCAGTTA ATCAGTTTACTGGTTATTTTAAACTTACTGACAAATGTTGCCATTAATGTGTTGACATC GTTAAGGAGGCACAAAGTGCTAATCCTATGGTGATTGTAATGCTGCTAACATACACC TGAAACATGGTGGTGGTGTAGCAGGTGCACTCAACAAGGCAACCAATGGTCCATG CAAAGGAGAGTGATGATTACATTAAGCTAAATGGCCCTCTTACAGTAGGAGGGTCT TGTTTGCTTTCTGGACATAATCTTGCTAAGAAGTGCTGCATGTTGTTGGACCTAACCC TAAATGCAGGTGAGGACATCCAGCTTCTTAAGGCAGCATATGAAATTTCAATTCCACA GGACATCTTACTTGACCACTTGTGTCAGCAGGCATATTTGGTGCTAAACCACTTCAG TCTTTACAAGTGTCGCTGCAGACGGTTCGTACACAGGTTTATATTGCAGTCAATGACA AAGCTCTTTATGAGCAGGTTGTGTCATGGATTATCTTGATAACCTGAAGCCTAGAGTGGA AGCACCTAAACAAGAGGAGGCCACCAACACAGAAGATTCCAAAACCTGAGGAGAAATC TGTCGTACAGAAGCCTGTCGATGTGAAGCCAAAAATTAAGGCCTGCATTGATGAGGT TACCACAACACTGGAAGAACTAAGTTTCTTACCAATAAGTACTCTGTTTGTGATA TCAATGGTAAGCTTTACCATGATTCTCAGAACATGCTTAGAGGTGAAGATATGTCTTT CCTTGAGAAAGATGCACCTTACATGGTAGGTGATGTTATCACTAGTGGTGATATCACT TGTGTTGTAATACCCTCCAAAAAGGCTGGTGGCACTACTGAGATGCTCTCAAGAGCT TTGAAGAAAGTGCCAGTTGATGAGTATATAACCACTACCTGGACAAGGATGTGCT GGTTATACACTTGAGGAAGCTAAGACTGCTCTTAAGAAATGCAAATCTGCATTTTATG TACTACCTTCAGAAACCACTAATGCTAAGGAAGAGATTCTAGGAAGTATCTCTGGAA TTTGAGAGAAATGCTTGTCTATGCTGAAGAGACAAGAAAAATTAATGCCATATGTCAT GATGTTAGAGCCATAATGGCAACCATCCAACGTAAGTATAAAGGAATTAATTAATCAAG AGGGCATCGTTGACTATGGTGTCCGATTCTTCTTTTACTAGTAAAGAGCCGTGATGAGC TTCTATTATTACGAAGCTGAAGTCTCTAATGAGCCGCTTGTACAATGCCAATTTGTT TATGTGACACATGGTTTTAATCTTGAAGAGGCTGCGCGCTGTATCGTTCTCTTAAAG CTCCTGCCGTAGTGTCAGTATCATCACCAGATGCTGTTACTACATATAATGGATACCT CACTTCGTATCAAGACATCTGAGGAGCACTTTGTAGAAACAGTTTCTTTGGCTGGC TCTTACAGAGATTGGTCTATTACAGGACAGCGTACAGAGTTAGGTGTTGAATTTCTTA AGCGTGGTGACAAAATTGTGTACCACACTCTGGAGAGCCCCGTGAGTTTCATCTTG ACGGTGAGGTTCTTTCACTTGACAACTAAAGAGTCTCTTATCCCTGCGGGAGGTTA AGACTATAAAAGTGTTCACAACTGTGGACAACACTAATCTCCACACACAGCTTGTGGA TATGTCTATGACATATGGACAGCAGTTTGGTCCAACATACTTGGATGGTGCTGATGTT ACAAAAATTAACCTCATGTAAATCATGAGGGTAAGACTTTCTTTGTACTACCTAGTGA TGACACACTACGTAGTGAAGCTTTTCGAGTACTACCATACTTGTATGAGAGATTTCTT GGTAGGTACATGTCTGCTTTAAACCACACAAAGAAATGGAATTTCTCAAGTTGGTG GTTTAACTTCAATTAATGGGCTGATAACAATTGTTATTTGTCTAGTGTTTTATTAGCA CTTCAACAGCTTGAAGTCAATTTCAATGCACCAGCACTTCAAGAGGCTTATTATAGAG CCCGTGCTGGTGATGCTGCTAACTTTTGTCACTCATACTCGCTTACAGTAAATAAAC TGTTGGCGAGCTTGGTGTGTCAGAGAACTATGACCCATCTTCTACAGCATGCTAA TTTGAATCTGCAAGCGAGTTCTTAATGTGGTGTGTAAACATTGTGGTCAGAAAACCT ACTACCTTAACGGGTGTAGAAGCTGTGATGTATATGGGTACTCTATCTTATGATAATC TTAAGACAGGTGTTTCCATTCATGTGTGTGGTGTGATGCTACACAATATCTAGT ACAACAAGAGTCTTCTTTTGTATGATGTCTGCACCACCTGCTGAGTATAAATACAG CAAGGTACATTCTTATGTGCAATGAGTACACTGGTAACATATCAGTGTGGTCATTACA CTCATATAACTGCTAAGGAGACCCCTCTATCGTATTGACGGAGCTCACCTTACAAAGAT GTCAGAGTACAAAGGACCAGTGAAGTATGTTTCTACAAGGAACATCTTACACTACA
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	ACCATCAAGCCTGTGTCGTATAAACTCGATGGAGTTACTTACACAGAGATTGAACCAA AATTGGATGGGTATTATAAAAAGGATAATGCTTACTATACAGAGCAGCCTATAGACCT TGTACCAACTCAACCATTACCAAATGCGAGTTTTGATAATTTCAAACCTCACATGTTCTA ACACAAAATTTGCTGATGATTTAAATCAAATGACAGGCTTACAAAAGCCAGCTTCACG AGAGCTATCTGTACATTCTTCCCAGACTTGAATGGCGATGTAGTGGCTATTGACTAT AGACACTATTACGCGAGTTTCAAGAAAGGTGCTAAATTACTGCATAAGCCAATTGTTT GGCACATTAACCAGGCTACAACCAAGACAACGTTCAAACCAACACTTGGTGTTTAC GTTGTCTTTGGAGTACAAAGCCAGTAGATACTTCAAATTCATTTGAAGTTCTGGCAGT AGAAGACACACAAGGAATGGACAATCTTGCTTGTAAGTCAACAACCCACCTCTGA AGAAGTAGTGGAAAATCCTACCATACAGAAGGAAGTCATAGAGTGTGACGTGAAAAAC TACCGAAGTTGTAGGCAATGTCATACTTAAACCATCAGATGAAGGTGTTAAAGTAACA CAAGAGTTAGGTGATGAGGATCTTATGGCTGCTTATGTGAAAAACACAAGCATTACC ATTAAGAAACCTAATGAGCTTTCACTAGCCTTAGGTTTAAAAACAATTGCCACTCATG GTATTGCTGCAATTAATAGTGTCTTGGAGTAAAATTTGGCTTATGTCAAACCATTC TTAGGACAAGCAGCAATTAACACATCAAATTCGCGTAAGAGATTAGCACAACGTGTGT TTAACAATTATATGCCCTTATGTGTTTACATTATTGTTCCAATTGTGTACTTTTACTAAAA GTACCAATTCTAGAATTAGAGCTTCACTACCTACAACCTATTGCTAAAAATAGTGTAAAG AGTGTGCTAAATTAATGTTGGATGCCGGCATTAAATATGTGAAGTCAACCAAAATTTT CTAAATGTTTCAATCGCTATGTGGCTATTGTTGTTAAGTATTTGCTTAGGTTCTCTA ATCTGTGTAACCTGCTGCTTTTGGTGTACTCTTATCTAATTTTGGTGCTCCTTCTTATTG TAATGGCGTTAGAGAATTGTATCTTAATTCGTCTAACGTTACTACTATGGATTCTGTG AAGGTTCTTTTCTTGCAGCATTTGTTTAAAGTGGATTAGACTCCCTTGATTCTTATCCA GCTCTTGAAACCATTCAGGTGACGATTTTCATCGTACAAGCTAGACTTGACAATTTTAG GTCTGGCCGCTGAGTGGGTTTTGGCATATATGTTGTTCAAAAATCTTTTATTATTATTA GGTCTTTTCACTATAATGCAGGTGTTCTTTGGCTATTTTGTAGTCAATTTTATCAGCA ATTCTTGGCTCATGTGTTTATCATTAGTATTGTACAAATGGCACCCGTTTCTGCAAT GGTTAGGATGTACATCTTCTTCTTCTTCTACTACATATGGAAGAGCTATGTTTCATA TCATGGATGTTGACACCTCTTCGACTTGCATGATGTGCTATAAGCGCAATCGGCCA CACGCGTTGAGTGTACAACCTATTGTTAATGGCATGAAGAGATCTTCTATGTCTATGC AAATGGAGGCCGTGGCTTCTGCAAGACTCACAAATGGAATTGTCTCAATTTGTGACAC ATTTTGCATGGTAGTACATTCAATAGTGATGAAGTTGCTCGTGATTGTCACCTCAG TTTAAAGACCAATCAACCCTACTGACCAGTCATCGTATATTGTTGATAGTGTGCTG TGAAAAATGGCGCGCTTCACCTCTACTTTGACAAGGCTGGTCAAAAAGACCTATGAGA GACATCCGCTCTCCATTTTGTCAATTTAGACAATTTGAGAGCTACAACACTAAAGG TTCACCTGCCTATTAATGTACATGTTTTGATGGCAAGTCCAAATGCGACGAGTCTGCT TCTAAGTCTGCTTCTGTGTACTACAGTCAGCTGATGTGCCAACCTATTCTGTTGCTTG ACCAAGCTCTTGATCAGACGTTGGAGATAGTACTGAAGTTTCCGTTAAGATGTTTGA TGCTTATGTGACACCTTTTTCAGCAACTTTTAGTGTTCTATGAAAAAATTTAAGGCA CTTGTTGCTACAGCTCACAGCGAGTTAGCAAAGGGTGTAGCTTTAGATGGTGTCTT TCTACATTCGTGTGAGCTGCCGACAAAGGTGTTGTTGATACCGATGTTGACACAAAG GATGTTATTGAATGTCTCAAACTTTACATCACTCTGACTTGAAGTGAACAGGTGACA GTTGTAACAATTTATGCTCACCTATAATAAGGTTGAAAACATGACGCCCAGAGATCT TGGCGCATGTATTGACTGTAATGCAAGGCATATCAATGCCCAAGTAGCAAAAAAGTCA CAATGTTTCACTCATCTGGAATGTAAAAGACTACATGCTTTATCTGAACAGCTGCGT AAACAAATTCGTAGTGTGCTGCCAAGAAAGAACACATACCTTTTATAGCTAATTTGTGCTA CAACTAGACAGGTTGTCAATGTCACTACTAAATCTCACTCAAGGGTGGTAAGAT TGTTAGTACTTGTTTAACTTATGCTTAAGGCCACATTATTGTGCGTTCTTGTGCTGAT TGGTTTGTATATCGTTATGCCAGTACATACATTGTCAATCCATGATGGTTACACAAAT GAAATCATTGGTTACAAAGCCATTCAAGGATGGTGTCACTCGTGACATCATTTCTACTG ATGATTGTTTTGCAAAATAACATGCTGGTTTTGACGCATGGTTTAGCCAGCGTGGTGG TTCATACAAAAATGACAAAAGCTGCCCTGTAGTAGCTGCTATCATTACAAGAGAGATT GGTTTCATAGTGCCTGGCTTACCGGGTACTGTGCTGAGAGCAATCAATGGTGACTTC TTGCATTTTCTACCTCGTGTTTTGTAGTGTGTTGGCAACATTTGCTACACACCTTCCAA ATTTTTAAGGATGCTATGGGCAACCTGTGCCATATTGTTATGACACTAATTTGCTAG AGGGTTCTATTTCTTATAGTGAGCTTCGTCCAGACACTCGTTATGTGCTTATGGATGG TTCCATCATACAGTTTCTAACACTTACCTGGAGGGTCTGTTAGAGTAGTAACAACT TTTGATGCTGAGTACTGTAGACATGGTACATGCCAAAGGTCAGAAGTAGGTATTTGCT CTATCTACCAGTGGTAGATGGGTCTTAATAATGAGCATTACAGAGCTCTATCAGGAG TTTTCTGTGGTGTGATGCGATGAATCTCATAGCTAACATCTTACTCCTCTTGTGCAA CCTGTGGGTGCTTTAGATGTGCTGCTTCAAGTAGTGGCTGGTGGTATTATTGCCATAT TGGTGACTTGTGCTGCCTACTACTTTATGAAATTCAGACGTGTTTTTGGTGAGTACAA CCATGTTGTTGCTGCTAATGCACTTTTGTGTTTGTGCTTTTCACTATACTCTGTCTGG TACCAGCTTACAGCTTCTGCCGGGAGTCTACTCAGTCTTTTACTGTACTGTGACATT CTATTTACCAATGATGTTTCATTCTTGGCTCACCTTCAATGGTTTGGCATGTTTTCTC CTATTGTGCCTTTTTGGATAACAGCAATCTATGTATTCTGTATTTCTCTGAAGCACTGC
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	CATTGGTTCTTTAACTATCTTAGGAAAAGAGTCATGTTTAAATGGAGTTACATTTAG TACCTTCGAGGAGGCTGCTTTGTGTACCTTTTTGCTCAACAAGGAAATGTACCTAAAA TTGCGTAGCGAGACACTGTTGCCACTTACACAGTATAACAGGTATCTTGCTCTATATA ACAAGTACAAGTATTTCACTGGAGCCTTAGATACTACCAGCTATCGTGAAGCAGCTT GCTGCCACTTAGCAAAGGCTCTAAATGACTTTAGCAACTCAGGTGCTGATGTTCTCTA CCAACCACCACAGACATCAATCACTTCTGCTGTTCTGCAGAGTGGTTTTAGGAAAATG GCATTCCCCTCAGGCAAAGTTGAAGGGTGCATGGTACAAGTAACCTGTGGAACATACA ACTCTTAATGGATTGTGGTTGGATGACACAGTATACTGTCCAAGACATGTCATTTGCA CAGCAGAAGACATGCTTAATCCTAATGAAGATCTGCTCATTGCGAAATCCAACCA TAGCTTTCTTTGTTGAGGCTGGCAATGTTCAACTTCGTGTTATTGGCCATTCTATGCAA AATTGTCTGCTTAGGCTTAAAGTTGATCTTCTAACCTTAAGACACCCAAGTATAAAT TGTCGTATCCAACCTGGTCAAACATTTTCAGTTCTAGCATGCTACAATGGTTCCACCA TCTGGTGTATTACAGTGTGCCATGAGACCTAATCATACCATTAAGGTTCTTTCTTAA TGGATCATGTGGTAGTGTGGTTTTAACATTGATTATGATTGCGTGTCTTTCTGCTATA TGCATCATATGGAGCTTCCAACAGGAGTACACGCTGGTACTGACTTAGAAGTAAAT TCTATGGTCCATTTGTTGACAGACAACTGCACAGGCTGCAGGTACAGACACAACCA TAACATTAATGTTTTGGCATGGCTGTATGCTGCTGTTATCAATGGTGATAGGTGGTT TCTTAATAGATTACCACTACTTTGAATGACTTTAACCTTGTGGCAATGAAGTACAAC ATGAACCTTTGACACAAGATCATGTTGACATATTGGGACCTCTTTCTGCTCAAACAGG AATTGCCGTCTTAGATATGTGTGCTGCTTTGAAAGAGCTGCTGCAGAAATGGTATGAAT GGTCGTACTATCCTTGGTAGCACTATTTAGAAGATGAGTTTACACCATTTGATGTTG TTAGACAATGCTCTGGTGTACCTTCCAAGGTAAGTTCAAGAAAATTTGTTAAGGGCAC TCATCATTGGATGCTTTTAACTTTCTTGACATCACTATTGATTCTTGTCCAAGATACAC AGTGGTCACTGTTTTCTTTGTTTACGAGAATGCTTTCTTGCCATTACTCTTGGTATT ATGGCAATTGCTGCTATGCTGCTGTTGTTAAGCATAAAGCAGCATTTCTGTGCT TGTTTCTGTTACCTTCTCTTGCAACAGTTGCTTACTTTAATATGGTCTACATGCTGCT AGCTGGGTGATGCGTATCATGACATGGCTTGAATGGCTGACACTAGCTTGTCTGGT TATAGGCTTAAGGATTGTGTTATGTATGCTTCAGCTTTAGTTTTGCTTATCTGATGAC AGCTCGCACTGTTTATGATGATGCTGCTAGACGTGTTGGACACTGATGAATGTCATT ACACTTGTTTACAAAGTCTACTATGGTAATGCTTTAGATCAAGCTATTTCCATGTGGG CCTTAGTTATTTCTGTAACCTCTAACTATTCTGGTGTGCTTACGCAATCATGTTTTTA GCTAGAGCTATAGTGTGTTGTGTGTTGAGTATTACCCATTGTTATTTACTGGCAA CACCTTACAGTGTATCATGCTTGTATTGTTTCTTAGGCTATTGTTGCTGCTGCTACT TTGGCCTTTTCTGTTTACTCAACCGTTACTTCAGGCTTACTTGGTGTATTGACTAC TTGGTCTCTACACAAGAATTTAGGTATATGAACCTCCAGGGGCTTTTGCCTCCTAAGA GTAGTATTGATGCTTTCAAGCTTAACATTAAGTTGTTGGGTATTGGAGGTAACCATG TATCAAGGTTGCTACTGTACAGTCTAAAATGTCTGACGTAAAGTGACATCTGTGGTA CTGCTCTCGGTTCTTCAACAACCTTAGAGTAGAGTCATCTTAAATTTGGGCAACA GTGTACAACCTCCACAATGATATTCTTCTTGCAAAAGACACAACCTGAAGCTTTGAGAA GATGGTTTCTCTTTTGTCTGTTTTGCTATCCATGCAGGGTGTGTAGACATTAATAGG TTGTGCGAGGAAATGCTCGATAACCGTGCTACTCTTCAGGCTATTGCTTCAGAAATTA GTTCTTTACCATCATATGCCGCTTATGCCACTGCCAGGAGGCTATGAGCAGGCTG TAGCTAATGGTGATTCTGAAGTCGTTCTCAAAAAGTTAAAGAAATCTTTGAATGTGCG TAAATCTGAGTTTGACCGTGATGCTGCCATGCAACGCAAGTTGGAAGATGGCAGA TCAGGCTATGACCCAAATGTACAAACAGGCAAGATCTGAGGACAAGAGGGGAGTAG AACTAGTGCTATGCAACAATGCTCTTCACTATGCTTAGGAAGCTTGATAATGATGCA CTTAACAACATTATCAACAATGCGCGTGATGGTTGTGTTCCACTCAACATCATACCAT TGACTACAGCAGCCAAACTCATGGTTGTTGTCCCTGATTATGGTACCTACAAGAACAC TTGTGATGGTAACACCTTTACATATGCATCTGCACTCTGGGAAATCCAGCAAGTTGTT GATGCGGATAGCAAGATTGTTCAACTTAGTGAAATTAACATGGACAATTCACCAAAAT TGGCTTGGCCTCTTATTGTTACAGCTCTAAGAGCCAACTCAGCTGTTAAACTACAGAA TAATGAAGTGAAGTCCAGTAGCACTACGACAGATGTCCTGTGCGGCTGGTACCACACA AACAGCTTGTACTGATGACAAATGCATTTGCCTACTATAACAATTCGAAGGGAGGTAG GTTTGTGCTGGCATTACTATCAGACCACCAAGATCTCAAATGGGCTAGATTCCTAAG AGTGATGGTACAGGTACAATTTACACAGAACTGGAACACCTTGTAGGTTTGTACAG ACACACCAAAGGGCCTAAAGTGAAATACTTGTACTTCATCAAAGGCTTAAACAACCT AAATAGAGGTATGGTGTGGGCAAGTTAGCTGCTACAGTACGCTTTCAGGCTGGAAA TGCTACAGAAGTACCTGCCAATTCAACTGTGCTTTCTTCTGTGCTTTTGAGTAGAC CCTGCTAAAGCATATAAGGATTACCTAGCAAGTGGAGGACAACCAATCACAACCTGT GTGAAGATGTTGTGTACACACTGGTACAGGACAGGCAATTAAGTGAACACCAGAA GCTAACATGGACCAAGAGTCTTTGGTGGTGCTTCATGTTGTCTGATTGTAGATGC CACATTGACCATCCAAATCCTAAAGGATTCTGTGACTTGAAGGTAAGTACGTCCAAA TACCTACCACTTGTGCTAATGACCCAGTGGGTTTTACACTTAGAAACACAGCTGTGAC CGTCTGCGAATGTGGAAGGTTATGGCTGTAGTTGTGACCAACTCCGCAACCTT GATGCACTGTGCGGATGCATCAACGTTTTTAAACGGGTTTGGGTTGAAGTGCAGCC CGTCTTACACCGTGCGGCACAGGCCTAGTACTGATGCTGCTACAGGGCTTTTATGAT
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	ATTACAAACGAAAAAGTTGCTGGTTTTGCAAAGTTCCTAAAACTAATTGCTGTCGCTT CCAGGAGAAGGATGAGGAAGGCAATTTATTAGACTCTTACTTTGTAGTTAAGAGGCA TACTATGTCTAACTACCAACATGAAGAGACTATTTATAACTTGGTTAAAGATTGTCCAG CGGTTGCTGCTCATGACTTTTTCAAGTTTAGAGTAGATGGTGACATGGTACCACATAT ATCACGTACAGCGTCTAACTAAATACACAATGGCTGATTTAGTCTATGCTCTACGTCAT TTTGATGAGGGTAATTGTGATACATTAAGAAATACTCGTCACATACAATTGCTGTG ATGATGATTATTTCAATAAGAAGGATTGGTATGACTTCGTAGAGAATCCTGACATCTT ACGCGTATATGCTAACTTAGGTGAGCGGTACGCCAATCAATTATTAAGACTGTACAA TTCTGCGATGCTATGCGTGATGCAGGCATTGTAGGCGTACTGACATTAGATAATCAG GATCTTAATGGGAACCTGGTACGATTTCCGGTGATTTCTGACAGTAGCACCAGGCTGC GGAGTTCCTATTGTGGATTCATATTACTCATTGCTGATGCCCATCCTCACTTTGACTA GGGCATTGGCTGCTGAGTCCCATATGGATGCTGATCTCGCAAAACCACTTATTAAGT GGGATTTGCTGAAATATGATTTTACGGAAGAGAGACTTTGTCTCTCGACCGTTATTT TAAATATTGGGACCAGACATACCATCCCAATTGTATTAAGTGTGGATGATAGGTGT ATCCTTCATTGTGCAAACTTTAATGTGTTATTTCTACTGTGTTCCACCTACAAGTTTT GGACCACTAGTAAGAAAAATATTTGTAGATGGTGTCTTTTGTGTTTCAACTGGAT ACCATTTTCGTGAGTTAGGAGTCGTACATAATCAGGATGTAACTTACATAGCTCGCG TCTCAGTTTCAAGGAACCTTTTAGTGATGCTGCTGATCCAGCTATGCATGCAGCTTCT GGCAATTTATTGCTAGATAAACGCACTACATGCTTTTCACTAGCTGCACTAACAAACA ATGTTGCTTTTCAAACTGTCAAACCCGGTAATTTTAAATAAGACTTTTATGACTTTGCT GTGCTAAAGGTTTCTTTAAGGAAGGAAGTTCTGTTGAACTAAACCACTTCTCTTTG CTCAGGATGGCAACGCTGCTATCAGTGATTATGACTATTATCGTTATAATCTGCCAAC AATGTGTGATATCAGACAACCTCTATTTCGTAGTTGAAGTTGTTGATAAATACTTTGATT GTTACGATGGTGGCTGTATTAATGCCAACCAAGTAATCGTTAACAACTCGGATAAATC AGCTGGTTTCCCATTTAATAAATGGGGTAAGGCTAGACTTTATTTAGCTCAATGAGT TATGAGGATCAAGATGCACCTTTTCGCGTATACTAAGCGTAATGTCACTCCCTACTATAA CTCAAAATGAATCTTAAGTATGCCATTAGTGCAAAAGATAGAGCTCGCACCCGTAGCTG GTGCTCTATCTGTAGTACTATGACAAATAGACAGTTTCATCAGAAATATTGAAGTCA ATAGCCGCCACTAGAGGAGCTACTGTGTAATTGGAACAAGCAAGTTTACGGTGGC TGGCATAATATGTTAAAACTGTTTACAGTGATGTAGAACTCCACACCTTATGGGTT GGGATTATCCTAAATGTGACAGAGCCATGCCTAACATGCTTAGGATAATGGCCTCTC TTGTTCTTGCTCGCAAAACATAACACTTGCTGTAACCTATCACACCGTTTCTACAGGTTA GCTAACGAGTGTGCGCAAGTATTAAGTGAGATGGTCACTGTGTGGCGGCTCACTATAT GTTAAACCAAGTGGAACATCATCCGGTGATGCTACAACCTGCTTATGCTAATAGTGTCT TTAACATTTGTCAAGCTGTTACAGCCAATGTAATGCACCTTCTTCAACTGATGGTAAT AAGATAGCTGACAAGTATGTCCGCAATCTACAACACAGGCTCTATGAGTGTCTCTATA GAAATAGGGATGTTGATCATGAATTCGTGGATGAGTTTACGCTTACCTGCGTAAACA TTTCTCCATGATGATTCTTTCTGATGATGCCGTTGTGTGCTATAACAGTAACATGCG GCTCAAGGTTTAGTAGCTAGCATTAGAAGCTTTAAGGCAGTTCCTTATTATCAAAATAA TGTGTTCTATGCTGAGGCAAAATGTTGGACTGAGACTGACCTTACTAAAGGACCTCA CGAATTTTGCTCAGCATACAATGCTAGTTAAACAAGGAGATGATTACGTGATCCCTG CCTTACCCAGATCCATCAAGAATATTAGGCGCAGGCTGTTTTGTCGATGATATTGTCA AAACAGATGGTACACTTATGATTGAAAGGTTTCGTGCTCACTGGCTATTGATGCTTACCC ACTTACAAAACATCCTAATCAGGAGTATGCTGATGCTTTCACTTGTATTACAAATACA TTAGAAAAGTTACATGATGAGCTTACTGGCCACATGTTGGACATGATTCCGTAATGCT AACTAATGATAACACCTCACGGTACTGGGAACCTGAGTTTTATGAGGCTATGTACACA CCACATACAGTCTTGCAGGCTGTAGGTGCTTGTGATTGTGCAATTCACAGACTTCAC TTGCTTGGCGTGCTGTATTAGGAGACCATTCTATGTTGCAAGTGTGCTATGACC ATGTCATTTCAACATCACACAAATAGTGTGTCTGTTAATCCCTATGTTGCAATGCC CCAGGTTGTGATGTCACTGATGTGACACAACCTGTATCTAGGAGGTATGAGCTATTATT GCAAGTCACATAAGCCTCCCATTAGTTTTCCATTATGTGCTAATGGTCAGGTTTTGG TTTATACAAAACACATGTGTAGGCAAGTACAAATGTCACTGACTTCAATGCGATAGCA ACATGTGATTGGACTAATGCTGGCGATTACATACTTGCCAAACACTTGTACTGAGAGAC TCAAGCTTTTCGACAGCAGAAACGCTCAAAGCCACTGAGGAAACATTTAAGCTGTCA ATGGTATTGCCACTGTACGCGAAGTACTCTCTGACAGAGAATTGCATCTTTCATGGG AGGTTGAAAAACCTAGACCACCATTTGAACAGAACTATGTCTTTACTGGTTACCGTGT AACTAAAAATAGTAAAGTACAGATTGGAGAGTACACCTTTGAAAAAGGTGACTATGGT GATGCTGTTGTGTACAGAGGTACTACGACATACAAGTTGAATGTTGGTGATTACTTTG TGTTGACATCTCACACTGTAATGCCACTTAGTGACCTACTCTAGTGCCACAAGAGCA CTATGTGAGAATTACTGGCTGTACCCAACTCAACATCTCAGATGAGTTTTCTAGC AATGTTGCAAAATTATCAAAAGGTCGGCATGCAAAAGTACTCTACACTCCAAGGACCAC CTGGTACTGGTAAGAGTCATTTTGCCATCGGACTTGCTCTCTATTACCCATCTGCTCG CATAGTGTATACGGCATGCTCTCATGCAGCTGTTGATGCCCTATGTGAAAAAGGCATT AAAATATTGCCCATAGATAAATGTAGTAGAATCATACCTGCGCGTGTGCGCGGTAGA GTGTTTTGATAAATTCAAAGTGAATTAACACTAGAACAGTATGTTTTCTGCACTGTAA ATGCATTGCCAGAAACACTGCTGACATTGTAGTCTTTGATGAAATCTCTATGGCTAC
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	TAATTATGACTTGAGTGTTGTCAATGCTAGACTTCGTGCAAAACACTACGTCTATATT GGCGATCCTGCTCAATTACCAGCCCCCGCACATTGCTGACTAAAGGCACACTAGAA CCAGAATATTTTAATTCAGTGTGCAGACTTATGAAAAAATAGGTCAGACATGTTCC TTGGAACCTTGTCGCCGTTGTCCTGCTGAAATTGTTGACACTGTGAGTGCTTTAGTTTA TGACAAATAAGCTAAAAGCACACAAGGATAAGTCAGCTCAATGCTTCAAAATGTTCTAC AAAGGTGTTATTACACATGATGTTTCATCTGCAATCAACAGACCTCAAATAGGCGTTG TAAGAGAATTTCTACACGCAATCCTGCTTGGAGAAAAGCTGTTTTATCTCACCTTAT AATTCACAGAACGCTGTAGCTTCAAAAATCTTAGGATTGCCTACGCAGACTGTTGATT CATCACAGGGTCTGAATATGACTATGTCATATTCACACAACTACTGAAACAGCACA CTCTTGTAATGTCAACCGCTTCAATGTGGCTATCACAAGGGCAAAAATTGGCATTGTTG TGCATAATGTCTGATAGAGATCTTTATGACAACTGCAATTTACAAGCTAGAAAATACC ACGTGCAATGTGGCTACATTACAAGCAGAAAATGTAAGTGGACTTTTTAAGGACTGT AGTAAGATCATTACTGGTCTTCATCCTACACAGGCACCTACACACCTCAGCGTTGATA TAAAGTTCAAGACTGAAGGATTATGTGTTGACATACCAGGCATACCAAGGACATGA CCTACCGTAGACTCATCTCTATGATGGGTTTCAAAATGAATTACCAAGTCAATGGTTA CCCTAATATGTTTATCACCCGCGAAGAAGCTATTGCTCAGCTTCGTGCGTGGATTGG CTTTGATGTAGAGGGCTGTCTGCAACTAGAGATGCTGTGGGTACTAACCTACCTCT CCAGCTAGGATTTTTCTACAGGTGTTAACTTAGTAGCTGTACCGACTGGTTATGTTGAC ACTGAAAATAACACAGAATTCACCAGAGTTAATGCAAAACCTCCACCAGGTGACCAG TTTAAACATCTTATACCACTCATGTATAAAGGCTTGCCTGGAATGTAGTGCGTATTA AGATAGTACAAATGCTCAGTGATACACTGAAAGGATTGTCAGACAGAGTCGTGTTG TCCTTTGGGCGCATGGCTTTGAGCTTACATCAATGAAGTACTTTGTCAAGATTGGACC TGAAAGAACGTGTTGTCTGTGTGACAAACGTGCAACTTGCTTTTCTACTTCATCAGAT ACTTATGCCTGCTGGAATCATTCTGTGGTTTTGACTATGTCTATAACCCATTATGAT TGATGTTACAGCAGTGGGCTTTACGGGTAACTTCAGAGTAACCATGACCAACATTG CCAGGTACATGGAAATGCACATGTGGCTAGTTGTGATGCTATCATGACTAGATGTTTA GCAGTCCATGAGTGCTTTGTTAAGCGCGTTGATTGGTCTGTTGAATACCCTATTATAG GAGATGAACGTGAGGTTAATTCTGCTTGCAAAAAGTACAAACATGCTGGTTGTGAAGT CTGCATTGCTTGCTGATAAGTTCCAGTTCTTCATGACATTGGAATCCAAAGGCTAT CAAGTGTGTGCTCAGGCTGAAGTGAATGGAAGTTCTACGATGCTCAGCCATGTAG TGACAAAGCTTACAAAATAGAGGAACCTTCTATTCTTATGCTACACATCAGATAAAT TCACTGATGGTGTGTTGTTTGGAAATTGAACGTTGATCGTTACCCAGCCAATGC AATTGTGTGTAGGTTTGACACAAGAGTCTTGTCAACTTGAACCTTACAGGGCTGTGAT GGTGGTAGTTTGATGTGAATAAGCATGCATTCCACACTCCAGCTTTCGATAAAGTG CATTTACTAATTTAAAGCAATTGCCTTTCTTTTACTATTCTGATAGTCTTTGTGAGCT CATGGCAAAACAAGTAGTGTCCGATATTGATTATGTTCCACTCAAATCTGCTACGTGTA TTACACGATGCAATTTAGGTGGTGTCTGTTGACAGACCATGCAAAATGAGTACCGAC AGTACTTGATGCATATAATATGATGATTTCTGCTGGATTTAGCCTATGGATTTACAAA CAATTTGATACTTATAACCTGTGGAATACATTTACCAGGTTACAGAGTTTAGAAAATGT GGCTTATAATGTTGTTAATAAAGGACACTTTGATGGACACGCCGGCGAAGCACCTGT TTCCATCATTAATAATGCTGTTTACACAAAGGTAGATGGTATTGATGGAGATCTTT GAAAATAAGACAACACTTCCTGTTAATGTTGCATTTGAGCTTTGGGCTAAGCGTAACA TTAAACCAAGTGCCAGAGATTAAAGATACTCAATAATTTGGGTGTTGATATCCGTGCTAA TACTGTAATCTGGGACTACAAAAGAGAAGCCCCAGCACATGTATCATAATAGGTG CTGCACAATGACTGACATTGCCAAGAACTACTGAGAGTGCTTGTCTTCACTTACT GTCTTGTTTGATGGTAGAGTGGAAGGACAGGTAGACCTTTTGTAGAAACGCCGTAAT GGTGTTTAATAACAGAAGGTTCAAGTCAAAAGGTCTAACACCTTCAAAGGGACCAGCA CAAGCTAGCGTCAATGGAGTCACATTAATTGGAGAATCAGTAAAAACACAGTTTAACT ACTTTAAGAAAGTAGACGGCATTATTCAACAGTTGCCTGAAACCTACTTTACTCAGAG CAGAGACTTAGAGGATTTTAAAGCCAGATCACAATGGAACCTGACTTTCTCGAGCT CGCTATGGATGAATTCATACAGCGATATAAGCTCGAGGGCTATGCCCTCGAACACAT CGTTTATGGAGATTTCAAGTCATGGACAACCTTGGCGGTCTTCATTTAATGATAGGCTTA GCCAAGCGCTCACAAGATTCAACCTTAAATTAGAGGATTTTATCCCTATGGACAGCA CAGTAAAAAATTACTTATAACAGATGCGCAACAGGTTCAATCAAAATGTGTGTTT TGTGATTGATCTTTACTTGATGACTTTGTGAGATAATAAAGTCACAAGATTGTGAG TGATTTCAAAAGTGGTCAAGGTTACAATTGACTATGCTGAAATTTCAATTCATGCTTTGG TGAAGGATGGACATGTTGAAACCTTACCCAAAACCTACAAGCAAGTCAAGCGTGG CAACCAGGTGTTGCGATGCCTAACTTGTACAAGATGCAAAAGAAATGCTTCTTGAAAAGT GTGACCTTCAGAATTATGGTGAAAATGCTGTTATACCAAAGGAATAATGATGAATGT CGCAAAGTATACTCAACTGTGTCAATACTTAAATACACTTACTTTAGCTGTACCCCTACA ACATGAGAGTTATTCACTTTGGTGCTGGCTCTGATAAAGGAGTTGCACCAGGTACAG CTGTGCTCAGACAATGGTTGCCAACTGGCACACTACTTGTGATTTCAGATCTTAATGA CTTCGTCTCCGACGCAGATTCTACTTTAATTGGAGACTGTGCAACAGTACATACGGCT AATAAATGGGACCTTATTATTAGCGATATGTATGACCTAGGACCAACATGTGACAA AAGAGAATGACTCTAAGAAGGGTTTTTCACTTATCTGTGTGATTTATAAGCAAAA ACTAGCCCTGGGTGGTCTATAGCTGTAAGATAACAGAGCATTCTTGAATGCTGA
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	CCTTTACAAGCTTATGGGCCATTTCTCATGGTGGACAGCTTTGTACAAATGTAAT GCATCATCATCGGAAGCATTTTTAATTGGGGCTAACTATCTTGGCAAGCCGAAGGAA CAAATTGATGGCTATACCATGCATGCTAACTACATTTTCTGGAGGAACACAAATCCTA TCCAGTTGTCTTCTATTCACTCTTTGACATGAGCAAATTTCTCTTAAATTAAGAGGA ACTGCTGTAATGTCTCTTAAGGAGAATCAAATCAATGATATGATTTATTCTCTTCTGGA AAAAGGTAGGCTTATCATTAGAGAAAACAACAGAGTTGTGGTTTCAAGTGATATTCTT GTTAACAACATAACGAACATGTTTATTTCTTATTATTTCTACTCTCACTAGTGGTAGT GACCTTGACCGGTGCACCACCTTTTGATGATGTTCAAGCTCCTAATTACACTCAACATA CTTCATCTATGAGGGGGTTTACTATCCTGATGAAATTTTATGATCAGACACTCTTTAT TTAACTCAGGATTTATTTCTTCCATTTTATTCTAATGTTACAGGGTTTCATACTATTAAT CATACGTTTGGCAACCCTGTCTATACCTTTTAAGGATGGTATTTATTTTGGCTGCCACAG AGAAATCAAATGTTGTCCGTGGTTGGGTTTTTGGTTCTACCATGAACAACAAGTCACA GTCGGTGATTATTATTAACAATTCTACTAATGTTGTTATACGAGCATGTAACTTTGAAT TGTGTGACAACCCTTTCTTGTCTTTCTAAACCATGGGTACACAGACACATACTAT GATATTCGATAATGCATTTAATTGCACTTTGAGTACATATCTGATGCCCTTTTGTGCTTG ATGTTTCAGAAAAGTCAGGTAATTTTAAACACTTACGAGAGTTTGTGTTTAAAAATAAA GATGGGTTTTCTCTATGTTTATAAGGGCTATCAACCTATAGATGTAGTTCGTGATCTAC CTTCTGGTTTTAACACTTTGAAACCTATTTTAAAGTTGCCCTTGGTATTAAACATTACA AATTTTAGAGCCATTCTTACAGCCTTTTCACTGCTCAAGACATTTGGGGCACGTCAG CTGCAGCCTATTTTGTGGCTATTTAAAGCCAACTACATTTATGCTCAAGTATGATGAA AATGGTACAATCACAGATGCTGTTGATTGTTCTCAAAATCCACTTGTGTAACCTCAAAT GCTCTGTTAAGAGCTTTGAGATTGACAAAGGAATTTACCAGACCTCTAATTTCAAGGT TGTTCCCTCAGGAGATGTTGTGAGATTCCCTAATATTACAAACTGTGTCCCTTTTGA GAGTTTTTAATGCTACTAAATCCCTTCTGTCTATGCATGGGAGAGAAAAAATTT CTAATTTGTGTTGCTGATTCTGTGCTCTACAACCTCAACATTTTTCACACCTTTAAG TGCTATGGCGTTTCTGCCACTAAGTTGAATGATCTTTGCTTCTCCAATGTCTATGCA ATTCTTTTGTAGTCAAGGGAGATGATGTAAGACAAATAGCGCCAGGACAACTGGTG TTATTGCTGATTATAATTATAAATTGCCAGATGATTTTCAAGGGTTGTCTCTTGG AATACTAGGAACATTGATGCTACTTCACTGGTAATTATAATTATAAATATAGGTATCT TAGACATGGCAAGCTTAGGCCCTTTGAGAGAGACATATCTAATGTGCCCTTCTCCCT GATGGCAAACCTTGCAACCCACCTGCTCTTAATTGTTATTGGCCATTAAATGATTATG GTTTTTACACCACTACTGGCATTGGCTACCAACCTTACAGAGTTGTAGTACTTTCTTTT GAACTTTTAAATGCACCGGCCACGGTTTGTGGACCAAAATATCCACTGACCTTATTA AGAACCAGTGTCAATTTTAAATTTAATGGACTCACTGGTGTGTTAACTCC TTCTTCAAAGAGATTTCAACCATTTCAACAATTTGGCCGTGATGTTTCTGATTCTACTG ATTCCGTTTCGAGATCCTAAAACATCTGAAATATTAGACATTTACCTTGGCGCTTTTGG GGGTGTAAGTGAATTACACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATAT CAAGATGTTAACTGCACTGATGTTTCTACAGCAATTCATGCAGATCAACTACACACAG CTTGGCGCATATATTCTACTGGAACAATGTATTCCAGACTCAAGCAGGCTGTCTTAT AGGAGCTGAGCATGTCGACACTTCTTATGAGTGCGACATTCTTATTGGAGCTGGCAT TTGTGCTAGTTACCATACAGTTTCTTTATTACGTAGTACTAGCCAAAAATCTATTGTG CTTATACTATGTCTTTAGGTGCTGATAGTTCAATTGCTTACTCTAATAACACCATTGCT ATACCTACTAATTTTCAATTAGCATTACTACAGAAGTAATGCCTGTTTCTATGGCTAA AACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAATGTGCTAATTTG CTTCTCCAATATGGTAGCTTTTGCACACAATAAATCGTGCATCTCAGGTATTGCTG CTGAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAAAACAAATGTACAAAA CCCCAACTTTGAAATATTTTGGTGGTTTTAATTTTCACAAATATTACCTGACCCTCTA AAGCCAACTAAGAGGTCTTTTATTGAGGACTTGCTCTTTAATAAGGTGACACTCGCTG ATGCTGGCTTCATGAAGCAATATGGCGAATGCCTAGGTGATATTAAATGCTAGAGATCT CATTTGTGCGCAGAAGTTCAATGGACTTACAGTGTGCCACCTCTGCTCACTGATGAT ATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCTGGATGGACA TTTGGTGTGGCGCTGCTCTTCAAATACCTTTTGTCTATGCAAATGGCATATAGGTTCA ATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCACCAAAATCGCCAACCA ATTTAACAAAGGCGATTAGTCAAATTCAGAATCACTTACAACAACATAACTGCATTG GGCAAGCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTAAAC AACTTAGCTCTAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCCGCACTT GATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGC CTTCAAACCTATGTAACACAACAATAATCAGGGCTGCTGAAATCAGGGCTTCTGCTA ATCTTGCTGCTACTAAAATGTCTGAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTT TTGTGGAAGGGCTACCACCTTATGTCCTTCCACAAGCAGCCCGCATGGTGTGT CTTCTACATGTCACGTATGTGCCATCCAGGAGAGGAACCTTACCACAGCGCCAGC AATTTGTCATGAAGGCAAAGCATACTCCCTCGTGAAGGTGTTTTGTGTTAATGGC ACTTCTTGGTTTTATTACACAGAGGAACCTTCTTTCTCCACAATAATTACTACAGACAA TACATTTGTCTCAGGAAATGTGATGTGTTATTGGCATCATTAAACAACACAGTTTATG ATCCTCTGCAACCTGAGCTTGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAA TCATACATCACCAGATGTTGATCTTGCGGACATTTCAAGGCATTAAACGCTTCTGTCGTC
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		AACATTCAAAAAGAAATTGACGCGCTCAATGAGGTGCTAAAAATTTAAATGAATCAC TCATTGACCTTCAAGAAATGGGAAAATATGAGCAATATATTAATGGCCTTGGTATGT TTGGCTCGGCTTCATTGCTGGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGT TGCATGACTAGTTGTTGCAGTTGCCTCAAGGGTGCATGCTCTTGTTGCTTCTGCTGC AAGTTTGATGAGGATGACTCTGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACAT AAACGAACTTATGGATTTGTTTATGAGATTTTTACTCTTAGATCAATTACTGCACAGC CAGTAAAAATTGACAATGCTTCTCCTGCAAGTACTGTTTATGCTACAGCAACGATACC GCTACAAGCCTCACTCCCTTTTCGGATGGCTTGTTATTGGCGTTGCAATTTCTTGCTGTT TTTCAGAGCGCTACCAAAAATAATTGCGCTCAATAAAAGATGGCAGCTAGCCCTTTATA AGGGCTTCCAGTTCAATTTGCAATTTACTGCTGCTATTTGTTACCATCTATTACATCTT TTGCTTGTGCTGCGAGGTATGGAGGCGCAATTTTTGTACCTCTATGCCCTTGATATATT TTCTACAATGCATCAACGCATGTAGAATTATTATGAGATGTTGGCTTTGTTGGAAGTG CAAATCCAAGAACCCATTACTTTATGATGCCAACTACTTTGTTTGTGGCAGACACACAT AACTATGACTACTGTATACCATATAACAGTGTACAGATACAATTGCTGTTACTGAAG GTGACGGCATTTCACACCAAACTCAAAGAAGACTACCAAAATGGTGTATTCTGTA GGATTAGGCACTCAGGTGTAAAGACTATGTCGTTGTACATGGCTATTTACCCGAAGTT TACTACCAGCTTGAGTCTACACAAATTAACAGACACTGGTATTGAAAAATGCTACAT TCTTCATCTTTAACAAGCTTGTTAAAGACCCACCGAATGTGCAAATACACACAATCGA CGGCTCTTCAGGAGTTGCTAATCCAGCAATGGATCCAATTTATGATGAGCCGACGAC GACTACTAGCGTGCTTTGTAAAGCACAAGAAAGTGAAGTACGAACTTATGCTACTACTC GTTTCGGAAGAAACAGGTACGTTAATAGTTAATAGCGTACTTCTTTTCTTGCTTCGT GGTATTCTTGCTAGTCACACTAGCCATCCTTACTGCGCTTCGATTGTGTGCGTACTGC TGCAATATTGTTAACGTGAGTTTAGTAAACCAACGGTTTACGCTACTCGCGTGTTA AAAATCTGAACCTCTTCTGAAGGAGTTCTGATCTTCTGGTCTAAACGAACCTAACTATT ATTATTATTCTGTTTGGAACTTTAACAATTGCTTATCATGGCAGACAAACGGTACTATTAC CGTTGAGGAGCTTAAACAACCTCTGGAACAATGGAACCTAGTAATAGGTTTCTATTTC CTAGCCTGGATTATGTTACTACAATTTGCCTATTCTAATCGGAACAGGTTTTGTACAT AATAAAGCTTGTTTTCTCTGGCTCTTGTTGGCCAGTAACACTTGCTTGTTTGTGCTT GCTGCTGTCTACAGAATTAATTGGGTGACTGGCGGGATTGCGATTGCAATGGCTTGT ATTGTAGGCTTGATGTGGCTTAGCTACTTCTGTTGCTTCTCAGGCTGTTTGTCTGTA CCCCTCAATGTGGTCAATCAACCCAGAAACAAACATTCTCTCAATGTGCCTCTCCG GGGGACAATTGTGACCAGACCGCTCATGGAAAGTGAACCTGTGCTTGGTGTGTGAT CATTCTGTGGTCACTTGCGAATGGCCGGACACTCCCTAGGGCGCTGTGACATTAAAG ACCTGCCAAAAGAGATCACTGTGGCTACATCAGAACGCTTTCTTATACAAATAGG AGCGTCGCAGCGTGTAGGCACTGATTAGGTTTTGCTGCATACAAACCGTACCGTAT TGGAACCTATAAATTAATACAGACCACGCCGGTAGCAACGACAATATTGCTTTGCTA GTACAGTAAGTGACAACAGATGTTTCATCTTGTGACTTCCAGGTTACAATAGCAGAG ATATTGATTATCATTATGAGGACTTTAGGATTGCTATTGGAATCTTGACGTTGATAAT AAGTTCAATAGTGAGACAATTAATTAAGCCTCTAACTAAGAAGAATTATTCGGAGTTA GATGATGAAGAACCTATGGAGTTAGATTATCCATAAAACGAACATGAAAAATTATTCTC TTCTGACATTGATTGTATTTACATCTTGCGAGCTATATCACTATCAGGAGTGTGTTA GAGGTACGACTGTACTACTAAAAGAACCTTGCCCATCAGGAACATACGAGGGCAATT CACCATTTACCCCTCTTGCTGACAATAAATTTGCACTAACTTGCACTAGCACACACTT TGCTTTTGCTTGCTGCTGACGGTACTCGACATACCTATCAGCTGCGTCAAGATCAGT TTCACCAAAACTTTTCTACAGACAAGAGGAGTTCAACAAGAGCTCTACTCGCCACTT TTTCTCATTGTTGCTGCTAGTATTTTTAATACTTTGCTTCACCATTAAAGAGAAAGAC AGAATGAATGAGCTCACTTTAATTGACTTCTATTTGTGCTTTTACGCTTTCTGCTATT CCTTGTTTTAATAATGCTTATTATATTTTGGTTTTCACTCGAAATCCAGGATCTAGAAG AACCTTGTAACAAAGTCTAAACGAACATGAACTTCTCATTGTTTGACTTGTATTTCT CTATGCAGTTGCATATGCACTGTAGTACAGCGCTGTGCATCTAATAAACCTCATGTGC TTGAAGATCCTTGTAAGGTACAACACTAGGGGTAATACCTTATAGCACTGCTTGCTTT GTGCTCTAGGAAAGGTTTTACCTTTTATAGATGGCACACTATGGTTCAAACATGCAC ACCTAATGTTACTATCAACTGTCAAGATCCAGCTGGTGGTGGCTTATAGCTAGGTGT TGGTACCTTATGAAGGTACCAAACTGCTGCATTTAGAGACGTACTGTTGTTTTAA ATAAACGAACAAATTAATGTCTGATAATGGACCCCAATCAAACCAACGTAAGTCCCC CCCGCATTACATTTGGTGGACCCACAGATTCAACTGACAATAACCAAGATGGAGGAC GCAATGGGGCAAGGCCAAAACAGCGCCGACCCCAAGGTTTACCAATAATACTGCG TCTTGGTTACAGCTCTCACTCAGCATGGCAAGGAGGAACTTAGATTCCCTCGAGGC CAGGGCGTTCCAATCAACACCAATAGTGGTCCAGATGACCAAAATGGCTACTACCGA AGAGCTACCCGACGAGTTGTTGGTGGTGACGGCAAAATGAAAGAGCTCAGCCCCAG ATGGTACTTCTATTACCTAGGAACCTGGCCAGAAGCTTCACTTCCCTACGGCGCTAA CAAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAATACACCCAAAGACCA CATTGGCACCCGCAATCCTAATAACAATGCTGCCACCGTGCTACAATTCCTCAAGG AACAACTTGC AAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCGAGTCAAGCCT CTTCTCGCTCCTCATCACGTAGTCGCGGTAATTCAAGAAATTAACCTCCTGGCAGCA GTAGGGGAAATTCCTCTGCTCGAATGGCTAGCGGAGGTGGTGAAACTGCCCTCGCG
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		CTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCAAAGTTTCTGGTAAAGGCCAA CAACAACAAGGCCAACTGTCACTAAGAAATCTGCTGCTGAGGCATCTAAAAAGCCT CGCCAAAAACGTACTGCCACAAAACAGTACAACGTCACTCAAGCATTTGGGAGACGT GGTCCAGAACAACCCAAAGGAAATTTGCGGGACCAAGACCTAATCAGACAAGGAACT GATTACAAACATTGGCCGCAAATTCACAAATTTGCTCCAAGTGCCTCTGCATTCTTTG GAATGTCACGCATTGGCATGGAAGTCACACCTTCGGGAACATGGCTGACTTATCATG GAGCCATTAATTTGGATGACAAAGATCCACAATTCAAAGACAACGTCACTGCTGAA CAAGCACATTGACGCATACAAAACATTCCCACCAACAGAGCCTAAAAAGGACAAAAA GAAAAAGACTGATGAAGCTCAGCCTTTGCCGCAGAGACAAAAGAAGCAGCCCCTGT GACTCTTCTTCTGCGGCTGACATGGATGATTTCTCCAGACAACCTCAAAATTCATG AGTGGAGCTTCTGCTGATTCAACTCAGGCATAAACTCATGATGACCACACAAGGC AGATGGGCTATGTAACGTTTTTCGCAATTCGTTTACGATACATAGTCTACTCTTGTG CAGAATGAATTTCTCGTAACATAACAGCACAAAGTAGGTTTAGTTAACTTTAATCTCACAT AGCAATCTTTAATCAATGTGAACATTAGGGAGGACTTGAAAGAGCCACCACATTTTC ATCGAGGCCACGCGGAGTACGATCGAGGGTACAGTGAATAATGCTAGGGGAGCTG CCTATATGGAAGAGCCCTAATGTGTAATAATTTTATAGTAGCTATCCCCATGTGA TTTTAATAGCTTCTTAGGGAATGACAAAAA
8	SARS-CoV-2 (GenBank: NC_045512.2)	ATTAAAGGTTTATACCTTCCAGGTAACAAACCAACCAACTTTTCGATCTCTTGATGAT CTGTTCTCTAAACGAACCTTTAAATCTGTGTGGCTGTCACTCGGCTGCATGCTTAGTG CACTCAGCAGTATAATTAATAACTAATTAATCTGTCGTTGACAGGACAGAGTAACTCG TCTATCTTCTGCAGGCTGCTTACGTTTCTGTCGTTGTCAGCCGATCATCATCAGCACA TCTAGGTTTCTGTCGGGTGTGACCGAAAGGTAAGATGGAGAGCCTTGTCCCTGGTTT CAACGAGAAAAACACACGTCCAACCTCAGTTTGCCTGTTTTACAGGTTCCGCGACGTGCT CGTACGTGGCTTTGGAGACTCCGTGGAGGAGGCTTATCAGAGGCACGTCAACATC TTAAAGATGGCACTTGTGGCTTAGTAGAAGTTGAAAAAGGCGTTTTCCTCAACTTGA ACAGCCCTATGTGTTCAACAGCTTCGGATGCTCGAAGTGCACCTCATGGTCATGT TATGGTTGAGCTGGTAGCAGAACTCGAAGGCATTGACGTCGTAGTGGTGAGA CACTTGGTGCTTGTCCCTCATGTGGGCGAAATACCAAGTGGCTTACCGCAAGGTTT TTCTTCGTAAGAACGGTAATAAAGGAGCTGGTGGCCATAGTTACGGCGCCGATCTAA AGTCATTTGACTTAGGCGACGAGCTTGGCACTGATCCTTATGAAGATTTTCAAGAAAA CTGGAACACTAAACATAGCAGTGGTGTACCCGTAAGTCACTGCGTGAGCTTAACGG AGGGGCATACACTCGCTATGTGATAACAACCTTCTGTGGCCCTGATGGCTACCCCTCT TGAGTGCATTAAAGACCTTCTAGCACGTGCTGGTAAAGCTTCATGCATTTTGTCCGAA CAACTGGACTTTATTGACACTAAGAGGGGTGATACTGCTGCCGTGAACATGAGCAT GAAATTTGCTTGGTACACGGAACGTTCTGAAAAAGAGCTATGAATTCAGACACCTTTTG AAATTAATTTGGCAAGAAATTTGACACCTTCAATGGGAATGTCCAAATTTTGTATTT CCCTTAATTTCCATAATCAAGACTATTCAACCAAGGGTTGAAAAAGAAAGCTTGATG GCTTTATGGGTAGAATTCGATCTGTCTATCCAGTTGCGTCACCAATGAATGCAACCA AATGTGCCTTTCAACTCTCATGAAGTGTGATCATTGTGGTGAAATTCATGGCAGACG GGCGATTTTGTAAAGCCACTTGCGAATTTTGTGGCACTGAGAATTTGACTAAAGAA GTGCCACTACTTGTGGTTACTTACCCCAAAATGCTGTTGTTAAATTTATTGTCCAGC ATGTCACAATTCAGAAGTAGGACCTGAGCATAGTCTTGCCGAATACCATAATGAATCT GGCTTGAACCACTTCTTCTGTAAGGGTGGTGCACATTTGCCTTTGGAGGCTGTGTG TTCTCTTATGTTGGTTGCCATAACAAGTGTGCCTATTGGGTTCCACGTGCTAGCGCTA ACATAGGTTGTAAACCATACAGGTGTTGTTGGAGAAGGTTCCGAAGGCTTAAAGTACA ACCTTCTTGAAATCTCCAAAAAGAGAAAGTCAACATCAATATTGTTGGTGACTTTAAA CTTAATGAAGAGATCGCCATTATTTTGGCATCTTTTCTGCTTCCACAAGTGCTTTTGT GGAACTGTGAAAGGTTTGGATTATAAAGCATTCAAAACAAATTGTTGAATCCTGTGGT AATTTTAAAGTTACAAAAGGAAAGCTAAAAAGGTGCCTGGAATATTGGTGAACAGA AATCAACTACTGAGTCTCTTATGCATTTGCATCAGAGGCTGCTCGTGTGTACGATC AATTTTCTCCCGCACTCTTGAACCTGCTCAAAATTTCTGCGTGTTTTACAGAAAGGCC GCTATAACAATACTAGATGGAATTTACAGTATTCACTGAGACTCATTGATGCTATGA TGTTACATCTGATTTGGCTACTAACAATCTAGTTGTAATGGCCTACATTACAGGTGG TGTTGTTCACTTACTTCCAGTGGCTAACTAACATCTTTGGCACTGTTTATGAAAA CTCAAAACCCGTCCTTGATTGGCTTGAAGAGAAGTTTAAAGGAAGGTGTAGAGTTTCTTA GAGACGGTTGGGAAATTTGTTAAATTTATCTCAACCTGTGCTTGTGAATTTGCGGTGG ACAAATTTGCACCTGTGCAAGGAAATTAAGGAGAGTGTTCAGACATTTCTTAAGCTT GTAAATAAATTTTGGCTTTGTGCTGACTCTATCATTATTGGTGGAGCTTAACTTAA AGCCTTGAATTTAGGTGAAACATTTGTCACGCACTCAAAGGGATTGTACAGAAAGTGT GTTAAATCCAGAGAAGAACTGGCCTACTCATGCCCTCAAAAGCCCCAAAGAAATTA TCTTCTTAGAGGGAGAAACACTTCCACAGAAGTGTAAACAGAGGAAGTTGCTTTGA AACTGGTGATTTACAACCATTAGAACAACCTACTAGTGAAGCTGTTGAAGCTCCATT GGTTGGTACACCAGTTTGTATTAACGGGCTTATGTTGCTCGAAATCAAGACACAGAA AAGTACTGTGCCCTTGACCTAATATGATGGTAACAAACAATACCTTACACTCAAG GCGGTGCACCAACAAAGGTTTACCTTTGGTGATGACACTGTGATAGAAGTCAAGGTT ACAAGAGTGTGAATATCACTTTTGAACCTGATGAAAGGATTGATAAGTACTTAATGA

