PROTEIN ANTIGEN-BINDING MOLECULES

FIELD

[0001] 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

[0002] 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.

[0003] Since 2002, we had three major human infectious disease pandemics caused by coronaviruses (CoVs), 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 loses 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, 372:109).

[0004] The recent emergence of SARS-CoV-2 variants, the UK COVID-19 variant SARS-CoV-2 B.1.1.7; the South Africa COVID-19 variant SARS-CoV-2 B.1.351 also known as 20H/501Y.V2, or 501Y.V2 variant; and the Brazil variant P.1.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 GX-P5L in pangolin and the SC2r-CoV RaTG13 in bats giving rise to a chance of future outbreaks (SARS3, SARS4, etc) caused by different, but related coronaviruses.

[0005] The current classification of coronaviruses has four genera, alpha, beta, delta and gamma. The coronaviruses that have caused human infection have all come from the Genus Beta Coronavirus (Nat Microbiol 2020, 5:536-544). The sub-genus: 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. The Sarbecoviruses include 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.

[0006] 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.

SUMMARY

[0007] Protein antigen-binding molecules, nucleic acid, expression vector, cell or composition suitable for use in treatment or prevention of coronaviral infection caused by sarbecoviruses is envisaged.

[0008] 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.

[0009] 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.

[0010] 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 herein above.

[0011] According to another aspect 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.

[0012] According to another aspect there is a cell of the cell line designated XXXX, deposited XXXXXXXX as ATCC accession number PTA-XXXXX or cell line YYYY, deposited YYYYYYYY as ATCC accession number PTA-YYYYY.

[0013] 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 as discussed herein above under conditions suitable for expression of an antigen-binding molecule by the cell.

[0014] 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, or a cell as discussed herein above, and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

[0015] 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, a cell as discussed herein above, or a composition as discussed herein above, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

[0016] 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, a cell as discussed herein above, or 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.

[0017] 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 above, an expression vector or a plurality of expression vectors as discussed herein above, a cell as discussed herein above, or a composition as discussed herein above.

[0018] 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.

[0019] 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

[0020] In the figures, which illustrate, by way of non-limiting examples only, embodiments of the present invention,

[0021] **Figure 1: 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).

[0022] **Figure 2:** Multiplex sVNT on six different RBDs (from left to right: SARS-CoV-2 WT, UK, SA strains; Bat virus RaTG13; Pangolin virus GX-P5L; SARS-CoV). **A)**. SARS patient (N=11). **B)** COVID-19 patient (N=40). **C)** Healthy-vaccinated (N=20). Serum samples were taken two weeks after second dose. **D)** SARS-vaccinated (N=9). Sera from SARS survivors taken 21-62 days after the first vaccination. All serum samples were tested at a single dilution of 1:20. A cut-off of 30% was set as previously determined.

[0023] **Figure 3:** Titration of neutralizing antibody levels (NT50) in the different groups against the six sarbecoviruses. Serum samples were tested at dilutions from 1:20 to 1:20480 by a 4-fold serial titration.

[0024] **Figure 4:** Confirmation of boosting pan-sarbecovirus cross-neutralizing antibodies in the SARS-vaccinated group. **A)** Pan-sarbecovirus neutralization of mAb 5B7D7 against SARS-CoV-2 variants of concern, bat SC2r-CoV RaTG13, Pangolin SC2r-CoV GX-P5L and SARS-CoV measured by the multiplex sVNT. **B)** Inhibition of 5B7D7 binding to different RBDs by the four different panels of sera as indicated.

[0025] **Figure 5:** Neutralization patterns from rabbit hyper immune sera targeting different beta coronavirus RBD proteins.

DETAILED DESCRIPTION

[0026] 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 combination of advantageous properties over known SARS-CoV-2 antibodies.

[0027] 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".

[0028] Furthermore, throughout the document, unless the context requires otherwise, the 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.

[0029] 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 herein belongs.

[0030] According to various embodiments there is an antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus.

[0031] 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.

[0032] 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 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 B.1.1.7, and/or capable of binding to SARS-CoV-2 B.1.351 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 any other sarbecovirus spike protein such as SARS-CoV-2 B.1.617.2; RmYN02; 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.

[0033] 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%, 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%, 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).

[0034] 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 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 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 B.1.1.7, and/or capable of binding to SARS-CoV-2 B.1.351 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 any other sarbecovirus spike protein such as SARS-CoV-2 B.1.617.2; RmYN02; RacCS203 or future unknown sarbecoviruses.

[0035] 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).

[0036] 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.

[0037] 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.

[0038] 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.

[0039] In various embodiments, the multispecific antigen-binding molecule is capable of binding 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 B.1.1.7, and/or capable of binding to SARS-CoV-2 B.1.351 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 any other sarbecovirus spike protein.

[0040] 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, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0041] 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.

[0042] 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.

[0043] 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).

[0044] 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).

[0045] 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.

[0046] 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 SARSr-CoV binds to ACE2 expressed by the host cells.

[0047] 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 SARSr-CoV-2 binds to ACE2 expressed by host cells.

[0048] 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 SARSr-CoV or other known sarbecoviruses.

[0049] 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.

[0050] 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. For example, an isoform, fragment, variant or homologue of the spike protein of sarbecovirus may display association with ACE2.

[0051] 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.

[0052] 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.

[0053] 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.

[0054] In various embodiments, the antigen-binding molecule comprises two antigen-binding molecules which binds to a sarbecovirus spike protein.

[0055] In various embodiments, the antigen-binding molecule binds to the receptor binding domain (RBD) of the Sarbecovirus spike protein.

[0056] In various embodiments, the antigen-binding molecule inhibits interaction between the sarbecovirus spike protein and Angiotensinogen converting enzyme 2 (ACE2).

[0057] In various embodiments, the antigen-binding molecule inhibits infection of ACE2-expressing cells by the sarbecovirus.

[0058] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0059] 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.

[0060] 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 B1.617, and the Brazil variant P.1.

[0061] 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.

[0062] 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.

[0063] 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.

[0064] In some 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 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.

[0065] 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, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0066] In various embodiments, the antigen-binding molecule comprises:

(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.

[0067] In various embodiments, the antigen-binding molecule comprises: a VH region comprising an amino acid sequence having at least 85% 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 85% sequence identity to the amino acid sequence of SEQ ID NO: 5, 6 or 7.

[0068] 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.

[0069] 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.

[0070] 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.

[0071] 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.

[0072] 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.

[0073] 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.

[0074] 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.

[0075] 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.

[0076] 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).

[0077] 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., Cκ or Cλ). 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).

[0078] In various embodiments, the antigen-binding molecule of the present disclosure comprises, or consists of, a Fab region which binds to sarbecovirus spike protein.

[0079] 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).

[0080] 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).

[0081] 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.

[0082] 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).

[0083] 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.

[0084] 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.

[0085] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[0086] In various embodiments, the antigen-binding molecule as discussed herein above, is suitable for use in in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[0087] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0088] 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.

[0089] 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.

[0090] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[0091] 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.

[0092] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0093] 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.

[0094] In various embodiments, the subject is an individual that has had SARS-CoV-2 vaccination or infection.

[0095] In various embodiments, the subject is an individual that has been diagnosed with a sarbecovirus infection

[0096] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[0097] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[0098] In various embodiments, the antigen-binding molecule is produced by cell line XXXX, deposited XXXXXXXX as ATCC accession number PTA-XXXXX or cell line YYYY, deposited YYYYYYYY as ATCC accession number PTA-YYYYY.

[0099] 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.

[00100] 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.

[00101] 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.

[00102] 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.

[00103] 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.

[00104] 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 in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00105] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00106] 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.

[00107] 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 infection.

[00108] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00109] 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.

[00110] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00111] 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 a as discussed herein above.

[00112] In various embodiments, the subject is an individual that has had SARS-CoV-2 vaccination or infection.

[00113] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00114] In various embodiments, the subject is an individual that have been diagnosed with a sarbecovirus infection.

[00115] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00116] 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.

[00117] According to various embodiments there is a cell of the cell line designated XXXX, deposited XXXXXXXX as ATCC accession number PTA-XXXXX or cell line YYYY, deposited YYYYYYYY as ATCC accession number PTA-YYYYY.

[00118] 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.

[00119] 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.

[00120] In various embodiments, the cell as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

[00121] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00122] In various embodiments, the cell as discussed herein above, is suitable for use in in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00123] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00124] 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.

[00125] 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.

[00126] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00127] 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.

[00128] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00129] 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.

[00130] In various embodiments, the subject is an individual that have had SARS-CoV-2 vaccination.

[00131] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00132] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00133] 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.

[00134] 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.

[00135] In various embodiments, the composition as discussed herein above, is suitable for use in individuals that have had SARS-CoV-2 infection or vaccination.

[00136] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00137] In various embodiments, the composition as discussed herein above, is suitable for use in in treatment of individuals that have been diagnosed with a sarbecovirus infection.

[00138] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00139] 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.

[00140] 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.

[00141] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00142] 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.

[00143] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00144] 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.

[00145] In various embodiments, the subject is an individual that have had SARS-CoV-2 vaccination or infection.

[00146] 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 B.1.1.7, or SARS-CoV-2 B.1.351.

[00147] In various embodiments, the subject is an individual that has been diagnosed with a sarbecovirus infection.

[00148] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

[00149] 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.

[00150] In various embodiments, the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L

[00151] Sequences

SEQ ID NO:	DESCRIPTION	SEQUENCE
1	Heavy chain variable region HC-CDR1	NNNNNNNNNNNNNNN
2	Heavy chain variable region HC-CDR2	NNNNNNNNNNNNNNN
3	Heavy chain variable region HC-CDR3	NNNNNNNNNNNNNNN
4	light chain variable region LC-CDR1	NNNNNNNNNNNNNNN
5	Light chain variable region LC-CDR2	NNNNNNNNNNNNNNN
6	Light chain variable region LC-CDR3	NNNNNNNNNNNNNNN
7	SARS-CoV (GenBank: NC_004718.3)	ATATTAGGTTTTTACCTACCCAGGAAAAGCCAACCAACCTCGATCTCTTGTAGATCTGT TCTCTAAACGAACTTTAAAATCTGTGTAGCTGTCGCTCGGCTGCATGCCTAGTGCACC TACGCAGTATAAACAATAATAAATTTTACTGTCGTTGACAAGAAACGAGTAACTCGTCC CTCTTCTGCAGACTGCTTACGGTTTCGTCCGTGTTGCAGTCGATCATCAGCATACCTA GGTTTCGTCCGGGTGTGACCGAAAGGTAAGATGGAGAGCCTTGTTCTTGGTGTCAAC GAGAAAACACACGTCCAACTCAGTTTGCCTGTCCTTCAGGTTAGAGACGTGCTAGTGC GTGGCTTCGGGGACTCTGTGGAAGAGGCCCTATCGGAGGCACGTGAACACCTCAAAA ATGGCACTTGTGGTCTAGTAGAGCTGGAAAAAGGCGTACTGCCCCAGCTTGAACAGC CCTATGTGTTCATTAAACGTTCTGATGCCTTAAGCACCAATCACGGCCACAAGGTCGTT GAGCTGGTTGCAGAAATGGACGGCATTCAGTACGGTCGTAGCGGTATAACACTGGGA GTACTCGTGCCACATGTGGGCGAAACCCCAATTGCATACCGCAATGTTCTTCTTCGTA AGAACGGTAATAAGGGAGCCGGTGGTCATAGCTATGGCATCGATCTAAAGTCTTATGA CTTAGGTGACGAGCTTGGCACTGATCCCATTGAAGATTATGAACAAAACTGGAACACT AAGCATGGCAGTGGTGCACTCCGTGAACTCACTCGTGAGCTCAATGGAGGTGCAGTC ACTCGCTATGTCGACAACAATTTCTGTGGCCCAGATGGGTACCCTCTTGATTGCATCA AAGATTTTCTCGCACGCGCGGGCAAGTCAATGTGCACTCTTTCCGAACAACTTGATTA CATCGAGTCGAAGAGAGGTGTCTACTGCTGCCGTGACCATGAGCATGAAATTGCCTG GTTCACTGAGCGCTCTGATAAGAGCTACGAGCACCAGACACCCTTCGAAATTAAGAGT GCCAAGAAATTTGACACTTTCAAAGGGGAATGCCCAAAGTTTGTGTTTCCTCTTAACTC AAAAGTCAAAGTCATTCAACCACGTGTTGAAAAGAAAAAGACTGAGGGTTTCATGGGG CGTATACGCTCTGTGTACCCTGTTGCATCTCCACAGGAGTGTAACAATATGCACTTGT CTACCTTGATGAAATGTAATCATTGCGATGAAGTTTCATGGCAGACGTGCGACTTTCTG AAAGCCACTTGTGAACATTGTGGCACTGAAAATTTAGTTATTGAAGGACCTACTACATG TGGGTACCTACCTACTAATGCTGTAGTGAAAATGCCATGTCCTGCCTGTCAAGACCCA GAGATTGGACCTGAGCATAGTGTTGCAGATTATCACAACCACTCAAACATTGAAACTC GACTCCGCAAGGGAGGTAGGACTAGATGTTTTGGAGGCTGTGTGTTTGCCTATGTTG GCTGCTATAATAAGCGTGCCTACTGGGTTCCTCGTGCTAGTGCTGATATTGGCTCAGG CCATACTGGCATTACTGGTGACAATGTGGAGACCTTGAATGAGGATCTCCTTGAGATA CTGAGTCGTGAACGTGTTAACATTAACATTGTTGGCGATTTTCATTTGAATGAAGAGGT TGCCATCATTTTGGCATCTTTCTCTGCTTCTACAAGTGCCTTTATTGACACTATAAAGAG TCTTGATTACAAGTCTTTCAAAACCATTGTTGAGTCCTGCGGTAACTATAAAGTTACCA AGGGAAAGCCCGTAAAAGGTGCTTGGAACATTGGACAACAGAGATCAGTTTTAACACC ACTGTGTGGTTTTCCCTCACAGGCTGCTGGTGTTATCAGATCAATTTTTGCGCGCACA CTTGATGCAGCAAACCACTCAATTCCTGATTTGCAAAGAGCAGCTGTCACCATACTTGA TGGTATTTCTGAACAGTCATTACGTCTTGTCGACGCCATGGTTTATACTTCAGACCTGC TCACCAACAGTGTCATTATTATGGCATATGTAACTGGTGGTCTTGTACAACAGACTTCT CAGTGGTTGTCTAATCTTTTGGGCACTACTGTTGAAAAACTCAGGCCTATCTTTGAATG

		GATTGAGGCGAAACTTAGTGCAGGAGTTGAATTTCTCAAGGATGCTTGGGAGATTCTC AAATTTCTCATTACAGGTGTTTTTGACATCGTCAAGGGTCAAATACAGGTTGCTTCAGA TAACATCAAGGATTGTGTAAAATGCTTCATTGATGTTGTTAACAAGGCACTCGAAATGT GCATTGATCAAGTCACTATCGCTGGCGCAAAGTTGCGATCACTCAACTTAGGTGAAGT CTTCATCGCTCAAAGCAAGGGACTTTACCGTCAGTGTATACGTGGCAAGGAGCAGCTG CAACTACTCATGCCTCTTAAGGCACCAAAAGAAGTAACCTTTCTTGAAGGTGATTCACA TGACACAGTACTTACCTCTGAGGAGGTTGTTCTCAAGAACGGTGAACTCGAAGCACTC GAGACGCCCGTTGATAGCTTCACAAATGGAGCTATCGTTGGCACACCAGTCTGTGTAA ATGGCCTCATGCTCTTAGAGATTAAGGACAAAGAACAATACTGCGCATTGTCTCCTGG TTTACTGGCTACAAACAATGTCTTTCGCTTAAAAGGGGGTGCACCAATTAAAGGTGTAA CCTTTGGAGAAGATACTGTTTGGGAAGTTCAAGGTTACAAGAATGTGAGAATCACATTT GAGCTTGATGAACGTGTTGACAAAGTGCTTAATGAAAAGTGCTCTGTCTACACTGTTGA ATCCGGTACCGAAGTTACTGAGTTTGCATGTGTTGTAGCAGAGGCTGTTGTGAAGACT TTACAACCAGTTTCTGATCTCCTTACCAACATGGGTATTGATCTTGATGAGTGGAGTGT AGCTACATTCTACTTATTTGATGATGCTGGTGAAGAAAACTTTTCATCACGTATGTATTG TTCCTTTTACCCTCCAGATGAGGAAGAAGAGGACGATGCAGAGTGTGAGGAAGAAGA AATTGATGAAACCTGTGAACATGAGTACGGTACAGAGGATGATTATCAAGGTCTCCCT CTGGAATTTGGTGCCTCAGCTGAAACAGTTCGAGTTGAGGAAGAAGAAGAGGAAGAC TGGCTGGATGATACTACTGAGCAATCAGAGATTGAGCCAGAACCAGAACCTACACCTG AAGAACCAGTTAATCAGTTTACTGGTTATTTAAAACTTACTGACAATGTTGCCATTAAAT GTGTTGACATCGTTAAGGAGGCACAAAGTGCTAATCCTATGGTGATTGTAAATGCTGC TAACATACACCTGAAACATGGTGGTGGTGTAGCAGGTGCACTCAACAAGGCAACCAAT GGTGCCATGCAAAAGGAGAGTGATGATTACATTAAGCTAAATGGCCCTCTTACAGTAG GAGGGTCTTGTTTGCTTTCTGGACATAATCTTGCTAAGAAGTGTCTGCATGTTGTTGGA CCTAACCTAAATGCAGGTGAGGACATCCAGCTTCTTAAGGCAGCATATGAAAATTTCAA TTCACAGGACATCTTACTTGCACCATTGTTGTCAGCAGGCATATTTGGTGCTAAACCAC TTCAGTCTTTACAAGTGTGCGTGCAGACGGTTCGTACACAGGTTTATATTGCAGTCAAT GACAAAGCTCTTTATGAGCAGGTTGTCATGGATTATCTTGATAACCTGAAGCCTAGAGT GGAAGCACCTAAACAAGAGGAGCCACCAAACACAGAAGATTCCAAAACTGAGGAGAA ATCTGTCGTACAGAAGCCTGTCGATGTGAAGCCAAAAATTAAGGCCTGCATTGATGAG GTTACCACAACACTGGAAGAAACTAAGTTTCTTACCAATAAGTTACTCTTGTTTGCTGA TATCAATGGTAAGCTTTACCATGATTCTCAGAACATGCTTAGAGGTGAAGATATGTCTT TCCTTGAGAAGGATGCACCTTACATGGTAGGTGATGTTATCACTAGTGGTGATATCACT TGTGTTGTAATACCCTCCAAAAAGGCTGGTGGCACTACTGAGATGCTCTCAAGAGCTT TGAAGAAAGTGCCAGTTGATGAGTATATAACCACGTACCCTGGACAAGGATGTGCTGG TTATACACTTGAGGAAGCTAAGACTGCTCTTAAGAAATGCAAATCTGCATTTTATGTAC TACCTTCAGAAGCACCTAATGCTAAGGAAGAGATTCTAGGAACTGTATCCTGGAATTTG AGAGAAATGCTTGCTCATGCTGAAGAGACAAGAAAATTAATGCCTATATGCATGGATGT TAGAGCCATAATGGCAACCATCCAACGTAAGTATAAAGGAATTAAAATTCAAGAGGGC ATCGTTGACTATGGTGTCCGATTCTTCTTTTATACTAGTAAAGAGCCTGTAGCTTCTATT ATTACGAAGCTGAACTCTCTAAATGAGCCGCTTGTCACAATGCCAATTGGTTATGTGAC ACATGGTTTTAATCTTGAAGAGGCTGCGCGCTGTATGCGTTCTCTTAAAGCTCCTGCC GTAGTGTCAGTATCATCACCAGATGCTGTTACTACATATAATGGATACCTCACTTCGTC ATCAAAGACATCTGAGGAGCACTTTGTAGAAACAGTTTCTTTGGCTGGCTCTTACAGA GATTGGTCCTATTCAGGACAGCGTACAGAGTTAGGTGTTGAATTTCTTAAGCGTGGTG ACAAAATTGTGTACCACACTCTGGAGAGCCCCGTCGAGTTTCATCTTGACGGTGAGGT TCTTTCACTTGACAAACTAAAGAGTCTCTTATCCCTGCGGGAGGTTAAGACTATAAAAG TGTTCACAACTGTGGACAACACTAATCTCCACACACAGCTTGTGGATATGTCTATGACA TATGGACAGCAGTTTGGTCCAACATACTTGGATGGTGCTGATGTTACAAAAATTAAACC TCATGTAAATCATGAGGGTAAGACTTTCTTTGTACTACCTAGTGATGACACACTACGTA GTGAAGCTTTCGAGTACTACCATACTCTTGATGAGAGTTTTCTTGGTAGGTACATGTCT GCTTTAAACCACACAAAGAAATGGAAATTTCCTCAAGTTGGTGGTTTAACTTCAATTAA ATGGGCTGATAACAATTGTTATTTGTCTAGTGTTTTATTAGCACTTCAACAGCTTGAAGT CAAATTCAATGCACCAGCACTTCAAGAGGCTTATTATAGAGCCCGTGCTGGTGATGCT GCTAACTTTTGTGCACTCATACTCGCTTACAGTAATAAAACTGTTGGCGAGCTTGGTGA TGTCAGAGAAACTATGACCCATCTTCTACAGCATGCTAATTTGGAATCTGCAAAGCGA GTTCTTAATGTGGTGTGTAAACATTGTGGTCAGAAAACTACTACCTTAACGGGTGTAGA AGCTGTGATGTATATGGGTACTCTATCTTATGATAATCTTAAGACAGGTGTTTCCATTC CATGTGTGTGTGGTCGTGATGCTACACAATATCTAGTACAACAAGAGTCTTCTTTTGTT ATGATGTCTGCACCACCTGCTGAGTATAAATTACAGCAAGGTACATTCTTATGTGCGAA TGAGTACACTGGTAACTATCAGTGTGGTCATTACACTCATATAACTGCTAAGGAGACCC TCTATCGTATTGACGGAGCTCACCTTACAAAGATGTCAGAGTACAAAGGACCAGTGAC TGATGTTTTCTACAAGGAAACATCTTACACTACAACCATCAAGCCTGTGTCGTATAAAC TCGATGGAGTTACTTACACAGAGATTGAACCAAAATTGGATGGGTATTATAAAAAGGAT AATGCTTACTATACAGAGCAGCCTATAGACCTTGTACCAACTCAACCATTACCAAATGC GAGTTTTGATAATTTCAAACTCACATGTTCTAACACAAAATTTGCTGATGATTTAAATCA