		GAAGTGCTCTGCCTATACAGTTGAACCTCGGTACAGAAAGTAAATGAGTTGCGCTGTGT TGTGGCAGATGCTGTCATAAAAACTTTGCAACCAGTATCTGAATTACTTACACCACTG GGCATTGATTTAGATGAGTGGAGTATGGCTACATACTACTTATTTGATGAGTCTGGTG AGTTTAAATTGGCTTCACATATGTATTGTTCTTTCTACCCTCCAGATGAGGATGAAGA AGAAGGTGATTGTGAAGAAGAAGAGTTTGAGCCATCAACTCAATATGAGTATGGTAC TGAAGATGATTACCAAGGTAAACCTTTGGAATTTGGTGCCACTTCTGCTGCTCTTCAA CCTGAAGAAGAGCAAGAAGAAGATTGGTTAGATGATGATAGTCAACAACTGTTGGT CAACAAGACGGCAGTGAGGACAATCAGACAACCTACTATTCAAACAATTGTTGAGGTT CAACCTCAATTAGAGATGGAACCTACACCACTGTTTTCAGACTATTGAAGTGAATAGTT TTAGTGGTTATTTAAACCTTACTGACAATGTATACATTAATAATGCAGACATTGTGGAA GAAGCTAAAAAGGTAAACCAACAGTGGTTGTTAATGCAGCCAATGTTTACCTTAAAC ATGGAGGAGGTGTTGCAGGAGCCTTAAATAAGGCTACTAACAATGCCATGCAAGTTG AATCTGATGATTACATAGCTACTAATGGACCACTTAAAGTGGGTGGTAGTTGTGTTTT AAGCGGACACAATCTTGCTAAACACTGTCTTCATGTTGTCGGCCCAATGTTAAACAAA GGTGAAGACATTCAACTCTTAAGAGTGCTTATGAAAAATTTAATCAGCAGCAAGTTT TACTTGACCACTATTATCAGCTGGTATTTTGGTGCTGACCCATATACATTCTTAAAGA GTTTGTGTAGATACTGTTCCGACAAATGTCTACTTAGCTGTCTTTGATAAAAACTCTA TGACAACTTGTTCAGCTTTTGGAAATGAAGAGTGAAGAGCAAGTTGAACAAAAG ATCGCTGAGATTCCTAAAGAGGAAGTTAAGCCATTTATAACTGAAAGTAAACCTTCAG TTGAACAGAGAAAAACAAGATGATAAGAAAAATCAAGCTTGTGTTGAAGAGATTACAAC AACTCTGGAAGAACTAAGTTCCTCACAGAAAACTTGTACTTTATATTGACATTAATG GCAATCTTCATCCAGATTCTGCCACTCTGTTAGTGACATTGACATCACTTTCTTAAAG AAAGATGCTCCATATATAGTGGGTGATGTTGTTCAAGAGGGTGTTTTAACTGCTGTGG TTATACCTACTAAAAAGGCTGGTGGCACTACTGAAATGCTAGCGAAAGCTTTGAGAAA AGTGCCAAACAGACAATTATATAACCACTTACCCGGGTGAGGGTTTAAATGTTACACT GTAGAGGAGGCAAGACAGTGTCTAAAAAGTGAAGAGTGCCTTTTACATTCTACCAT CTATTATCTCTAATGAGAAGCAAGAAATCTTGGAACTGTTTCTTGGAAATTTGCGAGA AATGCTTGCACATGCAGAAAGAAACACGCAAAATTAATGCCTGTCTGTGGAACTAAA GCCATAGTTTCAACTATACAGCGTAAATATAAGGGTATTTAAATACAAGAGGGTGTGG TTGATTATGGTGCTAGATTTTACTTTTACACCACTGTAACCACTGTAGCGTCACATTATC AACACACTTAACGATCTAAATGAACTCTTGTACAATGCCACTTGGCTATGTAACAC ATGGCTTAAATTTGGAAGAAGCTGCTCGGTATATGAGATCTCTCAAAGTGCCAGCTA CAGTTTCTGTTTCTTCACTGATGCTGTTACAGCGTATAATGGTTATCTTACTTCTTCT TCTAAACACCTGAAGAACATTTTATTGAAACCATCTCACTTGTCTGTTCTTAAAGA TTGGTCTATTCTGGACAATCTACACAACCTAGGTATAGAATTTCTTAAAGAGAGGTGAT AAAAGTGTATATTACACTAGTAATCCTACCACATTCCACCTAGATGGTGAAGTTATCA CCTTTGACAATCTTAAGACACTTCTTTCTTTGAGAGAAGTGAGGACTATTAAGGTGTT TACAACAGTAGACAACATTAACTCCACACGCAAGTTGTGGACATGCAATGACATAT GGACAACAGTTTGGTCCAACCTATTGATGGAGCTGATGTTACTAAATAAACCTC ATAATTCACATGAAGGTAAACATTTTATGTTTTACCTAATGATGACACTCTACGTGTT GAGGCTTTTGTAGTACTACCACACAACCTGATCCTAGTTTTCTGGGTGATCATGTGAG CATTAATCACACTAAAAAGTGGAATACCCACAAGTTAATGGTTAACTTCTATTAAA TGGGCAGATAACAACCTGTTATCTTGCCACTGCATTGTTAACTCCAACAAATAGAGT TGAAGTTTAAATCCACTGCTCTACAAGATGCTTATTACAGAGCAAGGGCTGGTGAAG CTGCTAATTTTGTGCACTTATCTTAGCCTACTGTAATAAGACAGTAGGTGAGTTAGG TGATGTTAGAGAAACAATGAGTTACTTGTTCACATGCCAATTTAGATTCTTGCAAAA GAGTCTTGAACGTGGTGTGTAACCTTGTGGACAACAGCAGACAACCTTAAAGGGTG TAGAAGCTGTTATGTACATGGGCACACTTTCTTATGAACAATTTAAGAAAGGTGTTCA GATACCTTGTACGTGTGGTAAACAAGCTACAAAATATCTAGTACAACAGGAGTACCT TTTGTATGATGTCAGCACCACTGCTCAGTATGAACCTTAAAGCATGGTACATTTACTT GTGCTAGTGAGTACACTGGTAATTACCACTGTGGTCACTATAAACATATAAATCTTAA AGAACTTTGTATTGCATAGACGGTGCTTTACTTACAAAGTCTCAGAATACAAAGGT CCTATTACGGATGTTTTCTACAAAGAAAAAGTTACACAACAACCATAAACCAAGTTA CTTATAAATTGGATGGTGTGTTTGTACAGAAATTGACCCTAAGTTGGACATATTATTAT AAGAAAGACAATTCTTATTTACAGAGCAACCAATTGATCTTGTACCAACCAACCAT ATCCAAACGCAAGCTTCGATAATTTTAAAGTTTGTATGTGATAATATCAAAATTTGCTGAT GATTTAAACCACTTAACTGGTTATAAGAAACCTGCTTCAAGAGAGCTTAAAGTTACAT TTTTCCCTGACTTAAATGGTGATGTGGTGGCTATTGATTATAAACACTACACACCCCTC TTTTAAGAAAGGAGCTAAATTTGTTACATAAACCTATTGTTTGGCATGTTAACAATGCAA CTAATAAAGCCACGTATAAACCAATACCTGGTGTATACGTTGTCTTTGGAGCACAAA ACCAGTTGAAACATCAAAATTCGTTTGTGATGACTGAAGTCAGAGGACGCGCAGGGAAT GGATAATCTTGCTGCGAAGATCTAAACCACTCTCTGAAGAAGTAGTGGAAAATCC TACCATACAGAAAGAGCTTCTTGAAGTGAATGTGAAAACTACCGAAGTTGTAGGAGA CATTATACTTAAACAGCAATAATAGTTTAAAAATTACAGAAGAGGTTGGCCACACA GATCTAATGGCTGCTTATGTAGACAATTCTAGTCTTACTATTAAGAAACCTAATGAATT ATCTAGAGTATTAGGTTTGAACACCCTTGCTACTCATGGTTAGCTGCTGTTAATAGT
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	GTCCCTTGGGATACTATAGCTAATTATGCTAAGCCTTTTCTTAACAAAGTTGTTAGTAC AACTACTAACATAGTTACACGGGTGTTTAAACCGTGTGTTGCTAATTATATGCCTTATT TCTTTACTTTTATTGCTACAATTGTGTACTTTTACTAGAAGTACAAATTCAGAAATTAAG CATCTATGCCGACTACTATAGCAAAGAATACTGTTAAGAGTGTGCGTAAATTTTGTCT AGAGGCTTCATTTAATTATTTGAAGTCACCTAATTTTCTAAACTGATAAATATTATAAT TTGGTTTTTACTATTAAAGTGTTTGCCTAGGTTCTTTAATCTACTCAACCGCTGCTTTAG GTGTTTTAATGTCTAATTTAGGCATGCCTTCTTACTGTACTGGTTACAGAGAAGGCTA TTTGAACCTCTACTAATGTCACTATTGCAACCTACTGTACTGGTTCTATACCTTTGTAGTG TTTGCTTAGTGGTTTAGATTCTTTAGACACCTATCCTTCTTTAGAACTATACAAATTA CCATTTTCATCTTTTAAATGGGATTTAACTGCTTTTGGCTTAGTTGCAGAGTGGTTTTTG GCATATATTCTTTTCACTAGGTTTTTCTATGTACTTGGATTGGCTGCAATCATGCAATT GTTTTTCAGCTATTTTGCAGTACATTTTATTAGTAATTCTTGGCTTATGTGGTTAATAAT TAATCTTGTACAAATGGCCCCGATTTTCACTATGGTTAGAATGTACATCTTCTTTGCAT CATTTTATTATGTATGGAAAAGTTATGTGCATGTTGTAGACGGTTGTAATTCATCAACT TGATGATGTGTTACAAACGTAATAGAGCAACAAGAGTCGAATGTACAACTATTGTTA ATGGTGTTAGAAGGTCCTTTTATGTCTATGCTAATGGAGGTAAAGGCTTTTGCAAACT ACACAATTGGAATTGTGTTAATTGTGATACATTCTGTGCTGGTAGTACATTTATTAGTG ATGAAGTTGCGAGAGACTTGTCACTACAGTTTAAAAGACCAATAAATCCTACTGTACCA GTCTTCTTACATCGTTGATAGTGTACAGTGAAGAATGGTCCATCCATCTTTACTTTG ATAAAGCTGGTCAAAAGACTTATGAAAGACATTCTCTCTCATTTTTGTTAACTTAGAC AACCTGAGAGCTAATAACACTAAAGGTTTATTGCTTATTAATGTTATAGTTTTGATGG TAAATCAAAATGTGAAGAATCATCTGCAAAATCAGCGTCTGTTTACTACAGTCAGCTT ATGTGTCAACCTATACTGTTACTAGATCAGGCATTAGTGTCTGATGTTGGTGATAGTG CGGAAGTTGCAGTTAAAATGTTTGTGCTTACGTTAATACGTTTTCATCAACTTTTAACT GTACCAATGGAAAACTCAAAACACTAGTTGCAACTGCAGAGCTGAACCTTGCAAG AATGTGTCTTAGACAATGTCTTATCTACTTTTATTTCAGCAGCTCGGCAAGGGTTTG TTGATTGAGATGTAGAACTAAAGATGTTGTTGAATGTCTTAAATTGTACATCAATCT GACATAGAAAGTTACTGGCGATAGTTGTAATAACTATATGCTCACCTATAACCAAGTTG AAAACATGACACCCCGTGACCTTGGTGCTTGTATTGACTGTAGTGCGCGTCATATTAA TGCGCAGGTAGCAAAAGTCAACAACATTGCTTTGATATGGAACGTTAAAGATTTTCATG TCATTGTCTGAACAACACTACGAAAACAAATACGTAGTGCTGCTAAAAGAAATAACTTAC CTTTTAAAGTTGACATGTGCAACTACTAGACAAGTTGTTAATGTTGTAACAACAAGATA GCACTTAAAGGGTGGTAAATTTGTTAATAATTGGTTGAAGCAGTTAATTAAGTTACAC TTGTGTTCCCTTTTGTGCTGCTATTTTCTATTTAATAACACCTGTTTCATGTCATGCTA AACATACTGACTTTTCAAGTGAAATCATAGGATACAAAGGCTATTGATGGTGGTGCTAC TCGTGACATAGCATCTACAGATACTTGTGTTGCTAACAAACATGCTGATTTTGACACAT GGTTTAGCCAGCGTGGTGGTAGTTATACTAATGACAAAGCTTGCCCATTTGATTGCTG CAGTCATAACAAGAGAGAGTGGGTTTTGCTGCTGCTGGTTTGGCTGGCACGATATTAC GCACAACATAATGGTGACTTTTTGCATTTCTTACCTAGAGTTTTTAGTGACAGTTGGTAA CATCTGTTACACACCATCAAACTTATAGAGTACACTGACTTTTGAACATCAGCTTGT GTTTTGGCTGCTGAATGTACAAATTTTAAAGATGCTTCTGGTAAGCCAGTACCATATT GTTATGATACCAATGTACTAGAAGGTTCTGTTGCTTATGAAAGTTTACGCCCTGACAC ACGTTATGTGCTCATGGATGGCTCTATTATTCAATTTTCTAACACCTACCTTGAAGGT TCTGTTAGAGTGGTAACAACTTTTGATTCTGAGTACTGTAGGCACGGCACTTTGAAA GATCAGAAGCTGGTGTGTTGTATCTACTAGTGGTAGATGGGTACTTAAACAATGATTA TTACAGATCTTTACCAGGAGTTTTCTGTGGTGTAGATGCTGTAAATTTACTTACTAATA TGTTTACACCACTAATTCACCTATTGGTGCTTTGGACATATCAGCATCTATAGTAGCT GGTGGTATTGTAGCTATCGTAGTAACATGCCTTGCTTACTATTTTATGAGGTTTAGAA GAGCTTTTGGTGAATACAGTCATGTAGTTGCCTTTAACTTTACTATTCTTATGTCA TTCAGTGTACTCTGTTTAAACACAGTTTACTCATTTCTACCTGGTGTATTCTGTATT TACTTGTACTTGACATTTTATCTTACTAATGATGTTTCTTTTTTAGCACATATTACAGTGG ATGGTTATGTTACACCTTTAGTACCTTTCTGGATAACAATTGCTTATATCATTTGTAT TTCCACAAAGCATTTCTATTGGTTCTTTAGTAATTACCTAAAGAGACGTGTAGTCTTTA ATGGTGTTTCTTTAGTACTTTTTGAAGAAGCTGCGCTGTGCACCTTTTTGTTAAATAAA GAAATGTATCTAAAGTTGCGTAGTGATGTGCTATTACCTCTTACGCAATATAATAGATA CTTAGCTCTTTATAATAAGTACAAGTATTTAGTGAGCAATGGATACAACTAGCTACA GAGAAGCTGCTTGTGTCATCTCGCAAAGGCTCTCAATGACTTCAGTAACTCAGGTT CTGATGTTCTTTACCAACCAACCAAACTCTATCACCTCAGCTGTTTTGAGAGTGG TTTTAGAAAAATGGCATTCCCATCTGGTAAAGTTGAGGGTTGTATGGTACAAGTAACT TGTGGTACAACCTACCTTAAACGGTCTTTGGCTTGATGACGTAGTTTACTGTCCAAGAC ATGTGATCTGCACCTCTGAAGACATGCTTAACCTAATTATGAAGATTTACTCATTG TAAGTCTAATCATAATTTCTTGGTACAGGCTGGTAATGTTCAACTCAGGGTTATTGGA CATTCTATGCAAAATTGTGACTTAAAGCTTAAAGTTGATACAGCAATCCTAAGACAC CTAAGTATAAGTTTGTTCGATTCAACCAGGACAGACTTTTTCACTGTGAGTTGTTA CAATGGTTCACCATCTGGTGTTTACCAATGTGCTATGAGGCCCAATTTCACTATTAAG GGTTCATTCTTAATGGTTCATGTGGTAGTGTGGTTTTAACATAGATTATGACTGTGT
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	CTCTTTTTGTTACATGCACCATATGGAATTACCAACTGGAGTTCATGCTGGCACAGAC TTAGAAGGTAACTTTTATGGACCTTTTGTGACAGGCAAAACAGCACAAAGCAGCTGGTA CGGACACAACCTATTACAGTTAATGTTTTAGCTTGTTGACGCTGCTGTTATAAATGG AGACAGGTGGTTTCTCAATCGATTTACCACAACCTTAATGACTTAACTTTGTGGCT ATGAAGTACAATTATGAACCTCTAACACAAGACCATGTTGACATACTAGGACCTCTTT CTGCTCAAACCTGGAATTGCCGTTTTAGATATGTGTGCTTCATTAAGAAATTAAGTGA AAATGGTATGAATGGACGTACCATATTGGGTAGTGCTTTATAGAAGATGAATTTACA CCTTTTGATGTTGTTAGACAATGCTCAGGTGTTACTTTCCAAAGTGCCAGTGAAAAGAA CAATCAAGGGTACACACCACTGGTTGTTACTCACAATTTTGACTTCACTTTTAGTTTTA GTCCAGAGTACTCAATGGTCTTTGTTCTTTTTTTGTATGAAAATGCCTTTTTACCTTTT GCTATGGGTATTATTGCTATGCTGCTTTTGCAATGATGTTTGTCAAACATAAGCATG CATTTCTCTGTTTGTGTTTTGTTACCTTCTCTTGCCACTGTAGCTTATTTAATATGGTCT ATATGCCTGCTAGTTGGGTGATGCGTATTATGACATGGTTGGATATGGTTGACTAG TTTGTCTGGTTTTAAGCTAAAAGACTGTGTTATGTATGCATCAGCTGTAGTGTTACTAA TCCTTATGACAGCAAGAAGCTGTGATGATGATGGTGCTAGGAGAGTGTGGACACTTA TGAATGTCTTGACACTCGTTTATAAAGTTTATTATGGTAATGCTTTAGATCAAGCCATT TCCATGTGGGCTCTTAATCTCTGTACTTCTAACTACTCAGGTGTAGTTACAACCTGT CATGTTTTTGGCCAGAGGTATTGTTTTTATGTGTGTTGAGTATTGCCCTATTTTCTTCA TAACTGGTAATACACTTCAGTGATAATGCTAGTTTATTGTTCTTAGGCTATTTTTGT ACTTGTTACTTTGGCCTCTTTTGTGTTACTCAACCGCTACTTTAGACTGACTCTTGGTG TTATGATTACTTAGTTTCTACACAGGAGTTTAGATATATGAATTCACAGGGACTACTCC CACCCAAGAATAGCATAGATGCCCTCAAACCTCAACATTAAATTGTTGGGTGTTGGTGG CAAACCTTGATCAAGTAGCCACTGTACAGTCTAAAAATGTCAGATGTAAAGTGCACA TCAGTAGTCTTACTCTCAGTTTTGCAACAACCTCAGAGTAGAATCATCTAAATGTTG GGCTCAATGTGTCCAGTTACACAATGACATTCTCTTAGCTAAAGATACTACTGAAGCC TTTGAAAAAATGGTTTCACTACTTTCTGTTTTGCTTTCCATGCAGGGTGCTGTAGACAT AAACAAGCTTTGTGAAGAAATGCTGGACAACAGGGCAACCTTACAAGCTATAGCCTC AGAGTTTAGTTCCCTTCCATCATATGCAGCTTTTGCTACTGCTCAAGAAGCTTATGAG CAGGCTGTTGCTAATGGTGATTCTGAAGTTGTTCTTAAAAAGTTGAAGAAGCTTTGA ATGTGGCTAAATCTGAATTTGACCGTGATGCAGCCATGCAACGTAAGTTGGAAAAGA TGGCTGATCAAGCTATGACCCAATGTATAAACAGGCTAGATCTGAGGACAAGAGGG CAAAAGTTACTAGTGCTATGCAGACAATGCTTTTCACTATGCTTAGAAAGTTGGATAA TGATGCACTCAACAACATTATCAACAATGCAAGAGATGGTTGTGTTCCCTTGAACATA ATACTCTTACAACAGCAGCCAACTAATGGTTGTCATACCAGACTAATACATATA AAAATACGTGTGATGGTACAACATTTACTTATGCATCAGCATTGTGGGAAATCCAACA GGTTGTAGATGCAGATAGTAAATTTGTTCAACTTAGTGAATTAAGTATGGACAATTCA CCTAATTTAGCATGGCCTCTTATTGTAACAGCTTTAAGGGCCAATTCTGCTGTCAAAT TACAGAATAATGAGCTTAGTCCCTGTTGCACTACGACAGATGCTTTGTGCTGCCGTA CTACACAACTGCTTGCACTGATGACAATGCGTTAGCTTACTACAACACAACAAAGG GAGGTAGGTTTGTACTTGCACTGTTATCCGATTACAGGATTTGAAATGGGCTAGATT CCCTAAGAGTGAAGCTAGTGAAGTGGTACTATCTATACAGAAGTGAACACCTTTGTAGGTTT GTTACAGACACACCTAAAGGTCCTAAAGTGAAGTATTTTACTTTTAAAGGATTAATA CAACCTAAATAGAGGTATGGTACTTGGTAGTTTAGCTGCCACAGTACGTCTACAGCT GGTAATGCAACAGAAGTGCCTGCCAATTCACTGTATTATCTTTCTGCTGTTTTGCTG TAGATGCTGCTAAAGCTTACAAGATTATCTAGCTAGTGGGGGACAACTACTAA TTGTGTTAAGATGTTGTGTACACACACTGGTACTGGTCAGGCAATAACAGTTACACCG GAAGCCAATATGGATCAAGATCCTTTGGTGGTGCATCGTGTGCTGTACTGCCGT TGCCACATAGATCATCCAATCCTAAAGGATTTTGTGACTTAAAGGTAAGTATGTAC AAATACCTACAACCTGTGCTAATGACCTGTGGGTTTTACACTTAAAAACACAGTCTG TACCGTCTGCGGTATGTGGAAGGTTATGGCTGTAGTTGTGATCAACTCCGCGAACC CATGCTTCAGTCAGCTGATGCACAATCGTTTTTAAACGGGTTTGGGCTGAAGTGCA GCCCGTCTTACACCGTGCGGCACAGGCACTAGTACTGATGTCGTATACAGGGCTTTT GACATCTACAATGATAAAGTAGCTGGTTTTGCTAAATTCCTAAAACTAATTGTTGTCG CTTCCAAGAAAAGGACGAAGATGACAATTTAATTGATTCTTACTTTGTAGTTAAGAGA CACACTTTCTTAACTACCAACATGAAGAAACAATTTATAATTTACTTAAGGATTGTCC AGCTGTTGCTAAACATGACTTCTTTAAGTTTAGAATAGACGGTGACATGGTACCACAT ATATCACGTCAACGTCTTACTAAATACACAATGGCAGACCTCGTCTATGCTTTAAGGC ATTTTGATGAAGGTAATTGTGACACATTAAGAAATACTTTGACATACAATTTGTTGT GATGATGATTATTTCAATAAAAAGGACTGGTATGATTTGTAGAAAACCCAGATATATT ACGCGTATACGCCAACTTAGGTGAACGTGTACGCCAAGCTTTGTTAAAAACAGTACA ATTCTGTGATGCCATGCGAAATGCTGGTATTGTTGGTGTACTGACATTAGATAATCAA GATCTCAATGGTAACTGGTATGATTTGCGGTGATTTATACAAACCACGCCAGGTAGTG GAGTTCCTGTTGTAGATTCTTATTATTCTTGTAAATGCCTATATTAACCTTGACCAGG GCTTTAACTGCAGAGTCACATGTTGACACTGACTTAACAAAGCCTTACATTAAGTGGG ATTTGTTAAATATGACTTCACGGAAGAGAGGTTAAACTCTTTGACCGTATTTTAA TATTGGGATCAGACATACCACCCAAATTGTGTTAACTGTTGGATGACAGATGCATT
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	TGCATTGTGCAAACTTTAATGTTTTATTCTCTACAGTGTTCACCTACAAGTTTGGACCACTAGTGAGAAAAATTTGTTGATGGTGTCCATTTGTAGTTTCACTGGATACC ACTTCAGAGAGCTAGGTGTTGTACATAATCAGGATGTAAACTTACATAGCTCTAGACT TAGTTTTAAGGAATTACTTGTGTATGCTGCTGACCTGCTATGCACGCTGCTTCTGGT AATCTATTACTAGATAAACGCACTACGTGCTTTTCAGTAGCTGCACTTACTAACAATGT TGCTTTTCAAACGTCAAACCCGGTAATTTTAAACAAAGACTTCTATGACTTTGCTGTGT CTAAGGGTTTCTTTAAGGAAGGAAGTTCTGTTGAATTAACAACTTCTTCTTGTCTCA GGATGGTAATGCTGCTATCAGCGATTATGACTACTATCGTTATAATCTACCAACAATG TGTGATATCAGACAACTACTATTTGTAGTTGAAGTTGTTGATAAGTACTTTGATTGTTA CGATGGTGGCTGTATTAATGCTAACCAGTCATCGTCAACAACTAGACAAATCAGCT GGTTTTCCATTTAATAAAATGGGTAAGGCTAGACTTTTATTATGATTCAATGAGTTATGA GGATCAAGATGCACCTTTTCGCATATACAAAACGTAATGTCATCCCTACTATAACTCAA ATGAATCTTAAGTATGCCATTAGTGCAAGAATAGAGCTCGCACCCGTAGCTGGTGTCT TCTATCTGTAGTACTATGACCAATAGACAGTTTCATCAAAAATTATTGAAATCAATAGC CGCCACTAGAGGAGCTACTGTAGTAATTGGAACAAGCAAATTCATGGTGGTGGCA CAACATGTTAAAACTGTTTATAGTGATGTAGAAAACCTCACCTTATGGGTTGGGAT TATCCTAAATGTGATAGAGCCATGCCTAACATGCTTAGAATTATGGCCTCACTTGTTC TTGCTCGCAAAACATACAACGTTGTTGAGCTTGTACACCCGTTTCTATAGATTAGCTAA TGAGTGTGCTCAAGTATTGAGTGAATGGTCATGTGTGGCGTTCACTATATGTTAAA CCAGGTGGAACCTCATCAGGAGATGCCACAACCTGCTTATGCTAATAGTGTTTTTAACA TTTGTCAAGCTGTACGGCCAATGTTAATGCACCTTTTCTACTGATGGTAACAAAT GCCGATAAGTATGTCCGCAATTTACAACACAGACTTTATGAGTGTCTCTATAGAAATA GAGATGTTGACACAGACTTTGTGAATGAGTTTTACGCATATTTGCCGTAAACATTTCTC AATGATGATACTCTCTGACGATGCTGTTGTGTGTTTCAATAGCACTTATGCATCTCAA GGTCTAGTGGCTAGCATAAAGAACTTTAAGTCAGTTCTTTATTATCAAAACAATGTTTT TATGTCTGAAGCAAAATGTTGGACTGAGACTGACCTTACTAAAGGACCTCATGAATTT TGCTCTCAACATACAATGCTAGTTAAACAGGGTGATGATTATGTGTACCTTCCTTACC CAGATCCATCAAGAAATCCTAGGGGCCGGCTGTTTTGTAGATGATATCGTAAACACAG ATGGTACACTTATGATTGAACGGTTCGTGCTTTAGCTATAGATGCTTACCCACTTAC TAAACATCCTAATCAGGAGTATGCTGATGTCCTTTCATTTGACTTACAATACATAAGAA AGCTACATGATGAGTTAACAGGACACATGTTAGACATGTATTCTGTTATGCTTACTAA TGATAACACTTCAAGGTATTGGGAACCTGAGTTTTATGAGGCTATGTACACACCCGAT ACAGTCTTACAGGCTGTTGGGGCTGTGTCTTTGCAATTCACAGACTTCATTAAGAT GTGGTGTGCTGCATACGTAGACCATTTCTATGTTGTAATGCTGTACGACCATGTCAT ATCAACATCACATAAAATAGTCTTGTCTGTTAATCCGTATGTTTGCATGCTCCAGGTT GTGATGTACAGATGTGACTCAACTTTACTTAGGAGGTATGAGCTATTATTGTAAATC ACATAAACCCACCCATTAGTTTTCCATTGTGTGCTAATGGACAAGTTTTGGTTTATATA AAAATACATGTGTTGGTAGCGATAATGTTACTGACTTTAATGCAATTCGAACATGTGA CTGGACAAATGCTGGTGATTACATTTTAGCTAACACCTGTACTGAAAGACTCAAGCTT TTTGACAGCAAAACGCTCAAAGCTACTGAGGAGACATTTAACTGTCTTATGGTATTG CTACTGTACGTGAAGTGCTGTCTGACAGAGAATTACATCTTTCATGGGAAGTTGGTAA ACCTAGACCACCCTTAACCGAAATTATGCTTTTACTGGTTATCGTGTAACATAAAAC AGTAAAGTACAAATAGGAGAGTACACCTTTGAAAAAGGTGACTATGGTGATGCTGTT GTTTACCGAGGTACAACAACCTTACAATTAATGTTGGTGATTATTTGTGTGACATC ACATACAGTAATGCCATTAAAGTGCACTTACACTAGTGCCACAAGAGCACTATGTTAGA ATTACTGGCTTATACCCAACACTCAATATCTCAGATGAGTTTTCTAGCAATGTTGCAAA TTATCAAAAGGTTGGTATGCAAAAAGTATTCTACACTCCAGGGACCACCTGGTACTGGT AAGAGTCATTTTGCTATTGGCCTAGCTCTCTACTACCCTTCTGCTGCGCATAGTGATA CAGCTTGCTCTCATGCCGCTGTTGATGCACTATGTGAGAAGGCATTAATAATTTGCC TATAGATAAATGTAGTAGAATTATACCTGCACGTGCTCGTGATAGAGTGTTTTGATAAA TTCAAAGTGAATTCACATTAGAACAGTATGTCTTTGTAAGTGAATGCAATGCCTGTA GACGACAGCAGATATAGTTGTCTTTGATGAAATTTCAATGGCCACAAATTATGATTTG AGTGTGTCAATGCCAGATTACGTGCTAAGCACTATGTGTACATTGGCGACCCCTGCT CAATTACCTGCACCCAGCATTGCTAAGTAAAGGGACACTAGAACCAGAAATATTCA ATTAGTGTGTAGACTTATGAAAACATAGGTCCAGACATGTTCTCGGAACTTGTCTG GCGTTGTCCTGCTGAAATTTGTTGACACTGTGAGTGCTTTGGTTTATGATAATAAGCTT AAAGCACATAAAGACAAATCAGCTCAATGCTTTAAATGTTTTATAAGGGTGTTATCAC GCATGATGTTTCATCTGCAATTAACAGGCCACAAATAGGCGTGGTAAGAGAATTCCTT ACACGTAACCCCTGCTTGGAGAAAAGCTGTCTTTATTTACCTTATAATTCACAGAATG CTGTAGCCTCAAAGATTTTGGGACTACCAACTCAAAGTGTGATTTCATCACAGGGCTC AGAATATGACTATGTCAATTTCACTCAAACCACTGAAACAGCTCACTCTTGTAAATGTAA ACAGATTTAATGTTGCTATTACCAGAGCAAAAGTAGGCATACTTTGCATAATGTCTGA TAGAGACCTTTATGACAAGTTGCAATTTACAAGTCTTGAAATTTCCACGTAGGAATGTG GCAACTTTACAAGCTGAAAAATGTAACAGGACTCTTAAAGATTGTAGTAAGGTAATCA CTGGGTTACATCCTACACAGGCACCTACACACCTCAGTGTTGACACTAAATTCAAAAC TGAAGGTTTATGTGTTGACATACCTGGCATACTAAGGACATGACCTATAGAAGACTC
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	ATCTCTATGATGGGTTTTAAATGAATTATCAAGTTAATGGTTACCCTAACATGTTTAT CACCCGCGAAGAAGCTATAAGACATGTACGTGCATGGATTGGCTTCGATGTCGAGG GGTGTCATGCTACTAGAGAAGCTGTTGGTACCAATTTACCTTTACAGCTAGGTTTTTC TACAGGTGTTAACCTAGTTGCTGTACCTACAGGTTATGTTGATACACCTAATAATACA GATTTTTCCAGAGTTAGTGCTAAACCACCGCTGGAGATCAATTTAAACACCTCATAC CACTTATGTACAAAGGACTTCCTTGGAAATGTAGTGCATATAAAGATTGTACAAATGTT AAGTGACACACTTAAAAATCTCTCTGACAGAGTCGTATTTGTCTTATGGGCACATGGC TTTGAGTTGACATCTATGAAGTATTTTGTGAAAATAGGACCTGAGCGCACCTGTTGTC TATGTGATAGACGTGCCACATGCTTTTCCACTGCTTCAGACACTTATGCCTGTTGGCA TCATTCTATTGGATTGATTACGTCTATAATCCGTTTATGATTGATGTTCAACAATGGG GTTTTACAGGTAACCTACAAAGCAACCATGATCTGTATTGTCAAGTCCATGGTAATGC ACATGTAGCTAGTTGTGATGCAATCATGACTAGGTGTCTAGCTGTCCACGAGTGCTTT GTTAAGCGTGTGACTGGACTATTGAATATCCTATAATTGGTGATGAAGTGAAGATTA ATGCGGCTGTGAGAAAGGTTCAACACATGGTTGTTAAAGCTGCATTATTAGCAGACAA ATTCCAGTTCTTCACGACATTGGTAACCCTAAAGCTATTAAGTGTGTACCTCAAGCT GATGTAGAAATGGAAGTTCTATGATGCACAGCCTTGATGTGACAAAGCTTATAAAATAG AAGAATTATTCTATTCTTATGCCACACATTCTGACAAATTCACAGATGGTGATGCCTA TTTTGGAATTGCAATGTCGATAGATATCCTGCTAATTCATTGTTGTAGATTTGACAC TAGAGTGCTATCTAACCTTAACCTGCCTGGTTGTGATGGTGGCAGTTTGTATGTAAT AAACATGCATTCCACACACCACTTTTGATAAAAGTGCTTTTGTTAATTTAAACAATT ACCATTTTTCTATTACTCTGACAGTCCATGTGAGTCTCATGGAACCAAGTAGTGCA GATATAGATTATGTACCACTAAAGTCTGCTACGTGTATAACACGTTGCAATTTAGGTG GTGCTGTCTGTAGACATCATGCTAATGAGTACAGATTGTATCTCGATGCTTATAACAT GATGATCTCAGCTGGCTTTAGCTTGTGGGTTTACAACAATTTGACTTTATAACCTC TGGAACACTTTTACAAGACTTCAGAGTTTAGAAAATGGGCTTTTAAATGTTGAAATAA GGGACACTTTTGATGGACAACAGGGTGAAGTACCAGTTTCTATCATTAATAACACTGTT TACACAAAAGTTGATGGTGTGATGTAGAATTGTTGAAAATAAAACAACATTACCTGT TAATGTAGCACTTTGAGCTTTGGGCTAAGCGCAACATTAACCAGTACCAGAGGTGAA AATACTCAATAATTTGGGTGTGGACATTGCTGCTAATACTGTGATCTGGGACTACAAA AGAGATGCTCCAGCACATATATCTACTATTGGTGTGTTGTTCTATGACTGACATAGCCA AGAAACCAACTGAAACGATTTGTGCACCACTCACTGTCTTTTTGATGGTAGAGTTGA TGGTCAAGTAGACTTATTTAGAAATGCCCGTAATGGTGTCTTATTACAGAAGGTAGT GTTAAAGGTTTACAACCATCTGTAGGTCCCAACAAGCTAGCTTAAATGGAGTCACAT TAATTGGAGAAGCCGTAAAAACACAGTTCAATTATTATAAGAAATGATGGTGATG CCAACAATTACCTGAACTTACTTTACTCAGAGTAGAAATTTACAAGAAATTTAAACCCA GGAGTCAAATGGAAATGATTTCTTAGAATTAGCTATGGATGAATTCATTGAACGGTA TAAATTAGAAGGCTATGCCTTCGAACATATCGTTTATGGAGATTTTAGTCATAGTCAG TTAGGTGGTTTACATCTACTGATTGGACTAGCTAAACGTTTTTAAAGGAATCACCTTTT AATTAGAAGATTTATTCCTATGGACAGTACAGTAAAAACTATTTTCATAACAGATGCG CAAACAGGTTTCATCTAAGTGTGTGTGTTCTGTTATTGATTTATTACTTGATGATTTTGT TGAAATAATAAAATCCCAAGATTTATCTGTAGTTTCTAAGGTTGTCAAAGTGACTATTG ACTATACAGAAATTTCAATTTATGCTTTGGTGAAAGATGGCCATGTAGAAACATTTTAC CCAAAATTACAATCTAGTCAAGCGTGGCAACCGGGTGTGCTATGCCTAATCTTTACA AAATGCAAGAATGCTATTAGAAAAGTGTGACCTTCAAAATTATGGTGATAGTGCAC ATTACCTAAAGGCATAATGATGAATGTGCAAAATATACTCAACTGTGCAATTTTAA ACACATTAACATTAGCTGTACCCTATAATATGAGAGTTATACATTTTGGTGCTGGTTCT GATAAAGGAGTTGCACCAGGTACAGCTGTTTTAAGACAGTGGTTGCCTACGGGTACG CTGCTTGTGCAATTGATCTTAATGACTTTGTCTCTGATGCAGATTCAACTTTGATTG GTGATTGTGCAACTGTACATACAGCTAATAAATGGGATCTCATTATTAGTGATATGTA CGACCTTAAGACTAAAAATGTTACAAAAGAAAAAGTACTTAAAGAGGGTTTTTCACT TACATTTGTGGGTTTATACAAACAAAAGCTAGCTCTTGAGGTTCCGTGGCTATAAAGA TAACAGAACATTCTTGAATGCTGATCTTTATAAGCTCATGGGACACTTCGCATGGTG GACAGCCTTTGTTACTAATGTGAATGCGTCATCATCTGAAGCATTTTAAATGGATGT AATTATCTTGGCAAACACGCGAACAATAGATGGTTATGTCATGCAGTGAATTACA TATTTTGGAGGAATACAAATCCAATTCAGTTGTCTTCTTATTCTTTATTTGACATGAGT AAATTTCCCTTAAATTAAGGGTACTGCTGTTATGTCTTTAAAGAAGGTCAAATCAA TGATATGATTTTATCTCTTCTAGTAAAGGTAGACTTATAATTAGAGAAAACAACAGAG TTGTTATTTCTAGTGATGTTCTTGTAAACAACTAAACGAACAATGTTTGTCTTCTGTT TTATTGCCACTAGTCTCTAGTCAAGTGTGTTAATCTTACAACCAGAATCAATTACCCC CTGCATACACTAATCTTTACACGTTGGTGTATTACCCTGACAAAGTTTTTCAGATCC TCAGTTTTACATTCAACTCAGGACTTGTCTTACCCTTTCTTTCCAATGTTACTGGTT CCATGCTATACATGCTCTGGGACCAATGGTACTAAGAGGTTTGATAACCCTGTCCTA CCATTTAATGATGGTGTATTGCTTCCACTGAGAAGTCTAACATAATAAGAGGCT GGATTTTTGGTACTACTTTAGATTGGAAGACCCAGTCCCTACTTTGTTAATAACGCT ACTAATGTTGTTATTAAGTCTGTGAATTTCAATTTGTAATGATCCATTTTGGGTGTT TATTACCACAAAACAACAAAAGTTGGATGGAAGTGAGTTCAGAGTTATTCTAGTG
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		CGAATAATTGCACCTTTGAATATGTCTCTCAGCCTTTTCTTATGGACCTTGAAGGAAAA CAGGGTAATTTCAAAAATCTTAGGGAATTTGTGTTAAGAATATTGATGGTTATTTTAA AATATATTCTAAGCACACGCCCTATTAATTTAGTGCGTGATCTCCCTCAGGGTTTTTCG GCTTAGAACCATTTGGTAGATTTGCCAATAGGTATTAACATCACTAGGTTTCAAACCTT ACTTGCTTTACATAGAAAGTTATTTGACTCCTGGTGATTCTTCTTCAGGTTGGACAGCT GGTGCTGCAGCTTATTATGTGGGTTATCTTCAACCTAGGACTTTTTCTATTAATAATAA TGA AAAATGGAACCATTACAGATGCTGTAGACTGTGCACCTGACCCTCTCTCAGAAAA AAGTGACGTTGAAATCCTTCACTGTAGAAAAAGGAATCTATCAAACTTCTAACTTTAG AGTCCAACCAACAGAATCTATTGTTAGATTTCTAATATTACAACTTGTGCCCTTTTG GTGAAGTTTTTAACGCCACCAGATTTGCATCTGTTTATGCTTGGAAACAGGAAGAGAAT CAGCAACTGTGTTGCTGATTATTCTGTCTATATAAATCCGCATCATTTTCCACTTTTA AGTGTATGGAGTGTCTCCTACTAAATTAATGATCTCTGCTTTACTAATGTCTATGCA GATTCATTTGTAATTAGAGGTGATGAAGTCAGACAAATCGCTCCAGGGCAAACCTGGA AAGATTGCTGATTATAATTATAAATTACCAGATGATTTTACAGGCTCGGTTATAGCTTG GAATTTCAACAATCTTGATTCTAAGGTTGGTGGTAATTATAATTACCTGTATAGATTGT TTAGGAAGTCTAATCTCAAACCTTTTGAGAGAGATATTCAACTGAAATCTATCAGGC CGGTAGCACACCTTGAATGGTGTGAAGGTTTTAATTGTTACTTTTCCCTTTACAATCAT ATGGTTTTCCAACCCACTAATGGTGTTGGTTACCAACCATACAGAGTAGTACTTTTC TTTTGAACCTTACATGCACCAGCAACTGTTTGTGGACCTAAAAAGTCTACTAATTTG GTTAAAAACAAATGTGTCAATTTCAACTTCAATGGTTTAAACAGGCACAGGTGTTCTTA CTGAGTCTAACAAAAAGTTTCTGCCCTTTCCAACAATTTGGCAGAGACATTGCTGACAC TACTGATGCTGTCCGTGATCCACAGACACTTGAGATTCTTGACATTACACCATGTTCT TTTGGTGGTGTCAGTGTTATAACACCAGGAACAAATCTTCTAACCAGGTTGCTGTTT TTTATCAGGATGTTAACTGCACAGAAGTCCCTGTTGCTATTCATGCAGATCAACTTAC TCCTACTTGGCGTGTTTATTCTACAGGTTCTAATGTTTTTCAACACAGCTGCAGGCTGT TTAATAGGGGCTGAACATGTCAACAACCTCATATGAGTGTGACATACCCATTGGTGCA GGTATATGCGCTAGTTATCAGACTCAGACTAATTTCTCCTCGGCGGGCACGTAGTGTA GCTAGTCAATCCATCATTGCCCTACACTATGTCACCTGGTGACAGAAATTCAGTTGCTT ACTCTAATAACTCTATTGCCATACCCACAAATTTTACTATTAGTGTACCACAGAAAT CTACCAAGTGTCTATGACCAAGACATCAGTAGATTGTACAATGTACATTTGTGGTGATT CAACTGAATGCAGCAATCTTTTGTGCAATATGGCAGTTTTTGTACACAATTAACCG TGCTTTAACTGGAATAGCTGTTGAACAAGACAAAAACCCCAAGAAGTTTTTGCACAA GTCAAAACAAATTTACAAAAACCCACCAATTAAGAGTTTTTGGTGGTTTTAATTTTTCACA AATATTACCAGATCCATCAAAACCAAGCAAGAGGTCAATTTATTGAAGATTTTCTTCA ACAAAGTGACACTTGCAGATGCTGGCTTCATCAAAACAATATGGTGATTGCTTGGTG ATATTGCTGCTAGAGACCTCATTTGTGCACAAAAGTTTAAACGGCCTTACTGTTTTGCC ACCTTTGCTCACAGATGAAATGATTGCTCAATACACTTCTGCACTGTTAGCGGGTACA ATCACTTCTGGTTGGACCTTTGGTGACAGGTGCTGCATTACAAATACCATTTGCTATGC AAATGGCTTATAGGTTTAAATGGTATTGGAGTTACACAGAATGTTCTCTATGAGAACCA AAAATTGATTGCCAACCAATTTAATAGTGCTATTGGCAAAATTCAGAGCTCACTTTCTT CCACAGCAAGTGCACTTGGAAAACTTCAAGATGTGGTCAACCAAAATGCAAGCTT TAAACACGCTTGTAAACAACCTAGCTCCAATTTTGGTGCAATTTCAAGTGTTTTAAAT GATATCCTTTACGCTCTTGACAAAGTTGAGGCTGAAGTGCAAAATGATAGGTTGATCA CAGGCAGACTTCAAAGTTTGCAGACATATGTGACTCAACAATTAATTAGAGCTGCGACA AATCAGAGCTTCTGCTAATCTTGCTGCTACTAAATGTCAGAGTGCTACTTGGACAA TCAAAAAGAGTTGATTTTTGTGGAAAGGGCTATCATCTTATGTCTTCCCTCAGTCAG CACCTCATGGTGATGCTTCTTGCTATGTGACTTATGTCCCTGCACAGAAAAAGAACTT CACAACTGCTCCTGCCATTTGTCATGATGGAAAAAGCACACTTTCCTGCTGAAGGTGT CTTTGTTTCAAATGGCACACACTGGTTTGTAAACACAAAGGAATTTTTATGAACCACAA ATCATTACTACAGACAACACATTTGTGTCTGGTAACTGTGATGTTGTAATAGGAATTG TCAACAACACAGTTTATGATCCTTTGCAACCTGAATTAGACTCATTCAAGGAGGAGTT AGATAAATATTTAAGAATCATACATCACCAGATGTTGATTTAGGTGACATCTCTGGCA TTAATGCTTCAGTTGTAACATTCAAAAAGAAATGACCGCCTCAATGAGGTTGCCAA GAATTTAAATGAATCTCTCATCGATCTCCAAGAACTTGGAAAGTATGAGCAGTATATA AAATGGCCATGGTACATTTGGCTAGGTTTTATAGCTGGCTTGATTGCCATAGTAATGG TGACAAATTATGCTTTGCTGTATGACCAGTTGCTGTAGTTGTCTCAAGGGCTGTTGTTT TTGTGGATCCTGCTGCAAAATTTGATGAAGACGACTCTGAGCCAGTGCTCAAAGGAGT CAAATTACATTACACATAAACGAACTTATGGATTTGTTTATGAGAATCTTCACAATTGG AACTGTAACCTTTGAAGCAAGGTGAAATCAAGGATGCTACTCCTTCAGATTTTGTTCGC GCTACTGCAACGATACCGATACAAGCCTCACTCCCTTTCCGATGGCTTATTGTTGGC GTTGCACTTCTGCTGTTTTTTCAGAGCGCTTCCAAAATCATAACCTCAAAAAAGAGAT GGCAACTAGCACTCTCCAAGGGTGTTCACCTTGTGCAACTGCTGTTGTTGTTTGT AACAGTTTACTCACACCTTTTGTCTGTTGCTGCTGGCCTTGAAGCCCTTTTCTCTAT CTTTATGCTTTAGTCTACTTCTTGCAGAGTATAAACTTTGTGAAGAATAAATAGAGGCT TTGGCTTTGCTGGAATGCCGTTCCAAAACCCATTACTTTATGATGCCAACTATTTT CTTTGCTGGCATACTAATTGTTACGACTATTGTATACCTTACAATAGTGAACCTCTTC
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	AATTGTCACTTACTTCAGGTGATGGCACAACAAGTCTATTTCTGAACATGACTACCA ATTGGTGGTTATACTGAAAAATGGGAATCTGGAGTAAAAGACTGTGTTGATTACACA GTTACTTCACTTCAGACTATTACCAAGCTGTACTCAACTCAATTGAGTACAGACACTGG TGTTGAACATGTTACCTTCTTCATCTACAATAAAATTTGTTGATGAGCCTGAAGAACATG TCCAAATTCACACAATCGACGGTTTCATCCGGAGTTGTTAATCCAGTAATGGAACCAAT TTATGATGAACCGACGACGACTACTAGCGTGCCTTTGTAAGCACAAGCTGATGAGTA CGAAGCTTATGACTCATTGCTTCGGAAGAGACAGGTACGTTAATAGTTAATAGCGTA CTTCTTTTTCTTGCCTTCGTGGTATTCTTGCTAGTTACACTAGCCATCCTTACTGCGCT TCGATTGTGTGCGTACTGCTGCAATATTGTTAACGTGAGTCTTGTAACACCTTCTTTTT ACGTTTACTCTCGTGTAAAAATCTGAATTTCTTAGAGTTCTGATCTTCTGGTCTAA ACGAAGCTAAATATTATATTAGTTTTCTGTTTGGAACTTTAATTTTAGCCATGGCAGAT TCCAACGGTACTATTACCGTTGAAGAGCTTAAAAAGCTCCTTGAACAATGGAACCTAG TAATAGGTTTCTTATTCCTTACATGGATTGTCTTCTACAATTTGCCATGCCAAACAGG AATAGGTTTTGTATATAATTAAGTTAATTTCTCTGGCTGTTATGGCCAGTAACCTT AGCTTGTGTTGTGCTTGTGCTGTTTACAGAATAAATTTGGATCACCAGTGGAAATGCT ATCGCAATGGCTTGTCTTGTAGGCTTGATGTGGCTCAGCTACTTCATTGCTTCTTTCA GACTGTTTGCCTGACGCTTCCATGTGGTCAATCCAGAACTAACATTTCTTCT CAACGTGCCACTCCATGGCACTATTCTGACCAGACCGCTTCTAGAAAGTGAACCTCGT AATCGGAGCTGTGATCCTTCGTGGACATCTTCGTATTGCTGGACACCATCTAGGACG CTGTGACATCAAGGACCTGCCTAAAGAAATCACTGTTGCTACATCAGCAACGCTTTCT TATTACAAATTTGGAGCTTTCGACGCTGTAGCAGGTGACTCAGGTTTTGCTGCATAC AGTCGCTACAGGATTGGCAACTATAATTAACACAGACCATTCAGTAGCAGTGAC AATATTGCTTTGCTTGTACAGTAAGTGACAACAGATGTTTCATCTCGTTGACTTTTCAG GTTACTATAGCAGAGATATTACTAATTATTATGAGGACTTTTAAAGTTTCCATTTGGAA TCTTGATTACATCATAAACCTCATAATTAATAATTTATCTAAGTCAACTGAGAATAA ATATTCTCAATTAGATGAAGAGCAACCAATGGAGATTGATTAAACGAACATTGAAAAAT ATTCTTTTCTTGGCACTGATAACACTCGCTACTTGTGAGCTTTATCACTACCAAGAGT GTGTTAGAGGTACAACAGTACTTTTAAAGAACTTGTCTTCTGGAACATACGAGGG CAATTCAACATTTTCATCCTTAGCTGATAACAAATTTGCACTGACTTGCTTTAGCACTC AATTTGCTTTTGTCTGCTGACGGCGTAAACACGCTCTATCAGTTACGTGCCAGATC AGTTTCACTAACTGTTTCATCAGACAAGAGGAAAGTTCAAGAACTTTACTCTCCAATT TTTTCTATTGTTGCGGCAATAGTGTTTAAACACTTTGCTTCACACTCAAAAGAAAGAC AGAATGATTGAACCTTTCATTAATTGACTTCTATTTGTGCTTTTACGCTTTCTGCTATTCT CTTGTTTTAATTATGCTTATTATCTTTTGGTTCTCACTTGAAGTCAAGATCATAATGAA ACTTGTCAAGCCTAAACGAACATGAAATTTCTGTTTTCTTAGGAATCATCACAACCTGT AGCTGCATTTCAACGAAGATGTAGTTTACAGTCATGTACTCAACATCAACCATATGTA GTTGATGACCCGTGTCCTATTCACTTCTATTCTAAATGGTATATTAGAGTAGGAGCTA GAAAATCAGCACCTTTAATTGAATTTGCGTGGATGAGGCTGTTCTAAATCAACCAT TCAGTACATCGATATCGGTAATTATACAGTTTCTGTTTACCTTTTACAATTAATTGCC AGGAACCTAAATTTGGGTAGTCTTGTAGTGCGTTGTTGCTTATGAAGACTTTTTAGA GTATCATGACGTTCTGTTGTTTATGATTTTCATCTAAACGAACAACTAAATCTCTGA TAATGGACCCCAAAATCAGCGAAATGCACCCCGCATTACGTTTGGTGGACCCCTCAGA TTCAACTGGCAGTAACCAAGATGGAGAAGCGAGTGGGGCGCGATCAAAACAACGCTG GGCCCCAAGGTTTACCAATAATACTGCGTCTTGGTTACCGCTCTCACTCAACATG GCAAGGAAGACCTTAAATTCCTCGAGGACAAGGCGTTCCAATTAAACCAATAGCA GTCCAGATGACCAAAATTTGGCTACTACCGAAGAGCTACCAGACGAATTCGTGGTGGTG ACGGTAAAAAGATCTCAGTCCAAGATGGTATTTCTACTACCTAGGAAGTGGGC CAGAAGCTGGACTTCCCTATGGTGCTAACAAAGACGGCATCATATGGGTTGCAACTG AGGGAGCCTTGAATACACCAAAAGATCACATTGGCACCCGCAATCCTGCTAACAATG CTGCAATCGTGCTACAACCTTCTCAAGGAACAACATTGCCAAAAGGCTTCTACGCGAG AAGGGAGCAGAGGCGGCGAGTCAAGCCTCTTCTCGTTCTCATCAGTATGTCGCAAC AGTTCAAGAAATTCACCTCCAGGCAGCAGTAGGGGAAGTCTCTCTGCTAGAATGGCT GGCAATGGCGGTGATGCTGCTTGTCTTGTCTGCTGCTTGACAGATTGAACCAAGCTT GAGAGCAAAATGTCTGGTAAAGGCCAACAACAAGGCCAAACTGTCAATAGAGAA TCTGCTGCTGAGGCTTCTAAGAAAGCCTCGGCAAAAACGTAAGTCCACTAAAGCATAAC AATGTAACACAAGCTTTGCGCAGACGTGGTCCAGAACAACCCAAAGGAAATTTGGG GACCAGGAAGTAAATCAGACAAGGAAGTATTACAAACATTGGCCGCAAAATTTGCACAA TTTTCCCCCAGCGCTTCAGCGTTCTTCGGAATGTCGCGCATTGGCATGGAAGTCACA CCTTCGGGAACGTGGTTGACCTACACAGGTGCCATCAAATTTGGATGACAAAGATCCA AATTTCAAAGATCAAGTCAATTTTCTGCTGAATAAGCATATTGACGCATACAAAACATTCCC ACCAACAGAGCCTAAAAAGGACAAAAAGAAAGGCTGATGAACTCAAGCCTTACC GCAGAGACAGAAAGAACGCAAACTGTGACTCTTCTCTGCTGCAGATTTGGATGA TTTTCTCAAACAATTTGCAACAATCCATGAGCAGTGCTGACTCAACTCAGGCTTAACT CATGCAGACCACACAAGGCAGATGGGTATATAAACGTTTTTCGCTTTTCGCTTACGA TATATAGTCTACTTGTGCGAGAATGAATTCCTGTAACATACATAGCACAAGTAGATGT AGTTAACTTTAATCTCACATAGCAATCTTTAATCAGTGTTAACATTAGGGAGGACTT
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		GAAAGAGCCACCACATTTTCACCGAGGCCACGCGGAGTACGATCGAGTGACAGTG ACAATGCTAGGGAGAGCTGCCTATATGGAAGAGCCCTAATGTGTAATAATTTTA GTAGTGCTATCCCCATGTGATTTAATAGCTTCTTAGGAGAATGACAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAA
9	SARS-CoV spike protein	MFIFLLFLTLSGSDLDRCITTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFLP FYSNVTGFHTINHTFDNPVIFPKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTN VVIRACNFELCDNPFFAVSKPMGTQTHTMIFDNFNFCTFEYISDAFSLDVSEKSGNFKHL REFVFNKNDGFLVYKGYQPIDVVRDLPSGFNTLKPFIKPLPLGINITNFRAITAFSPAQDT WGTSAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSN FRVVPDGDVVRFPNITNLCPFGEVFNATKFPVYAWERKKISNCVADYSLYNSTFFSTF KCYGVSATKLNLCFSNVYADSFVVGDDVVRQIAPGQTGVIADYNYKLDDDFMGCVLAW NTRNIDATSTGNYNKYRYLRHGKLRPFERDISNVFSPDGKPTPPALNCYWPLNDYG FYTTTGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSK RFQPFQFGRDVSDFDTSVRDPKTSEILDISPCSFGGVSVITPGTNASSEVAVLYQDVNC TDVSTAIHADQLTPAWRIYSTGNNVFQTAAGCLIGAEHVDTSYECDDIPGAGICASYHTVS LLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMKTSVDCNMYICG DSTECANLLQYGSFCTQLNRLSGIAAEQDRNTRVFAQVKQMYKTPTLYKFGGFNFS QILPDPLKPTKRSFIEDLLFNKVTADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLL TDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFGIGVQTNVLYENQKQIA NQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRG KVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSCEVLGQSKRVDFCGK GYHLSFPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVVFNGTSWFI TQRNFFSPQIITDNTFVSGNCDVVGIIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVL GDISGINASVVNIQKEIDRLNEVAKNLSLIDLQELGKYEQYIKWPVYVWLGFIAGLIAIV MVTILLCCMTSCCCLKGACSCGCKFDEDDSEPVLKGVKLHYT
10	SARS-CoV-2 spike protein	MFLTLTKRTMFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHST QDLFLPFFSNVTWFAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDS KTQSLIIVNNATNVVIKVCFEYQFCNDPFLGVYHKNKNSWMESEFRVYSSANNCTFEYV SQPFLMDLEGKQGNFKNLREFVFNKIDGYFKIYSKHTPINLVRDLPGQFSALEPLVDLPIGI NITRFQTLALHRSYLTGDSSSGWTAGAAAYVGYLQPRFTLLKYNENGITDAVDCAL DPLSETKCTLKSFTEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATKFPVYAWN RKRISSNCVADYSLYNASFSFTKCYGVSPTKLNLCFTNVYADSFVIRGDEVVRQIAPGQ TGKIADYNYKLDDFTGCVIWNNSNLDLKVGGNYYLYRLFRKSNLKPFERDISTEYIQ AGSTPCNGVEGFNCFYPLQSYGFQPTNGVGYQPYRVVLSFELLHAPATVCGPKKSTN LVKNKCVNFNFNGLTGTGVLTESNKKFLPFQFGRDIADTTDAVRDPQTLLEILDITPCSF GVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGNNVFQTRAGCLIGA EHVNNSYECDDIPGAGICASYQTQTNSPRRARSVASQSIAYTMSLGAENSVAYSNNSIAIP TNFTISVTEILPVSMTKTSVDCVTMYICGDSSTECNLLQYGSFCTQLNRLALTGIAVEQDK NTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTADAGFIKQYG DCLGDIARDLICAQKFNGLTVLPPLLTDEMIAYTSALLAGTITSGWTFGAGAALQIPFA MQMAYRFGIGVQTNVLYENQKLIANQFNISAIGKIQDLSSTASALGKLQDVVNQNAQAL NTLVKQLSSNFGAISSVLNDILSRDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASA NLAATKMSCEVLGQSKRVDFCGKGYHLSFPQSAAPHGVVFLHVTYVPAQEKFTTAPAI CHDGAHFPPREGVVFVSNGTWFWVTQRNFYEPQIITDNTFVSGNCDVVGIIINNTVYDPL QPELDSFKEELDKYFKNHTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLSLIDLQEL GKYEQYIKWPVYIWLGFIAGLIAIVMVTIMLCCMTSCCCLKGCCSCGCKFDEDDSEP VLKGVKLHYT
11	SARS-CoV spike protein S1 subunit	SDLDRCITTFDDVQAPNYTQHTSSMRGVVYPDEIFRSDTLYLTQDLFLPFYSNVTGFHTIN HTFDNPVIFPKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVIRACNFELCD NPFFAVSKPMGTQTHTMIFDNFNFCTFEYISDAFSLDVSEKSGNFKHLREFVFNKNDGFL YVYKGYQPIDVVRDLPSGFNTLKPFIKPLPLGINITNFRAITAFSPAQDTWGTSAAAYFVGY LKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPDGDVVRFP NITNLCPFGEVFNATKFPVYAWERKKISNCVADYSLYNSTFFSTFKCYGVSATKLNLC LFSNVYADSFVVGDDVVRQIAPGQTGVIADYNYKLDDDFMGCVLAWNTRNIDATSTGN YNKYRYLRHGKLRPFERDISNVFSPDGKPTPPALNCYWPLNDYGFTYTTTGIGYQPY RVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQFGRD VSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNASSEVAVLYQDVNCTDVSTAIHADQL TPAWRIYSTGNNVFQTAAGCLIGAEHVDTSYECDDIPGAGICASYHTVSLR
12	SARS-CoV spike protein RBD	RVVPDGDVVRFPNITNLCPFGEVFNATKFPVYAWERKKISNCVADYSLYNSTFFSTFK CYGVSATKLNLCFSNVYADSFVVGDDVVRQIAPGQTGVIADYNYKLDDDFMGCVLAWN TRNIDATSTGNYNKYRYLRHGKLRPFERDISNVFSPDGKPTPPALNCYWPLNDYGFT YTTTGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNF
13	SARS-CoV-2 spike protein S1 subunit	SQCYNLTTRTQLPPAYTNSFTRGVVYPDKVFRSSVLHSTQDLFLPFFSNVTWFAIHVSG TNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLIIVNNATNVVIKVC FQFCNDPFLGVYHKNKNSWMESEFRVYSSANNCTFEYVYVQPFLLMDLEGKQGNFKNL FVFNKIDGYFKIYSKHTPINLVRDLPGQFSALEPLVDLPIGINITRFQTLALHRSYLTGDS