		AATGACAGGCTTCACAAAGCCAGCTTCACGAGAGCTATCTGTCACATTCTTCCCAGAC TTGAATGGCGATGTAGTGGCTATTGACTATAGACACTATTCAGCGAGTTTCAAGAAAG GTGCTAAATTACTGCATAAGCCAATTGTTTGGCACATTAACCAGGCTACAACCAAGACA ACGTTCAAACCAAACACTTGGTGTTTACGTTGTCTTTGGAGTACAAAGCCAGTAGATAC TTCAAATTCATTTGAAGTTCTGGCAGTAGAAGACACACAAGGAATGGACAATCTTGCTT GTGAAAGTCAACAACCCACCTCTGAAGAAGTAGTGGAAAATCCTACCATACAGAAGGA AGTCATAGAGTGTGACGTGAAAACTACCGAAGTTGTAGGCAATGTCATACTTAAACCAT CAGATGAAGGTGTTAAAGTAACACAAGAGTTAGGTCATGAGGATCTTATGGCTGCTTA TGTGGAAAACACAAGCATTACCATTAAGAAACCTAATGAGCTTTCACTAGCCTTAGGTT TAAAAACAATTGCCACTCATGGTATTGCTGCAATTAATAGTGTTCCTTGGAGTAAAATTT TGGCTTATGTCAAACCATTCTTAGGACAAGCAGCAATTACAACATCAAATTGCGCTAAG AGATTAGCACAACGTGTGTTTAACAATTATATGCCTTATGTGTTTACATTATTGTTCCAA TTGTGTACTTTTACTAAAAGTACCAATTCTAGAATTAGAGCTTCACTACCTACAACTATT GCTAAAAATAGTGTTAAGAGTGTTGCTAAATTATGTTTGGATGCCGGCATTAATTATGT GAAGTCACCCAAATTTTCTAAATTGTTCACAATCGCTATGTGGCTATTGTTGTTAAGTAT TTGCTTAGGTTCTCTAATCTGTGTAACTGCTGCTTTTGGTGTACTCTTATCTAATTTTGG TGCTCCTTCTTATTGTAATGGCGTTAGAGAATTGTATCTTAATTCGTCTAACGTTACTAC TATGGATTTCTGTGAAGGTTCTTTTCCTTGCAGCATTTGTTTAAGTGGATTAGACTCCC TTGATTCTTATCCAGCTCTTGAAACCATTCAGGTGACGATTTCATCGTACAAGCTAGAC TTGACAATTTTAGGTCTGGCCGCTGAGTGGGTTTTGGCATATATGTTGTTCACAAAATT CTTTTATTTATTAGGTCTTTCAGCTATAATGCAGGTGTTCTTTGGCTATTTTGCTAGTCA TTTCATCAGCAATTCTTGGCTCATGTGGTTTATCATTAGTATTGTACAAATGGCACCCG TTTCTGCAATGGTTAGGATGTACATCTTCTTTGCTTCTTTCTACTACATATGGAAGAGCT ATGTTCATATCATGGATGGTTGCACCTCTTCGACTTGCATGATGTGCTATAAGCGCAAT CGTGCCACACGCGTTGAGTGTACAACTATTGTTAATGGCATGAAGAGATCTTTCTATGT CTATGCAAATGGAGGCCGTGGCTTCTGCAAGACTCACAATTGGAATTGTCTCAATTGT GACACATTTTGCACTGGTAGTACATTCATTAGTGATGAAGTTGCTCGTGATTTGTCACT CCAGTTTAAAAGACCAATCAACCCTACTGACCAGTCATCGTATATTGTTGATAGTGTTG CTGTGAAAAATGGCGCGCTTCACCTCTACTTTGACAAGGCTGGTCAAAAGACCTATGA GAGACATCCGCTCTCCCATTTTGTCAATTTAGACAATTTGAGAGCTAACAACACTAAAG GTTCACTGCCTATTAATGTCATAGTTTTTGATGGCAAGTCCAAATGCGACGAGTCTGCT TCTAAGTCTGCTTCTGTGTACTACAGTCAGCTGATGTGCCAACCTATTCTGTTGCTTGA CCAAGCTCTTGTATCAGACGTTGGAGATAGTACTGAAGTTTCCGTTAAGATGTTTGATG CTTATGTCGACACCTTTTCAGCAACTTTTAGTGTTCCTATGGAAAAACTTAAGGCACTT GTTGCTACAGCTCACAGCGAGTTAGCAAAGGGTGTAGCTTTAGATGGTGTCCTTTCTA CATTCGTGTCAGCTGCCCGACAAGGTGTTGTTGATACCGATGTTGACACAAAGGATGT TATTGAATGTCTCAAACTTTCACATCACTCTGACTTAGAAGTGACAGGTGACAGTTGTA ACAATTTCATGCTCACCTATAATAAGGTTGAAAACATGACGCCCAGAGATCTTGGCGC ATGTATTGACTGTAATGCAAGGCATATCAATGCCCAAGTAGCAAAAAGTCACAATGTTT CACTCATCTGGAATGTAAAAGACTACATGTCTTTATCTGAACAGCTGCGTAAACAAATT CGTAGTGCTGCCAAGAAGAACAACATACCTTTTAGACTAACTTGTGCTACAACTAGACA GGTTGTCAATGTCATAACTACTAAAATCTCACTCAAGGGTGGTAAGATTGTTAGTACTT GTTTTAAACTTATGCTTAAGGCCACATTATTGTGCGTTCTTGCTGCATTGGTTTGTTATA TCGTTATGCCAGTACATACATTGTCAATCCATGATGGTTACACAAATGAAATCATTGGT TACAAAGCCATTCAGGATGGTGTCACTCGTGACATCATTTCTACTGATGATTGTTTTGC AAATAAACATGCTGGTTTTGACGCATGGTTTAGCCAGCGTGGTGGTTCATACAAAAAT GACAAAAGCTGCCCTGTAGTAGCTGCTATCATTACAAGAGAGATTGGTTTCATAGTGC CTGGCTTACCGGGTACTGTGCTGAGAGCAATCAATGGTGACTTCTTGCATTTTCTACC TCGTGTTTTTAGTGCTGTTGGCAACATTTGCTACACACCTTCCAAACTCATTGAGTATA GTGATTTTGCTACCTCTGCTTGCGTTCTTGCTGCTGAGTGTACAATTTTTAAGGATGCT ATGGGCAAACCTGTGCCATATTGTTATGACACTAATTTGCTAGAGGGTTCTATTTCTTA TAGTGAGCTTCGTCCAGACACTCGTTATGTGCTTATGGATGGTTCCATCATACAGTTTC CTAACACTTACCTGGAGGGTTCTGTTAGAGTAGTAACAACTTTTGATGCTGAGTACTGT AGACATGGTACATGCGAAAGGTCAGAAGTAGGTATTTGCCTATCTACCAGTGGTAGAT GGGTTCTTAATAATGAGCATTACAGAGCTCTATCAGGAGTTTTCTGTGGTGTTGATGCG ATGAATCTCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGT GTCTGCTTCAGTAGTGGCTGGTGGTATTATTGCCATATTGGTGACTTGTGCTGCCTAC TACTTTATGAAATTCAGACGTGTTTTTGGTGAGTACAACCATGTTGTTGCTGCTAATGC ACTTTTGTTTTTGATGTCTTTCACTATACTCTGTCTGGTACCAGCTTACAGCTTTCTGCC GGGAGTCTACTCAGTCTTTTACTTGTACTTGACATTCTATTTCACCAATGATGTTTCATT CTTGGCTCACCTTCAATGGTTTGCCATGTTTTCTCCTATTGTGCCTTTTTGGATAACAG CAATCTATGTATTCTGTATTTCTCTGAAGCACTGCCATTGGTTCTTTAACAACTATCTTA GGAAAAGAGTCATGTTTAATGGAGTTACATTTAGTACCTTCGAGGAGGCTGCTTTGTGT ACCTTTTTGCTCAACAAGGAAATGTACCTAAAATTGCGTAGCGAGACACTGTTGCCACT TACACAGTATAACAGGTATCTTGCTCTATATAACAAGTACAAGTATTTCAGTGGAGCCT TAGATACTACCAGCTATCGTGAAGCAGCTTGCTGCCACTTAGCAAAGGCTCTAAATGA

		CTTTAGCAACTCAGGTGCTGATGTTCTCTACCAACCACCACAGACATCAATCACTTCTG CTGTTCTGCAGAGTGGTTTTAGGAAAATGGCATTCCCGTCAGGCAAAGTTGAAGGGTG CATGGTACAAGTAACCTGTGGAACTACAACTCTTAATGGATTGTGGTTGGATGACACA GTATACTGTCCAAGACATGTCATTTGCACAGCAGAAGACATGCTTAATCCTAACTATGA AGATCTGCTCATTCGCAAATCCAACCATAGCTTTCTTGTTCAGGCTGGCAATGTTCAAC TTCGTGTTATTGGCCATTCTATGCAAAATTGTCTGCTTAGGCTTAAAGTTGATACTTCTA ACCCTAAGACACCCAAGTATAAATTTGTCCGTATCCAACCTGGTCAAACATTTTCAGTT CTAGCATGCTACAATGGTTCACCATCTGGTGTTTATCAGTGTGCCATGAGACCTAATCA TACCATTAAAGGTTCTTTCCTTAATGGATCATGTGGTAGTGTTGGTTTTAACATTGATTA TGATTGCGTGTCTTTCTGCTATATGCATCATATGGAGCTTCCAACAGGAGTACACGCT GGTACTGACTTAGAAGGTAAATTCTATGGTCCATTTGTTGACAGACAAACTGCACAGG CTGCAGGTACAGACACAACCATAACATTAAATGTTTTGGCATGGCTGTATGCTGCTGTT ATCAATGGTGATAGGTGGTTTCTTAATAGATTCACCACTACTTTGAATGACTTTAACCTT GTGGCAATGAAGTACAACTATGAACCTTTGACACAAGATCATGTTGACATATTGGGAC CTCTTTCTGCTCAAACAGGAATTGCCGTCTTAGATATGTGTGCTGCTTTGAAAGAGCTG CTGCAGAATGGTATGAATGGTCGTACTATCCTTGGTAGCACTATTTTAGAAGATGAGTT TACACCATTTGATGTTGTTAGACAATGCTCTGGTGTTACCTTCCAAGGTAAGTTCAAGA AAATTGTTAAGGGCACTCATCATTGGATGCTTTTAACTTTCTTGACATCACTATTGATTC TTGTTCAAAGTACACAGTGGTCACTGTTTTTCTTTGTTTACGAGAATGCTTTCTTGCCAT TTACTCTTGGTATTATGGCAATTGCTGCATGTGCTATGCTGCTTGTTAAGCATAAGCAC GCATTCTTGTGCTTGTTTCTGTTACCTTCTCTTGCAACAGTTGCTTACTTTAATATGGTC TACATGCCTGCTAGCTGGGTGATGCGTATCATGACATGGCTTGAATTGGCTGACACTA GCTTGTCTGGTTATAGGCTTAAGGATTGTGTTATGTATGCTTCAGCTTTAGTTTTGCTTA TTCTCATGACAGCTCGCACTGTTTATGATGATGCTGCTAGACGTGTTTGGACACTGAT GAATGTCATTACACTTGTTTACAAAGTCTACTATGGTAATGCTTTAGATCAAGCTATTTC CATGTGGGCCTTAGTTATTTCTGTAACCTCTAACTATTCTGGTGTCGTTACGACTATCA TGTTTTTAGCTAGAGCTATAGTGTTTGTGTGTGTTGAGTATTACCCATTGTTATTTATTA CTGGCAACACCTTACAGTGTATCATGCTTGTTTATTGTTTCTTAGGCTATTGTTGCTGC TGCTACTTTGGCCTTTTCTGTTTACTCAACCGTTACTTCAGGCTTACTCTTGGTGTTTAT GACTACTTGGTCTCTACACAAGAATTTAGGTATATGAACTCCCAGGGGCTTTTGCCTCC TAAGAGTAGTATTGATGCTTTCAAGCTTAACATTAAGTTGTTGGGTATTGGAGGTAAAC CATGTATCAAGGTTGCTACTGTACAGTCTAAAATGTCTGACGTAAAGTGCACATCTGTG GTACTGCTCTCGGTTCTTCAACAACTTAGAGTAGAGTCATCTTCTAAATTGTGGGCACA ATGTGTACAACTCCACAATGATATTCTTCTTGCAAAAGACACAACTGAAGCTTTCGAGA AGATGGTTTCTCTTTTGTCTGTTTTGCTATCCATGCAGGGTGCTGTAGACATTAATAGG TTGTGCGAGGAAATGCTCGATAACCGTGCTACTCTTCAGGCTATTGCTTCAGAATTTAG TTCTTTACCATCATATGCCGCTTATGCCACTGCCCAGGAGGCCTATGAGCAGGCTGTA GCTAATGGTGATTCTGAAGTCGTTCTCAAAAAGTTAAAGAAATCTTTGAATGTGGCTAA ATCTGAGTTTGACCGTGATGCTGCCATGCAACGCAAGTTGGAAAAGATGGCAGATCAG GCTATGACCCAAATGTACAAACAGGCAAGATCTGAGGACAAGAGGGCAAAAGTAACTA GTGCTATGCAAACAATGCTCTTCACTATGCTTAGGAAGCTTGATAATGATGCACTTAAC AACATTATCAACAATGCGCGTGATGGTTGTGTTCCACTCAACATCATACCATTGACTAC AGCAGCCAAACTCATGGTTGTTGTCCCTGATTATGGTACCTACAAGAACACTTGTGAT GGTAACACCTTTACATATGCATCTGCACTCTGGGAAATCCAGCAAGTTGTTGATGCGG ATAGCAAGATTGTTCAACTTAGTGAAATTAACATGGACAATTCACCAAATTTGGCTTGG CCTCTTATTGTTACAGCTCTAAGAGCCAACTCAGCTGTTAAACTACAGAATAATGAACT GAGTCCAGTAGCACTACGACAGATGTCCTGTGCGGCTGGTACCACACAAACAGCTTG TACTGATGACAATGCACTTGCCTACTATAACAATTCGAAGGGAGGTAGGTTTGTGCTG GCATTACTATCAGACCACCAAGATCTCAAATGGGCTAGATTCCCTAAGAGTGATGGTA CAGGTACAATTTACACAGAACTGGAACCACCTTGTAGGTTTGTTACAGACACACCAAAA GGGCCTAAAGTGAAATACTTGTACTTCATCAAAGGCTTAAACAACCTAAATAGAGGTAT GGTGCTGGGCAGTTTAGCTGCTACAGTACGTCTTCAGGCTGGAAATGCTACAGAAGTA CCTGCCAATTCAACTGTGCTTTCCTTCTGTGCTTTTGCAGTAGACCCTGCTAAAGCATA TAAGGATTACCTAGCAAGTGGAGGACAACCAATCACCAACTGTGTGAAGATGTTGTGT ACACACACTGGTACAGGACAGGCAATTACTGTAACACCAGAAGCTAACATGGACCAAG AGTCCTTTGGTGGTGCTTCATGTTGTCTGTATTGTAGATGCCACATTGACCATCCAAAT CCTAAAGGATTCTGTGACTTGAAAGGTAAGTACGTCCAAATACCTACCACTTGTGCTAA TGACCCAGTGGGTTTTACACTTAGAAACACAGTCTGTACCGTCTGCGGAATGTGGAAA GGTTATGGCTGTAGTTGTGACCAACTCCGCGAACCCTTGATGCAGTCTGCGGATGCAT CAACGTTTTTAAACGGGTTTGCGGTGTAAGTGCAGCCCGTCTTACACCGTGCGGCACA GGCACTAGTACTGATGTCGTCTACAGGGCTTTTGATATTTACAACGAAAAAGTTGCTG GTTTTGCAAAGTTCCTAAAAACTAATTGCTGTCGCTTCCAGGAGAAGGATGAGGAAGG CAATTTATTAGACTCTTACTTTGTAGTTAAGAGGCATACTATGTCTAACTACCAACATGA AGAGACTATTTATAACTTGGTTAAAGATTGTCCAGCGGTTGCTGTCCATGACTTTTTCA AGTTTAGAGTAGATGGTGACATGGTACCACATATATCACGTCAGCGTCTAACTAAATAC ACAATGGCTGATTTAGTCTATGCTCTACGTCATTTTGATGAGGGTAATTGTGATACATT