		SSGWTAGAAAYVGYLQPRFTLLKYNENGTITDAVDCALDPLSETKCTLKSTVEKGIYQ TSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNKRKISNCVADYSLVYNSASF STFKCYGVSPTKLNLCFTNVYADSFVIRGDEVQRAPGQTGKIADYNYKLPDDFTGCVIA WNSNNLDSKVGNNYNYLYRFLFRKSNLKPFERDISTEIQAGSTPCNGVEGFNCYFPLQS YGFQPTNGVGYQPYRVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNGLTGTGVL ESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQD VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAHEVNNSEYCDIPIGAGICASY QTQTNSPRRAR
14	SARS-CoV-2 spike protein RBD	RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNKRKISNCVADYSLVYNSASFSTFK CYGVSPTKLNLCFTNVYADSFVIRGDEVQRAPGQTGKIADYNYKLPDDFTGCVIAWNS NNLDSKVGNNYNYLYRFLFRKSNLKPFERDISTEIQAGSTPCNGVEGFNCYFPLQSYGF QPTNGVGYQPYRVVLSFELLHAPATVCGPKKSTNLVKNKCVNF
15	SARS-CoV-2 spike protein RBD	PNITNLCPFGEVFNATRFASVYAWNKRKISNCVADYSLVYNSASFSTFKCYGVSPTKLN LCFTNVYDSFVIRGDEVQRAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGNNY LYRFLFRKSNLKPFERDISTEIQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYR VVLSFELLHAPATVCGPKKS
16	SARS-CoV-2 spike protein S1 subunit	MLLVNQSHQGFNKEHTSKMVSAILVYVLLAAAAHSAFAQCYNLTTRTQLPPAYTNSFTRG VYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGTKRFDNPVLPNDGVYFAST EKSNIIRGWIFGTTLDSTQSLIVNNATNVVIVKCEFCNDPFLGVYHKNKNSWMESE FRVYSSANNCTFEYVSQPFLLMDLEGKQGNFKNLREFVFNIDGYFKIYKHTPINLVRL PQGFSALEPLVDLPIGINITRFQTLALHRSYLTGPDSSSGWTAGAAAYVGYLQPRFTLL KYNENGTITDAVDCALDPLSETKCTLKSTVEKGIYQTSNFRVQPTESIVRFPNITNLCPF GEVFNATRFASVYAWNKRKISNCVADYSLVYNSASFSTFKCYGVSPTKLNLCFTNVYA DSFVIRGDEVQRAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGNNYNYLYRFLR KSNLKPFERDISTEIQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVLSFE LLHAPATVCGPKKSTNLVKNKCVNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAV RDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYS TGSNVFQTRAGCLIGAHEVNNSEYCDIPIGAGICASYQTQTNSPRRAR
17	SARS-CoV spike protein RBD	MNITNLCPFGEVFNATKFPVSVAWERKKISNCVADYSLYNSTFFSTFKCYGVSATKLN LCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDATSTGN YNYKYRYLRHGKLRPFERDISNVFSPDGKPCPPALNCYWPLNDYGYFTTTGIGYQPY RVVLSFELLNAPATYLSLNTAAAL
18	Artificial Sarbecovirus spike consensus 1	MFIFLLFTLVSGSTIEKCTTFDDVQPPNYTQFLSSHrgvYYPDDIFRSDVLHLTQDHLFP FDSNVTGFITFGLNFDNPIPFKDGIFYAATEKSNVIRGWVFGSTMNNKSQSVIIMNNSTNV VIRACNFELCDNPFVFAVSKPNNQIPSYIFNNAFNCTFEYVSDDFNLDVGEKPGNFKHLR EFVFNKNDGFLVYVSGYQPIDVASGLPSGFNALKPIFKLPLGINITNFRLLTAFPPRPDYW GTSAAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFR VVPDGDVVRFPNITNLCPFGEVFNATKFPVSVAWERKRISNCVADYSLYNSTFFSTFKC YGVSATKLNLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNT RNIDATSTGNNYKYRYLRHGKLRPFERDISNVFSPDGKPCPPALNCYWPLNDYGYFT TTTGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNGLTGTGVLTPSSKRF QPQFQGRDVSDFTDSDVRDPKTSEILDSPCSFGGVSVITPGTNTSSEVAVLYQDVNCTD VPVAIHADQLTPAWRVYSTGNNVFQTAGCLIGAHEVDTSEYCDIPIGAGICASYHTVSSL RSTSQKSIVAYTMSLGADSSIAYSNNITAIPTNFSISITTEVMVPVMAKTSVDCNMYICGDS TECANLLLQYGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFSQIL PDPLKPTKRSFIEDLLFNKVTADAGFMKQYGECLGDINARDLCAQKFNGLTVLPLLLTD DMIAAYTAALVSGTATAGWTFGAGALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQ FNKAISQIQESLTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRDPPE AEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYH LMSFPQAAPHGVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVVFNGTSWVITQR NFFSPQIITDNTFVSGSCDVIIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVLGDI SGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWVWVYVWLGFIAGLIAIVMTI LLCCMTSCCCLKGACSCGSCCKFEDEDDSEPVLGKVKLHYT
19	Artificial Sarbecovirus spike consensus 2	MFIFLLFTLTSGSDLRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLP FYSNVTGFHTINHTFDNPIPFKDGIFYAATEKSNVVRGWVFGSTMNNKSQSVIIMNNSTN VVIRACNFELCDNPFVVSQPMGTRTHTMIFDNFNCTFEYISDAFSLDVSEKSGNFKHL REFVFNKNDGFLVYKGYQPIDVVRDLPSGFNTLKIPIFKLPLGIKITNFRILTAQSPAQGT WGTSAAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSN FRVVPDGDVVRFPNITNLCPFGEVFNATKFPVSVAWERKRISNCVADYSLYNSTSFSTF KCYGVSATKLNLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAW NTRNIDATSTGNHNYKYRYLRHGKLRPFERDISNVFSPDGKPCPPAPNCYWPLRGY FYTTSGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNGLTGTGVLTPSSK RFQPFQGRDVSDFTDSDVRDPKTSEILDSPRSFGGVSVITPGTNASSEVAVLYQDVN TDVSTLHAEQLTPAWRIYSTGNNVFQTAGCLIGAHEVDTSEYCDIPIGAGICASYHTVS SLRSTSQKSIVAYTMSLGADSSIAYSNNITAIPTNFSISITTEVMVPVSMTKTSVDCNMYICG DSTECANLLLQYGSFRCQLNRALSGIAAEQDRNTREVFAQVKQMYKTPTLKDFGGFNFS

		QILPDPLKPTKRSFIEDLLFNKVTADAGFMKQYGECLGDINARDLICAQKFNGLTVPPLL TVDMAIAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVQTQNVLYENQKQIA NQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRD PPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGK GYHLSFPPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVVFVNGTSWFI TQRNFFSPQIITDNTFVSGNCDVIGIINNNTVYDPLQPELDSFKEELDKYFKNHTSPDVL GDISGINASVNIQEEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIV MVTILLCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVLHYT
20	Artificial Sarbecovirus spike consensus 3	MFIFLFFLTLVSGSDLESCITTFDDVQAPNPYQHSSRRGVYYPDEFISDITLYLTQDLFLP FDSNVTGFHTINHRFDNPVIFPKDGVYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNT NVVIRACNFELCDNPFPAVSKPTGTQHTMIFNNAFNCTFEYISDSFLDVAEKSNGFKHL REFVFNKNDGFLYVYKGYQPIDVVRDLPSGFNLIKPIFKLPLGINITNFRILATFLPAQDWTW GTSAAAAYFVGYLKPTATFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNF RVAPSKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLNNTSFSTFK CYGVSATKLNLDLCSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAWN TRNIDATQTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCTPPAFNCYWPLNDYGF YTTNGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSK RFQPFQFGGRDVSDFDTSVRDPKTSEILDISPCSFGGVSVITPGTNTSSEVAVLYQDVNC TDVPVAIHADQLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVS SLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMKTSVDCNMICYG DSTECANLLLQYGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFS QILPDPLKPTKRSFIEDLLFNKVTADAGFMKQYGECLGDINARDLICAQKFNGLTVPPLL TDDMAIAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVQTQNVLYENQKQIA NQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRD PPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGK GYHLSFPPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVVFVNGTSWFI TQRNFFSPQIITDNTFVSGNCDVIGIINNNTVYDPLQPELDSFKEELDKYFKNHTSPDVL GDISGINASVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIV MVTILLCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVLHYT
21	Artificial Sarbecovirus spike consensus 4	MFIFLFFLTLVSGSTIEKCTTFDDVQPPNYTQFLSSHRGVYYPDDIFRSDVLHLTQDHFPL FDSNVTGFITGLNFDNPIPFKDGIFYAATEKSNVIRGWVFGSTMNNKSQSVIIMNNTNV VIRACNFELCDNPFPAVSKPNNTQIPSYIFNNAFNCTFEYVSDDFNLDVGEKPGNFKHLR EFVFNKNDGFLYVYSGYQPIDVASGLPSGFNALKPIFKLPLGINITNFRILLTAFPPRPDYW GTSAAAAYFVGYLKPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFR VAPSKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLNNTSFSTFKC YGVSATKLNLDLCSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNT RNIDATSTGNYNKYRSLRHGKLRPFERDISNVFSPDGKPCTPPAFNCYWPLNDYGF YTTNGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSK RFQPFQFGGRDVSDFDTSVRDPKTSEILDISPCSFGGVSVITPGTNTSSEVAVLYQDVNCT DVPVAIHADQLTPAWRVYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVS SLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMKTSVDCNMICYG DSTECANLLLQYGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFS QILPDPLKPTKRSFIEDLLFNKVTADAGFMKQYGECLGDINARDLICAQKFNGLTVPPLL TDDMAIAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVQTQNVLYENQKQIA NQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRD PPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGK GYHLSFPPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVVFVNGTSWFI TQRNFFSPQIITDNTFVSGNCDVIGIINNNTVYDPLQPELDSFKEELDKYFKNHTSPDVL GDISGINASVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIV MVTILLCCMTSCCCLKGACSCGSCCKFDEDDSEPVLKGVLHYT
22	Artificial Sarbecovirus spike consensus 5	MFVFLFLLPLVSSQCVNLTTTRTGIPIPGYTNSSTRGVYYPDKVFRSSVLHLTQDLFLPFFSN VTWVFNAINYQGGFKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLTDLARTQSLIVNNAT NVVIVCEFCQCTDPFLGVYHNNKNTWVNEFRVYSSANNCTFEYVSQPFLLMDLEGKQ GNFKNLREFVFNKNDGFKIYKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFTQLLALH RSYLTGKLESWTTGAAAYYVGYLQPRFTLLSYNENGITDAVDCALDPLSETKCTLKS LTVEKGIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYS VLNNTSFSTFKCYGVSPTKLNLDLCTNVYADSFVVRGDEVRIAPGQTGVIADYNYKLP DDFTGCVIAWNSVKQDALTTGGNYYNYLRLFRKSKLPFERDISTEIQAGSTPCNGVVGL NCYYPLQRYGFHPTTGVGYPYRVVLSFELLNAPATVCGPKKSTNLVKNKCVNFNFNG LTGTGVLTESNKKLFPQFGGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSN QVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGNSVQTRAGCLIGAEHVNSYECDIPI GAGICASYQTQTNPRRARSVNSQSIAYTMSLGAENSVAYSNNIAIPTNFTISVTTEILP VSMTKTSVDCTMYICGDSIECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQI YKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTADAGFIKQYGDCLGDIARDLI CAQKFNGLTVPPLLTDemiaQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIG VTQNVLYENQKLIANQFNSAIGKIQDSLSTASALGKLQDVVNQNAQALNTLVKQLSSNF

		GAISSVLNDILSRDPPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSEC VLGQSKRVDFCGKGYHLSMFPQSAPHGVVFLHVTYVPAQEKNTTAPAICHEGKAHFPR EGVFSNGTHWVFTQRFYEPQIITDNTFVSGSCDVVIGVNNTVYDPLQPELDSFKEEL DKYFKNHTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYIKWP WYIWLGFIAGLIAIMVTIMLCCMTSCCCLKGCCSCGSCCKFDEDDSEPVLGKVKLHYT
23	Artificial Sarbecovirus spike consensus 6	MFVFLFLLPLVSSQCVNLTTRTGIPPGYTNSSTRGVYYPDKVFRSSVLHLTQDLFLPFFSN VTWFNAINYQGGFKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDARTQSLIVNNAT NVVIKVECFQFCTDPFLGVYHNNNKTWVNEFRVYSSANNCTFEYVSQPFLLMDLEGKQ GNFKNLREFVFKNVDGYFYKSHKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFQTLALH RSYLTGKLESWTTGAAAYVGYLQPRFTLLSYNENGITDAVDCALDPLSETKCTLKS FTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYS VLYNSASFSTFKCYGVSPKTLNDLCFTNVYADSFVIRGDEVQIAPGQTGKIADYNYKLP DDFTGCVIAWNSNNLDSKVGGNYNLYRLFRKSNLKPFERDISTEIQAGSTPCNGVEG FNCYFPLQSYGFQPTNGVGYQPYRVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFN GLTGTGVLTESNKKFLPFQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTS NQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSEYCDI PIGAGICASYQTQTNPRRARSVNSQSIIAYTMSLGAENSVAYSNNISAIPTNFTISVTTEIL PVSMKTSTVDCMTYICGDSIECSNLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQ IYKTPPIKDFGGFNFSQILPDPSPKSKRSFIEDLLFNKVTADAGFIKQYGDCLGDIARDLI CAQKFNGLTVLPPLLTDEMAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIG VTQNVLYENQKLIANQFNSAIGKIQDLSSTASALGKLQDVVNQNAQALNTLVKQLSSNF GAISSVLNDILSRDPPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSEC VLGQSKRVDFCGKGYHLSMFPQSAPHGVVFLHVTYVPAQEKNTTAPAICHEGKAHFPR EGVFSNGTHWVFTQRFYEPQIITDNTFVSGSCDVVIGVNNTVYDPLQPELDSFKEEL DKYFKNHTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYIKWP WYIWLGFIAGLIAIMVTIMLCCMTSCCCLKGCCSCGSCCKFDEDDSEPVLGKVKLHYT
24	Artificial Sarbecovirus spike consensus 7	MFVFLFLLPLVSSQCVNLTTRTGIPPGYTNSSTRGVYYPDKVFRSSVLHLTQDLFLPFFSN VTWFNTINYQGGFKFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDNTTQSLIVNNAT NVVIKVECFQFCTDPFLGVYHNNNKTWVNEFRVYSSANNCTFEYVSQPFLLMDLEGKQ GNFKNLREFVFKNVDGYFYKSHKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFQTLALH RSYLTGKLESWTTGAAAYVGYLQPRFTLLSYNENGITDAVDCALDPLSETKCTLKS LTVEKGIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATKFAVYAWNRKRISNCVADYS VLYNSTSFSTFKCYGVSPKTLNDLCFTNVYADSFVVRGDEVQIAPGQTGVIADYNYKLP DDFTGC VIAWNSVKQDAKTGGNYNLYRLFRKSKLKPFERDISTEIQAGSTPCNGVVLNLCYYP ERYGFHPTNGVGYQPYRVVLSFELLNAPATVCGPKLSTTLVKNKCVNFNFNGLTGTGV LTTSKKKFLPFQFGRDISDITDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLY QDVNCTEVPMAIHADQLTPTWRVYSTGANVFQTRAGCLIGAEHVNNSEYCDIPIGAGICA SYHTQTNRSVNSQSIIAYTMSLGAENSVAYSNNISAIPTNFTISVTTEILPVSMKTSTVDC MTYICGDSIECSNLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGG FNFSQILPDPSPKSKRSFIEDLLFNKVTADAGFIKQYGDCLGDIARDLICAQKFNGLTVL PPLLTDEMAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQK LIANQFNSAIGKIQDLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSR LDPEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCG KGYHLSMFPQSAPHGVVFLHVTYVPAQEKNTTAPAICHEGKAHFPRREGVFSNGTHW FVTQRFYEPQIITDNTFVSGSCDVVIGVNNTVYDPLQPELDSFKEELDKYFKNHTSPD VDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYIKWPWYIWLGFIAGLIA IIMVTIMLCCMTSCCCLKGCCSCGSCCKFDEDDSEPVLGKVKLHYT
25	Artificial Sarbecovirus spike consensus 8	MFIFLFFLLTVSSQCVNFDDRTPPPTQTNSSTRGVYYPDDIFRSSVLHLTQDLFLPFFSN VTWFHTINYRFDNPVPIPKDGYFAATEKSNVIRGWIFGSTMNKSQSIVVNNSTNVVIR VCNFKLCDNPFFAVYNKWTQIESRVYSNAFNCTFEYVSKSFLDLGEKGNFKHLREF VFNKDGFLKVYSGYTPIDLVRDLPSGFNALKPIFKLPLGINITNFTLLTAFRPGQSGWG TSAAAYFVGYLKPRTFMLKYDENGITDAVDCSQDPLAELKCTLKSFEVEKGIYQTSNFR VQPTKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFSTFKC YGVSPKTLNDLCFSNVYADSFVVGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAWNT RNIDATTGGNYNLYRLFRHSLKLPFERDISNVIYSPGGKPCPPGFNCYWPLNDYGFYP TNGVGYQPYRVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNFNGLTGTGVLTPSSKR FQPFQFGRDVSDFDTSVRDPKTEILDISPSCSFGGVSVITPGTNTSSEAVLYQDVNCT DVPVAIHADQLTPAWRVYSTGNNVFQTAGCLIGAEHVNNSEYCDIPIGAGICASYHTVS SLRSTSQKSIVAYTMSLGAENSIYNNISAIPTNFTISVTTEVLPVSMKTSTVDCMTYICG DSTECSNLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFSQI LPDPSKPSKRSFIEDLLFNKVTADAGFMKQYGDCLGDINARDLICAQKFNGLTVLPPLLT DEMAIYAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIAN QFNKAISIQIESLTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRDP PEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGK YHLSMFPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAHFPRREGVFSNGTHWFIT

		QRNFYSPQIITDNTFVSGSCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVL GDISGINASVNNIQEKIDRLNEVAKNLNESLIDLQELGKYEQYIKWPVYVWLGFIAGLIAIV MVTIMLCCMTSCCSCCLKGCCSCGSCCKFDEDDSEPVKGVKLHYY
26	Artificial Sarbecovirus RBD consensus 1	SNFRVVPSCDVVRFPNITNLCPFGEVFNATKFPVYAWERKRISNCVADYSVLYNSTSFS TFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVADYNYKLPDDFMGCVL AWNTRNIDATSTGNHNYKYRSLRHGKLRPFERDISNVFSPDGKPCPTPPAFNCYWPLNDY GYGYFTTSGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNGLTGTGVLTPSS KRFPQFQGRDVSDFDTSVRDPKTSEIL
27	Artificial Sarbecovirus RBD consensus 2	SNFRVAPSKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFS TFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVADYNYKLPDDFMGCVLA WNTRNIDATSTGNHNYKYRSLRHGKLRPFERDISNVFSPDGKPCPTPPAFNCYWPLNDY GYTTNGIGYQPYRVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNGLTGTGVLTPSS RFQFQFQGRDVSDFDTSVRDPKTSEIL
28	Artificial Sarbecovirus RBD consensus 3	SNFRVQPTISIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSTSFS FKCYGVSA TKLNDLCFTNVYADSFVVRGDEVQRQIAPGQTGVADYNYKLPDDFMGCVIAW NSVKQDALTTGGNYYLYRFRKSKLPFERDISTEIQAGSTPCNGVGLNCYPLQRY GFHPTTGVGYQPYRVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNGLTGTGVLTE SNKKFLPFQFQGRDIADTTDAVRDPQTLLEIL
29	Artificial Sarbecovirus RBD consensus 4	SNFRVQPTISIVRFPNITNLCPFGEVFNATKFAVYAWNRKRISNCVADYSVLYNSTSFS FKCYGVSA TKLNDLCFTNVYADSFVVRGDEVQRQIAPGQTGVADYNYKLPDDFMGCVIAW NSVKQDAKTGGNYYLYRFRKSKLPFERDISTEIQAGSTPCNGVGLNCYPLERY GFHPTNGVGYQPYRVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNGLTGTGVLTT SKKKFLPFQFQGRDISDTTDAVRDPQTLLEIL
30	Artificial Sarbecovirus RBD consensus 5	SNFRVQPTKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFS TFKCYGVSA TKLNDLCFTNVYADSFVVKGDDVRQIAPGQTGVADYNYKLPDDFMGCVLA WNTRNIDATTTGGNYYLYRFRHSLKLPFERDISNVIYSPGGKPCPTPPGFNCYWPLNDY GFYPTNGVGYQPYRVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNGLTGTGVLTP SSKRFPFQFQGRDVSDFDTSVRDPKTLEIL
31	Antibody 1 (SS6V1-B5) VH NT sequence	GAGGTGCAGCTGGTGGAGCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGA GACTCTCCTGTGCAGCCTCTGGATTCACTCAGGAACACAGATGAGTGGGT CGCCAAGCTCCAGGAAAGGCTGGAGTGGGTCTCAGTAATTGGTAATACGGGTGG CACATTCTATGCAGGCTCCGTGAAGGGCCGATTACCATCTCCAGAGAAAATGCCAA GAATCCTTGTATCTTCAAATGAATAGCCTGAGAGCCGAGGACACGGCCTGTATTA CTGTGCAAGAGTAACCTATACAGCAGCCCTCTCCATTCTGGTTCCTCGATCTCTG GGGCCGTGGCACCCTGGTCACCGTCTCTTCA
32	Antibody 1 (SS6V1-B5) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGGCAAGTCAGAGCATTGGCAACTATTAAATTGGTATCAGCAG AAATCAGGGAAAGCCCTAAGATCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGG GTCCCATCAAGGTTCAAGTGGCAGTGGATCTGGGACAGATTCTACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGAACCTACTATTGTCAACAGACGTATCGTACCCCT CCGGAGGACAGTTTGGCCAGGGGACCAAGGTGGAAATCAAA
33	Antibody 2 (SS6V2-G1) VH NT sequence	GAGGTGCAGCTGGTGGAGCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGA GACTCTCCTGTGCAGCCTCTGGATTCACTCAGTAGCAACTACATGAGCTGGGT CGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGTTATTATAGCGGTGGTA GCACATTCTACGACAGCTCCGTGAAGGGCAGATTACCATCTCCAGAGAAAATGCCAA AGAACACGCTGTATCTTCAAATGAATAGCCTGAGAGCCGAGGACACGGCTGTCTATT ACTGTGCGAGGGAGTTAAGGCACTACTTTGACTACTGGGGCCAGGGAACCCCTGGT CACCGTCTCTTCA
34	Antibody 2 (SS6V2-G1) VL NT sequence	GACATCCAGTTGACCCAGTCTCCATCCTCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGGCAAGTCAGGGCATTAGCAGTTATTAGCCTGGTATCAGCAA AAACCAGGGAAAGCCCTAAGCTCCTGATCTATGCTGCATCAACTTTGCAAAGTGGG GTCCCATCAAGGTTCAAGGCGCAGTGGATCTGGGACAGAAATCACTCTCACAATCAGC AGCCTGCAGCCTGAAGATTTTGAACCTATTACTGTCAACAGCTTAATAGTTACCCCT CGTACAGTTTGGCCAGGGGACCAAGGTGGAAATCAAA
35	Antibody 3 (SS6V3-G2) VH NT sequence	CAGGTTCACTGGTGCAGTCTGGAGCTGAGGTGAAGAGCCTGGGGCCTCAGTGAA GGTCTCCTGCAAGGCCTCTGGTTAGAGCTTTACCAACTCTGGAATCACCTGGGTGC GACAGGCCCCCTGGACAAGGGCTTGAAGTGGATGGGCGGGACCAACTTTTATAATGGT ATCACA AATTATCCACAGAACATCCAGGGCAGAGTCACCATGACTACAGACACGTCC ACGAATACAGCCTATCTGGAGCTGACGAGCCTGAGATCTGAAGACACGGCCATGTAT TACTGTGCGTTAAATCGTGTGCGGATTTTCAACGATGGTTACAACCCCTTGGGGTAC TGGGGCCAGGGAACCCCTGGTCACCGTCTCTTCA
36	Antibody 3 (SS6V3-G2) VL NT sequence	GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGC CACCATCAACTGCAAGTCCAGCCAGAGTGTTTTATACAGTTCCAACAATAAGAACTA CTTAGCTTGGTACCAGCAGAAACAGGACAGCCTCCTAAACTGCTATTACTGGGC TTCTTCCCGGAATCCGGGGTCCCGGACCGATTCACTGGCAGCGGGTCTGGGACA