		AAAAGAAATACTCGTCACATACAATTGCTGTGATGATGATTATTTCAATAAGAAGGATT GGTATGACTTCGTAGAGAATCCTGACATCTTACGCGTATATGCTAACTTAGGTGAGCG TGTACGCCAATCATTATTAAAGACTGTACAATTCTGCGATGCTATGCGTGATGCAGGCA TTGTAGGCGTACTGACATTAGATAATCAGGATCTTAATGGGAACTGGTACGATTTCGGT GATTTCGTACAAGTAGCACCAGGCTGCGGAGTTCCTATTGTGGATTCATATTACTCATT GCTGATGCCCATCCTCACTTTGACTAGGGCATTGGCTGCTGAGTCCCATATGGATGCT GATCTCGCAAAACCACTTATTAAGTGGGATTTGCTGAAATATGATTTTACGGAAGAGAG ACTTTGTCTCTTCGACCGTTATTTTAAATATTGGGACCAGACATACCATCCCAATTGTAT TAACTGTTTGGATGATAGGTGTATCCTTCATTGTGCAAACTTTAATGTGTTATTTTCTAC TGTGTTTCCACCTACAAGTTTTGGACCACTAGTAAGAAAAATATTTGTAGATGGTGTTC CTTTTGTTGTTTCAACTGGATACCATTTTCGTGAGTTAGGAGTCGTACATAATCAGGAT GTAAACTTACATAGCTCGCGTCTCAGTTTCAAGGAACTTTTAGTGTATGCTGCTGATCC AGCTATGCATGCAGCTTCTGGCAATTTATTGCTAGATAAACGCACTACATGCTTTTCAG TAGCTGCACTAACAAACAATGTTGCTTTTCAAACTGTCAAACCCGGTAATTTTAATAAA GACTTTTATGACTTTGCTGTGTCTAAAGGTTTCTTTAAGGAAGGAAGTTCTGTTGAACT AAAACACTTCTTCTTTGCTCAGGATGGCAACGCTGCTATCAGTGATTATGACTATTATC GTTATAATCTGCCAACAATGTGTGATATCAGACAACTCCTATTCGTAGTTGAAGTTGTT GATAAATACTTTGATTGTTACGATGGTGGCTGTATTAATGCCAACCAAGTAATCGTTAA CAATCTGGATAAATCAGCTGGTTTCCCATTTAATAAATGGGGTAAGGCTAGACTTTATT ATGACTCAATGAGTTATGAGGATCAAGATGCACTTTTCGCGTATACTAAGCGTAATGTC ATCCCTACTATAACTCAAATGAATCTTAAGTATGCCATTAGTGCAAAGAATAGAGCTCG CACCGTAGCTGGTGTCTCTATCTGTAGTACTATGACAAATAGACAGTTTCATCAGAAAT TATTGAAGTCAATAGCCGCCACTAGAGGAGCTACTGTGGTAATTGGAACAAGCAAGTT TTACGGTGGCTGGCATAATATGTTAAAAACTGTTTACAGTGATGTAGAAACTCCACACC TTATGGGTTGGGATTATCCAAAATGTGACAGAGCCATGCCTAACATGCTTAGGATAAT GGCCTCTCTTGTTCTTGCTCGCAAACATAACACTTGCTGTAACTTATCACACCGTTTCT ACAGGTTAGCTAACGAGTGTGCGCAAGTATTAAGTGAGATGGTCATGTGTGGCGGCT CACTATATGTTAAACCAGGTGGAACATCATCCGGTGATGCTACAACTGCTTATGCTAAT AGTGTCTTTAACATTTGTCAAGCTGTTACAGCCAATGTAAATGCACTTCTTTCAACTGAT GGTAATAAGATAGCTGACAAGTATGTCCGCAATCTACAACACAGGCTCTATGAGTGTC TCTATAGAAATAGGGATGTTGATCATGAATTCGTGGATGAGTTTTACGCTTACCTGCGT AAACATTTCTCCATGATGATTCTTTCTGATGATGCCGTTGTGTGCTATAACAGTAACTAT GCGGCTCAAGGTTTAGTAGCTAGCATTAAGAACTTTAAGGCAGTTCTTTATTATCAAAA TAATGTGTTCATGTCTGAGGCAAAATGTTGGACTGAGACTGACCTTACTAAAGGACCT CACGAATTTTGCTCACAGCATACAATGCTAGTTAAACAAGGAGATGATTACGTGTACCT GCCTTACCCAGATCCATCAAGAATATTAGGCGCAGGCTGTTTTGTCGATGATATTGTCA AAACAGATGGTACACTTATGATTGAAAGGTTCGTGTCACTGGCTATTGATGCTTACCCA CTTACAAAACATCCTAATCAGGAGTATGCTGATGTCTTTCACTTGTATTTACAATACATT AGAAAGTTACATGATGAGCTTACTGGCCACATGTTGGACATGTATTCCGTAATGCTAAC TAATGATAACACCTCACGGTACTGGGAACCTGAGTTTTATGAGGCTATGTACACACCA CATACAGTCTTGCAGGCTGTAGGTGCTTGTGTATTGTGCAATTCACAGACTTCACTTCG TTGCGGTGCCTGTATTAGGAGACCATTCCTATGTTGCAAGTGCTGCTATGACCATGTC ATTTCAACATCACACAAATTAGTGTTGTCTGTTAATCCCTATGTTTGCAATGCCCCAGG TTGTGATGTCACTGATGTGACACAACTGTATCTAGGAGGTATGAGCTATTATTGCAAGT CACATAAGCCTCCCATTAGTTTTCCATTATGTGCTAATGGTCAGGTTTTTGGTTTATACA AAAACACATGTGTAGGCAGTGACAATGTCACTGACTTCAATGCGATAGCAACATGTGA TTGGACTAATGCTGGCGATTACATACTTGCCAACACTTGTACTGAGAGACTCAAGCTTT TCGCAGCAGAAACGCTCAAAGCCACTGAGGAAACATTTAAGCTGTCATATGGTATTGC CACTGTACGCGAAGTACTCTCTGACAGAGAATTGCATCTTTCATGGGAGGTTGGAAAA CCTAGACCACCATTGAACAGAAACTATGTCTTTACTGGTTACCGTGTAACTAAAAATAG TAAAGTACAGATTGGAGAGTACACCTTTGAAAAAGGTGACTATGGTGATGCTGTTGTG TACAGAGGTACTACGACATACAAGTTGAATGTTGGTGATTACTTTGTGTTGACATCTCA CACTGTAATGCCACTTAGTGCACCTACTCTAGTGCCACAAGAGCACTATGTGAGAATT ACTGGCTTGTACCCAACACTCAACATCTCAGATGAGTTTTCTAGCAATGTTGCAAATTA TCAAAAGGTCGGCATGCAAAAGTACTCTACACTCCAAGGACCACCTGGTACTGGTAAG AGTCATTTTGCCATCGGACTTGCTCTCTATTACCCATCTGCTCGCATAGTGTATACGGC ATGCTCTCATGCAGCTGTTGATGCCCTATGTGAAAAGGCATTAAAATATTTGCCCATAG ATAAATGTAGTAGAATCATACCTGCGCGTGCGCGCGTAGAGTGTTTTGATAAATTCAAA GTGAATTCAACACTAGAACAGTATGTTTTCTGCACTGTAAATGCATTGCCAGAAACAAC TGCTGACATTGTAGTCTTTGATGAAATCTCTATGGCTACTAATTATGACTTGAGTGTTGT CAATGCTAGACTTCGTGCAAAACACTACGTCTATATTGGCGATCCTGCTCAATTACCAG CCCCCCGCACATTGCTGACTAAAGGCACACTAGAACCAGAATATTTTAATTCAGTGTG CAGACTTATGAAAACAATAGGTCCAGACATGTTCCTTGGAACTTGTCGCCGTTGTCCT GCTGAAATTGTTGACACTGTGAGTGCTTTAGTTTATGACAATAAGCTAAAAGCACACAA GGATAAGTCAGCTCAATGCTTCAAAATGTTCTACAAAGGTGTTATTACACATGATGTTT CATCTGCAATCAACAGACCTCAAATAGGCGTTGTAAGAGAATTTCTTACACGCAATCCT

		GCTTGGAGAAAAGCTGTTTTTATCTCACCTTATAATTCACAGAACGCTGTAGCTTCAAA AATCTTAGGATTGCCTACGCAGACTGTTGATTCATCACAGGGTTCTGAATATGACTATG TCATATTCACACAAACTACTGAAACAGCACACTCTTGTAATGTCAACCGCTTCAATGTG GCTATCACAAGGGCAAAAATTGGCATTTTGTGCATAATGTCTGATAGAGATCTTTATGA CAAACTGCAATTTACAAGTCTAGAAATACCACGTCGCAATGTGGCTACATTACAAGCAG AAAATGTAACTGGACTTTTTAAGGACTGTAGTAAGATCATTACTGGTCTTCATCCTACA CAGGCACCTACACACCTCAGCGTTGATATAAAGTTCAAGACTGAAGGATTATGTGTTG ACATACCAGGCATACCAAAGGACATGACCTACCGTAGACTCATCTCTATGATGGGTTT CAAAATGAATTACCAAGTCAATGGTTACCCTAATATGTTTATCACCCGCGAAGAAGCTA TTCGTCACGTTCGTGCGTGGATTGGCTTTGATGTAGAGGGCTGTCATGCAACTAGAGA TGCTGTGGGTACTAACCTACCTCTCCAGCTAGGATTTTCTACAGGTGTTAACTTAGTAG CTGTACCGACTGGTTATGTTGACACTGAAAATAACACAGAATTCACCAGAGTTAATGCA AAACCTCCACCAGGTGACCAGTTTAAACATCTTATACCACTCATGTATAAAGGCTTGCC CTGGAATGTAGTGCGTATTAAGATAGTACAAATGCTCAGTGATACACTGAAAGGATTGT CAGACAGAGTCGTGTTCGTCCTTTGGGCGCATGGCTTTGAGCTTACATCAATGAAGTA CTTTGTCAAGATTGGACCTGAAAGAACGTGTTGTCTGTGTGACAAACGTGCAACTTGC TTTTCTACTTCATCAGATACTTATGCCTGCTGGAATCATTCTGTGGGTTTTGACTATGTC TATAACCCATTTATGATTGATGTTCAGCAGTGGGGCTTTACGGGTAACCTTCAGAGTAA CCATGACCAACATTGCCAGGTACATGGAAATGCACATGTGGCTAGTTGTGATGCTATC ATGACTAGATGTTTAGCAGTCCATGAGTGCTTTGTTAAGCGCGTTGATTGGTCTGTTGA ATACCCTATTATAGGAGATGAACTGAGGGTTAATTCTGCTTGCAGAAAAGTACAACACA TGGTTGTGAAGTCTGCATTGCTTGCTGATAAGTTTCCAGTTCTTCATGACATTGGAAAT CCAAAGGCTATCAAGTGTGTGCCTCAGGCTGAAGTAGAATGGAAGTTCTACGATGCTC AGCCATGTAGTGACAAAGCTTACAAAATAGAGGAACTCTTCTATTCTTATGCTACACAT CACGATAAATTCACTGATGGTGTTTGTTTGTTTTGGAATTGTAACGTTGATCGTTACCC AGCCAATGCAATTGTGTGTAGGTTTGACACAAGAGTCTTGTCAAACTTGAACTTACCAG GCTGTGATGGTGGTAGTTTGTATGTGAATAAGCATGCATTCCACACTCCAGCTTTCGAT AAAAGTGCATTTACTAATTTAAAGCAATTGCCTTTCTTTTACTATTCTGATAGTCCTTGT GAGTCTCATGGCAAACAAGTAGTGTCGGATATTGATTATGTTCCACTCAAATCTGCTAC GTGTATTACACGATGCAATTTAGGTGGTGCTGTTTGCAGACACCATGCAAATGAGTAC CGACAGTACTTGGATGCATATAATATGATGATTTCTGCTGGATTTAGCCTATGGATTTA CAAACAATTTGATACTTATAACCTGTGGAATACATTTACCAGGTTACAGAGTTTAGAAAA TGTGGCTTATAATGTTGTTAATAAAGGACACTTTGATGGACACGCCGGCGAAGCACCT GTTTCCATCATTAATAATGCTGTTTACACAAAGGTAGATGGTATTGATGTGGAGATCTT TGAAAATAAGACAACACTTCCTGTTAATGTTGCATTTGAGCTTTGGGCTAAGCGTAACA TTAAACCAGTGCCAGAGATTAAGATACTCAATAATTTGGGTGTTGATATCGCTGCTAAT ACTGTAATCTGGGACTACAAAAGAGAAGCCCCAGCACATGTATCTACAATAGGTGTCT GCACAATGACTGACATTGCCAAGAAACCTACTGAGAGTGCTTGTTCTTCACTTACTGTC TTGTTTGATGGTAGAGTGGAAGGACAGGTAGACCTTTTTAGAAACGCCCGTAATGGTG TTTTAATAACAGAAGGTTCAGTCAAAGGTCTAACACCTTCAAAGGGACCAGCACAAGC TAGCGTCAATGGAGTCACATTAATTGGAGAATCAGTAAAAACACAGTTTAACTACTTTA AGAAAGTAGACGGCATTATTCAACAGTTGCCTGAAACCTACTTTACTCAGAGCAGAGA CTTAGAGGATTTTAAGCCCAGATCACAAATGGAAACTGACTTTCTCGAGCTCGCTATG GATGAATTCATACAGCGATATAAGCTCGAGGGCTATGCCTTCGAACACATCGTTTATG GAGATTTCAGTCATGGACAACTTGGCGGTCTTCATTTAATGATAGGCTTAGCCAAGCG CTCACAAGATTCACCACTTAAATTAGAGGATTTTATCCCTATGGACAGCACAGTGAAAA ATTACTTCATAACAGATGCGCAAACAGGTTCATCAAAATGTGTGTGTTCTGTGATTGAT CTTTTACTTGATGACTTTGTCGAGATAATAAAGTCACAAGATTTGTCAGTGATTTCAAAA GTGGTCAAGGTTACAATTGACTATGCTGAAATTTCATTCATGCTTTGGTGTAAGGATGG ACATGTTGAAACCTTCTACCCAAAACTACAAGCAAGTCAAGCGTGGCAACCAGGTGTT GCGATGCCTAACTTGTACAAGATGCAAAGAATGCTTCTTGAAAAGTGTGACCTTCAGA ATTATGGTGAAAATGCTGTTATACCAAAAGGAATAATGATGAATGTCGCAAAGTATACT CAACTGTGTCAATACTTAAATACACTTACTTTAGCTGTACCCTACAACATGAGAGTTATT CACTTTGGTGCTGGCTCTGATAAAGGAGTTGCACCAGGTACAGCTGTGCTCAGACAAT GGTTGCCAACTGGCACACTACTTGTCGATTCAGATCTTAATGACTTCGTCTCCGACGC AGATTCTACTTTAATTGGAGACTGTGCAACAGTACATACGGCTAATAAATGGGACCTTA TTATTAGCGATATGTATGACCCTAGGACCAAACATGTGACAAAAGAGAATGACTCTAAA GAAGGGTTTTTCACTTATCTGTGTGGATTTATAAAGCAAAAACTAGCCCTGGGTGGTTC TATAGCTGTAAAGATAACAGAGCATTCTTGGAATGCTGACCTTTACAAGCTTATGGGCC ATTTCTCATGGTGGACAGCTTTTGTTACAAATGTAAATGCATCATCATCGGAAGCATTT TTAATTGGGGCTAACTATCTTGGCAAGCCGAAGGAACAAATTGATGGCTATACCATGC ATGCTAACTACATTTTCTGGAGGAACACAAATCCTATCCAGTTGTCTTCCTATTCACTCT TTGACATGAGCAAATTTCCTCTTAAATTAAGAGGAACTGCTGTAATGTCTCTTAAGGAG AATCAAATCAATGATATGATTTATTCTCTTCTGGAAAAAGGTAGGCTTATCATTAGAGAA AACAACAGAGTTGTGGTTTCAAGTGATATTCTTGTTAACAACTAAACGAACATGTTTATT TTCTTATTATTTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACTTTTGAT

		GATGTTCAAGCTCCTAATTACACTCAACATACTTCATCTATGAGGGGGGTTTACTATCC TGATGAAATTTTTAGATCAGACACTCTTTATTTAACTCAGGATTTATTTCTTCCATTTTAT TCTAATGTTACAGGGTTTCATACTATTAATCATACGTTTGGCAACCCTGTCATACCTTTT AAGGATGGTATTTATTTTGCTGCCACAGAGAAATCAAATGTTGTCCGTGGTTGGGTTTT TGGTTCTACCATGAACAACAAGTCACAGTCGGTGATTATTATTAACAATTCTACTAATGT TGTTATACGAGCATGTAACTTTGAATTGTGTGACAACCCTTTCTTTGCTGTTTCTAAACC CATGGGTACACAGACACATACTATGATATTCGATAATGCATTTAATTGCACTTTCGAGT ACATATCTGATGCCTTTTCGCTTGATGTTTCAGAAAAGTCAGGTAATTTTAAACACTTAC GAGAGTTTGTGTTTAAAAATAAAGATGGGTTTCTCTATGTTTATAAGGGCTATCAACCT ATAGATGTAGTTCGTGATCTACCTTCTGGTTTTAACACTTTGAAACCTATTTTTAAGTTG CCTCTTGGTATTAACATTACAAATTTTAGAGCCATTCTTACAGCCTTTTCACCTGCTCAA GACATTTGGGGCACGTCAGCTGCAGCCTATTTTGTTGGCTATTTAAAGCCAACTACATT TATGCTCAAGTATGATGAAAATGGTACAATCACAGATGCTGTTGATTGTTCTCAAAATC CACTTGCTGAACTCAAATGCTCTGTTAAGAGCTTTGAGATTGACAAAGGAATTTACCAG ACCTCTAATTTCAGGGTTGTTCCCTCAGGAGATGTTGTGAGATTCCCTAATATTACAAA CTTGTGTCCTTTTGGAGAGGTTTTTAATGCTACTAAATTCCCTTCTGTCTATGCATGGG AGAGAAAAAAAATTTCTAATTGTGTTGCTGATTACTCTGTGCTCTACAACTCAACATTTT TTTCAACCTTTAAGTGCTATGGCGTTTCTGCCACTAAGTTGAATGATCTTTGCTTCTCC AATGTCTATGCAGATTCTTTTGTAGTCAAGGGAGATGATGTAAGACAAATAGCGCCAG GACAAACTGGTGTTATTGCTGATTATAATTATAAATTGCCAGATGATTTCATGGGTTGT GTCCTTGCTTGGAATACTAGGAACATTGATGCTACTTCAACTGGTAATTATAATTATAAA TATAGGTATCTTAGACATGGCAAGCTTAGGCCCTTTGAGAGAGACATATCTAATGTGC CTTTCTCCCCTGATGGCAAACCTTGCACCCCACCTGCTCTTAATTGTTATTGGCCATTA AATGATTATGGTTTTTACACCACTACTGGCATTGGCTACCAACCTTACAGAGTTGTAGT ACTTTCTTTTGAACTTTTAAATGCACCGGCCACGGTTTGTGGACCAAAATTATCCACTG ACCTTATTAAGAACCAGTGTGTCAATTTTAATTTTAATGGACTCACTGGTACTGGTGTG TTAACTCCTTCTTCAAAGAGATTTCAACCATTTCAACAATTTGGCCGTGATGTTTCTGAT TTCACTGATTCCGTTCGAGATCCTAAAACATCTGAAATATTAGACATTTCACCTTGCGC TTTTGGGGGTGTAAGTGTAATTACACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTC TATATCAAGATGTTAACTGCACTGATGTTTCTACAGCAATTCATGCAGATCAACTCACA CCAGCTTGGCGCATATATTCTACTGGAAACAATGTATTCCAGACTCAAGCAGGCTGTC TTATAGGAGCTGAGCATGTCGACACTTCTTATGAGTGCGACATTCCTATTGGAGCTGG CATTTGTGCTAGTTACCATACAGTTTCTTTATTACGTAGTACTAGCCAAAAATCTATTGT GGCTTATACTATGTCTTTAGGTGCTGATAGTTCAATTGCTTACTCTAATAACACCATTGC TATACCTACTAACTTTTCAATTAGCATTACTACAGAAGTAATGCCTGTTTCTATGGCTAA AACCTCCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAATGTGCTAATTTGC TTCTCCAATATGGTAGCTTTTGCACACAACTAAATCGTGCACTCTCAGGTATTGCTGCT GAACAGGATCGCAACACACGTGAAGTGTTCGCTCAAGTCAAACAAATGTACAAAACCC CAACTTTGAAATATTTTGGTGGTTTTAATTTTTCACAAATATTACCTGACCCTCTAAAGC CAACTAAGAGGTCTTTTATTGAGGACTTGCTCTTTAATAAGGTGACACTCGCTGATGCT GGCTTCATGAAGCAATATGGCGAATGCCTAGGTGATATTAATGCTAGAGATCTCATTTG TGCGCAGAAGTTCAATGGACTTACAGTGTTGCCACCTCTGCTCACTGATGATATGATT GCTGCCTACACTGCTGCTCTAGTTAGTGGTACTGCCACTGCTGGATGGACATTTGGTG CTGGCGCTGCTCTTCAAATACCTTTTGCTATGCAAATGGCATATAGGTTCAATGGCATT GGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAACAAATCGCCAACCAATTTAACAA GGCGATTAGTCAAATTCAAGAATCACTTACAACAACATCAACTGCATTGGGCAAGCTG CAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTTAAACAACTTAGCTC TAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCGCGACTTGATAAAGTCG AGGCGGAGGTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCTTCAAACCTA TGTAACACAACAACTAATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCT ACTAAAATGTCTGAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAAAGGG CTACCACCTTATGTCCTTCCCACAAGCAGCCCCGCATGGTGTTGTCTTCCTACATGTC ACGTATGTGCCATCCCAGGAGAGGAACTTCACCACAGCGCCAGCAATTTGTCATGAAG GCAAAGCATACTTCCCTCGTGAAGGTGTTTTTGTGTTTAATGGCACTTCTTGGTTTATT ACACAGAGGAACTTCTTTTCTCCACAAATAATTACTACAGACAATACATTTGTCTCAGG AAATTGTGATGTCGTTATTGGCATCATTAACAACACAGTTTATGATCCTCTGCAACCTG AGCTTGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAATCATACATCACCAGAT GTTGATCTTGGCGACATTTCAGGCATTAACGCTTCTGTCGTCAACATTCAAAAAGAAAT TGACCGCCTCAATGAGGTCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAAT TGGGAAAATATGAGCAATATATTAAATGGCCTTGGTATGTTTGGCTCGGCTTCATTGCT GGACTAATTGCCATCGTCATGGTTACAATCTTGCTTTGTTGCATGACTAGTTGTTGCAG TTGCCTCAAGGGTGCATGCTCTTGTGGTTCTTGCTGCAAGTTTGATGAGGATGACTCT GAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAAACGAACTTATGGATTTGTTT ATGAGATTTTTTACTCTTAGATCAATTACTGCACAGCCAGTAAAAATTGACAATGCTTCT CCTGCAAGTACTGTTCATGCTACAGCAACGATACCGCTACAAGCCTCACTCCCTTTCG GATGGCTTGTTATTGGCGTTGCATTTCTTGCTGTTTTTCAGAGCGCTACCAAAATAATT

		GCGCTCAATAAAAGATGGCAGCTAGCCCTTTATAAGGGCTTCCAGTTCATTTGCAATTT ACTGCTGCTATTTGTTACCATCTATTCACATCTTTTGCTTGTCGCTGCAGGTATGGAGG CGCAATTTTTGTACCTCTATGCCTTGATATATTTTCTACAATGCATCAACGCATGTAGAA TTATTATGAGATGTTGGCTTTGTTGGAAGTGCAAATCCAAGAACCCATTACTTTATGAT GCCAACTACTTTGTTTGCTGGCACACACATAACTATGACTACTGTATACCATATAACAG TGTCACAGATACAATTGTCGTTACTGAAGGTGACGGCATTTCAACACCAAAACTCAAAG AAGACTACCAAATTGGTGGTTATTCTGAGGATAGGCACTCAGGTGTTAAAGACTATGT CGTTGTACATGGCTATTTCACCGAAGTTTACTACCAGCTTGAGTCTACACAAATTACTA CAGACACTGGTATTGAAAATGCTACATTCTTCATCTTTAACAAGCTTGTTAAAGACCCA CCGAATGTGCAAATACACACAATCGACGGCTCTTCAGGAGTTGCTAATCCAGCAATGG ATCCAATTTATGATGAGCCGACGACGACTACTAGCGTGCCTTTGTAAGCACAAGAAAG TGAGTACGAACTTATGTACTCATTCGTTTCGGAAGAAACAGGTACGTTAATAGTTAATA GCGTACTTCTTTTTCTTGCTTTCGTGGTATTCTTGCTAGTCACACTAGCCATCCTTACT GCGCTTCGATTGTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAAACCAAC GGTTTACGTCTACTCGCGTGTTAAAAATCTGAACTCTTCTGAAGGAGTTCCTGATCTTC TGGTCTAAACGAACTAACTATTATTATTATTCTGTTTGGAACTTTAACATTGCTTATCAT GGCAGACAACGGTACTATTACCGTTGAGGAGCTTAAACAACTCCTGGAACAATGGAAC CTAGTAATAGGTTTCCTATTCCTAGCCTGGATTATGTTACTACAATTTGCCTATTCTAAT CGGAACAGGTTTTTGTACATAATAAAGCTTGTTTTCCTCTGGCTCTTGTGGCCAGTAAC ACTTGCTTGTTTTGTGCTTGCTGCTGTCTACAGAATTAATTGGGTGACTGGCGGGATT GCGATTGCAATGGCTTGTATTGTAGGCTTGATGTGGCTTAGCTACTTCGTTGCTTCCTT CAGGCTGTTTGCTCGTACCCGCTCAATGTGGTCATTCAACCCAGAAACAAACATTCTT CTCAATGTGCCTCTCCGGGGGACAATTGTGACCAGACCGCTCATGGAAAGTGAACTT GTCATTGGTGCTGTGATCATTCGTGGTCACTTGCGAATGGCCGGACACTCCCTAGGG CGCTGTGACATTAAGGACCTGCCAAAAGAGATCACTGTGGCTACATCACGAACGCTTT CTTATTACAAATTAGGAGCGTCGCAGCGTGTAGGCACTGATTCAGGTTTTGCTGCATA CAACCGCTACCGTATTGGAAACTATAAATTAAATACAGACCACGCCGGTAGCAACGAC AATATTGCTTTGCTAGTACAGTAAGTGACAACAGATGTTTCATCTTGTTGACTTCCAGG TTACAATAGCAGAGATATTGATTATCATTATGAGGACTTTCAGGATTGCTATTTGGAATC TTGACGTTATAATAAGTTCAATAGTGAGACAATTATTTAAGCCTCTAACTAAGAAGAATT ATTCGGAGTTAGATGATGAAGAACCTATGGAGTTAGATTATCCATAAAACGAACATGAA AATTATTCTCTTCCTGACATTGATTGTATTTACATCTTGCGAGCTATATCACTATCAGGA GTGTGTTAGAGGTACGACTGTACTACTAAAAGAACCTTGCCCATCAGGAACATACGAG GGCAATTCACCATTTCACCCTCTTGCTGACAATAAATTTGCACTAACTTGCACTAGCAC ACACTTTGCTTTTGCTTGTGCTGACGGTACTCGACATACCTATCAGCTGCGTGCAAGA TCAGTTTCACCAAAACTTTTCATCAGACAAGAGGAGGTTCAACAAGAGCTCTACTCGC CACTTTTTCTCATTGTTGCTGCTCTAGTATTTTTAATACTTTGCTTCACCATTAAGAGAA AGACAGAATGAATGAGCTCACTTTAATTGACTTCTATTTGTGCTTTTTAGCCTTTCTGCT ATTCCTTGTTTTAATAATGCTTATTATATTTTGGTTTTCACTCGAAATCCAGGATCTAGA AGAACCTTGTACCAAAGTCTAAACGAACATGAAACTTCTCATTGTTTTGACTTGTATTTC TCTATGCAGTTGCATATGCACTGTAGTACAGCGCTGTGCATCTAATAAACCTCATGTGC TTGAAGATCCTTGTAAGGTACAACACTAGGGGTAATACTTATAGCACTGCTTGGCTTTG TGCTCTAGGAAAGGTTTTACCTTTTCATAGATGGCACACTATGGTTCAAACATGCACAC CTAATGTTACTATCAACTGTCAAGATCCAGCTGGTGGTGCGCTTATAGCTAGGTGTTG GTACCTTCATGAAGGTCACCAAACTGCTGCATTTAGAGACGTACTTGTTGTTTTAAATA AACGAACAAATTAAAATGTCTGATAATGGACCCCAATCAAACCAACGTAGTGCCCCCC GCATTACATTTGGTGGACCCACAGATTCAACTGACAATAACCAGAATGGAGGACGCAA TGGGGCAAGGCCAAAACAGCGCCGACCCCAAGGTTTACCCAATAATACTGCGTCTTG GTTCACAGCTCTCACTCAGCATGGCAAGGAGGAACTTAGATTCCCTCGAGGCCAGGG CGTTCCAATCAACACCAATAGTGGTCCAGATGACCAAATTGGCTACTACCGAAGAGCT ACCCGACGAGTTCGTGGTGGTGACGGCAAAATGAAAGAGCTCAGCCCCAGATGGTAC TTCTATTACCTAGGAACTGGCCCAGAAGCTTCACTTCCCTACGGCGCTAACAAAGAAG GCATCGTATGGGTTGCAACTGAGGGAGCCTTGAATACACCCAAAGACCACATTGGCA CCCGCAATCCTAATAACAATGCTGCCACCGTGCTACAACTTCCTCAAGGAACAACATT GCCAAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCAGTCAAGCCTCTTCTCGCTC CTCATCACGTAGTCGCGGTAATTCAAGAAATTCAACTCCTGGCAGCAGTAGGGGAAAT TCTCCTGCTCGAATGGCTAGCGGAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTA GACAGATTGAACCAGCTTGAGAGCAAAGTTTCTGGTAAAGGCCAACAACAACAAGGCC AAACTGTCACTAAGAAATCTGCTGCTGAGGCATCTAAAAAGCCTCGCCAAAAACGTAC TGCCACAAAACAGTACAACGTCACTCAAGCATTTGGGAGACGTGGTCCAGAACAAACC CAAGGAAATTTCGGGGACCAAGACCTAATCAGACAAGGAACTGATTACAAACATTGGC CGCAAATTGCACAATTTGCTCCAAGTGCCTCTGCATTCTTTGGAATGTCACGCATTGG CATGGAAGTCACACCTTCGGGAACATGGCTGACTTATCATGGAGCCATTAAATTGGAT GACAAAGATCCACAATTCAAAGACAACGTCATACTGCTGAACAAGCACATTGACGCAT ACAAAACATTCCCACCAACAGAGCCTAAAAAGGACAAAAAGAAAAAGACTGATGAAGC TCAGCCTTTGCCGCAGAGACAAAAGAAGCAGCCCACTGTGACTCTTCTTCCTGCGGCT

		GACATGGATGATTTCTCCAGACAACTTCAAAATTCCATGAGTGGAGCTTCTGCTGATTC AACTCAGGCATAAACACTCATGATGACCACACAAGGCAGATGGGCTATGTAAACGTTT TCGCAATTCCGTTTACGATACATAGTCTACTCTTGTGCAGAATGAATTCTCGTAACTAA ACAGCACAAGTAGGTTTAGTTAACTTTAATCTCACATAGCAATCTTTAATCAATGTGTAA CATTAGGGAGGACTTGAAAGAGCCACCACATTTTCATCGAGGCCACGCGGAGTACGA TCGAGGGTACAGTGAATAATGCTAGGGAGAGCTGCCTATATGGAAGAGCCCTAATGT GTAAAATTAATTTTAGTAGTGCTATCCCCATGTGATTTTAATAGCTTCTTAGGAGAATGA CAAAAAAAAAAAAAAAAAAAAAAA
8	SARS-CoV-2 (GenBank: NC_045512.2)	ATTAAAGGTTTATACCTTCCCAGGTAACAAACCAACCAACTTTCGATCTCTTGTAGATC TGTTCTCTAAACGAACTTTAAAATCTGTGTGGCTGTCACTCGGCTGCATGCTTAGTGCA CTCACGCAGTATAATTAATAACTAATTACTGTCGTTGACAGGACACGAGTAACTCGTCT ATCTTCTGCAGGCTGCTTACGGTTTCGTCCGTGTTGCAGCCGATCATCAGCACATCTA GGTTTCGTCCGGGTGTGACCGAAAGGTAAGATGGAGAGCCTTGTCCCTGGTTTCAAC GAGAAAACACACGTCCAACTCAGTTTGCCTGTTTTACAGGTTCGCGACGTGCTCGTAC GTGGCTTTGGAGACTCCGTGGAGGAGGTCTTATCAGAGGCACGTCAACATCTTAAAGA TGGCACTTGTGGCTTAGTAGAAGTTGAAAAAGGCGTTTTGCCTCAACTTGAACAGCCC TATGTGTTCATCAAACGTTCGGATGCTCGAACTGCACCTCATGGTCATGTTATGGTTGA GCTGGTAGCAGAACTCGAAGGCATTCAGTACGGTCGTAGTGGTGAGACACTTGGTGT CCTTGTCCCTCATGTGGGCGAAATACCAGTGGCTTACCGCAAGGTTCTTCTTCGTAAG AACGGTAATAAAGGAGCTGGTGGCCATAGTTACGGCGCCGATCTAAAGTCATTTGACT TAGGCGACGAGCTTGGCACTGATCCTTATGAAGATTTTCAAGAAAACTGGAACACTAA ACATAGCAGTGGTGTTACCCGTGAACTCATGCGTGAGCTTAACGGAGGGGCATACAC TCGCTATGTCGATAACAACTTCTGTGGCCCTGATGGCTACCCTCTTGAGTGCATTAAA GACCTTCTAGCACGTGCTGGTAAAGCTTCATGCACTTTGTCCGAACAACTGGACTTTAT TGACACTAAGAGGGGTGTATACTGCTGCCGTGAACATGAGCATGAAATTGCTTGGTAC ACGGAACGTTCTGAAAAGAGCTATGAATTGCAGACACCTTTTGAAATTAAATTGGCAAA GAAATTTGACACCTTCAATGGGGAATGTCCAAATTTTGTATTTCCCTTAAATTCCATAAT CAAGACTATTCAACCAAGGGTTGAAAAGAAAAAGCTTGATGGCTTTATGGGTAGAATTC GATCTGTCTATCCAGTTGCGTCACCAAATGAATGCAACCAAATGTGCCTTTCAACTCTC ATGAAGTGTGATCATTGTGGTGAAACTTCATGGCAGACGGGCGATTTTGTTAAAGCCA CTTGCGAATTTTGTGGCACTGAGAATTTGACTAAAGAAGGTGCCACTACTTGTGGTTAC TTACCCCAAAATGCTGTTGTTAAAATTTATTGTCCAGCATGTCACAATTCAGAAGTAGG ACCTGAGCATAGTCTTGCCGAATACCATAATGAATCTGGCTTGAAAACCATTCTTCGTA AGGGTGGTCGCACTATTGCCTTTGGAGGCTGTGTGTTCTCTTATGTTGGTTGCCATAA CAAGTGTGCCTATTGGGTTCCACGTGCTAGCGCTAACATAGGTTGTAACCATACAGGT GTTGTTGGAGAAGGTTCCGAAGGTCTTAATGACAACCTTCTTGAAATACTCCAAAAAGA GAAAGTCAACATCAATATTGTTGGTGACTTTAAACTTAATGAAGAGATCGCCATTATTTT GGCATCTTTTTCTGCTTCCACAAGTGCTTTTGTGGAAACTGTGAAAGGTTTGGATTATA AAGCATTCAAACAAATTGTTGAATCCTGTGGTAATTTTAAAGTTACAAAAGGAAAAGCT AAAAAAGGTGCCTGGAATATTGGTGAACAGAAATCAATACTGAGTCCTCTTTATGCATT TGCATCAGAGGCTGCTCGTGTTGTACGATCAATTTTCTCCCGCACTCTTGAAACTGCT CAAAATTCTGTGCGTGTTTTACAGAAGGCCGCTATAACAATACTAGATGGAATTTCACA GTATTCACTGAGACTCATTGATGCTATGATGTTCACATCTGATTTGGCTACTAACAATC TAGTTGTAATGGCCTACATTACAGGTGGTGTTGTTCAGTTGACTTCGCAGTGGCTAACT AACATCTTTGGCACTGTTTATGAAAAACTCAAACCCGTCCTTGATTGGCTTGAAGAGAA GTTTAAGGAAGGTGTAGAGTTTCTTAGAGACGGTTGGGAAATTGTTAAATTTATCTCAA CCTGTGCTTGTGAAATTGTCGGTGGACAAATTGTCACCTGTGCAAAGGAAATTAAGGA GAGTGTTCAGACATTCTTTAAGCTTGTAAATAAATTTTTGGCTTTGTGTGCTGACTCTAT CATTATTGGTGGAGCTAAACTTAAAGCCTTGAATTTAGGTGAAACATTTGTCACGCACT CAAAGGGATTGTACAGAAAGTGTGTTAAATCCAGAGAAGAAACTGGCCTACTCATGCC TCTAAAAGCCCCAAAAGAAATTATCTTCTTAGAGGGAGAAACACTTCCCACAGAAGTGT TAACAGAGGAAGTTGTCTTGAAAACTGGTGATTTACAACCATTAGAACAACCTACTAGT GAAGCTGTTGAAGCTCCATTGGTTGGTACACCAGTTTGTATTAACGGGCTTATGTTGCT CGAAATCAAAGACACAGAAAAGTACTGTGCCCTTGCACCTAATATGATGGTAACAAAC AATACCTTCACACTCAAAGGCGGTGCACCAACAAAGGTTACTTTTGGTGATGACACTG TGATAGAAGTGCAAGGTTACAAGAGTGTGAATATCACTTTTGAACTTGATGAAAGGATT GATAAAGTACTTAATGAGAAGTGCTCTGCCTATACAGTTGAACTCGGTACAGAAGTAAA TGAGTTCGCCTGTGTTGTGGCAGATGCTGTCATAAAAACTTTGCAACCAGTATCTGAAT TACTTACACCACTGGGCATTGATTTAGATGAGTGGAGTATGGCTACATACTACTTATTT GATGAGTCTGGTGAGTTTAAATTGGCTTCACATATGTATTGTTCTTTCTACCCTCCAGA TGAGGATGAAGAAGAAGGTGATTGTGAAGAAGAAGAGTTTGAGCCATCAACTCAATAT GAGTATGGTACTGAAGATGATTACCAAGGTAAACCTTTGGAATTTGGTGCCACTTCTG CTGCTCTTCAACCTGAAGAAGAGCAAGAAGAAGATTGGTTAGATGATGATAGTCAACA AACTGTTGGTCAACAAGACGGCAGTGAGGACAATCAGACAACTACTATTCAAACAATT GTTGAGGTTCAACCTCAATTAGAGATGGAACTTACACCAGTTGTTCAGACTATTGAAGT GAATAGTTTTAGTGGTTATTTAAAACTTACTGACAATGTATACATTAAAAATGCAGACAT