		GATTTCACTCTCACCATCGACAGGCTGCAGGCTGAAGATGTGGCAATTTTACTGT CAGCAATATTTTAGTTCTCCCTTCTCTTTCGGCGGAGGGACCAAGGTGGAAATCAAA
37	Antibody 4 (SS6V4-A1) VH NT sequence	GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCCGGGAGGCTCTGA AGATCTCCTGTGAGGGTTCT GGATACACCTTTAGTATGTACTGG ATCGCCTGGGTGC GCCAGATGCCCGGAAAGGCCCTGGAGTGGATGGGAATC ATCTATCCTGATGACTCT GATAGA AGATATAGTCCGTCTTTCAAGGCCAGGTCACCATCTCAGTCGACAAGTCC ATCAGCACCGCCTACCTACAGTGGAGCAGCCTGAAGGCCTCGGACACCGCCATATA TTACTGT CGGAGACTCCAGAATGGATATAGTTATGGCCCTCTTGAAAAAT TGGGGCC AGGGAACCCTGGTCACCGTCTCCTCA
38	Antibody 4 (SS6V4-A1) VL NT sequence	GACATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGC CACCATCAACTGCAAGTCCAGCC CAGAGTACTTTATACAGGTCCAACAATAAGAATT A CTTAGCTTGGTACCAGCAGAAGCCAGGACAGCCTCCTAACTTCTCATTAACTGGGC ATCT ACCCGGGAATACGGGGTCCCTGATCGATTCACTGGCAGCGGGTCTGGGACAG ATTTCACTCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCAGTTTACTACTGT C AGCAATAATTATAGTTATCCGTGGACG TTCCGCCAAGGGACCAAGGTGGAGATCAAA
39	Antibody 5 (SS6V5-C3) VH NT sequence	GAGGTGCAGCTGGTGCAGTCTGGCGCAGAGGTGAGAAAGCCCCGGGAGTCTCTGA AGATCTCCTGTAAAGACTTCT GGATACACCTTTACCCACTATTGG ATCGGCTGGGTGC GCCAGCTGCCCGGAAAGGCCCTCGAGTGGATGGGCATC ATCTATCCTGATGACTCT GATACCA AAATACAGTCCGTCTTCCAAGGCCAAATCACCATCTCAGCCGACAAGTCC ATCAGCACCGCCTACCTGCAGTGGAACAGCCTGAAGGCCTCGGACACCGCCATGTA TTTCTGT CGGACCGGGATATTGGTGGGGTCCAACCTCTTTGACCAC TGGGGCC AGGGAACGCTGGTCACCGTCTCCTCA
40	Antibody 5 (SS6V5-C3) VL NT sequence	GACATCCAGATGACCCAGTCTCCTTCCACCTGTCTGCGTCTGTTGGAGACAGAGTC ACCATCACTTGCCGGGGCAGT CAGAGTATTAGTACCTGG TTGGCCTGGTATCAGCA GAAACCAGGGAAACCCCTAAGGTCCTGATCTAT AAGGCGTCT ATTTTAAAGAGTGG GGTCTCATCAAGATTCAGCGGCAGTGGATCTGGGACAGAATTCCTCTCACCATCAG CAGCCTGCAGCCTGATGATTTTGAACCTATTACTG CCAACACTATAATAGTTATATA AAAACATT CGGCCAAGGGACCAAGGTGGAAATCAAA
41	Antibody 6 (SS6V6-C4) VH NT sequence	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGA GACTCTCCTGTTCAAGCCTCT GGATTACCTTCAATACCTATGCT ATGCACTGGGTCC GCCAGGCTCCAGGGAAGGGACCAAGTATGTTTCAGGT ATTAGTTCTAATGGGGGT ATCAC AGACTACGAGACTCCGTGAAGGGCAGATTACCATCTCCAGAGACAATTCC AAGAACACGCTGTATCTTCAAATGAGCAGTCTGAGACCTGAGGACACGGCTGTGTAT TACTGT GTGAAAGACTCCCTGGCTACGGTGGTAACTCTCTTATCTTAC TGGGGCCA GGGAACCTGGTCACCGTCTCCTCA
42	Antibody 6 (SS6V6-C4) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGCCGGGGCAAGT CAGACCATTAGCAGCTA TTTAAATTGGTTTCAGCAG AAACCAGGTAAGGCCCTAAACTCCTGATCTAT GCTGCATCC AGTTTGCAAAGTGGG GTCCCATCAAAGTTCACTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGCCATTTACTACTGT CAACAGAGTTACAGTACCCCT GGGACG TTCCGCCAAGGGACCAAGGTGGAAATCAAA
43	Antibody 7 (SS6V7-C5) VH NT sequence	GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCCGGGAGTCTCTGA AGATCTCCTGTAAAGGTTCT GAAAAACATCTTTCCGGCTACTGG ATCGGCTGGGTGC GCCAGATGCCCGGAAAGGCCCTGGAGTGGATGGGGAT ATCTATCCTGATGACTCT GATACC AGATACAACCCGTCTTCCAAGGCCAGGTCACCATCTCAGCCGACCAATTC CATCAGCACCGCCTACCTGCAGTGGAGCAGACTGAAGGCCTCGGACACCGCCATGT ATTACTGT CGGAGACATTTAGGGGGTGGCAGCAGTTGGCCATTGACTACT TGGGGC CAGGGAACCCTGGTCACCGTCTCCTCA
44	Antibody 7 (SS6V7-C5) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCACTGTCTGCATCTGTAGGAGACAGAGTC ACCATCACTTGTCGGGGCAAT CAGGGCATTAGCAATT ATTAGCCTGGTTTCAGCAG AAACCAGGGAAGGCCCTAAGTCCCTGATCTAT GCTGCATCC AGTTTGCAAAGTGGG GTCCCATCAAAGTTCAAGCGGCAATAGATCTGGGACAGATTTCACTCTCACCATCAGC AGCCTACAGCCTGAAGATTTTGCAACTTATTACTGC CAACAGTATAGTAGTTACCCC TTCACT TTCCGGCGGAGGGACCAAGGTGGAGATCAAA
45	Antibody 8 (SS6V8-D3) VH NT sequence	GAGGTGCAGCTGGTGGAGTCTGGGGGAGACTTGGTCCAGCCTGGGGGGTCCCTGA GACTCTCCTGTTCAAGCCTCT GGATTACCTTCAGCACCTATGCT ATGCACTGGGTCC GCCAGGCTCCAGGGAAGGGACTGGATTATGTGGCATCC ATTGCTAGTGTATGGGGGT ATCAC AACTTACGCACTCCGTGAAGGGCAGATTACCATCTCCAGAGACAATTCC AAGAACGCGCTGTATCTTCAAATGAGTAGTCTGAGAGTTGAGGACACCGGCTGTGTAT TACTGT GTGAAAGATTCTTGACTTCGGTGACTACGATTTTTGACTGCT TGGGGCCAG GGAAACCCTGGTCACCGTCTCCTCA
46	Antibody 8 (SS6V8-D3) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCTGTCTGCATCTGTAGGAGACAGCGTC ACCATCACTTGCCGGGGCAAGT CAGAACATTAACAGTTAT TTACATTGGTATCAGCAG AAGCCAGGGAAAGCCCTAAGTCCCTGATCTAT ACTGCATCC AGTTTGCAAAGTGGG GTCCCATCAAAGTTCACTGCCAGTGGATCTGGGACACATTTCACTCTCACCATCAGC

		AGTCTGCAACCTGAAGATTTTGAACCTTACTACTGT CAACAGAGTTACACTGACCCC TACACTTTTGGCCAGGGGTCCAAGGTGGAAATCAAA
47	Antibody 9 (SS6V9-D11) VH NT sequence	CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGGGACCCCTGT CCCTCACCTGCGCTGTCTCT GGTGGCTCCATCAGCAGTAATATCTGGT GGAGTTGG GTCCGCCAGCCCCCGGAAAGGGGCTGGAGTGGATTGGGGAC ATCTATCACAGTG GGAGTACCA ACTACAACCCGTCCCTCGAGGGTCGAGTCACCATATCAATAGACAAGT CCAAGAACCAATTCTCCCTGAGGCTGACGTCTCTGACCGCCCGGGACACGGCCGTG TATTACTGT GCGAGAGCGATTTCGCGAGCAGTACTTTGATAGCAGTGTCTGGGGCTA CTGGGGCCAGGGAATTCTGGTCACCGTCTCCTCA
48	Antibody 9 (SS6V9-D11) VL NT sequence	GAAATAGTGATGACGCACTCTCCAGCCACCCCTGTCTGTCTCCAGGGGAAAGAGT CACCCCTCTCCTGCAGGGCCAGT CAGAGTGTGTGACCAAC TTAGCCTGGTACCAGC AGAAACCTGGCCAGGCTCCAGGCTCCTCATCTAT GGTGGCTTCC ACCAGGGCCACT GGTATCCCAGCCAGGTTCACTGGCAGTGGGTCTGGGACAGAGTTCACTCTCACCAT CAGCAGCCTGCAGTCTGAAGATTTTGAATTTATCACTGT CAGCAGTATAATAACTG GCCTGGGTACACTTTTGGCCAGGGGACCAAGTGGATATCAAA
49	Antibody 10 (SS6V10-E1) VH NT sequence	GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCCGGGGAGTCTCTGA AGATCTCCTGTGAGGGTTCT GAAGACAGCTTTACCGGCTACTGGAT CGGTTGGGTG CGCCAGCTGCCCGGAAAGGCCCTGGAGTGGATGGGGTT ATCTATCCAGATGAGC GCGATACC AGATACAGCCCGGCTTCCAAGGCCTGGTCACCTTCTCAGCCGACAAG TCCATCACCAACCGCTACCTGCACTGGAGTGAAGTTTAAAGGCCTCGACACCGCCATA TATTTCTGT GCGAGACATTTAGGGGGAGGCGAGCTGGCCCCATTGACTCC TGGG GCCAGGGAACCCAGGTCAACCTCTCCTCA
50	Antibody 10 (SS6V10-E1) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCACTGTCTGCATCTGTAGGAGACAGAGTC ACTATCACTTGTGCGGGCGAGT CAGGGCATTAGAAATTA TTAGCCTGGTTTCAGCAG AAACCAGGGAAAGCCCCCTAAGTCCCTGATCTAT GCTGCATCC AGTTTGCAAAGTGGG GTCCCATCAAAGTTACAGCGGCAGTGGATATGGGACAGACTTCACTCTCACCATCAAC AGCCTGCAGCCTGAAGATTTTGAACCTTATTACTGC CAACAGTATAATAATCACCCC TTCACTTTTGGCGGAGGGACCAAGGTGGAAATCAAA
51	Antibody 11 (SS6V11-E7) VH NT sequence	CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAGACCCCTGT CCCTCACTTGCACTGTCTCT GGTGGCTTCATCGGTCCTCACTACT GGAGCTGGGTCC GCCAGCCCCCAGGGAAGGGAGTGGAGTGGATTGGTTAT ATCTATATCAGCGGGAGC ACCAACTACAATCCCTCCCTCAAGAGTCGACTCACTATATCAGTAGACATGTCCAAGA GCCAGTTCTCCCTGACACTGAGCTCTGCGACCGCTGCGGACACGGCCGTCTATTAC TGT GCGAGAGGGGGGGGATATTTGGAACCGGCCCCTTTGAGTACT GGGGCCAGG GAACCTGGTCACCGTCTCCTCA
52	Antibody 11 (SS6V11-E7) VL NT sequence	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGC CTCCATCTCCTGCAGGTCTAGT CAGAGCCTCCTGCAAAATAATGGATACA ACTATT GGCTTGGTACCTGCAGAAGCCAGGGCAGTCTCCAACTCCTCATCT ATTGAGTTC TACTCGGGCTCCGGGGTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGATT TTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGC ATGC AATCTCTACAAATTCAGGCACCTTC Ggccaagggacacgactggagattgaa
53	Antibody 12 (SS6V12-E11) VH NT sequence	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCCTGGTCAAGCCTGGGGGGTCCCTGA GACTCTCCTGTGCAGCCTCT GGATTACCTTCAGTACCTATAAC ATGAAGTGGGTCC GCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCATCC ATTAGCAGTAGTAGAG TTTCATGT TTCTACGCAGACTCAGTGAAGGGCCGATTACCATCTCCAGAGACAACGC CAATAACTCACTGTATCTGCAAAATGAATAGCCTGAGAGCCGAGGACACGGCTGTGTA TTATTGT GCGAGAGATTACTATGATAACAGTGGTTACTACTACTACGGTATGGACGT CTGGGGCCAAAGGGACACGGTCACCGTCTCTTCA
54	Antibody 12 (SS6V12-E11) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGCGACAGAGTC ACCATCACTTGCCGGGCAAGT CAGAGCATTAGGACCTAT TTAAGTTGGTATCAGCAG AAACCAGGGAAAGCCCCCTGAGCTCCTGATCTAT GCTGCATCC AATTTGCAAAGTGGG GTCCCATCAAGGTTCACTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGAACCTTACTACTGT CTACAGACTTACAGTACCCCTC AAATCACCTTC Ggccaagggacacgactggagattgaa
55	Antibody 13 (SS6V13-F1) VH NT sequence	CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTTAAGCCTTCGGAGACCCCTGTC CCTCACCTGCTCTGTCTCT GGTGTCTCCATCCTTGGTTCTTAT TGGGGCTGGATCCG GCAGCCCCCGGGACGGGGCTGCAGTGGATTGGCTAT ATCTATTTCACTGAGAACA CCA ACTACAACCCCTCCCTCCAGAGTCGAGTCACCATGTCACCTTGACACGTCCAAGA ACCTGTTGTCCCTGAAGCTGAGCTCTGTGACCGCTGCTGACACGGCCGTCTATTACT GT GCGAGAGGGGGGGGATATTTGGAACCGGCCCTTTGACTCC TGGGGCCAGGG AACCTGGTCACCGTCTCCTCA
56	Antibody 13 (SS6V13-F1) VL NT sequence	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGC CTCCATCTCCTGCAGGTCTAGT CAGGGCCTCGTGCGAGTAATGGATACA ACTATT TGGCTTGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT TTGGGTT CTA ATCGGGCCTCCGGGGTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGAT

		TTTACACTGAAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTACTACTGC ATG CAAGGTCTACAAATCCagggcacttcggccaagggacacgactggagattaaa
57	Antibody 14 (SS6V14-F2) VH NT sequence	CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCCTCGGAGACCCTGT CCCTCACCTGCACTGTCTCT GGTGGCCCCATCAGTAGTTACTACT GGACCTGGATC CGGCAGCCCCCAGGGAAGGGGACTGGAGTGGATTGGATAT ATCTACTACAGTGGGA GCACCA ACTACAGCCCCCTCCCTCAAGAGTCGAGTCACCATGTCACTAGAAACGTCCA AGAACCAGTTCTCCCTGAAGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTAT TACTGT GCGCGAGATCCCCCTTGGCGGAGGGTGCCGCCTCGTCAGGGTTTGACAAC T GGGGCCAGGGAACCTGGTCACCGTCTCTCTCA
58	Antibody 14 (SS6V14-F2) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCCGTCGGAGACAGAGTC ACCATCACTTGCCGGGCAAGT CAGAGCATTAGCAGCTA TTTAAATTGGTATCAGCAG AAACCCGGGAAAGCCCCCTAAGCTCCTGATCTAT GCTGCATCC CGCTTTGCAAAGTGGG GTCCCATCAAGGTTCACTGGTAGTGGATCTGGGACACATTTCACTCTCACCATTAAAC GGTCTGCAACCTGAAGATTTTGAACCTACTCCTGT CAACAGAGTTACACTACCCCT CGGACTTT CGGCCCTGGGACCAAGGTGGAGATCAAA
59	Antibody 15 (SS6V15-F6) VH NT sequence	GAACTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGA GACTCTCCTGTGCAGCCTCT GGATTACCTTCAGTAGTTATGCT TATACACTGGGTCC GCCAGGCTCCAGGCAAGGCGCTGGAGTGGGTGGCACT GATATCATATGATGGACG TACAAAA TACTACGCAGACTCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTC CAAGAACACCCTGTATCTGCAAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTCTA TTACTGT GCGGAGACTTGATATTAATAATACACCACCTGCTAACGACTACT GGGGCCA GGGAACCCCTGGTCACCGTCTCTCTCA
60	Antibody 15 (SS6V15-F6) VL NT sequence	GAAATTGTGTTGACGAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGACAGAGCC ACCGTCTCCTGCAGGGCCAGT CAGATTGTTAGCAGCAATTAC TTAGCCTGGTACCA GCAGAAACCTGGCCAGGTTCCAGACTCCTCATCTAT GATGCATCC AGCAGGGCCA CTGGCATCCAGACAGGTTCACTGGCAGTGGGTCTGGGACAGACTTCACTCTCACC ATCAGCAGACTGGAGCCTGAGGATTTTGCAGTGATTAAGTGT CACCAGTATGGTGAC TCTCGCAGGACGTT CGGCCAAGGGACCAAGGTGGATATCAAA
61	Antibody 16 (L8N16-C7) VH NT sequence	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCGTGGTCAAGCCGGGGGGGTCCCTGA GACTCTCCTGTGTAGCCTCT GAATTCACCTTCAGTCGTTATACC ATGAAGTGGGTCC GCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGCGATCC ATTGGTGGTAGTACTCC TCTCTCA TTTCTACGCAGACTCATTGAGGGGCCGATTACCATCTCCAGAGACAACGC CAAGAATTCACTCTATCTGAAATGAGCAGCCTAAGAGCCGACGACACGGCTGTGTA TTACTGT GCGCGAGATTCCGATTGCTCGGGGACTACGTTGTTCCGATCTCT GGGGGCC GTGGCACCCCGTCACTGTCTCTCTCA
62	Antibody 16 (L8N16-C7) VL NT sequence	GACATCCAGATGACCCAGTCTCCAGTCTCCCTGTCTGCATCTGTGGGAGACAGAGTC ACCATCACTTGCCGGGCAAGT CAGGCCATTAGTAGCTA TTTAAATTGGTATCAGCAG AAACCCAGGAAAGCCCCCTAGGCTCCTGATCCAT GCTGCATCC AGTTACATACTGGG GTCCCATCAAGGTTCACTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGC AGTCTGCAACCTGAAGATTTTGAACCTACTATTGT CAACAGAGTTACATCACCCTC CGGAGTACAGT TTTGGCCAGGGGACCAAGCTGGAATGAAA
63	Antibody 17 (L8N17-G3) VH NT sequence	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGCGGTCCAGCCTGGGAAGTCCCTGA GACTCTCCTGTGCAGCCTCT GGCTTCACCTTCAGTTCCATGCT ATGCACTGGGTCC GCCAGGCTCCAGGCAAGGGGCTAGAGTGGGTGGCAGAT ATATCATATGATGGACG TAATAAA TACTACGCAGACTCCGTGAAGGGCCGACTCATCATCTCCAGAGACAATTC CAAGAACACGCTGTATCTGCAAAATGGACAGCCTGAGACCTGAAGACACGGCTATATA TTACTGT GCGAGAGGAGAGGGCCGAACGATGGCTACAATTTGGGTTTCGTATATG ACTACT GGGGCCAGGGATCCCTGGTCACCGTCTCC
64	Antibody 17 (L8N17-G3) VL NT sequence	GATATTGTGATGACCCAGACTCCACTCTCCTCACCTGTCAACCTTGGACAGCCGGCC TCCATCTCCTGCAGGTCTAGT CAAAGCCTCGTACACAGTGATGGAAACACCTACGT GAGTTGGCTTCAGCAGAGGCCAGGCCAGCCTCCAAGACTCCTAATTTAT AAGATTTC TAACCGGTTCTCTGGGGTCC CAGACAGATTCACTGGCAGTGGGGCAGGGACAGATT TCACACTGAAAATCAGCAGGGGTGAAAGCTGAGGATGTCGGGGTTTATTTCTGC ATGC AAGCTACACAATTTCCCCCGACGTT CGGCCAAGGGACCAAGGTGGAAATC
65	Antibody 18 (SS6V18-E3) VH NT sequence	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCGGGGGGTCCCTGA GACTCTCCTGTGCGGCCTCT GGATTACCTTCAGTTCCATGCT ATGCACTGGGTCC GCCAGGTTCCAGGGAAGGGGACTGGAATATGTTTCTTCT ATTACTAGTAATGGGGGC GGCACA TTTTATGCAGACTCTGTGAAGGGCAGATTACCATCTCCAGAGACAATTC AAGAACACAGTGTATCTGCAAAATGGGAGCCTGAGCACTGAGGACATGGCTTTATAT TACTGT GCGAGAGAAGGGATACAGGGATGGGTGACCTACTTTGACTACT GGGGGCC GGGGAATCCTGGTCACCGTCTCTCTCA
66	Antibody 18 (SS6V18-E3) VL NT sequence	GACATCCAGATGACCCAGTCTCCATCCTCCTCTCTGCATCTATAGGAGACAGAGTC ACCATCACTTGCCGGGCAAGT CAGAGCATTAGCACCAAT TTAAATTGGTATCAGCAA AAACCCAGGAAAGCCCCCAAGCTCCTGATCTAT GCTGCATCC AGTTTGCCAAAGTGG GGTCCCATCAAGGTTCACTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAG

		CAGTCTGCAACCTGAGGACTTTGCAAATTATCTCTGT CAACAGACTTACACTACGCC CCAGTACAGT TTTGGCCAGGGGACCAAGGTGGAGATCAAA
67	Antibody 19 (SS6V19-F4) VH NT sequence	GAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCAGTGAA GGTTTCCTGCAAGGTTTCT GGATACACCTTCACTGACTATAAT ATGAATTGGGTGCG ACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGATGG ATCAACACCAACACTGGG ATCCCA ACTTATGCCCAAGGGCTTACAGGACGGTTTGTCTTCTCCTTGGACACCTCT GTCAGCACGGCATATCTGCAGATCAGCAGCCTAAAGGCTGAGGACACTGCCATTTAT TACTGT GCGAGAGATGGGGGGTGGCAGTTACCTTACTGGTACTTCGATCTC TGGGG CCGTGGCACCCTGGTCACCGTCTCTTCA
68	Antibody 19 (SS6V19-F4) VL NT sequence	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTCTCCAGGGGAAAGAGT CACCTCTCCTGCAGGGCCAGT TACAGTTTTAGCAGCAGCT TAGCCTGGTACCAGC AGAAACCTGGCCAGGCTCCAGGCTCCTCATCTAC GGTACATCC ACCAGGGCCACT GGTGTCCCACTCAGGTTCACTGGCAGTGGGTCTGGGACAGAGTTCACTCTCACCAT CAGCAGCCTCCAGTCTGAAGATTAGCAGTTTATTACTGT CAACAGTATTATAGTTGG CCCCTGACGT TCGGCCAAAGGACCAAAAGTGGATATCAAA
69	Antibody 20 (SS6V20-F5) VH NT sequence	CAGGTGCAGCTGCAAGAGTCGGGCCCGGGACTGGTGAAGCCTTCGGAGACCCTGT CCCTCACCTGCACTGTCTCT GGTGGCTCCATCATTGGTTACTACT TGGAGCTGGATCC GGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTAT ATCTATTTACGCGCGAACC ACCA ACTACAACCCCTCCCTGAAGAGTCGAGTCACCATGTCACTAGACATGTCCAAG AAACAGTTCTCCCTGAAATTGAGGTCTGTGACCGCTGCGGACACGGCCGTTTATTAC TGT GCGAGAGGGGGGGATATTGGAAACCGGCCCCCTCGACTTC TGGGGCCAGG GAATCCTGGTCACCGTCTCTCTCA
70	Antibody 20 (SS6V20-F5) VL NT sequence	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCTGGAGAGCCGGC CTCCATCTCCTGCAGGTCTAGT CAGAGCCTCATGCAGCTTAATGGATACA ACTATTT GGCCTGGTACCTGCAGAGGCCAGGGCAGTCTCACAGCTCCTGATTTAT TTGGGT CT ACTCGGGCTCCGGGGTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGAT TTTACACTGAAATCACCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTATTGC ATG CAAGGTCTACAAATTCAGGCACCT TCGGCCAAGGACACGACTGGAGATTAA
71	Antibody 1 (SS6V1-B5) VH aa sequence	EVQLVESGGGLVQPGGSLRLSCAAS GFILRNY EMQWVRQAPGKGLEWVSV IGNTG TF YAGSVKGRFTISRENAKNSLYLQMNSLRADETALYYC ARVTYTSSPLPFWFLDL WGRGT LVTVSS
72	Antibody 1 (SS6V1-B5) VL aa sequence	DIQMTQSPSSLSASVGDRVITCRAS QSIGNYL NWYQQKSGKAPKILY AAS SLQSGVPS RFGSGSGTDFTLTISLQPEDFATYYC QQTYRTPPEDS FGQGTKVEIK
73	Antibody 2 (SS6V2-G1) VH aa sequence	EVQLVESGGGLVQPGGSLRLSCAAS GFTVSSNY MSWVRQAPGKLEWVSV YSGGS TF YADSVKGRFTISRDNKNTLYLQMNSLRADETAVYYC ARELRHYFDY WGQGLTVTVSS
74	Antibody 2 (SS6V2-G1) VL aa sequence	DIQLTQSPSFLSASVGDRVITCRAS QGISSYL AWYQQKPGKAPKLLIY AAS TLQSGVPS RFGSGSGTEFTLTISLQPEDFATYYC QQLNSYPYPS FGQGTKVEIK
75	Antibody 3 (SS6V3-G2) VH aa sequence	QVQLVQSGAEVKRPGASVKVSKCAS GYSFTNSG ITWVRQAPGQGLEWMGG TNIFYNGI INYPQNIQGRVTMT TDSTNTAYLELTLRSEDAMYYC ALNRVAIFNDGYNPLGY WGQ GTLTVTVSS
76	Antibody 3 (SS6V3-G2) VL aa sequence	DIVMTQSPDSLAVSLGERATINCKSS QSVLYSSNNKNY LAWYQQKPGQPPLIY WASS RESGVPDRFSGSGSGTDFTLTIDRLQAEDVAIYYC QQYFSSPFS FGQGTKVEIK
77	Antibody 4 (SS6V4-A1) VH aa sequence	EVQLVQSGAEVKRPGKGLKISCKGS GYTFSMY WIAWVRQMPGKLEWVG IYPDDSDR RYSFSGGQVTISVDKSISTAYLQWSSLKASDTAIYYC ARLQNGYSYGLEN WGQGLTV TVSS
78	Antibody 4 (SS6V4-A1) VL aa sequence	DIVMTQSPDSLTVSLGERATINCKSS QSTLYRSNNKNY LAWYQQKPGQPPLIN WAST REYGVPRDFSGSGSGTDFTLTISLQAEDVAIYYC QQYYSYPWF FGQGTKVEIK
79	Antibody 5 (SS6V5-C3) VH aa sequence	EVQLVQSGAEVRKPGESLKISCKTS GYTFTHY WIGWVRQLPGKLEWVG IYPDDSDTK YSPFSGGQITISADKSISTAYLQWNSLKASDTAMFYC ATADIVVGSNFFDH WGQGLTVTV SS
80	Antibody 5 (SS6V5-C3) VL aa sequence	DIQMTQSPSTLSASVGDRVITCRAS QSISTWL AWYQQKPGKPPKVLIIY KAS ILESGVSS RFGSGSGTEFTLTISLQPDDEFATYYC QHYNYSYIKT FGQGTKVEIK
81	Antibody 6 (SS6V6-C4) VH aa sequence	EVQLVESGGGLVQPGGSLRLSCSAS GFTFNTY AMHWRQAPGKPEYVSG ISSNGGIT DYADSVKGRFTISRDNKNTLYLQMSSLRPEDTAVYYC VKDSLATVVTLLSY WGQGLTV TVSS
82	Antibody 6 (SS6V6-C4) VL aa sequence	DIQMTQSPSSLSASVGDRVITCRAS QTISSYL NWFQQKPGKAPKLLIY AAS SLQSGVPS RFGSGSGTDFTLTISLQPEDFAIYYC QQSYSTPGTF FGQGTKVEIK

83	Antibody 7 (SS6V7-C5) VH aa sequence	EVQLVQSGAEVKKPGESLKISCKGSENI FGSYWIGWVRQMPGKGLEWMGIIYPDDSDTR YNPSFQGGQVTISADQSISTAYLQWSRLKASDTAMYYC ARHLGGGSSWPIDY WGQGTLLV TVSS
84	Antibody 7 (SS6V7-C5) VL aa sequence	DIQMTQSPSSLSASVGDRVITITCRAN QGISNYLAWFQQKPGKAPKSLIY AAS SLQSGVPS KFSGNRSRGTDFTLTISLQPEDFATYYC QQYSSYPFT FGGGTKVEIK
85	Antibody 8 (SS6V8-D3) VH aa sequence	EVQLVESGGDLVQPGGSLRLSCSAS GFTFSTYAMHWRQAPGKGLDYVASIASDGGIT TYADSVKGRFTISRDN SKNALYLQMSSLRVEDTAVYYC VKDSLTSVTITFDC WGQGTLLV VSS
86	Antibody 8 (SS6V8-D3) VL aa sequence	DIQMTQSPSSLSASVGDSVTITCRAS QINISYLHWYQQKPGKAPKLLIY TAS SLQSGVPS RFSASGSGTHFTLTISLQPEDFATYYC QQSYTDPYT FGGGSKVEIK
87	Antibody 9 (SS6V9-D11) VH aa sequence	QVQLQESGPGLVKPSGTLSTCAVS GGSSISNIWWSWVRQPPGKGLEWIGDIYHSGST NYPNPLEGRVTISIDSKNQFSLRLTSLTAADTAVYYC ARAISSQQYFDS SLGLYWGQGIL VTSS
88	Antibody 9 (SS6V9-D11) VL aa sequence	EIVMTQSPATLSVSPGERVTLSRCSAS QSVVTNLAWYQQKPGQAPRLLIY GASTRATGIPA RFSGSGSGTEFTLTISLQSEDFAIYHC QQYNNWPGYT FGGGTKVDIK
89	Antibody 10 (SS6V10-E1) VH aa sequence	EVQLVQSGAEVKKPGESLKISCKGSE EDSFTGYWIGWVRQLPGKGLEWMGFYIPDDGDT RYSPAFQGLVTFSDAKSITTAYLQWSSLKASDTAIYFC ARHLGGGSSWPIDS WGQGTQV TVSS
90	Antibody 10 (SS6V10-E1) VL aa sequence	DIQMTQSPSSLSASVGDRVITITCRAS QGIRNYLAWFQQKPGKAPKSLIY AAS SLQSGVPS KFSGSGYGTDFLTINSLQPEDFATYYC QQYNNHPFT FGGGTKVEIK
91	Antibody 11 (SS6V11-E7) VH aa sequence	QVQLQESGPGLVKPSSETLSLTCTVS GGFIGPHYWSWVRQPPGKGLEWIGYIYISGSTNY NPSLKSRLTISVDMSKQFSLTLSSATAADTAVYYC ARGGGYLETGPF EYWGQGTLLVTV SS
92	Antibody 11 (SS6V11-E7) VL aa sequence	DIVMTQSPLSLPVTGPGEPAISCRSS QSLQNNGYNYLAWYLQKPGQSPQLLIY LS STRA SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC MQSLQIPGT FGGGTRLEIK
93	Antibody 12 (SS6V12-E11) VH aa sequence	EVQLVESGGGLVKPGGSLRLSCAAS GFTFSTYMNWVRQAPGKLEWVSSISSSSSFM FYADSVKGRFTISRDNANNSLYLQMNSLRAEDTAVYYC ARDYYDNSGYYYGM DVWG QGTTVTSS
94	Antibody 12 (SS6V12-E11) VL aa sequence	DIQMTQSPSSLSASVGDRVITITCRAS QSIRTYLSWYQQKPGKAPPELLIY AAS NLQSGVPS RFSGSGSGTDFTLTISLQPEDFATYYC CLQTYSTPQIT FGGGTRLEIE
95	Antibody 13 (SS6V13-F1) VH aa sequence	QVQLQESGPGLVKPSSETLSLTCSVS GVSILGSYWGWRQPPGTGLQWIGYIYFSENTNY NPSLQSRVTMSLDTSKNLLSLKSSVTAADTAVYYC ARGGGYLETGPF DSWGQGTLLVTV SS
96	Antibody 13 (SS6V13-F1) VL aa sequence	DIVMTQSPLSLPVTGPGEPAISCRSS QGLVQSNGYNYLAWYLQKPGQSPQLLIY LGS NR ASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC MQGLQTPGT FGGGTRLEIK
97	Antibody 14 (SS6V14-F2) VH aa sequence	QVQLQESGPGLVKPSSETLSLTCTVS GGPISSYYWTWIRQPPGKGLEWIGYIYSGSTNY SPSLKSRVTMSLET SKNQFSLKLTSTVTAADTAVYYC ARDPLAEGAASSG FDNWGQGTLL VTSS
98	Antibody 14 (SS6V14-F2) VL aa sequence	DIQMTQSPSSLSASVGDRVITITCRAS QSISSYLNWYQQKPGKAPKLLIY AAS ALQSGVPS RFSGSGSGTHFSLTINGLQPEDFATYSC QQSYTTPRT FGPGTKVEIK
99	Antibody 15 (SS6V15-F6) VH aa sequence	EVQLVESGGGVVQPGSLRLSCAAS GFTFSSYAIHWRQAPGKALEWVALISYDGRTK YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC ARLDIIITPPANDY WGQGTLLV VSS
100	Antibody 15 (SS6V15-F6) VL aa sequence	EIVLTQSPGTLSTLSPGDRATVSCRAS QIVSSNYLAWYQQKPGQVPRLLIY DAS SRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYC HQYGD SRRTFGGGTKVDIK
101	Antibody 16 (L8N16-C7) VH aa sequence	EVQLLESGGGLVKPGGSLRLSCVASE EFTFSRYTMNWVRQAPGKLEWVASIGGSTPLS FYADSLRGRFTISRDN AKNSLYLEMSSLRADDTAVYYC ARDSIASATTL FDLWGRGTPV TVSS
102	Antibody 16 (L8N16-C7) VL aa sequence	DIQMTQSPVLSASVGDRVITITCRAS QAISSYLNWYQHKPGKAPRLLIH AAS SLHTGVPS RFSGSGSGTDFTLTISLQPEDFATYYC QQSYITPPEYS FGGGTKLEMK
103	Antibody 17 (L8N17-G3) VH aa sequence	QVQLVESGGGAVQPGKSLRLSCAAS GFTFSSYAMHWRQAPGKLEWVADISYDGRN K YYADSVKGRLLISRDN SKNTLYLQMDSLRPEDTAIYYC ARGEAGTMAI WVSSYDYG QGSLVTVS

104	Antibody 17 (L8N17-G3) VL aa sequence	DIVMTQTPLSSPVTLGQPASISCRSS <u>QSLVHSDGNTY</u> VS W LQQRPGQPPRLLIY <u>KIS</u> NRF SGVPDRFSGSGAGTDFTLKISRVAEDVG V YFC <u>MQATQFPPT</u> FGGQTKVEI
105	Antibody 18 (SS6V18-E3) VH aa sequence	EVQLVESGGGLVQPGGSLRLSCAAS <u>GFTFSSY</u> AMHWRQVPGKLEYVSS <u>ITSN</u> GGGT FYADSVKGRFTISRDNKNTVYLQMGSLSTEDMALYYC <u>AREGIQGWVTFDY</u> WGRGILV TVSS
106	Antibody 18 (SS6V18-E3) VL aa sequence	DIQMTQSPSSLSASIGDRVTITCRAS <u>QSISTNL</u> NWYQQKPGKAPKLLIY <u>AAS</u> SLPSGVPSR FSGSGSGTDFLTITSSLPEDFANYLC <u>QQTYTTPQYS</u> FGGQTKVEIK
107	Antibody 19 (SS6V19-F4) VH aa sequence	EVQLVQSGSELKPKGASVKVSCKVS <u>GYTFDYN</u> MNWRQAPGQGLEWMGW <u>INTNTGI</u> <u>P</u> TYAQGFTGRFVSLDTSVSTAYLQISSLKAE T AIYYC <u>ARDGGWQLPYWYFDL</u> WGRGT LVTSS
108	Antibody 19 (SS6V19-F4) VL aa sequence	EIVMTQSPATLSVSPGERVTLSCRAS <u>YFSSS</u> LAWYQQKPGQAPRLLIY <u>GTS</u> STRATGVPV RFSGSGSGTEFTLTITSSLQSEDLAVYYC <u>QQYYSWPLT</u> FGGQTKVDIK
109	Antibody 20 (SS6V20-F5) VH aa sequence	QVQLQESGPGLVKPSSETLSLTCTVS <u>GGSII</u> GYWSWIRQPPGKLEWIGY <u>IYFSANT</u> NYN PSLKSRTMSVDMSKKQFSLKLRVTAADTA V YYC <u>ARGGGYLETGPLDF</u> WGGQILVT SS
110	Antibody 20 (SS6V20-F5) VL aa sequence	DIVMTQSPLSLPVTGEPASISCRSS <u>QSLMQLNGYNY</u> LAWYLQRPQGPQQLLIY <u>LGS</u> TR ASGVDRFSGSGSGTDFTLKITRVEAEDVG V YYC <u>MQGLQIPGT</u> FGGQTRLEIK
111	Heavy chain variable region HC-CDR1	ESTPXTXG
112	Heavy chain variable region HC-CDR2	IVXSVAN
113	Heavy chain variable region HC-CDR3	DXDTXTTXXHSXSPVP
114	light chain variable region LC-CDR1	RTIATX
115	light chain variable region LC-CDR2	ADS
116	light chain variable region LC-CDR3	QRSXXTXRGAX

[00191] In sequence ID Nos. 31-70 listed above the nucleic acids encoding the CDR regions are bold and underlined. In sequence ID Nos. 71-110 listed above the amino acids of the CDR regions are bold and underlined.

[00192] Examples

- 5 **[00193]** In the following, the inventors present by way of example only, antigen-binding molecule which binds to a wide range of sarbecovirus spike protein.

[00194] Example 1 human serum panels

- 10 **[00195]** The four serum panels included in this study were described as below. (1) SARS patient (n = 11): these were sera collected from SARS survivors in Singapore at different time points (2003, 2012 and 2020) before the vaccination program started in February 2021; (2) COVID-19 patient (n = 40): this group of sera was collected during 2020 as part of a

national longitudinal study (Chia et al.: Lancet Microbe 2021). (3) Healthy individuals-vaccinated with COVID-19 vaccine (in this case the Pfizer mRNA vaccine) (n = 20): these were sera collected at day 14 after second dose (or 35 days after the first dose) of the Pfizer-BioNTech BNT162b2 mRNA vaccine. (4) SARS survivors-vaccinated with COVID-19 vaccine (in this case the Pfizer mRNA vaccine) (n=9): sera taken from SARS survivors 21-62 days post first vaccination of the Pfizer-BioNTech BNT162b2 mRNA vaccine.

[00196] To our surprise, when SARS survivors were immunized with COVID-19 vaccine (in this case the Pfizer mRNA vaccine), we found an unexpected high-level boost of anti-SARS-CoV NABs (See **[Table 1]**).

[Table 1]. Boost of SARS-CoV NAB after immunization with COVID-19 vaccine (NT50%).

SARS Survivors		Patient #1	Patient #2
SARS NABs	Pre-vaccine	170	266
	Post-vaccine	1,077	1,266
	Fold of change	6.34	4.76
COVID NABs	Post-vaccine	719	1,115

[00197] Although some level of boosting was deemed possible considering that the SARS-CoV and SARS-CoV-2 share genome identity at approximately 80% (Zhou et al.: Nature 2020, 579:270-273.), the fold of increase (5-6 fold) SARS-CoV specific NABs was not expected. Importantly, this observation was not limited to the first two SARS survivors tested, the trend maintained (see below) when more individuals (N=9) were tested.

[00198] Multiplex surrogate Virus Neutralizing Test (sVNT) based on RBD from six different sarbecoviruses

[00199] The viral RBD were immobilized on a solid phase (a magnetic bead) and used with a fluorescent dye, in this case phycoerythrin (PE), conjugated to ACE2 to measure the virus-receptor binding ([Fig. 2]) which allowed multiplex detection of NABs against different sarbecoviruses. Altogether six RBD proteins from six different sarbecoviruses were used SARS-CoV; SARS-CoV-2; SARS-CoV-2 B.1.1.7; SARS-CoV-2 B.1.351; SC2r-CoV GX-P5L and SC2r-CoV RaTG13.

[00200] Six AviTag-biotinylated RBDs from different sarbecoviruses were coated on the MagPlex Avidin microsphere (Luminex) at 5 µg/1 million beads. In multiplex sVNT, RBD-coated microspheres (600 beads/antigen) were pre-incubated with serum at a final concentration of 1:20 or greater for 1h at 37°C with 800 rpm agitation. After 1h incubation,
 5 **50 µl of PE-conjugated hACE2** (GenScript, 1000 ng/ml) were added to the well and incubated for 30 min at 37°C with agitation, followed by two PBS-1% BSA washes. The data were acquired using MAGPIX system.

[00201] The cross-NAb data demonstrated two highly important features: 1) vaccination of SARS survivors produced very high NABs against all viruses studied ([Fig. 3D]), even
 10 against the bat and pangolin viruses; 2) they neutralized the SARS-CoV-2 variants better than the naïve individuals who received the normal two doses ([Fig. 3C]); 3) SARS patients had minimal cross- NABs to any of the other five viruses before vaccination ([Fig. 3A]) whereas the COVID-19 patients had cross-NABs against other viruses (all of them are SARS-CoV-2 related), they did not have much against the SARS-CoV ([Fig. 3B]).

15 **[00202]** The mRNA vaccine has been demonstrated to have an exceptional capability of inducing very high level of neutralizing antibodies (Nabs) against SARS-CoV-2. But from the breakthrough infections reported (Hacisuleyman et al.: N Engl J Med 2021) and the data in [Fig. 3C], it is clear that the NABs have a relatively narrow spectrum as some individuals had lower NABs against the Alpha COVID-19 variant SARS-CoV-2 B.1.1.7; and/or the Beta
 20 COVID-19 variant SARS-CoV-2 B.1.351 also known as 20H/501Y.V2, or 501Y.V2 variant; , i.e., the NABs are highly specific to the virus sequence used in the mRNA vaccine. The same was observed with the COVID-19 patient sera ([Fig. 3B]).

[00203] Although SARS-CoV and SARS-CoV-2 share 80% genome identify and cross-NABs have been discovered in the past (both in human and animals), majority of the key
 25 immune dominant neutralizing epitopes in the RBD region of their spike protein (S) are highly virus- or variant-specific. However unexpectedly, when cross immunization is conducted (either through infection or vaccination), it is possible to make the cross-NAb epitope(s) more immune dominant.

[00204] Pan-sarbecovirus mAb inhibition assay

30 **[00205]** Using the multiplex sVNT developed above, the study was extended to examine cross-NABs to the SARS-CoV-2 variants and, more importantly, to other sarbecoviruses that are detected in bats and pangolins which are deemed to be potentially at risk for human infection (Lam et al.: Nature 2020, 583:282-285.).

[00206] RBD-coated microspheres (600 beads/antigen) were pre-incubated with 1:100 diluted serum for 1h at 37°C with agitation. Unbound antibodies were removed by two PBS-1% BSA washes. Pan-sarbecovirus mAbs (1000 ng/ml) were then added, followed by 1h incubation at 37°C with agitation followed by washing. The binding of the pan-sarbecovirus mAb on RBD was detected by PE-conjugated anti-mouse IgG antibodies. The data were acquired using MAGPIX system.

[00207] Using serial dilutions, we have further illustrated the best performance of pan-sarbecovirus cross-neutralization by the SARS-vaccinated group ([Fig. 4]). This is the first real life human study/data demonstrating the feasibility of a pan-sarbecovirus antigen-binding molecule.

[00208] While previous studies, had shown there is limited cross neutralization between SARS-CoV and SARS-CoV-2 (Yang R, et al. EBioMedicine 2020, 58:102890), when SARS survivors were immunized with COVID-19 vaccine (in this case the Pfizer mRNA vaccine), we found that a high level of cross-NAbs were produced which can neutralize six different sarbecoviruses used in the current study ([Fig. 4]). This is the first-in-human study/data demonstrating the feasibility of producing pan-sarbecovirus NAbs with high potency and broad spectrum.

[00209] The mRNA vaccine has been demonstrated to have an exceptional capability of inducing very high level of NAbs against SARS-CoV-2. But from the breakthrough infections reported (Hacisuleyman, et al. N Engl J Med 2021.) and the data in [Fig. 4], it is clear that the NAbs have a relatively narrow spectrum as some individuals had lower NAbs against the Alpha COVID-19 variant SARS-CoV-2 B.1.1.7; and/or the Beta COVID-19 variant SARS-CoV-2 B.1.351 also known as 20H/501Y.V2, or 501Y.V2 variant; and even lower NAbs against the pre-emergent bat and pangolin viruses, with the NAs against SARS-CoV-1 at the lowest.

[00210] As depicted in [Fig. 5] it is postulated that the most likely mechanism of this cross-neutralization boosting is via exposure to two separate epitopes from two different sarbecoviruses: although SARS-CoV-1 and SARS-CoV-2 share 80% genome identity and cross-NAbs have been discovered in the past (both in human and animals), majority of the key immune dominant neutralizing epitopes in the RBD region of their spike protein (S) are highly virus- or variant-specific. However, when cross immunization is conducted (either through infection or vaccination), it is possible to make the cross-NAb epitope(s) more immune dominant.

[00211] SARS-CoV-1 survivors who received the BNT162b2 mRNA vaccine generated broad neutralizing antibodies against ten sarbecoviruses in clades 1a and 1b, including multiple VOCs of SARS-CoV-2 and zoonotic sarbecoviruses.

[00212] Example 2. Mouse studies

5 **[00213]** In this study, the mouse mAb 5B7D7 (Genscript) was used. As shown in [Fig. 6A], the mAb is able to neutralize all six viruses, albeit with slightly lower efficacy against GX-P5L. Using a blocking assay, same principle as the sVNT by replacing the PE-hACE2 with the mAb, we have determined the ability of the four different serum panels to block the mAb's ability in neutralization ([Fig. 6B]). Several important findings were made from this
10 analysis. First, it is clear that the cross-neutralizing ability of the SARS-Vaccinated group is the best among the four groups. Second, during natural infection (for either SARS and COVID-19), there is minimal activation of cross-neutralizing antibodies across the two lineages between SARS-CoV-2 (and related viruses) and SARS-CoV-1. Third, although the mRNA vaccination boosted overall neutralizing ability against SARS-CoV-2 related viruses,
15 it had minimal impact on cross-neutralization against SARS-CoV-1.

[00214] Although cross neutralization between SARS-CoV-1 and SARS-CoV-2 is not common, this monoclonal antibody binds to RBD and cross-neutralize both SARS-CoV-1 and SARS-CoV-2 as well as other sarbecoviruses.

[00215] B-cell profiling by staining with RBD from SARS-CoV-1 and SARS-CoV-2

20 **[00216]** For flow cytometry analysis, cryopreserved PBMCs were thawed and surface stained for SARS-CoV-1 and SARS-CoV-2 specific B cells using bait tetramers prepared with biotinylated SARS-CoV-1 RBD or SARS-CoV-2 RBD (custom-made by GenScript) tetramerised with Streptavidin-conjugated with BV421 (Biolegend, Cat#405225) or Streptavidin-conjugated with PE (BD Pharmingen, Cat#554061). Briefly, thawed PBMCs were
25 incubated for 40 min at room temperature with SARS-CoV-1-RBD tetramers and SARS-CoV-2-RBD tetramers with 10% FBS in FACS staining buffer (PBS supplemented with 2mM EDTA and 2% FBS) before proceeding to staining with surface panel fluorochrome-conjugated antibodies. Surface staining was performed with viability dye (Invitrogen, LIVE/DEAD® Fixable AQUA Dead Cell Stain), anti-human CD3 antibody conjugated with
30 FITC, anti-human CD14 antibody conjugated with FITC, anti-human CD56 antibody conjugated with FITC, anti-human CD19 antibody conjugated with PE-Cyanine5, anti-human CD27 antibody conjugated with APC-H7 and anti-human CD38 antibody conjugated with BV786, for 30 min in FACS staining buffer at 4 °C. Stained cells were washed twice with

FACS staining buffer and acquired on the same day. Samples were acquired on BD LSR Fortessa™ analyser or BD FACS Aria III equipped with 355, 405, 488, 561, and 640 nm lasers. SARS-CoV-1 and SARS-CoV-2 specific B cells were quantified by gating on CD19+ B cells after excluding AQUA-positive dead cells and CD3+, CD14+, CD56+ cells. The boosting of cross-NAbs in the SARS-Vaccinated group was further confirmed by direct staining of B-cells using virus-specific RBD proteins. As shown in [Fig. 7], the double stained B-cells, i.e., B-cells which bind RBDs from both SARS-CoV-1 and SARS-CoV-2, were significantly enriched, by more than 10-fold, in the SARS-Vaccinated group in comparison to the Healthy-Vaccinated group.

10 **[00217]** Example 3 Rabbit studies

[00218] The virus/strain-specific immunodominant antibody responses were further confirmed using rabbit hyper immune serum targeting specific virus/strain. In addition to the four key viruses used in this study (i.e., SARS-CoV, RaTG13, GX-P5L and SARS-CoV-2), we have also included RmYN02 and HKU1. RmYN02 is a bat sarbecovirus which has a very close genetic relationship with SARS-CoV-2, but its RBD failed to bind hACE2 (Wacharapluesadee et al.: Nat Commun 2021, 12:972). RmYN02 is also very closely related to another bat sarbecovirus, RacCS203, discovered in bats in Thailand (Wacharapluesadee et al.: Nat Commun 2021, 12:972). HKU1 is a human beta coronavirus, but not a sarbecovirus, and is included here as a negative control.

20 **[00219]** Multiplex sVNT analysis using rabbit hyper immune sera targeting RBD of six different beta coronaviruses.

[00220] The rabbit anti-RBD sera were produced by commercial contract with GenScript Biotech using the RBD of each virus as the antigen. The testing was conducted essentially the same as those described above. Rabbit sera were used by a 4-fold serial dilution starting at 1:20.

[00221] The data presented in [Fig. 8] demonstrates that cross-neutralization is limited only to the strain/lineage level among the five Sarbecoviruses SC2r-CoVs. There is no cross-neutralization between SC2r-CoV and SARS-CoV and the negative control HKU1 did not neutralize any virus/strain as shown. It is worth noting that the RmYN02, although shown to be non-hACE2 binding (Wacharapluesadee et al.: Nat Commun 2021, 12:972), is still able to produce neutralizing antibodies to the bat sarbecovirus RaTG13.

[00222] Based on various embodiments described above from the SARS-Vaccinated donors, human pan-sarbecovirus NABs are formed as follows:

[00223] Sorting out SARS1-SARS2 double positive B-cells: as shown in [Fig. 9], using RBDs from SRARS-CoV-1 and SARS-CoV-2, B-cells which produce antibodies that can recognize both RBDs (type C in the figure) are selected and tested for neutralization across different sarbecoviruses.

[00224] Cloning and culture B-cells for production of small scale monoclonal antibodies: two methods are used for detecting the B-cell receptors. First, the single B cells are grown on 3T3 feeder system which will allow continual secretion of mAbs into the supernatant for initial screening, followed by B cell receptor cloning of the best clones. Second, the sorted B are lysed directly to cells and B cell receptors sequences are detected from the RNA followed by subcloning the sequences into an mAb expression plasmid.

[00225] Testing for pan-sarbecovirus neutralization activity: supernatant containing individual mAb are used to test for cross-NAB activity using the multiplex sVNT platform described herein above.

[00226] Large scale production and further characterization: top candidates are taken for further characterization such as structural analysis for epitope mapping, determination of neutralization activity against live virus and checking in-vivo protection in animal challenge models.

[00227] Example 4. Isolation of broadly sarbecovirus-neutralizing mAbs from a BNT162b2-vaccinated SARS1 survivor donor.

[00228] Blood was obtained from a SARS-CoV-1 survivor, SS6V, and the neutralization capacity of the donor's sera to SARS-CoV-1 and SARS-CoV-2 was confirmed pre- and post-BNT162b2 vaccination using a surrogate virus neutralization test. PBMCs and plasma from day 23 post first vaccination dose were separated from EDTA whole blood and cryopreserved for long term storage. PBMCs were thawed, first stained for SARS-CoV-1 RBD and SARS-CoV-2 RBD tetramers, then surface stained with LIVE/DEAD Fixable aqua dead cell stain (Invitrogen), anti-human CD3-FITC, anti-human CD14-FITC, anti-human CD56-FITC, anti-human CD19-PE-Cy5, anti-human CD27-APC-H7, anti-human CD38-BV786 were single cell sorted into 96-well PCR plates (Axygen) pre-filled with 10 μ l/well of RT-PCR catch buffer containing 10 mM TRIS pH 8.0 and 10 U of RNasin Ribonuclease Inhibitor (Promega) using BD FACSAria III (BD Biosciences) equipped with 355-nm, 405-

nm, 488-nm, 561-nm and 640-nm lasers. The plates were then flash frozen on dry ice and kept at -80 °C until use.

[00229] Reverse transcription was next performed using Qiagen OneStep RT-PCR kit on each plate of sorted B cells. Nested PCR was done using Q5 polymerase (NEB) and the wells containing corresponding heavy and light chains were purified for sequencing. After analyzing the sequences, specific primers were then used to amplify for individual gene families and the PCR products were cloned into pTRIOZ expression vector (Invivogen).

[00230] pTRIOZ constructs were transfection into HEK293 cells using Eugene6 (Promega) and the supernatant was harvested to check for small scale efficacy screening using SARS-CoV-1 and SARS-CoV-2 RBD binding ELISA and surrogate virus neutralization tests (sVNT). For the binding ELISA assay, 100 ng of protein was coated onto Maxisorp plates (Nunc) overnight at 4 °C. After blocking with OptEIA blocking buffer (BD), 50 µl of each supernatant were added neat per well and incubated at 37 °C for 1 h. 1:5000 of Goat anti-human IgG-HRP (Bethyl) diluted in OptEIA was then added which will convert TMB substrate into a colorimetric readout for quantification using Cytation 5 reader (BioTek). For sVNT, a commercially available kit for SARS-CoV-2 (cPass; Genscript) was used and the manufacturer's protocol was followed. The same kit was used to measure the amount of neutralizing antibodies against SARS-CoV-1 by substituting the SARS-CoV-2 RBD-HRP reagent with 6ng/well of SARS-CoV-1 RBD-HRP (Genscript). The best mAbs (SS6V1-B5, SS6V11-E7, SS6V12-E11, SS6V13-F1, SS6V19-F4 and SS6V20-F5) and control mAbs (S309, CR3022, S2X259 and LyCoV-1404) from the initial binding and neutralization screening were then batch produced by transfection into EXPI293 cells for large-scale expression and purified using Protein G agarose beads (Millipore) for downstream characterizations.