		TGTGGAAGAAGCTAAAAAGGTAAAACCAACAGTGGTTGTTAATGCAGCCAATGTTTAC CTTAAACATGGAGGAGGTGTTGCAGGAGCCTTAAATAAGGCTACTAACAATGCCATGC AAGTTGAATCTGATGATTACATAGCTACTAATGGACCACTTAAAGTGGGTGGTAGTTGT GTTTTAAGCGGACACAATCTTGCTAAACACTGTCTTCATGTTGTCGGCCCAAATGTTAA CAAAGGTGAAGACATTCAACTTCTTAAGAGTGCTTATGAAAATTTTAATCAGCACGAAG TTCTACTTGCACCATTATTATCAGCTGGTATTTTTGGTGCTGACCCTATACATTCTTTAA GAGTTTGTGTAGATACTGTTCGCACAAATGTCTACTTAGCTGTCTTTGATAAAAATCTCT ATGACAAACTTGTTTCAAGCTTTTTGGAAATGAAGAGTGAAAAGCAAGTTGAACAAAAG ATCGCTGAGATTCCTAAAGAGGAAGTTAAGCCATTTATAACTGAAAGTAAACCTTCAGT TGAACAGAGAAAACAAGATGATAAGAAAATCAAAGCTTGTGTTGAAGAAGTTACAACAA CTCTGGAAGAAACTAAGTTCCTCACAGAAAACTTGTTACTTTATATTGACATTAATGGC AATCTTCATCCAGATTCTGCCACTCTTGTTAGTGACATTGACATCACTTTCTTAAAGAAA GATGCTCCATATATAGTGGGTGATGTTGTTCAAGAGGGTGTTTTAACTGCTGTGGTTAT ACCTACTAAAAAGGCTGGTGGCACTACTGAAATGCTAGCGAAAGCTTTGAGAAAAGTG CCAACAGACAATTATATAACCACTTACCCGGGTCAGGGTTTAAATGGTTACACTGTAGA GGAGGCAAAGACAGTGCTTAAAAAGTGTAAAAGTGCCTTTTACATTCTACCATCTATTA TCTCTAATGAGAAGCAAGAAATTCTTGGAACTGTTTCTTGGAATTTGCGAGAAATGCTT GCACATGCAGAAGAAACACGCAAATTAATGCCTGTCTGTGTGGAAACTAAAGCCATAG TTTCAACTATACAGCGTAAATATAAGGGTATTAAAATACAAGAGGGTGTGGTTGATTAT GGTGCTAGATTTTACTTTTACACCAGTAAAACAACTGTAGCGTCACTTATCAACACACT TAACGATCTAAATGAAACTCTTGTTACAATGCCACTTGGCTATGTAACACATGGCTTAA ATTTGGAAGAAGCTGCTCGGTATATGAGATCTCTCAAAGTGCCAGCTACAGTTTCTGTT TCTTCACCTGATGCTGTTACAGCGTATAATGGTTATCTTACTTCTTCTTCTAAAACACCT GAAGAACATTTTATTGAAACCATCTCACTTGCTGGTTCCTATAAAGATTGGTCCTATTCT GGACAATCTACACAACTAGGTATAGAATTTCTTAAGAGAGGTGATAAAAGTGTATATTA CACTAGTAATCCTACCACATTCCACCTAGATGGTGAAGTTATCACCTTTGACAATCTTA AGACACTTCTTTCTTTGAGAGAAGTGAGGACTATTAAGGTGTTTACAACAGTAGACAAC ATTAACCTCCACACGCAAGTTGTGGACATGTCAATGACATATGGACAACAGTTTGGTC CAACTTATTTGGATGGAGCTGATGTTACTAAAATAAAACCTCATAATTCACATGAAGGT AAAACATTTTATGTTTTACCTAATGATGACACTCTACGTGTTGAGGCTTTTGAGTACTAC CACACAACTGATCCTAGTTTTCTGGGTAGGTACATGTCAGCATTAAATCACACTAAAAA GTGGAAATACCCACAAGTTAATGGTTTAACTTCTATTAAATGGGCAGATAACAACTGTT ATCTTGCCACTGCATTGTTAACACTCCAACAAATAGAGTTGAAGTTTAATCCACCTGCT CTACAAGATGCTTATTACAGAGCAAGGGCTGGTGAAGCTGCTAACTTTTGTGCACTTAT CTTAGCCTACTGTAATAAGACAGTAGGTGAGTTAGGTGATGTTAGAGAAACAATGAGTT ACTTGTTTCAACATGCCAATTTAGATTCTTGCAAAAGAGTCTTGAACGTGGTGTGTAAA ACTTGTGGACAACAGCAGACAACCCTTAAGGGTGTAGAAGCTGTTATGTACATGGGCA CACTTTCTTATGAACAATTTAAGAAAGGTGTTCAGATACCTTGTACGTGTGGTAAACAA GCTACAAAATATCTAGTACAACAGGAGTCACCTTTTGTTATGATGTCAGCACCACCTGC TCAGTATGAACTTAAGCATGGTACATTTACTTGTGCTAGTGAGTACACTGGTAATTACC AGTGTGGTCACTATAAACATATAACTTCTAAAGAAACTTTGTATTGCATAGACGGTGCT TTACTTACAAAGTCCTCAGAATACAAAGGTCCTATTACGGATGTTTTCTACAAAGAAAA CAGTTACACAACAACCATAAAACCAGTTACTTATAAATTGGATGGTGTTGTTTGTACAG AAATTGACCCTAAGTTGGACAATTATTATAAGAAAGACAATTCTTATTTCACAGAGCAAC CAATTGATCTTGTACCAAACCAACCATATCCAAACGCAAGCTTCGATAATTTTAAGTTT GTATGTGATAATATCAAATTTGCTGATGATTTAAACCAGTTAACTGGTTATAAGAAACCT GCTTCAAGAGAGCTTAAAGTTACATTTTTCCCTGACTTAAATGGTGATGTGGTGGCTAT TGATTATAAACACTACACACCCTCTTTTAAGAAAGGAGCTAAATTGTTACATAAACCTAT TGTTTGGCATGTTAACAATGCAACTAATAAAGCCACGTATAAACCAAATACCTGGTGTA TACGTTGTCTTTGGAGCACAAAACCAGTTGAAACATCAAATTCGTTTGATGTACTGAAG TCAGAGGACGCGCAGGGAATGGATAATCTTGCCTGCGAAGATCTAAAACCAGTCTCTG AAGAAGTAGTGGAAAATCCTACCATACAGAAAGACGTTCTTGAGTGTAATGTGAAAACT ACCGAAGTTGTAGGAGACATTATACTTAAACCAGCAAATAATAGTTTAAAAATTACAGA AGAGGTTGGCCACACAGATCTAATGGCTGCTTATGTAGACAATTCTAGTCTTACTATTA AGAAACCTAATGAATTATCTAGAGTATTAGGTTTGAAAACCCTTGCTACTCATGGTTTA GCTGCTGTTAATAGTGTCCCTTGGGATACTATAGCTAATTATGCTAAGCCTTTTCTTAA CAAAGTTGTTAGTACAACTACTAACATAGTTACACGGTGTTTAAACCGTGTTTGTACTA ATTATATGCCTTATTTCTTTACTTTATTGCTACAATTGTGTACTTTTACTAGAAGTACAAA TTCTAGAATTAAAGCATCTATGCCGACTACTATAGCAAAGAATACTGTTAAGAGTGTCG GTAAATTTTGTCTAGAGGCTTCATTTAATTATTTGAAGTCACCTAATTTTTCTAAACTGAT AAATATTATAATTTGGTTTTTACTATTAAGTGTTTGCCTAGGTTCTTTAATCTACTCAACC GCTGCTTTAGGTGTTTTAATGTCTAATTTAGGCATGCCTTCTTACTGTACTGGTTACAG AGAAGGCTATTTGAACTCTACTAATGTCACTATTGCAACCTACTGTACTGGTTCTATAC CTTGTAGTGTTTGTCTTAGTGGTTTAGATTCTTTAGACACCTATCCTTCTTTAGAAACTA TACAAATTACCATTTCATCTTTTAAATGGGATTTAACTGCTTTTGGCTTAGTTGCAGAGT GGTTTTTGGCATATATTCTTTTCACTAGGTTTTTCTATGTACTTGGATTGGCTGCAATCA

		TGCAATTGTTTTTCAGCTATTTTGCAGTACATTTTATTAGTAATTCTTGGCTTATGTGGT TAATAATTAATCTTGTACAAATGGCCCCGATTTCAGCTATGGTTAGAATGTACATCTTCT TTGCATCATTTTATTATGTATGGAAAAGTTATGTGCATGTTGTAGACGGTTGTAATTCAT CAACTTGTATGATGTGTTACAAACGTAATAGAGCAACAAGAGTCGAATGTACAACTATT GTTAATGGTGTTAGAAGGTCCTTTTATGTCTATGCTAATGGAGGTAAAGGCTTTTGCAA ACTACACAATTGGAATTGTGTTAATTGTGATACATTCTGTGCTGGTAGTACATTTATTAG TGATGAAGTTGCGAGAGACTTGTCACTACAGTTTAAAAGACCAATAAATCCTACTGACC AGTCTTCTTACATCGTTGATAGTGTTACAGTGAAGAATGGTTCCATCCATCTTTACTTTG ATAAAGCTGGTCAAAAGACTTATGAAAGACATTCTCTCTCTCATTTTGTTAACTTAGACA ACCTGAGAGCTAATAACACTAAAGGTTCATTGCCTATTAATGTTATAGTTTTTGATGGTA AATCAAAATGTGAAGAATCATCTGCAAAATCAGCGTCTGTTTACTACAGTCAGCTTATG TGTCAACCTATACTGTTACTAGATCAGGCATTAGTGTCTGATGTTGGTGATAGTGCGGA AGTTGCAGTTAAAATGTTTGATGCTTACGTTAATACGTTTTCATCAACTTTTAACGTACC AATGGAAAAACTCAAAACACTAGTTGCAACTGCAGAAGCTGAACTTGCAAAGAATGTG TCCTTAGACAATGTCTTATCTACTTTTATTTCAGCAGCTCGGCAAGGGTTTGTTGATTC AGATGTAGAAACTAAAGATGTTGTTGAATGTCTTAAATTGTCACATCAATCTGACATAG AAGTTACTGGCGATAGTTGTAATAACTATATGCTCACCTATAACAAAGTTGAAAACATG ACACCCCGTGACCTTGGTGCTTGTATTGACTGTAGTGCGCGTCATATTAATGCGCAGG TAGCAAAAAGTCACAACATTGCTTTGATATGGAACGTTAAAGATTTCATGTCATTGTCT GAACAACTACGAAAACAAATACGTAGTGCTGCTAAAAAGAATAACTTACCTTTTAAGTT GACATGTGCAACTACTAGACAAGTTGTTAATGTTGTAACAACAAAGATAGCACTTAAGG GTGGTAAAATTGTTAATAATTGGTTGAAGCAGTTAATTAAAGTTACACTTGTGTTCCTTT TTGTTGCTGCTATTTTCTATTTAATAACACCTGTTCATGTCATGTCTAAACATACTGACT TTTCAAGTGAAATCATAGGATACAAGGCTATTGATGGTGGTGTCACTCGTGACATAGC ATCTACAGATACTTGTTTTGCTAACAAACATGCTGATTTTGACACATGGTTTAGCCAGC GTGGTGGTAGTTATACTAATGACAAAGCTTGCCCATTGATTGCTGCAGTCATAACAAGA GAAGTGGGTTTTGTCGTGCCTGGTTTGCCTGGCACGATATTACGCACAACTAATGGTG ACTTTTTGCATTTCTTACCTAGAGTTTTTAGTGCAGTTGGTAACATCTGTTACACACCAT CAAAACTTATAGAGTACACTGACTTTGCAACATCAGCTTGTGTTTTGGCTGCTGAATGT ACAATTTTTAAAGATGCTTCTGGTAAGCCAGTACCATATTGTTATGATACCAATGTACTA GAAGGTTCTGTTGCTTATGAAAGTTTACGCCCTGACACACGTTATGTGCTCATGGATG GCTCTATTATTCAATTTCCTAACACCTACCTTGAAGGTTCTGTTAGAGTGGTAACAACTT TTGATTCTGAGTACTGTAGGCACGGCACTTGTGAAAGATCAGAAGCTGGTGTTTGTGT ATCTACTAGTGGTAGATGGGTACTTAACAATGATTATTACAGATCTTTACCAGGAGTTT TCTGTGGTGTAGATGCTGTAAATTTACTTACTAATATGTTTACACCACTAATTCAACCTA TTGGTGCTTTGGACATATCAGCATCTATAGTAGCTGGTGGTATTGTAGCTATCGTAGTA ACATGCCTTGCCTACTATTTTATGAGGTTTAGAAGAGCTTTTGGTGAATACAGTCATGT AGTTGCCTTTAATACTTTACTATTCCTTATGTCATTCACTGTACTCTGTTTAACACCAGT TTACTCATTCTTACCTGGTGTTTATTCTGTTATTTACTTGTACTTGACATTTTATCTTACT AATGATGTTTCTTTTTTAGCACATATTCAGTGGATGGTTATGTTCACACCTTTAGTACCT TTCTGGATAACAATTGCTTATATCATTTGTATTTCCACAAAGCATTTCTATTGGTTCTTTA GTAATTACCTAAAGAGACGTGTAGTCTTTAATGGTGTTTCCTTTAGTACTTTTGAAGAA GCTGCGCTGTGCACCTTTTTGTTAAATAAAGAAATGTATCTAAAGTTGCGTAGTGATGT GCTATTACCTCTTACGCAATATAATAGATACTTAGCTCTTTATAATAAGTACAAGTATTT TAGTGGAGCAATGGATACAACTAGCTACAGAGAAGCTGCTTGTTGTCATCTCGCAAAG GCTCTCAATGACTTCAGTAACTCAGGTTCTGATGTTCTTTACCAACCACCACAAACCTC TATCACCTCAGCTGTTTTGCAGAGTGGTTTTAGAAAAATGGCATTCCCATCTGGTAAAG TTGAGGGTTGTATGGTACAAGTAACTTGTGGTACAACTACACTTAACGGTCTTTGGCTT GATGACGTAGTTTACTGTCCAAGACATGTGATCTGCACCTCTGAAGACATGCTTAACC CTAATTATGAAGATTTACTCATTCGTAAGTCTAATCATAATTTCTTGGTACAGGCTGGTA ATGTTCAACTCAGGGTTATTGGACATTCTATGCAAAATTGTGTACTTAAGCTTAAGGTT GATACAGCCAATCCTAAGACACCTAAGTATAAGTTTGTTCGCATTCAACCAGGACAGA CTTTTTCAGTGTTAGCTTGTTACAATGGTTCACCATCTGGTGTTTACCAATGTGCTATG AGGCCCAATTTCACTATTAAGGGTTCATTCCTTAATGGTTCATGTGGTAGTGTTGGTTT TAACATAGATTATGACTGTGTCTCTTTTTGTTACATGCACCATATGGAATTACCAACTGG AGTTCATGCTGGCACAGACTTAGAAGGTAACTTTTATGGACCTTTTGTTGACAGGCAAA CAGCACAAGCAGCTGGTACGGACACAACTATTACAGTTAATGTTTTAGCTTGGTTGTAC GCTGCTGTTATAAATGGAGACAGGTGGTTTCTCAATCGATTTACCACAACTCTTAATGA CTTTAACCTTGTGGCTATGAAGTACAATTATGAACCTCTAACACAAGACCATGTTGACA TACTAGGACCTCTTTCTGCTCAAACTGGAATTGCCGTTTTAGATATGTGTGCTTCATTA AAAGAATTACTGCAAAATGGTATGAATGGACGTACCATATTGGGTAGTGCTTTATTAGA AGATGAATTTACACCTTTTGATGTTGTTAGACAATGCTCAGGTGTTACTTTCCAAAGTG CAGTGAAAAGAACAATCAAGGGTACACACCACTGGTTGTTACTCACAATTTTGACTTCA CTTTTAGTTTTAGTCCAGAGTACTCAATGGTCTTTGTTCTTTTTTTTGTATGAAAATGCC TTTTTACCTTTTGCTATGGGTATTATTGCTATGTCTGCTTTTGCAATGATGTTTGTCAAA CATAAGCATGCATTTCTCTGTTTGTTTTTGTTACCTTCTCTTGCCACTGTAGCTTATTTT

		AATATGGTCTATATGCCTGCTAGTTGGGTGATGCGTATTATGACATGGTTGGATATGGT TGATACTAGTTTGTCTGGTTTTAAGCTAAAAGACTGTGTTATGTATGCATCAGCTGTAG TGTTACTAATCCTTATGACAGCAAGAACTGTGTATGATGATGGTGCTAGGAGAGTGTG GACACTTATGAATGTCTTGACACTCGTTTATAAAGTTTATTATGGTAATGCTTTAGATCA AGCCATTTCCATGTGGGCTCTTATAATCTCTGTTACTTCTAACTACTCAGGTGTAGTTA CAACTGTCATGTTTTTGGCCAGAGGTATTGTTTTTATGTGTGTTGAGTATTGCCCTATTT TCTTCATAACTGGTAATACACTTCAGTGTATAATGCTAGTTTATTGTTTCTTAGGCTATT TTTGTACTTGTTACTTTGGCCTCTTTTGTTTACTCAACCGCTACTTTAGACTGACTCTTG GTGTTTATGATTACTTAGTTTCTACACAGGAGTTTAGATATATGAATTCACAGGGACTA CTCCCACCCAAGAATAGCATAGATGCCTTCAAACTCAACATTAAATTGTTGGGTGTTGG TGGCAAACCTTGTATCAAAGTAGCCACTGTACAGTCTAAAATGTCAGATGTAAAGTGCA CATCAGTAGTCTTACTCTCAGTTTTGCAACAACTCAGAGTAGAATCATCATCTAAATTGT GGGCTCAATGTGTCCAGTTACACAATGACATTCTCTTAGCTAAAGATACTACTGAAGCC TTTGAAAAAATGGTTTCACTACTTTCTGTTTTGCTTTCCATGCAGGGTGCTGTAGACAT AAACAAGCTTTGTGAAGAAATGCTGGACAACAGGGCAACCTTACAAGCTATAGCCTCA GAGTTTAGTTCCCTTCCATCATATGCAGCTTTTGCTACTGCTCAAGAAGCTTATGAGCA GGCTGTTGCTAATGGTGATTCTGAAGTTGTTCTTAAAAAGTTGAAGAAGTCTTTGAATG TGGCTAAATCTGAATTTGACCGTGATGCAGCCATGCAACGTAAGTTGGAAAAGATGGC TGATCAAGCTATGACCCAAATGTATAAACAGGCTAGATCTGAGGACAAGAGGGCAAAA GTTACTAGTGCTATGCAGACAATGCTTTTCACTATGCTTAGAAAGTTGGATAATGATGC ACTCAACAACATTATCAACAATGCAAGAGATGGTTGTGTTCCCTTGAACATAATACCTC TTACAACAGCAGCCAAACTAATGGTTGTCATACCAGACTATAACACATATAAAAATACG TGTGATGGTACAACATTTACTTATGCATCAGCATTGTGGGAAATCCAACAGGTTGTAGA TGCAGATAGTAAAATTGTTCAACTTAGTGAAATTAGTATGGACAATTCACCTAATTTAGC ATGGCCTCTTATTGTAACAGCTTTAAGGGCCAATTCTGCTGTCAAATTACAGAATAATG AGCTTAGTCCTGTTGCACTACGACAGATGTCTTGTGCTGCCGGTACTACACAAACTGC TTGCACTGATGACAATGCGTTAGCTTACTACAACACAACAAAGGGAGGTAGGTTTGTA CTTGCACTGTTATCCGATTTACAGGATTTGAAATGGGCTAGATTCCCTAAGAGTGATGG AACTGGTACTATCTATACAGAACTGGAACCACCTTGTAGGTTTGTTACAGACACACCTA AAGGTCCTAAAGTGAAGTATTTATACTTTATTAAAGGATTAAACAACCTAAATAGAGGTA TGGTACTTGGTAGTTTAGCTGCCACAGTACGTCTACAAGCTGGTAATGCAACAGAAGT GCCTGCCAATTCAACTGTATTATCTTTCTGTGCTTTTGCTGTAGATGCTGCTAAAGCTT ACAAAGATTATCTAGCTAGTGGGGGACAACCAATCACTAATTGTGTTAAGATGTTGTGT ACACACACTGGTACTGGTCAGGCAATAACAGTTACACCGGAAGCCAATATGGATCAAG AATCCTTTGGTGGTGCATCGTGTTGTCTGTACTGCCGTTGCCACATAGATCATCCAAAT CCTAAAGGATTTTGTGACTTAAAAGGTAAGTATGTACAAATACCTACAACTTGTGCTAA TGACCCTGTGGGTTTTACACTTAAAAACACAGTCTGTACCGTCTGCGGTATGTGGAAA GGTTATGGCTGTAGTTGTGATCAACTCCGCGAACCCATGCTTCAGTCAGCTGATGCAC AATCGTTTTTAAACGGGTTTGCGGTGTAAGTGCAGCCCGTCTTACACCGTGCGGCACA GGCACTAGTACTGATGTCGTATACAGGGCTTTTGACATCTACAATGATAAAGTAGCTG GTTTTGCTAAATTCCTAAAAACTAATTGTTGTCGCTTCCAAGAAAAGGACGAAGATGAC AATTTAATTGATTCTTACTTTGTAGTTAAGAGACACACTTTCTCTAACTACCAACATGAA GAAACAATTTATAATTTACTTAAGGATTGTCCAGCTGTTGCTAAACATGACTTCTTTAAG TTTAGAATAGACGGTGACATGGTACCACATATATCACGTCAACGTCTTACTAAATACAC AATGGCAGACCTCGTCTATGCTTTAAGGCATTTTGATGAAGGTAATTGTGACACATTAA AAGAAATACTTGTCACATACAATTGTTGTGATGATGATTATTTCAATAAAAAGGACTGGT ATGATTTTGTAGAAAACCCAGATATATTACGCGTATACGCCAACTTAGGTGAACGTGTA CGCCAAGCTTTGTTAAAAACAGTACAATTCTGTGATGCCATGCGAAATGCTGGTATTGT TGGTGTACTGACATTAGATAATCAAGATCTCAATGGTAACTGGTATGATTTCGGTGATT TCATACAAACCACGCCAGGTAGTGGAGTTCCTGTTGTAGATTCTTATTATTCATTGTTA ATGCCTATATTAACCTTGACCAGGGCTTTAACTGCAGAGTCACATGTTGACACTGACTT AACAAAGCCTTACATTAAGTGGGATTTGTTAAAATATGACTTCACGGAAGAGAGGTTAA AACTCTTTGACCGTTATTTTAAATATTGGGATCAGACATACCACCCAAATTGTGTTAACT GTTTGGATGACAGATGCATTCTGCATTGTGCAAACTTTAATGTTTTATTCTCTACAGTGT TCCCACCTACAAGTTTTGGACCACTAGTGAGAAAAATATTTGTTGATGGTGTTCCATTT GTAGTTTCAACTGGATACCACTTCAGAGAGCTAGGTGTTGTACATAATCAGGATGTAAA CTTACATAGCTCTAGACTTAGTTTTAAGGAATTACTTGTGTATGCTGCTGACCCTGCTA TGCACGCTGCTTCTGGTAATCTATTACTAGATAAACGCACTACGTGCTTTTCAGTAGCT GCACTTACTAACAATGTTGCTTTTCAAACTGTCAAACCCGGTAATTTTAACAAAGACTTC TATGACTTTGCTGTGTCTAAGGGTTTCTTTAAGGAAGGAAGTTCTGTTGAATTAAAACA CTTCTTCTTTGCTCAGGATGGTAATGCTGCTATCAGCGATTATGACTACTATCGTTATA ATCTACCAACAATGTGTGATATCAGACAACTACTATTTGTAGTTGAAGTTGTTGATAAGT ACTTTGATTGTTACGATGGTGGCTGTATTAATGCTAACCAAGTCATCGTCAACAACCTA GACAAATCAGCTGGTTTTCCATTTAATAAATGGGGTAAGGCTAGACTTTATTATGATTC AATGAGTTATGAGGATCAAGATGCACTTTTCGCATATACAAAACGTAATGTCATCCCTA CTATAACTCAAATGAATCTTAAGTATGCCATTAGTGCAAAGAATAGAGCTCGCACCGTA

		GCTGGTGTCTCTATCTGTAGTACTATGACCAATAGACAGTTTCATCAAAAATTATTGAA ATCAATAGCCGCCACTAGAGGAGCTACTGTAGTAATTGGAACAAGCAAATTCTATGGT GGTTGGCACAACATGTTAAAAACTGTTTATAGTGATGTAGAAAACCCTCACCTTATGGG TTGGGATTATCCTAAATGTGATAGAGCCATGCCTAACATGCTTAGAATTATGGCCTCAC TTGTTCTTGCTCGCAAACATACAACGTGTTGTAGCTTGTCACACCGTTTCTATAGATTA GCTAATGAGTGTGCTCAAGTATTGAGTGAAATGGTCATGTGTGGCGGTTCACTATATG TTAAACCAGGTGGAACCTCATCAGGAGATGCCACAACTGCTTATGCTAATAGTGTTTTT AACATTTGTCAAGCTGTCACGGCCAATGTTAATGCACTTTTATCTACTGATGGTAACAA AATTGCCGATAAGTATGTCCGCAATTTACAACACAGACTTTATGAGTGTCTCTATAGAA ATAGAGATGTTGACACAGACTTTGTGAATGAGTTTTACGCATATTTGCGTAAACATTTC TCAATGATGATACTCTCTGACGATGCTGTTGTGTGTTTCAATAGCACTTATGCATCTCA AGGTCTAGTGGCTAGCATAAAGAACTTTAAGTCAGTTCTTTATTATCAAAACAATGTTTT TATGTCTGAAGCAAAATGTTGGACTGAGACTGACCTTACTAAAGGACCTCATGAATTTT GCTCTCAACATACAATGCTAGTTAAACAGGGTGATGATTATGTGTACCTTCCTTACCCA GATCCATCAAGAATCCTAGGGGCCGGCTGTTTTGTAGATGATATCGTAAAAACAGATG GTACACTTATGATTGAACGGTTCGTGTCTTTAGCTATAGATGCTTACCCACTTACTAAA CATCCTAATCAGGAGTATGCTGATGTCTTTCATTTGTACTTACAATACATAAGAAAGCTA CATGATGAGTTAACAGGACACATGTTAGACATGTATTCTGTTATGCTTACTAATGATAA CACTTCAAGGTATTGGGAACCTGAGTTTTATGAGGCTATGTACACACCGCATACAGTC TTACAGGCTGTTGGGGCTTGTGTTCTTTGCAATTCACAGACTTCATTAAGATGTGGTGC TTGCATACGTAGACCATTCTTATGTTGTAAATGCTGTTACGACCATGTCATATCAACAT CACATAAATTAGTCTTGTCTGTTAATCCGTATGTTTGCAATGCTCCAGGTTGTGATGTC ACAGATGTGACTCAACTTTACTTAGGAGGTATGAGCTATTATTGTAAATCACATAAACC ACCCATTAGTTTTCCATTGTGTGCTAATGGACAAGTTTTTGGTTTATATAAAAATACATG TGTTGGTAGCGATAATGTTACTGACTTTAATGCAATTGCAACATGTGACTGGACAAATG CTGGTGATTACATTTTAGCTAACACCTGTACTGAAAGACTCAAGCTTTTTGCAGCAGAA ACGCTCAAAGCTACTGAGGAGACATTTAAACTGTCTTATGGTATTGCTACTGTACGTGA AGTGCTGTCTGACAGAGAATTACATCTTTCATGGGAAGTTGGTAAACCTAGACCACCA CTTAACCGAAATTATGTCTTTACTGGTTATCGTGTAACTAAAAACAGTAAAGTACAAATA GGAGAGTACACCTTTGAAAAAGGTGACTATGGTGATGCTGTTGTTTACCGAGGTACAA CAACTTACAAATTAAATGTTGGTGATTATTTTGTGCTGACATCACATACAGTAATGCCAT TAAGTGCACCTACACTAGTGCCACAAGAGCACTATGTTAGAATTACTGGCTTATACCCA ACACTCAATATCTCAGATGAGTTTTCTAGCAATGTTGCAAATTATCAAAAGGTTGGTAT GCAAAAGTATTCTACACTCCAGGGACCACCTGGTACTGGTAAGAGTCATTTTGCTATT GGCCTAGCTCTCTACTACCCTTCTGCTCGCATAGTGTATACAGCTTGCTCTCATGCCG CTGTTGATGCACTATGTGAGAAGGCATTAAAATATTTGCCTATAGATAAATGTAGTAGA ATTATACCTGCACGTGCTCGTGTAGAGTGTTTTGATAAATTCAAAGTGAATTCAACATT AGAACAGTATGTCTTTTGTACTGTAAATGCATTGCCTGAGACGACAGCAGATATAGTTG TCTTTGATGAAATTTCAATGGCCACAAATTATGATTTGAGTGTTGTCAATGCCAGATTAC GTGCTAAGCACTATGTGTACATTGGCGACCCTGCTCAATTACCTGCACCACGCACATT GCTAACTAAGGGCACACTAGAACCAGAATATTTCAATTCAGTGTGTAGACTTATGAAAA CTATAGGTCCAGACATGTTCCTCGGAACTTGTCGGCGTTGTCCTGCTGAAATTGTTGA CACTGTGAGTGCTTTGGTTTATGATAATAAGCTTAAAGCACATAAAGACAAATCAGCTC AATGCTTTAAAATGTTTTATAAGGGTGTTATCACGCATGATGTTTCATCTGCAATTAACA GGCCACAAATAGGCGTGGTAAGAGAATTCCTTACACGTAACCCTGCTTGGAGAAAAGC TGTCTTTATTTCACCTTATAATTCACAGAATGCTGTAGCCTCAAAGATTTTGGGACTACC AACTCAAACTGTTGATTCATCACAGGGCTCAGAATATGACTATGTCATATTCACTCAAA CCACTGAAACAGCTCACTCTTGTAATGTAAACAGATTTAATGTTGCTATTACCAGAGCA AAAGTAGGCATACTTTGCATAATGTCTGATAGAGACCTTTATGACAAGTTGCAATTTAC AAGTCTTGAAATTCCACGTAGGAATGTGGCAACTTTACAAGCTGAAAATGTAACAGGA CTCTTTAAAGATTGTAGTAAGGTAATCACTGGGTTACATCCTACACAGGCACCTACACA CCTCAGTGTTGACACTAAATTCAAAACTGAAGGTTTATGTGTTGACATACCTGGCATAC CTAAGGACATGACCTATAGAAGACTCATCTCTATGATGGGTTTTAAAATGAATTATCAA GTTAATGGTTACCCTAACATGTTTATCACCCGCGAAGAAGCTATAAGACATGTACGTGC ATGGATTGGCTTCGATGTCGAGGGGTGTCATGCTACTAGAGAAGCTGTTGGTACCAAT TTACCTTTACAGCTAGGTTTTTCTACAGGTGTTAACCTAGTTGCTGTACCTACAGGTTA TGTTGATACACCTAATAATACAGATTTTTCCAGAGTTAGTGCTAAACCACCGCCTGGAG ATCAATTTAAACACCTCATACCACTTATGTACAAAGGACTTCCTTGGAATGTAGTGCGT ATAAAGATTGTACAAATGTTAAGTGACACACTTAAAAATCTCTCTGACAGAGTCGTATTT GTCTTATGGGCACATGGCTTTGAGTTGACATCTATGAAGTATTTTGTGAAAATAGGACC TGAGCGCACCTGTTGTCTATGTGATAGACGTGCCACATGCTTTTCCACTGCTTCAGAC ACTTATGCCTGTTGGCATCATTCTATTGGATTTGATTACGTCTATAATCCGTTTATGATT GATGTTCAACAATGGGGTTTTACAGGTAACCTACAAAGCAACCATGATCTGTATTGTCA AGTCCATGGTAATGCACATGTAGCTAGTTGTGATGCAATCATGACTAGGTGTCTAGCT GTCCACGAGTGCTTTGTTAAGCGTGTTGACTGGACTATTGAATATCCTATAATTGGTGA TGAACTGAAGATTAATGCGGCTTGTAGAAAGGTTCAACACATGGTTGTTAAAGCTGCAT

		TATTAGCAGACAAATTCCCAGTTCTTCACGACATTGGTAACCCTAAAGCTATTAAGTGT GTACCTCAAGCTGATGTAGAATGGAAGTTCTATGATGCACAGCCTTGTAGTGACAAAG CTTATAAAATAGAAGAATTATTCTATTCTTATGCCACACATTCTGACAAATTCACAGATG GTGTATGCCTATTTTGGAATTGCAATGTCGATAGATATCCTGCTAATTCCATTGTTTGTA GATTTGACACTAGAGTGCTATCTAACCTTAACTTGCCTGGTTGTGATGGTGGCAGTTTG TATGTAAATAAACATGCATTCCACACACCAGCTTTTGATAAAAGTGCTTTTGTTAATTTA AAACAATTACCATTTTTCTATTACTCTGACAGTCCATGTGAGTCTCATGGAAAACAAGTA GTGTCAGATATAGATTATGTACCACTAAAGTCTGCTACGTGTATAACACGTTGCAATTT AGGTGGTGCTGTCTGTAGACATCATGCTAATGAGTACAGATTGTATCTCGATGCTTATA ACATGATGATCTCAGCTGGCTTTAGCTTGTGGGTTTACAAACAATTTGATACTTATAAC CTCTGGAACACTTTTACAAGACTTCAGAGTTTAGAAAATGTGGCTTTTAATGTTGTAAAT AAGGGACACTTTGATGGACAACAGGGTGAAGTACCAGTTTCTATCATTAATAACACTGT TTACACAAAAGTTGATGGTGTTGATGTAGAATTGTTTGAAAATAAAACAACATTACCTGT TAATGTAGCATTTGAGCTTTGGGCTAAGCGCAACATTAAACCAGTACCAGAGGTGAAA ATACTCAATAATTTGGGTGTGGACATTGCTGCTAATACTGTGATCTGGGACTACAAAAG AGATGCTCCAGCACATATATCTACTATTGGTGTTTGTTCTATGACTGACATAGCCAAGA AACCAACTGAAACGATTTGTGCACCACTCACTGTCTTTTTTGATGGTAGAGTTGATGGT CAAGTAGACTTATTTAGAAATGCCCGTAATGGTGTTCTTATTACAGAAGGTAGTGTTAA AGGTTTACAACCATCTGTAGGTCCCAAACAAGCTAGTCTTAATGGAGTCACATTAATTG GAGAAGCCGTAAAAACACAGTTCAATTATTATAAGAAAGTTGATGGTGTTGTCCAACAA TTACCTGAAACTTACTTTACTCAGAGTAGAAATTTACAAGAATTTAAACCCAGGAGTCA AATGGAAATTGATTTCTTAGAATTAGCTATGGATGAATTCATTGAACGGTATAAATTAGA AGGCTATGCCTTCGAACATATCGTTTATGGAGATTTTAGTCATAGTCAGTTAGGTGGTT TACATCTACTGATTGGACTAGCTAAACGTTTTAAGGAATCACCTTTTGAATTAGAAGATT TTATTCCTATGGACAGTACAGTTAAAAACTATTTCATAACAGATGCGCAAACAGGTTCA TCTAAGTGTGTGTGTTCTGTTATTGATTTATTACTTGATGATTTTGTTGAAATAATAAAAT CCCAAGATTTATCTGTAGTTTCTAAGGTTGTCAAAGTGACTATTGACTATACAGAAATTT CATTTATGCTTTGGTGTAAAGATGGCCATGTAGAAACATTTTACCCAAAATTACAATCTA GTCAAGCGTGGCAACCGGGTGTTGCTATGCCTAATCTTTACAAAATGCAAAGAATGCT ATTAGAAAAGTGTGACCTTCAAAATTATGGTGATAGTGCAACATTACCTAAAGGCATAA TGATGAATGTCGCAAAATATACTCAACTGTGTCAATATTTAAACACATTAACATTAGCTG TACCCTATAATATGAGAGTTATACATTTTGGTGCTGGTTCTGATAAAGGAGTTGCACCA GGTACAGCTGTTTTAAGACAGTGGTTGCCTACGGGTACGCTGCTTGTCGATTCAGATC TTAATGACTTTGTCTCTGATGCAGATTCAACTTTGATTGGTGATTGTGCAACTGTACATA CAGCTAATAAATGGGATCTCATTATTAGTGATATGTACGACCCTAAGACTAAAAATGTT ACAAAAGAAAATGACTCTAAAGAGGGTTTTTTCACTTACATTTGTGGGTTTATACAACAA AAGCTAGCTCTTGGAGGTTCCGTGGCTATAAAGATAACAGAACATTCTTGGAATGCTG ATCTTTATAAGCTCATGGGACACTTCGCATGGTGGACAGCCTTTGTTACTAATGTGAAT GCGTCATCATCTGAAGCATTTTTAATTGGATGTAATTATCTTGGCAAACCACGCGAACA AATAGATGGTTATGTCATGCATGCAAATTACATATTTTGGAGGAATACAAATCCAATTCA GTTGTCTTCCTATTCTTTATTTGACATGAGTAAATTTCCCCTTAAATTAAGGGGTACTGC TGTTATGTCTTTAAAAGAAGGTCAAATCAATGATATGATTTTATCTCTTCTTAGTAAAGG TAGACTTATAATTAGAGAAAACAACAGAGTTGTTATTTCTAGTGATGTTCTTGTTAACAA CTAAACGAACAATGTTTGTTTTTCTTGTTTTATTGCCACTAGTCTCTAGTCAGTGTGTTA ATCTTACAACCAGAACTCAATTACCCCCTGCATACACTAATTCTTTCACACGTGGTGTT TATTACCCTGACAAAGTTTTCAGATCCTCAGTTTTACATTCAACTCAGGACTTGTTCTTA CCTTTCTTTTCCAATGTTACTTGGTTCCATGCTATACATGTCTCTGGGACCAATGGTAC TAAGAGGTTTGATAACCCTGTCCTACCATTTAATGATGGTGTTTATTTTGCTTCCACTGA GAAGTCTAACATAATAAGAGGCTGGATTTTTGGTACTACTTTAGATTCGAAGACCCAGT CCCTACTTATTGTTAATAACGCTACTAATGTTGTTATTAAAGTCTGTGAATTTCAATTTT GTAATGATCCATTTTTGGGTGTTTATTACCACAAAAACAACAAAAGTTGGATGGAAAGT GAGTTCAGAGTTTATTCTAGTGCGAATAATTGCACTTTTGAATATGTCTCTCAGCCTTTT CTTATGGACCTTGAAGGAAAACAGGGTAATTTCAAAAATCTTAGGGAATTTGTGTTTAA GAATATTGATGGTTATTTTAAAATATATTCTAAGCACACGCCTATTAATTTAGTGCGTGA TCTCCCTCAGGGTTTTTCGGCTTTAGAACCATTGGTAGATTTGCCAATAGGTATTAACA TCACTAGGTTTCAAACTTTACTTGCTTTACATAGAAGTTATTTGACTCCTGGTGATTCTT CTTCAGGTTGGACAGCTGGTGCTGCAGCTTATTATGTGGGTTATCTTCAACCTAGGAC TTTTCTATTAAAATATAATGAAAATGGAACCATTACAGATGCTGTAGACTGTGCACTTGA CCCTCTCTCAGAAACAAAGTGTACGTTGAAATCCTTCACTGTAGAAAAAGGAATCTATC AAACTTCTAACTTTAGAGTCCAACCAACAGAATCTATTGTTAGATTTCCTAATATTACAA ACTTGTGCCCTTTTGGTGAAGTTTTTAACGCCACCAGATTTGCATCTGTTTATGCTTGG AACAGGAAGAGAATCAGCAACTGTGTTGCTGATTATTCTGTCCTATATAATTCCGCATC ATTTTCCACTTTTAAGTGTTATGGAGTGTCTCCTACTAAATTAAATGATCTCTGCTTTAC TAATGTCTATGCAGATTCATTTGTAATTAGAGGTGATGAAGTCAGACAAATCGCTCCAG GGCAAACTGGAAAGATTGCTGATTATAATTATAAATTACCAGATGATTTTACAGGCTGC GTTATAGCTTGGAATTCTAACAATCTTGATTCTAAGGTTGGTGGTAATTATAATTACCTG