[00231] The results are summarized in [Table 2]

[Table 2]: Pre- and post-vaccination neutralizing antibody levels of the donor recruited in this study measured by sVNT

Pre-vaccination	Post dose 1	Post dose 2
SARS-CoV-1 sVNT (% inhibition)		
73.05	98.12	97.74
SARS-CoV-2 sVNT (% inhibition)		
37.31	97.72	97.06

[00232] The peripheral blood mononuclear (PBMCs) at day 23 after the first dose of BNT162b2 vaccine were taken for B cell enrichment and isolation. CD19+ B cells that were positive for binding to SARS-CoV-1 (SC1+) and SARS-CoV-2 (SC2+) RBD tetramers [Fig. 11] were sorted and their antibody genes amplified and cloned. In total, 19 paired heavy and light kappa fragments were recovered from single B cells, reconstructed into pTRIOZ expression vector and monoclonal antibodies (mAbs) were expressed *in vitro*. Majority (17 out of 19) were from the double-positive (SC1+SC2+) B cells, while two from SC2+ and none from the SC1+ single-positive B cells were recovered.

[00233] For control and comparative studies, we also included four published broad spectrum mAbs, S309 (Sotrovimab, GSK), CR3022, S2X259 (VirBiotech) and LyCoV-1404 (Eli Lilly) in this study. The two mAbs cloned from SC2+ single positive B cells showed minimal reactivity to SARS-CoV-1 RBD [Table 3]. All 17 mAbs recovered from SC1+SC2+ B cells showed binding to both SARS-CoV-1 and SARS-CoV-2 RBDs, but their neutralization capacities varied across different mAbs. Six of the most potent neutralizers (SS6V11-B5, SS6V11-E7, SS6V12-E11, SS6V13-F1, SS6V19-F4 and SS6V20-F5) were selected for large-scale production and further characterization. These are listed as antibodies 1, 11-13, 19 and 20 above. The most potent mAbs (SS6V11-E7, SS6V13-F1 and SS6V20-F5) utilize a unique heavy and light chain gene family combination that has not been reported to date. These are listed as antibodies 11, 13 and 20 above. All three mAbs use IGHV4-59 heavy chains and IGKV2-28/IGKJ5 light chains, suggesting that the B cells most likely originated from the same clonal family and the slight variations of the heavy and light chains occurred through hypersomatic mutation.

[Table 3]: Binding and neutralization activities of the mAbs obtained in this study (H = heavy gene family, K = kappa light gene family, L = lambda light gene family)

	Type	Construct name	Gene class	sVNT SARS-CoV-1 (% I)	sVNT SARS-CoV-2 (% I)	Binding SARS-CoV-1	Binding SARS-CoV-2
1	SC2+	mAb2 (SS6V2-G1)	H = 3-66, K = 1-9	1.346	20.159	0.008	0.947
2	SC2+	mAb3 (SS6V3-G2)	H = 1-18, K = 4-1	8.882	17.704	0.010	1.088

3	SC1+SC2+	mAb4 (SS6V4-A1)	H = 5-51, K = 4-1	15.311	22.372	0.960	1.251
4	SC1+SC2+	mAb1 (SS6V1-B5)	H = 3-13, K = 1-39	52.063	46.266	1.346	1.731
5	SC1+SC2+	mAb5 (SS6V5-C3)	H = 5-51, K = 1-5	11.693	32.296	1.159	1.677
6	SC1+SC2+	mAb6 (SS6V6-C4)	H = 3-64, K = 1-39	30.472	31.708	1.293	1.917
7	SC1+SC2+	mAb7 (SS6V7-C5)	H = 5-51, K = 1-16	20.813	14.903	0.972	1.164
8	SC1+SC2+	mAb8 (SS6V8-D3)	H = 3-64, K = 1-39	36.094	33.057	1.417	1.938
10	SC1+SC2+	mAb9 (SS6V9-D11)	H = 4-4, K = 3-15	45.215	39.177	1.295	1.815
11	SC1+SC2+	mAb10 (SS6V10-E1)	H = 5-51, K = 1-16	15.401	22.683	1.096	1.308
12	SC1+SC2+	mAb18 (SS6V18-E3)	H = 3-64, K = 1-39	43.660	15.526	1.329	1.109
13	SC1+SC2+	mAb11 (SS6V11-E7)	H = 4-59, K = 2-28	96.890	96.196	1.133	1.676
14	SC1+SC2+	mAb12 (SS6V12-E11)	H = 3-21, K = 1-39	50.389	45.021	1.213	1.445
15	SC1+SC2+	mAb13 (SS6V13-F1)	H = 4-59, K = 2-28	95.903	94.537	1.248	1.694
16	SC1+SC2+	mAb14 (SS6V14-F2)	H = 4-59, K = 1-39	18.122	33.402	1.062	1.539

17	SC1+SC2+	mAb19 (SS6V19-F4)	H = 7-4-1, K = 3-15	61.214	38.797	1.149	0.641
18	SC1+SC2+	mAb20 (SS6V20-F5)	H = 4-59, K = 2-28	96.651	96.058	1.246	1.805
19	SC1+SC2+	mAb15 (SS6V15-F6)	H = 3-30, K = 3-20	17.494	15.664	0.831	0.674
20	Control	S309	H = 1-18, K = 3-20	36.513	39.592	1.216	1.546
21	Control	CR3022	H = 5-51, K = 4-1	32.536	24.205	1.185	1.463
22	Control	S2X259	H = 1-69, L = 1-40	92.793	94.018	0.973	1.731
23	Control	LyCoV140 4	H = 2-5, L = 2-14	94.522	0.144	1.544	0.445

[00234] Example 5 Potency, breadth and variant escapability of pan-sarbecovirus mAbs

[00235] An 18-plex sVNT was performed based on RBDs derived from SARS-CoV-2 ancestral virus and its variants (Alpha, Beta, Delta, Delta Plus, Gamma, Lambda, Mu); zoonotic sarbecoviruses BANAL-52, BANAL-236, GD-1, RaTG13, GX-P5L, Rs2018B, LYRa11, RsSHC014, WIV-1; and SARS-CoV-1. Data for the top six mAbs identified in the preliminary screen and three control mAbs are shown in [Fig. 12]. SS6V11-E7, SS6V13-F1 and SS6V20-F5 mAbs exhibited ultrapotent ability to neutralize all 18 sarbecoviruses with neutralizing titer 50% (NT50) ranging from 10.44-120.30 ng/ml (0.070 – 0.802 nM). These are listed as antibodies 11, 13 and 20 above. The remaining three mAbs SS6V1-B5, SS6V12-E11 and SS6V19-F4 also displayed broad spectrum neutralizing activity, but they were less active/inactive against some viruses tested, i.e. SS6V12-E11 on Lambda, SS6V19-F4 on Lambda, GX-P5L and RsSHC014. These are listed as antibodies 1, 12 and 19 above. Their NT50 could be in the higher than 1,000 ng/ml (6.67 nM) range for some Clade-1b sarbecoviruses and higher than 200 ng/ml (1.33 nM) range for Clade-1a sarbecoviruses. For the four control mAbs, there were also some immune escape observed, i.e. S309 by Lambda and WIV-1, LyCoV-1404 by some Clade-1b zoonotic sarbecovirus (RaTG13 and GX-P5L), and all the Clade-1a sarbecoviruses (WIV-1, RsSHC014, Rs2018B and SARS-CoV-1) [Fig. 13]. Thus, it was concluded that although LyCoV-1404 retains potent activity against multiple variants i.e. variant-proof, it is not a pan-sarbecovirus mAb. As the primary aim is to develop pan-sarbecovirus, broadly neutralizing mAbs, LyCoV-1404 was not

included as a comparator in the rest of the assays. S2X259 is the only tested control mAb that retained pan-sarbecovirus neutralizing activity on all 18 strains tested, with NT50 ranging between 47.39-370.50 ng/ml (0.316 – 2.47 nM).

[00236] Example 6 Functionality of pan-sarbecovirus neutralizing mAbs

5 **[00237]** With the data presented above from multiple assays, SS6V11-E7, SS6V13-F1 and SS6V20-F5 were chosen for further characterizations together with the three control mAbs S309, CR3022 and S2X257, all sourced from commercial suppliers with either direct purchase or contract production.

10 **[00238]** The functionality of these mAbs in their ability to neutralize different sarbecoviruses was further assessed against eight spike-pseudotyped reporter viruses which included SARS-CoV-2 ancestral and four VOCs (Alpha, Delta, Beta and Gamma), two zoonotic sarbecoviruses (GX-P5L and WIV-1), and SARS-CoV-1. It was observed that all three test mAbs retained highly potent neutralizing activity against all the eight pseudoviruses with relative half maximal neutralizing titre (NT50) of less than 10 ng/ml (0.067 nM) (Fig. 14).
15 S309 has an NT50 of 100-1000 ng/ml (0.667 – 6.67 nM) on SARS-CoV-2 VOCs and pre-emergent sarbecoviruses. In general, S2X259 performed better than S309. However, it was ~10-fold less potent compared to the three mAbs identified in the current study. CR3022 was only able to neutralize some Clade-1a sarbecoviruses (WIV-1 and SARS-CoV-1), but none of the Clade-1b sarbecoviruses.

20 **[00239]** Example 7 Ability to neutralize Omicron viruses of different sublineages

[00240] During the final stage of the current study, a new sublineage, Omicron BA.2, emerged and is becoming an equally dominant virus as the original Omicron BA.1 virus. To determine the neutralizing ability of the newly identified mAbs against these two virus variants, testing was conducted using three different platforms – multiplex sVNT,
25 pseudovirus neutralization test (pVNT) and plaque reduction neutralization test (PRNT).

[00241] Serum samples were tested with a newly developed multiplex-sVNT assay. Briefly, AviTag-biotinylated RBD proteins from ancestral SARS-CoV-2 and SARS-CoV-1, nine VOCs/VOIs (Alpha, Delta, Beta, Gamma, Delta Plus, Lambda, Mu, Omicron BA.1, Omicron BA.2) and ten zoonotic sarbecoviruses (BANAL-52, BANAL-236, GD-1, RaTG13,
30 GX-P5L, Rs2018B, LYRa11, RsSHC014 and WIV-1), were coated on a MagPlex Avidin microsphere (Luminex) at 5 µg/1 million beads. The RBD-coated microspheres (600 beads/antigen) were pre-incubated with mAbs at a starting concentration of 10,000 ng/ml

serially diluted four-fold for 15 min at 37°C with 250 rpm agitation. After 15 min incubation, 50 µL of 2 µg/mL phycoerythrin (PE)-conjugated hACE2 (GenScript) were added to the well and incubated for 15 min at 37°C with agitation, followed by two PBS-1% BSA washes. The final readings were acquired using the MAGPIX system (Luminex Corporation). Data shown in [Fig. 15] indicates that SS6V11-E7 and SS6V20-F5 retained potent activity on both BA.1 and BA.2 Omicron with average NT50 ranging between 177-315 ng/ml (1.18 – 2.10 nM) on multiplex sVNT.

[00242] SARS-CoV-2 Wuhan-hu-1 (ancestral), Alpha, Delta, Beta, Gamma, Omicron BA.1, Omicron BA.2, GX-P5L, WIV-1 and SARS-CoV-1 full-length spike pseudotyped viruses were produced and packaged. Briefly, 5 million of HEK293T cells were transfected with 20 µg of pCAGGS spike plasmid using FuGENE6 (Promega). At 24h post transfection, cells were incubated with VSVΔG luc seed virus (at MOI of 5) for 2h. Following two PBS washes, infected cells were replenished with complete growth media supplemented with 1:5000 diluted anti-VSV-G mAb (Clone 8GF11, Kerafast). At 24h post infection, pseudoviruses were harvested by centrifugation at 2,000 x g for 5 min. For the pVNT assay, 3 x 10⁶ RLU of pseudoviruses were pre-incubated with four-fold serially diluted mAb at a starting concentration of 20 µg/ml into a final volume of 50 µl for 1 h at 37°C, followed by infection of ACE2-stable-expressing A549 cells. At 20-24 h post-infection, an equal volume of ONE-Glo luciferase substrate (Promega) was added and the luminescence signal was measured using the Cytation 5 microplate reader (BioTek) with Gen5 software version 3.10.

[00243] The mAbs were serially diluted four-fold using DMEM containing 2% FBS, at a starting concentration of 20 µg/ml. SARS-CoV-2 virus (ancestral or Omicron BA.1 and BA.2 strains) were then diluted to 500 PFU/ml and mixed with the diluted mAbs and incubated at 37°C for 1 h for the mAbs and viruses to bind. After 1 h, the mAbs-virus mixture were added to A549-ACE2 monolayer and incubated for a further 1 h at 37°C. The inoculum was then decontaminated. The cells were replenished with plaque medium (DMEM supplemented with 2% FBS, 0.8% Avicel and 0.2% carboxymethylcellulose) and incubated at 37°C for 3 days. Plaques were fixed and stained with 10% buffered formalin and 0.2% crystal violet, respectively.

[00244] In authentic virus neutralization tests only SS6V11-E7, listed above as antibody 11, continued to show a capacity to neutralize BA.2 at NT50 of 1400 ng/ml (9.3 nM) or 500 ng/ml (3.33 nM) using pVNT or PRNT assays respectively see [Fig. 15B and 15C]. The ~2-4-fold discrepancy in neutralization potency to the BA.2 variant measured by the live virus assays (pVNT and PRNT) compared to the biochemical multiplex-sVNT assay suggested

that there may be additional antibody escaping effects aided by mutations present in the full BA.2 spike, which became pronounced in the live virus assays. Regardless, we observed that only SS6V11-E7 maintained neutralization capacity against Omicron BA.2 whereas all the other mAbs tested, including the three control mAbs, had completely lost potency.

5 **[00245]**

[00246] It should be further appreciated by the person skilled in the art that variations and combinations of features described above, not being alternatives or substitutes, may be combined to form yet further embodiments falling within the intended scope of the invention.

[00247] As would be understood by a person skilled in the art, each embodiment may be
10 used in combination with other embodiment or several embodiments.

Claims

[Claim 1]. An antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

5 HC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO:1 or SEQ ID NO:111

HC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO:2 or SEQ ID NO:112

10 HC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:3 or SEQ ID NO:113; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID NO:114

15 LC-CDR2 having the amino acid having at least 85% sequence identity to SEQ ID NO: 5 or SEQ ID NO:115

LC-CDR3 having the amino acid having at least 85% sequence identity to SEQ ID NO:6 or SEQ ID NO:116.

20 [Claim 2]. An antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid having formula I: $X_1-X_2-X_3-\Phi-X_4-X_{n1}-X_5-X_6$:

wherein X_1 is selected from one of G and E;

X_2 is selected from one of F, Y, N, G, D, and V;

25 X_3 is selected from one of P, T, S, I and F;

Φ is selected from one of F, V, L, or I;

X_4 is selected from one of S, T, R, N, G, L, and I;

X_{n1} is selected from one of S, SN, N, M, H, T, G, P, G and D;

X_5 is selected from one of Y, S, N, I and H;

30 X_6 is selected from one of Y, G, W, E, A, N, and T;

HC-CDR2 having the amino acid formula II: $X_7-X_8-X_9-X_{n2}-\Pi-X_{n3}-X_{10}$.

wherein X_7 is selected from one of I and T;

X_8 is selected from one of Y, S, N, G, A and T;

X_9 is selected from one of S, F, P, N, H, I, Y, G, and T;

X_{n2} is selected from one of G, YN, DD, T, NG, DG, S, SS, D, ST, and NT;

5 π is selected from one of G, S, P, A and E;

X_{n3} is selected from one of S, I, D, G, F, N, RT, L, and RN;

X_{10} is selected from one of T, R, M, K, S, and P;

HC-CDR3 having the amino acid having formula III: $\Psi\text{-}\zeta_1\text{-}X_{n4}\text{-}X_{11}\text{-}X_{n5}\text{-}X_{12}\text{-}X_{13}\text{-}X_{14}\text{-}\zeta_2\text{-}X_{15}$;

10 wherein Ψ is selected from one of A and V,

ζ_1 is selected from one of R, T, K and L-N

X_{n4} is selected from one of E, HLGGG, GGG, LDIII, DSI, GEAG, RVAIF, LQNG, VTYTS, ADIV, DSLA, DSL, AISQQ, DYYDN, DPL, EGIQG, and DGG;

X_{11} is selected from one of L, S, Y, T, A, N, V, and W;

15 X_{n5} is selected from one of R, S, LET, P, SAT, MATIWV, DGY, SY, PLPF, GS, VV, SVT, FDS, GYYY, EGAAS, V, and QLPY;

X_{12} is selected from one of H, W, G, P, T, S, N, and Y;

X_{13} is selected from one of Y, P, A, L, S, F, I, V, and G;

X_{14} is selected from one of F, I, N, Y, L, and M;

20 ζ_2 is selected from one of D, E, G, and S;

X_{15} is selected from one of Y, S, L, N, H, C, V, and F;

and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid having formula IV: $X_{16}\text{-}X_{17}\text{-}X_{18}\text{-}X_{n6}\text{-}\zeta_3\text{-}X_{19}$;

25 wherein X_{16} is selected from one of Q and Y;

X_{17} is selected from one of G, S, T, N, I, and A;

X_{18} is selected from one of V, I, T, F and L;

X_{n6} is selected from one of S, G, N, V, R, LYSSNNK, LYRSNNK, LQNNGY, VQSNGY, VHSDGN, MQLNGY and SS;

30 ζ_3 is selected from one of S, N, and T;

X_{19} is selected from one of W, Y, S and N;

LC-CDR2 having the amino acid having formula V: $X_{20}\text{-}X_{21}\text{-}S$;

wherein X_{20} is selected from one of A, W, K, T, G, L, and D;

X_{21} is selected from one of A, S, G, I, and T

LC-CDR3 having the amino acid having formula VI: $X_{22}\text{-}\zeta_4\text{-}X_{23}\text{-}X_{n7}\text{-}\zeta_5\text{-}X_{24}\text{-}X_{25}\text{-}$

$X_{n8}\text{-}\zeta_6$:

5 wherein X_{22} is selected from one of Q, H, and M;

ζ_4 is selected from one of Q and H;

X_{23} is selected from one of Y, S, G, A, L, and T;

X_{n7} is selected from one of F, Y, N, S, L, G, T, YR, and YI;

ζ_5 is selected from one of S, T, N, Q, and D;

10 X_{24} is selected from one of S, Y, T, D, H, F, P, W, and I;

X_{25} is selected from one of P, I, and R;

X_{n8} is selected from one of F, W, K, G, Y, R, P, L, PY, EY, ED, GY, QY, and QI;

ζ_6 is selected from one of T and S.

15 [Claim 3]. The antigen-binding molecule according to claim 2, wherein:

Φ is selected from one of F, L, or I;

X_5 is selected from one of Y, S, I and H;

X_6 is selected from one of Y, W, E, A, N, and T;

X_8 is I;

20 X_{n2} is selected from one of DD, T, NG, DG, S, SS, D, ST, and NT;

ζ_1 is selected from one of R, T, and K;

X_{n4} is selected from one of HLGGG, GGG, LDIII, DSI, GEAG, LQNG, VTYTS, ADIV, DSLA, DSL, AISQQ, DYYDN, DPL, EGIQG, and DGG;

X_{11} is selected from one of S, Y, T, A, V, and W;

25 X_{n5} is selected from one of S, LET, P, SAT, MATIWW, SY, PLPF, GS, VV, SVT, FDS, GYYY, EGAAS, V, and QLPY;

X_{12} is selected from one of W, G, P, T, S, N, and Y;

X_{n6} is selected from one of S, G, N, V, R, LYRSNNK, LQNNGY, VQSNGY, VHSDGN, MQLNGY and SS;

30 X_{23} is selected from one of Y, S, G, A, and T;

X_{n8} is selected from one of F, W, K, G, Y, R, P, L, EY, ED, GY, QY, and QI.

[Claim 4]. The antigen-binding molecule according to claim 2 or 3, wherein:

- 5 X_1 is G;
 X_2 is selected from one of G, F, Y and V;
 X_3 is selected from one of S, I, T and F;
 Φ is selected from one of F, L and I;
 X_4 is selected from one of R, S, G, L, T and I;
- 10 X_{n1} is selected from one of P, N, T, D and G;
 X_5 is selected from one of Y, S and H;
 X_6 is selected from one of E, N and Y;
 X_7 is I;
 X_8 is selected from one of G, S, N and Y;
- 15 X_9 is selected from one of I, N, S, T and F;
 X_{n2} is selected from one of T, S, SS and NT;
 π is selected from one of G, E, S and A;
 X_{n3} is selected from one of G, S, F, I and N;
 X_{10} is selected from one of T, M and P;
- 20 **Ψ is A;**
 ζ_1 is R;
 X_{n4} is selected from one of VTYTS, GGG, DYYDN, and DGG;
 X_{11} is selected from one of S, Y and W;
 X_{n5} is selected from one of PLPF, LET, GYYY and QLPY;
- 25 X_{12} is selected from one of W, Y and G;
 X_{13} is selected from one of F, P, G, and Y;
 X_{14} is selected from one of F, M and L;
 ζ_2 is selected from one of D and E;

- X_{15} is selected from one of Y, L, V, F and S;
 X_{16} is selected from one of Q and Y;
 X_{17} is selected from one of G and S;
 X_{18} is selected from one of I, F and L;
 5 X_{n6} is selected from one of G, LQNNGY, R, VQSNGY, S and MQLNGY;
 ζ_3 is selected from one of N, S and T;
 X_{19} is selected from one of Y or S;
 X_{20} is selected from one of A, L and G;
 X_{21} is selected from one of A, S, T and G;
 10 X_{22} is selected from one of Q, M and L;
 ζ_4 is Q;
 X_{23} is selected from one of T, S, Y and G;
 X_{n7} is selected from one of YR, L, and Y;
 ζ_5 is selected from one of T, Q, and S;
 15 X_{24} is selected from one of P, I, W and T;
 X_{25} is P;
 X_{n8} is selected from one of ED, G, QI and L;
 ζ_6 is selected from one of S and T.
- 20 [Claim 5]. The antigen-binding molecule according to any one of claims 2 to 4,
 wherein:
- X_1 is G;
 X_2 is selected from one of G and V;
 X_3 is selected from one of S, and F;
 25 Φ is I;
 X_4 is selected from one of G, L and I;
 X_{n1} is selected from one of P and G;
 X_5 is selected from one of Y, S and H;

- X_6 is Y;
 X_7 is I;
 X_8 is Y;
 X_9 is selected from one of I and F;
5 X_{n2} is S; π is selected from one of G, E and A;
 X_{n3} is selected from one of S and N;
 X_{10} is T;
 Ψ is A;
 ζ_1 is R;
10 X_{n4} is GGG;
 X_{11} is Y;
 X_{n5} is LET;
 X_{12} is G;
 X_{13} is P;
15 X_{14} is selected from one of F and L;
 ζ_2 is selected from one of D, and E;
 X_{15} is selected from one of Y, F and S;
 X_{16} is Q;
 X_{17} is selected from one of G and S;
20 X_{18} is L;
 X_{n6} is selected from one of LQNNGY, VQSNGY and MQLNGY;
 ζ_3 is N;
 X_{19} is Y;
 X_{20} is L;
25 X_{21} is selected from one of S and G;
 X_{22} is M;
 ζ_4 is Q;
 X_{23} is selected from one of S and G;

X_{n7} is L;
 ζ_5 is Q;
 X_{24} is selected from one of I and T;
 X_{25} is P;
 5 X_{n8} is G;
 ζ_6 is T.

[Claim 6]. The antigen-binding molecule according to any one of claims 2 to 5,
 10 wherein:

X_1 is G;
 X_2 is G;
 X_3 is selected from one of S, and F;
 Φ is I;
 15 X_4 is selected from one of G, and I;
 X_{n1} is selected from one of P and G;
 X_5 is selected from one of Y and H;
 X_6 is Y;
 X_7 is I;
 20 X_8 is Y;
 X_9 is selected from one of I and F;
 X_{n2} is S;
 π is selected from one of G and A;
 X_{n3} is selected from one of S and N;
 25 X_{10} is T;
 Ψ is A;
 ζ_1 is R;
 X_{n4} is GGG;

- X_{17} is Y;
 X_{n5} is LET;
 X_{12} is G;
 X_{13} is P;
5 X_{14} is selected from one of F and L;
 ζ_2 is selected from one of D, and E;
 X_{15} is selected from one of Y and F;
 X_{16} is Q;
 X_{17} is S;
10 X_{18} is L;
 X_{n6} is selected from one of LQNNGY, and MQLNGY;
 ζ_3 is N;
 X_{19} is Y;
 X_{20} is L;
15 X_{21} is selected from one of S and G;
 X_{22} is M;
 ζ_4 is Q;
 X_{23} is selected from one of S and G;
 X_{n7} is L;
20 ζ_5 is Q;
 X_{24} is I;
 X_{25} is P;
 X_{n8} is G;
 ζ_6 is T.
- 25 [Claim 7]. The antigen-binding molecule according to any one of claims 1 to 6,
 comprising two antigen-binding molecules which binds to different sarbecovirus spike
 protein.

[Claim 8]. The antigen-binding molecule according to any one of claims 1 to 7, wherein the antigen-binding molecule binds to the receptor binding domain (RBD) of the Sarbecovirus spike protein.

5 [Claim 9]. The antigen-binding molecule according to any one of claims 1 to 8, wherein the antigen-binding molecule inhibits interaction between a sarbecovirus spike protein and Angiotensinogen converting enzyme 2 (ACE2).

[Claim 10]. The antigen-binding molecule according to any one of claims 1 to 9, wherein
10 the antigen-binding molecule inhibits infection of ACE2-expressing cells by a sarbecovirus.

[Claim 11]. The antigen-binding molecule according to any one of claims 1 to 10, wherein the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2
15 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

20 [Claim 12]. The antigen-binding molecule according to claim 1, wherein the antigen-binding molecule comprises:

a VH region comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 1, 2, and 3; and

a VL region comprising an amino acid sequence having at least 95% sequence
25 identity to the amino acid sequence of SEQ ID NO: 4, 5, and 6.

[Claim 13]. A nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding the antigen-binding molecule according to any one of claims 1 to 12.

30 [Claim 14]. An expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids according to claim 13.

[Claim 15]. A method for producing antigen-binding molecule which binds to a sarbecovirus spike protein, comprising culturing a cell capable of expressing an antigen binding molecule according to any one of claims 1 to 12 under conditions suitable for expression of an antigen-binding molecule by the cell.

[Claim 16]. A composition comprising the antigen-binding molecule according to any one of claims 1 to 12, the nucleic acid or the plurality of nucleic acids according to claim 13, the expression vector or the plurality of expression vectors according to claim 14, and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

[Claim 17]. The antigen-binding molecule according to any one of claims 1 to 12, a nucleic acid or a plurality of nucleic acids according to claim 13, an expression vector or a plurality of expression vectors according to claim 14, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[Claim 18]. The antigen-binding molecule according to any one of claims 1 to 12, a nucleic acid or a plurality of nucleic acids according to claim 13, an expression vector or a plurality of expression vectors according to claim 14 or a composition according to claim 16, for use according to claim 17, wherein the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[Claim 19]. Use of the antigen-binding molecule according to any one of claims 1 to 12, a nucleic acid or a plurality of nucleic acids according to claim 13, an expression vector or a plurality of expression vectors according to claim 14, or a composition according to claim 16, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[Claim 20]. The use according to claim 19, wherein the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1,
 5 SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.

[Claim 21]. A method of treating or preventing a disease caused by infection with a sarbecovirus, comprising administering to a subject a therapeutically or prophylactically
 10 effective amount of the antigen-binding molecule according to any one of claims 1 to 12, the nucleic acid or a plurality of nucleic acids according to claim 13, an expression vector or a plurality of expression vectors according to claim 14, or a composition according to claim 16.

[Claim 22]. The method of claim 21, wherein the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV
 15 RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.
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[Claim 23]. Use of the antigen-binding molecule according to any one of claims 1 to 12 to inhibit infection of ACE2-expressing cells by a sarbecovirus.

[Claim 24]. Use of claim 23, wherein the sarbecovirus is selected from the group comprising SARS-CoV-2, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SARS-CoV-2 B.1.617.2, SARS-CoV-2 C37, SARS-CoV-2 B.1.621, SARS-CoV-2 P.1, SARS-CoV-2 BA.1, SARS-CoV-2 BA.2, SC2r-CoV BANAL-52, SC2r-CoV BANAL-236, SC2r-CoV GD-1, SC2r-CoV RaTG13, SC2r-CoV GX-P5L, SC1r-CoV Rs2018B, SC1r-CoV
 25 RsSHC014, SC1r-CoV LYRa11, SC1r-CoV WIV-1, and SARS-CoV.
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