		TATAGATTGTTTAGGAAGTCTAATCTCAAACCTTTTGAGAGAGATATTTCAACTGAAATC TATCAGGCCGGTAGCACACCTTGTAATGGTGTTGAAGGTTTTAATTGTTACTTTCCTTT ACAATCATATGGTTTCCAACCCACTAATGGTGTTGGTTACCAACCATACAGAGTAGTAG TACTTTCTTTTGAACTTCTACATGCACCAGCAACTGTTTGTGGACCTAAAAAGTCTACTA ATTTGGTTAAAAACAAATGTGTCAATTTCAACTTCAATGGTTTAACAGGCACAGGTGTT CTTACTGAGTCTAACAAAAAGTTTCTGCCTTTCCAACAATTTGGCAGAGACATTGCTGA CACTACTGATGCTGTCCGTGATCCACAGACACTTGAGATTCTTGACATTACACCATGTT CTTTTGGTGGTGTCAGTGTTATAACACCAGGAACAAATACTTCTAACCAGGTTGCTGTT CTTTATCAGGATGTTAACTGCACAGAAGTCCCTGTTGCTATTCATGCAGATCAACTTAC TCCTACTTGGCGTGTTTATTCTACAGGTTCTAATGTTTTTCAAACACGTGCAGGCTGTT TAATAGGGGCTGAACATGTCAACAACTCATATGAGTGTGACATACCCATTGGTGCAGG TATATGCGCTAGTTATCAGACTCAGACTAATTCTCCTCGGCGGGCACGTAGTGTAGCT AGTCAATCCATCATTGCCTACACTATGTCACTTGGTGCAGAAAATTCAGTTGCTTACTC TAATAACTCTATTGCCATACCCACAAATTTTACTATTAGTGTTACCACAGAAATTCTACC AGTGTCTATGACCAAGACATCAGTAGATTGTACAATGTACATTTGTGGTGATTCAACTG AATGCAGCAATCTTTTGTTGCAATATGGCAGTTTTTGTACACAATTAAACCGTGCTTTAA CTGGAATAGCTGTTGAACAAGACAAAAACACCCAAGAAGTTTTTGCACAAGTCAAACAA ATTTACAAAACACCACCAATTAAAGATTTTGGTGGTTTTAATTTTTCACAAATATTACCA GATCCATCAAAACCAAGCAAGAGGTCATTTATTGAAGATCTACTTTTCAACAAAGTGAC ACTTGCAGATGCTGGCTTCATCAAACAATATGGTGATTGCCTTGGTGATATTGCTGCTA GAGACCTCATTTGTGCACAAAAGTTTAACGGCCTTACTGTTTTGCCACCTTTGCTCACA GATGAAATGATTGCTCAATACACTTCTGCACTGTTAGCGGGTACAATCACTTCTGGTTG GACCTTTGGTGCAGGTGCTGCATTACAAATACCATTTGCTATGCAAATGGCTTATAGGT TTAATGGTATTGGAGTTACACAGAATGTTCTCTATGAGAACCAAAAATTGATTGCCAAC CAATTTAATAGTGCTATTGGCAAAATTCAAGACTCACTTTCTTCCACAGCAAGTGCACT TGGAAAACTTCAAGATGTGGTCAACCAAAATGCACAAGCTTTAAACACGCTTGTTAAAC AACTTAGCTCCAATTTTGGTGCAATTTCAAGTGTTTTAAATGATATCCTTTCACGTCTTG ACAAAGTTGAGGCTGAAGTGCAAATTGATAGGTTGATCACAGGCAGACTTCAAAGTTT GCAGACATATGTGACTCAACAATTAATTAGAGCTGCAGAAATCAGAGCTTCTGCTAATC TTGCTGCTACTAAAATGTCAGAGTGTGTACTTGGACAATCAAAAAGAGTTGATTTTTGT GGAAAGGGCTATCATCTTATGTCCTTCCCTCAGTCAGCACCTCATGGTGTAGTCTTCTT GCATGTGACTTATGTCCCTGCACAAGAAAAGAACTTCACAACTGCTCCTGCCATTTGTC ATGATGGAAAAGCACACTTTCCTCGTGAAGGTGTCTTTGTTTCAAATGGCACACACTG GTTTGTAACACAAAGGAATTTTTATGAACCACAAATCATTACTACAGACAACACATTTGT GTCTGGTAACTGTGATGTTGTAATAGGAATTGTCAACAACACAGTTTATGATCCTTTGC AACCTGAATTAGACTCATTCAAGGAGGAGTTAGATAAATATTTTAAGAATCATACATCA CCAGATGTTGATTTAGGTGACATCTCTGGCATTAATGCTTCAGTTGTAAACATTCAAAA AGAAATTGACCGCCTCAATGAGGTTGCCAAGAATTTAAATGAATCTCTCATCGATCTCC AAGAACTTGGAAAGTATGAGCAGTATATAAAATGGCCATGGTACATTTGGCTAGGTTTT ATAGCTGGCTTGATTGCCATAGTAATGGTGACAATTATGCTTTGCTGTATGACCAGTTG CTGTAGTTGTCTCAAGGGCTGTTGTTCTTGTGGATCCTGCTGCAAATTTGATGAAGAC GACTCTGAGCCAGTGCTCAAAGGAGTCAAATTACATTACACATAAACGAACTTATGGAT TTGTTTATGAGAATCTTCACAATTGGAACTGTAACTTTGAAGCAAGGTGAAATCAAGGA TGCTACTCCTTCAGATTTTGTTCGCGCTACTGCAACGATACCGATACAAGCCTCACTCC CTTTCGGATGGCTTATTGTTGGCGTTGCACTTCTTGCTGTTTTTCAGAGCGCTTCCAAA ATCATAACCCTCAAAAAGAGATGGCAACTAGCACTCTCCAAGGGTGTTCACTTTGTTTG CAACTTGCTGTTGTTGTTTGTAACAGTTTACTCACACCTTTTGCTCGTTGCTGCTGGCC TTGAAGCCCCTTTTCTCTATCTTTATGCTTTAGTCTACTTCTTGCAGAGTATAAACTTTG TAAGAATAATAATGAGGCTTTGGCTTTGCTGGAAATGCCGTTCCAAAAACCCATTACTT TATGATGCCAACTATTTTCTTTGCTGGCATACTAATTGTTACGACTATTGTATACCTTAC AATAGTGTAACTTCTTCAATTGTCATTACTTCAGGTGATGGCACAACAAGTCCTATTTCT GAACATGACTACCAGATTGGTGGTTATACTGAAAAATGGGAATCTGGAGTAAAAGACT GTGTTGTATTACACAGTTACTTCACTTCAGACTATTACCAGCTGTACTCAACTCAATTGA GTACAGACACTGGTGTTGAACATGTTACCTTCTTCATCTACAATAAAATTGTTGATGAG CCTGAAGAACATGTCCAAATTCACACAATCGACGGTTCATCCGGAGTTGTTAATCCAG TAATGGAACCAATTTATGATGAACCGACGACGACTACTAGCGTGCCTTTGTAAGCACA AGCTGATGAGTACGAACTTATGTACTCATTCGTTTCGGAAGAGACAGGTACGTTAATA GTTAATAGCGTACTTCTTTTTCTTGCTTTCGTGGTATTCTTGCTAGTTACACTAGCCATC CTTACTGCGCTTCGATTGTGTGCGTACTGCTGCAATATTGTTAACGTGAGTCTTGTAAA ACCTTCTTTTTACGTTTACTCTCGTGTTAAAAATCTGAATTCTTCTAGAGTTCCTGATCT TCTGGTCTAAACGAACTAAATATTATATTAGTTTTTCTGTTTGGAACTTTAATTTTAGCCA TGGCAGATTCCAACGGTACTATTACCGTTGAAGAGCTTAAAAAGCTCCTTGAACAATG GAACCTAGTAATAGGTTTCCTATTCCTTACATGGATTTGTCTTCTACAATTTGCCTATGC CAACAGGAATAGGTTTTTGTATATAATTAAGTTAATTTTCCTCTGGCTGTTATGGCCAGT AACTTTAGCTTGTTTTGTGCTTGCTGCTGTTTACAGAATAAATTGGATCACCGGTGGAA TTGCTATCGCAATGGCTTGTCTTGTAGGCTTGATGTGGCTCAGCTACTTCATTGCTTCT

		TTCAGACTGTTTGCGCGTACGCGTTCCATGTGGTCATTCAATCCAGAAACTAACATTCT TCTCAACGTGCCACTCCATGGCACTATTCTGACCAGACCGCTTCTAGAAAGTGAACTC GTAATCGGAGCTGTGATCCTTCGTGGACATCTTCGTATTGCTGGACACCATCTAGGAC GCTGTGACATCAAGGACCTGCCTAAAGAAATCACTGTTGCTACATCACGAACGCTTTC TTATTACAAATTGGGAGCTTCGCAGCGTGTAGCAGGTGACTCAGGTTTTGCTGCATAC AGTCGCTACAGGATTGGCAACTATAAATTAAACACAGACCATTCCAGTAGCAGTGACA ATATTGCTTTGCTTGTACAGTAAGTGACAACAGATGTTTCATCTCGTTGACTTTCAGGT TACTATAGCAGAGATATTACTAATTATTATGAGGACTTTTAAAGTTTCCATTTGGAATCT TGATTACATCATAAACCTCATAATTAAAAATTTATCTAAGTCACTAACTGAGAATAAATAT TCTCAATTAGATGAAGAGCAACCAATGGAGATTGATTAAACGAACATGAAAATTATTCT TTTCTTGGCACTGATAACACTCGCTACTTGTGAGCTTTATCACTACCAAGAGTGTGTTA GAGGTACAACAGTACTTTTAAAAGAACCTTGCTCTTCTGGAACATACGAGGGCAATTCA CCATTTCATCCTCTAGCTGATAACAAATTTGCACTGACTTGCTTTAGCACTCAATTTGCT TTTGCTTGTCCTGACGGCGTAAAACACGTCTATCAGTTACGTGCCAGATCAGTTTCAC CTAAACTGTTCATCAGACAAGAGGAAGTTCAAGAACTTTACTCTCCAATTTTTCTTATTG TTGCGGCAATAGTGTTTATAACACTTTGCTTCACACTCAAAAGAAAGACAGAATGATTG AACTTTCATTAATTGACTTCTATTTGTGCTTTTTAGCCTTTCTGCTATTCCTTGTTTTAAT TATGCTTATTATCTTTTGGTTCTCACTTGAACTGCAAGATCATAATGAAACTTGTCACGC CTAAACGAACATGAAATTTCTTGTTTTCTTAGGAATCATCACAACTGTAGCTGCATTTCA CCAAGAATGTAGTTTACAGTCATGTACTCAACATCAACCATATGTAGTTGATGACCCGT GTCCTATTCACTTCTATTCTAAATGGTATATTAGAGTAGGAGCTAGAAAATCAGCACCT TTAATTGAATTGTGCGTGGATGAGGCTGGTTCTAAATCACCCATTCAGTACATCGATAT CGGTAATTATACAGTTTCCTGTTTACCTTTTACAATTAATTGCCAGGAACCTAAATTGGG TAGTCTTGTAGTGCGTTGTTCGTTCTATGAAGACTTTTTAGAGTATCATGACGTTCGTG TTGTTTTAGATTTCATCTAAACGAACAAACTAAAATGTCTGATAATGGACCCCAAAATCA GCGAAATGCACCCCGCATTACGTTTGGTGGACCCTCAGATTCAACTGGCAGTAACCAG AATGGAGAACGCAGTGGGGCGCGATCAAAACAACGTCGGCCCCAAGGTTTACCCAAT AATACTGCGTCTTGGTTCACCGCTCTCACTCAACATGGCAAGGAAGACCTTAAATTCC CTCGAGGACAAGGCGTTCCAATTAACACCAATAGCAGTCCAGATGACCAAATTGGCTA CTACCGAAGAGCTACCAGACGAATTCGTGGTGGTGACGGTAAAATGAAAGATCTCAGT CCAAGATGGTATTTCTACTACCTAGGAACTGGGCCAGAAGCTGGACTTCCCTATGGTG CTAACAAAGACGGCATCATATGGGTTGCAACTGAGGGAGCCTTGAATACACCAAAAGA TCACATTGGCACCCGCAATCCTGCTAACAATGCTGCAATCGTGCTACAACTTCCTCAA GGAACAACATTGCCAAAAGGCTTCTACGCAGAAGGGAGCAGAGGCGGCAGTCAAGCC TCTTCTCGTTCCTCATCACGTAGTCGCAACAGTTCAAGAAATTCAACTCCAGGCAGCA GTAGGGGAACTTCTCCTGCTAGAATGGCTGGCAATGGCGGTGATGCTGCTCTTGCTTT GCTGCTGCTTGACAGATTGAACCAGCTTGAGAGCAAAATGTCTGGTAAAGGCCAACAA CAACAAGGCCAAACTGTCACTAAGAAATCTGCTGCTGAGGCTTCTAAGAAGCCTCGGC AAAAACGTACTGCCACTAAAGCATACAATGTAACACAAGCTTTCGGCAGACGTGGTCC AGAACAAACCCAAGGAAATTTTGGGGACCAGGAACTAATCAGACAAGGAACTGATTAC AAACATTGGCCGCAAATTGCACAATTTGCCCCCAGCGCTTCAGCGTTCTTCGGAATGT CGCGCATTGGCATGGAAGTCACACCTTCGGGAACGTGGTTGACCTACACAGGTGCCA TCAAATTGGATGACAAAGATCCAAATTTCAAAGATCAAGTCATTTTGCTGAATAAGCAT ATTGACGCATACAAAACATTCCCACCAACAGAGCCTAAAAAGGACAAAAAGAAGAAGG CTGATGAAACTCAAGCCTTACCGCAGAGACAGAAGAAACAGCAAACTGTGACTCTTCT TCCTGCTGCAGATTTGGATGATTTCTCCAAACAATTGCAACAATCCATGAGCAGTGCTG ACTCAACTCAGGCCTAAACTCATGCAGACCACACAAGGCAGATGGGCTATATAAACGT TTTCGCTTTTCCGTTTACGATATATAGTCTACTCTTGTGCAGAATGAATTCTCGTAACTA CATAGCACAAGTAGATGTAGTTAACTTTAATCTCACATAGCAATCTTTAATCAGTGTGTA ACATTAGGGAGGACTTGAAAGAGCCACCACATTTTCACCGAGGCCACGCGGAGTACG ATCGAGTGTACAGTGAACAATGCTAGGGAGAGCTGCCTATATGGAAGAGCCCTAATGT GTAAAATTAATTTTAGTAGTGCTATCCCCATGTGATTTTAATAGCTTCTTAGGAGAATGA CAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
9	SARS-CoV spike protein	MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLPF YSNVTGFHTINHTFDNPVIPFKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVI RACNFELCDNPFFAVSKPMGTQTHTMIFDNAFNCTFEYISDAFSLDVSEKSGNFKHLREFV FKNKDGFLYVYKGYQPIDVVRDLPSGFNTLKPIFKLPLGINITNFRAILTAFSPAQDTWGTSA AAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPS GDVVRFPNITNLCPFGEVFNATKFPSVYAWERKKISNCVADYSVLYNSTFFSTFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDAT STGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLNDYGFYTTTGIGY QPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQF GRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNASSEVAVLYQDVNCTDVSTAIHAD QLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSLLRSTSQKSIV AYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQY GSFCTQLNRALSGIAAEQDRNTREVFAQVKQMYKTPTLKYFGGFNFSQILPDPLKPTKRSF

		IEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAALVS GTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTT TSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQ SLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVVF LHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSG NCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLN EVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACS CGSCCKFDEDDSEPVLKGVKLHYT
10	SARS-CoV-2 spike protein	MFLLTTKRTMFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQ DLFLPFFSNVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKT QSLLIVNNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQP FLMDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITR FQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISN CVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADY NYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNG VEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNFN FNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNT SNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDI PIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILP VSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIY KTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICA QKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIGVTQ NVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISS VLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSK RVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAICHDGKAHFPREGVFVS NGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKN HTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFI AGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHYT
11	SARS-CoV spike protein S1 subunit	SDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLPFYSNVTGFHTINH TFDNPVIPFKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVIRACNFELCDNP FFAVSKPMGTQTHTMIFDNAFNCTFEYISDAFSLDVSEKSGNFKHLREFVFKNKDGFLYVY KGYQPIDVVRDLPSGFNTLKPIFKLPLGINITNFRAILTAFSPAQDTWGTSAAAYFVGYLKPT TFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPSGDVVRFPNITNL CPFGEVFNATKFPSVYAWERKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNDLCFSNVY ADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDATSTGNYNYKYRYL RHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLNDYGFYTTTGIGYQPYRVVVLSFELL NAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQFGRDVSDFTDSVRD PKTSEILDISPCSFGGVSVITPGTNASSEVAVLYQDVNCTDVSTAIHADQLTPAWRIYSTGN NVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSLLR
12	SARS-CoV spike protein RBD	RVVPSGDVVRFPNITNLCPFGEVFNATKFPSVYAWERKKISNCVADYSVLYNSTFFSTFKC YGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTR NIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLNDYGFYTT TGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNF
13	SARS-CoV-2 spike protein S1 subunit	SQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGT NGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIVNNATNVVIKVCEFQF CNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVF KNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQTLLALHRSYLTPGDSSSG WTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSNF RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKC YGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNN LDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPT NGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNKKFL PFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVP VAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYQTQTNSPR RAR
14	SARS-CoV-2 spike protein RBD	RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKC YGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNN LDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPT NGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNF
15	SARS-CoV-2 spike protein RBD	PNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDL CFTNVYDSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNY LYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVV VLSFELLHAPATVCGPKKS

16	SARS-CoV-2 spike protein S1 subunit	MLLVNQSHQGFNKEHTSKMVSAIVLYVLLAAAAHSAFAQCVNLTTRTQLPPAYTNSFTRG VYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFAST EKSNIIRGWIFGTTLDSKTQSLLIVNNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEF RVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQ GFSALEPLVDLPIGINITRFQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYN ENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVF NATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIR GDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKP FERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPAT VCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEI LDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQT RAGCLIGAEHVNNSYECDIPIGAGICASYQTQTNSPRRAR
17	SARS-CoV spike protein RBD	MNITNLCPFGEVFNATKFPSVYAWERKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNDL CFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDATSTGNYN YKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLNDYGFYTTTGIGYQPYRVV VLSFELLNAPATYLSLNTAAAL
18	Artificial Sarbecovirus spike consensus 1	MFIFLFFLTLVSGSTIEKCTTFDDVQPPNYTQFLSSHRGVYYPDDIFRSDVLHLTQDHFLPF DSNVTGFITFGLNFDNPIIPFKDGIYFAATEKSNVIRGWVFGSTMNNKSQSVIIMNNSTNVVI RACNFELCDNPFFAVSKPNNTQIPSYIFBNAFNCTFEYVSDDFNLDVGEKPGNFKHLREFV FKNKDGFLYVYSGYQPIDVASGLPSGFNALKPIFKLPLGINITNFRTLLTAFPPRPDYWGTS AAAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPS GDVVRFPNITNLCPFGEVFNATKFPSVYAWERKRISNCVADYSVLYNSTFFSTFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDAT STGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLNDYGFYTTTGIGY QPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQF GRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNTSSEVAVLYQDVNCTDVPVAIHAD QLTPAWRVYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSSLRSTSQKSI VAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQ YGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFSQILPDPLKPTKR SFIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAAL VSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESL TTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQIDRLITGRL QSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVV FLHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVS GSCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRL NEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGAC SCGSCCKFDEDDSEPVLKGVKLHYT
19	Artificial Sarbecovirus spike consensus 2	MFIFLLFFTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLPF YSNVTGFHTINHTFDNPVIPFKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVI RACNFELCDNPFFVVSKPMGTRTHTMIFDNAFNCTFEYISDAFSLDVSEKSGNFKHLREFV FKNKDGFLYVYKGYQPIDVVRDLPSGFNTLKPIFKLPLGIKITNFRAILTAFSPAQGTWGTSA AAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVVPS GDVVRFPNITNLCPFGEVFNATKFPSVYAWERKRISNCVADYSVLYNSTSFSTFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDAT STGNHNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPAPNCYWPLRGYGFYTTSGIGY QPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQF GRDVSDFTDSVRDPKTSEILDISPRSFGGVSVITPGTNASSEVAVLYQDVNCTDVSTLIHAE QLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSSLRSTSQKSIV AYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMTKTSVDCNMYICGDSTECANLLLQY GSFCRQLNRALSGIAAEQDRNTREVFVQVKQMYKTPTLKDFGGFNFSQILPDPLKPTKRS FIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTVDMIAAYTAALVS GTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTT TSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQIDRLITGRLQ SLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVGFCGKGYHLMSFPQAAPHGVVF LHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFSGTSWFITQRNFFSPQIITTDNTFVSG NCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQEEIDRLN EVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACS CGSCCKFDEDDSEPVLKGVKLHYT
20	Artificial Sarbecovirus spike consensus 3	MFIFLFFLTLVSGSDLESCTTFDDVQAPNYPQHSSSRRGVYYPDEIFRSDTLYLTQDLFLPF DSNVTGFHTINHRFDNPVIPFKDGVYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNV VIRACNFELCDNPFFAVSKPTGTQTHTMIFBNAFNCTFEYISDSFSLDVAEKSGNFKHLREF VFKNKDGFLYVYKGYQPIDVVRDLPSGFNILKPIFKLPLGINITNFRAILTAFLPAQDTWGTS AAAYFVGYLKPATFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVAP SKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFSTFKCYGVS ATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAWNTRNIDAT QTGNYNYKYRSLRHGKLRPFERDISNVPFSPDGKPCTPPAFNCYWPLNDYGFYTTNGIGY

		QPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQF GRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNTSSEVAVLYQDVNCTDVPVAIHAD QLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSSLRSTSQKSIV AYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQY GSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFSQILPDPLKPTKRSF IEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAALVS GTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTT TSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQIDRLITGRLQ SLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVVF LHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSG NCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLN EVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACS CGSCCKFDEDDSEPVLKGVKLHYT
21	Artificial Sarbecovirus spike consensus 4	MFIFLFFLTLVSGSTIEKCTTFDDVQPPNYTQFLSSHRGVYYPDDIFRSDVLHLTQDHFLPF DSNVTGFITFGLNFDNPIIPFKDGIYFAATEKSNVIRGWVFGSTMNNKSQSVIIMNNSTNVVI RACNFELCDNPFFAVSKPNNTQIPSYIFBNAFNCTFEYVSDDFNLDVGEKPGNFKHLREFV FKNKDGFLYVYSGYQPIDVASGLPSGFNALKPIFKLPLGINITNFRTLLTAFPPRPDYWGTS AAAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTSNFRVAPS KEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFSTFKCYGVSA TKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAWNTRNIDAT STGNYNYKYRSLRHGKLRPFERDISNVPFSPDGKPCTPPAFNCYWPLNDYGFFTTNGIGY QPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQPFQQF GRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNTSSEVAVLYQDVNCTDVPVAIHAD QLTPAWRVYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSSLRSTSQKSI VAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQ YGSFCTQLNRALSGIAVEQDRNTREVFAQVKQMYKTPTLKDFGGFNFSQILPDPLKPTKR SFIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAAL VSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESL TTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQIDRLITGRL QSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVV FLHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVS GSCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRL NEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGAC SCGSCCKFDEDDSEPVLKGVKLHYT
22	Artificial Sarbecovirus spike consensus 5	MFVFLFLLPLVSSQCVNLTTRTGIPPGYTNSSTRGVYYPDKVFRSSVLHLTQDLFLPFFSNV TWFNAINYQGGFKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDARTQSLLIVNNATNV VIKVCEFQFCTDPFLGVYYHNNNKTWVENEFRVYSSANNCTFEYVSQPFLMDLEGKQGN FKNLREFVFKNVDGYFKIYSKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFQTLLALHRSYL TPGKLESGWTTGAAAYYVGYLQPRTFLLSYNENGTITDAVDCALDPLSETKCTLKSLTVEK GIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNST SFSTFKCYGVSPTKLNDLCFTNVYADSFVVRGDEVRQIAPGQTGVIADYNYKLPDDFTGC VIAWNSVKQDALTGGNYNYLYRLFRKSKLKPFERDISTEIYQAGSTPCNGVVGLNCYYPLQ RYGFHPTTGVGYQPYRVVVLSFELLNAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLT ESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDV NCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYQT QTNSPRRARSVNSQSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTKTSVDCT MYICGDSIECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFN FSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICAQKFNGLTVLPPL LTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKLIAN QFNSAIGKIQDSLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPP EAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYH LMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAICHEGKAHFPREGVFVSNGTHWFVTQR NFYEPQIITTDNTFVSGSCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDIS GINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIIMVTIMLC CMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHYT
23	Artificial Sarbecovirus spike consensus 6	MFVFLFLLPLVSSQCVNLTTRTGIPPGYTNSSTRGVYYPDKVFRSSVLHLTQDLFLPFFSNV TWFNAINYQGGFKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDARTQSLLIVNNATNV VIKVCEFQFCTDPFLGVYYHNNNKTWVENEFRVYSSANNCTFEYVSQPFLMDLEGKQGN FKNLREFVFKNVDGYFKIYSKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFQTLLALHRSYL TPGKLESGWTTGAAAYYVGYLQPRTFLLSYNENGTITDAVDCALDPLSETKCTLKSFTVEK GIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNS ASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGC VIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQ SYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLT ESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDV NCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYQT

		QTNSPRRARSVNSQSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTKTSVDCT MYICGDSIECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFN FSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICAQKFNGLTVLPPL LTDEMIAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKLIAN QFNSAIGKIQDSLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPP EAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYH LMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAICHEGKAHFPREGVFVSNGTHWFVTQR NFYEPQIITTDNTFVSGSCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDIS GINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIIMVTIMLC CMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHYT
24	Artificial Sarbecovirus spike consensus 7	MFVFLFLLPLVSSQCVNLTTRTGIPPGYTNSSTRGVYYPDKVFRSSILHLTQDLFLPFFSNV TWFNTINYQGGFKKFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDNTTQSLLIVNNATNV VIKVCEFQFCTDPFLGVYYHNNNKTWVENEFRVYSSANNCTFEYVSQPFLMDLEGKQGN FKNLREFVFKNVDGYFKIYSKHTPIDLVRDLPRGFSALEPLVDLPIGINITRFQTLLALHRSYL TPGKLESGWTTGAAAYYVGYLQQRTFLLSYNENGTITDAVDCSLDPLSETKCTLKSLTVEK GIYQTSNFRVQPTISIVRFPNITNLCPFGEVFNATKFASVYAWNRKRISNCVADYSVLYNST SFSTFKCYGVSPTKLNDLCFTNVYADSFVVRGDEVRQIAPGQTGVIADYNYKLPDDFTGC VIAWNSVKQDAKTGGNYNYLYRLFRKSKLKPFERDISTEIYQAGSTPCNGVVGLNCYYPLE RYGFHPTNGVGYQPYRVVVLSFELLNAPATVCGPKLSTTLVKNKCVNFNFNGLTGTGVLT TSKKKFLPFQQFGRDISDTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQVAVLYQDV NCTEVPMAIHADQLTPTWRVYSTGANVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYHT QTNSRSVNSQSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTKTSVDCTMYIC GDSIECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFSQI LPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICAQKFNGLTVLPPLLTDE MIAQYTSALLAGTITSGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKLIANQFNS AIGKIQDSLSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEV QIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSF PQSAPHGVVFLHVTYVPAQEKNFTTAPAICHEGKAHFPREGVFVSNGTHWFVTQRNFYE PQIITTDNTFVSGSCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINA SVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIIMVTIMLCCMT SCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHYT
25	Artificial Sarbecovirus spike consensus 8	MFIFLFFLTLVSSQCVNFDDRTPPPPTQTNSSTRGVYYPDDIFRSSVLHLTQDLFLPFFSNV TWFHTINYRFDNPVIPFKDGVYFAATEKSNVIRGWIFGSTMDNKSQSVIIVNNSTNVVIRVC NFQLCDNPFFAVYNKTWTQIESRVYSNAFNCTFEYVSKSFLLDLGEKQGNFKHLREFVFK NKDGFLKVYSGYTPIDLVRDLPSGFNALKPIFKLPLGINITNFRTLLTAFRPGQSGWGTSAA AYFVGYLKPRTFMLKYDENGTITDAVDCSQDPLAELKCTLKSFEVEKGIYQTSNFRVQPTK EVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFSTFKCYGVSPT KLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAWNTRNIDATT GGNYNYLYRLFRHSKLKPFERDISNVIYSPGGKPCTPPGFNCYWPLNDYGFYPTNGVGYQ PYRVVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNFNGLTGTGVLTPSSKRFQPFQQFG RDVSDFTDSVRDPKTLEILDISPCSFGGVSVITPGTNTSSZVAVLYQDVNCTDVPVAIHADQ LTPAWRVYSTGNNVFQTQAGCLIGAEHVNNSYECDIPIGAGICASYHTVSSLRSTSQKSIV AYTMSLGAENSIAYSNNSIAIPTNFSISVTTEVLPVSMTKTSVDCTMYICGDSTECSNLLLQY GSFCTQLNRALSGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFI EDLLFNKVTLADAGFMKQYGDCLGDINARDLICAQKFNGLTVLPPLLTDEMIAAYTAALVSG TATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTTT STALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQIDRLITGRLQS LQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVVFL HVTYVPSQERNFTTAPAICHEGKAHFPREGVFVSNGTHWFITQRNFYSPQIITTDNTFVSG SCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLN EVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCS CGSCCKFDEDDSEPVLKGVKLHYT
26	Artificial Sarbecovirus RBD consensus 1	SNFRVVPSGDVVRFPNITNLCPFGEVFNATKFPSVYAWERKRISNCVADYSVLYNSTSFST FKCYGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAW NTRNIDATSTGNHNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPAPNCYWPLRGYGF YTTSGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKR FQPFQQFGRDVSDFTDSVRDPKTSEIL
27	Artificial Sarbecovirus RBD consensus 2	SNFRVAPSKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFST FKCYGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAW NTRNIDATQTGNYNYKYRSLRHGKLRPFERDISNVPFSPDGKPCTPPAFNCYWPLNDYGY TTNGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSRFQ PFQQFGRDVSDFTDSVRDPKTSEIL
28	Artificial Sarbecovirus RBD consensus 3	SNFRVQPTISIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSTSFSTF KCYGVSPTKLNDLCFTNVYADSFVVRGDEVRQIAPGQTGVIADYNYKLPDDFTGCVIAWN SVKQDALTGGNYNYLYRLFRKSKLKPFERDISTEIYQAGSTPCNGVVGLNCYYPLQRYGF

		HPTTGVGYQPYRVVVLSFELLNAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNK KFLPFQQFGRDIADTTDAVRDPQTLEIL
29	Artificial Sarbecovirus RBD consensus 4	SNFRVQPTISIVRFPNITNLCPFGEVFNATKFASVYAWNRKRISNCVADYSVLYNSTSFSTF KCYGVSPTKLNDLCFTNVYADSFVVRGDEVRQIAPGQTGVIADYNYKLPDDFTGCVIAWN SVKQDAKTGGNYNYLYRLFRKSKLKPFERDISTEIYQAGSTPCNGVVGLNCYYPLERYGF HPTNGVGYQPYRVVVLSFELLNAPATVCGPKLSTTLVKNKCVNFNFNGLTGTGVLTTSKK KFLPFQQFGRDISDTTDAVRDPQTLEIL
30	Artificial Sarbecovirus RBD consensus 5	SNFRVQPTKEVVRFPNITNLCPFGEVFNATTFPSVYAWERKRISNCVADYSVLYNSTSFST FKCYGVSPTKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFTGCVLAW NTRNIDATTGGNYNYLYRLFRHSKLKPFERDISNVIYSPGGKPCTPPGFNCYWPLNDYGFY PTNGVGYQPYRVVVLSFELLNAPATVCGPKLSTDLVKNKCVNFNFNGLTGTGVLTPSSKR FQPFQQFGRDVSDFTDSVRDPKTLEIL

[00152] Examples

[00153] In the following Examples, the inventors present antigen-binding molecule which binds to a wide range of sarbecovirus spike protein.

[00154] **Example 1 human serum panels**

[00155] 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.

[00156] 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**).

[00157] **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

[00158] 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.

[00159] Multiplex surrogate Virus Neutralizing Test (sVNT) based on RBD from six different sarbecoviruses

[00160] 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 (Figure 1) 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 B1.351; SC2r-CoV GX-P5L and SC2r-CoV RaTG13.

[00161] 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, 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.

[00162] The cross-NAb data demonstrated two highly important features: 1) vaccination of SARS survivors produced very high NAbs against all viruses studied (Figure 2D), even 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 (Figure 2C); 3) SARS patients had minimal cross- NAbs to any of the other five viruses before vaccination (Figure 2A) 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 (Figure 2B).

[00163] 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 Figure 2C, it is clear that the NAbs have a relatively narrow spectrum as some individuals had lower NAbs against the UK and/or SA variants, 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 (Figure 2B).

[00164] 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 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.

[00165] Pan-sarbecovirus mAb inhibition assay

[00166] 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.).

[00167] 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.

[00168] Using serial dilutions, we have further illustrated the best performance of pan-sarbecovirus cross-neutralization by the SARS-vaccinated group (Figure 3). This is the first real life human study/data demonstrating the feasibility of a pan-sarbecovirus antigen-binding molecule.

[00169] Example 2. Mouse studies

[00170] In this study, the mouse mAb 5B7D7 was used. As shown in Figure 4A, 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 (Figure 4B). Several important findings were made from this 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 representing SC2r-CoVs and SARS-CoV. Third, although the mRNA vaccination boosted overall neutralizing ability against SCr2-CoVs, it had minimal impact on cross-neutralization against SARS-CoV.

[00171] Example 3 Rabbit studies

[00172] 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.

[00173] Multiplex sVNT analysis using rabbit hyper immune sera targeting RBD of six different beta coronaviruses.

[00174] 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.

[00175] The data presented in Figure 5 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.

[00176] 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.

[00177] As would be understood by a person skilled in the art, each embodiment may be used in combination with other embodiment or several embodiments.

Claims

1. An antigen-binding molecule which binds to a sarbecovirus spike protein from two or more different sarbecovirus.

2. The antigen-binding molecule according to claim 1, comprising two antigen-binding molecules which binds to different sarbecovirus spike protein.

3. The antigen-binding molecule according to claim 1 or 2, wherein the antigen-binding molecule binds to the receptor binding domain (RBD) of the Sarbecovirus spike protein.

4 The antigen-binding molecule according to any one of claims 1 to 3, wherein the antigen-binding molecule inhibits interaction between a sarbecovirus spike protein and Angiotensinogen converting enzyme 2 (ACE2).

5. The antigen-binding molecule according to any one of claims 1 to 4, wherein the antigen-binding molecule inhibits infection of ACE2-expressing cells by a sarbecovirus.

6. The antigen-binding molecule according to any one of claims 1 to 5, wherein the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

7. The antigen-binding molecule according to any one of claims 1 to 6, wherein the antigen-binding molecule comprises:

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

HC-CDR1 having the amino acid sequence of SEQ ID NO:2

HC-CDR2 having the amino acid sequence of SEQ ID NO:3

HC-CDR3 having the amino acid sequence of SEQ ID NO:4; and

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

LC-CDR1 having the amino acid sequence of SEQ ID NO: 5

LC-CDR2 having the amino acid sequence of SEQ ID NO: 6

LC-CDR3 having the amino acid sequence of SEQ ID NO:7.

8. The antigen-binding molecule according to any one of claims 1 to 7, wherein the antigen-binding molecule comprises:

a VH region comprising an amino acid sequence having at least 85% 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 85% sequence identity to the amino acid sequence of SEQ ID NO: 5, 6 or 7.

9. The antigen-binding molecule produced by cell line XXXX, deposited XXXXXXXX as ATCC accession number PTA-XXXXX or cell line YYYY, deposited YYYYYYYY as ATCC accession number PTA-YYYYY.

10. A nucleic acid, or a plurality of nucleic acids, optionally isolated, encoding the antigen-binding molecule according to any one of claims 1 to 9.

11. An expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids according to claim 10.

12. A cell comprising an antigen-binding molecule according to any one of claims 1 to 9, a nucleic acid or a plurality of nucleic acids according to claim 10, or an expression vector or a plurality of expression vectors according to claim 11.

13. A cell of the cell line designated XXXX, deposited XXXXXXXX as ATCC accession number PTA-XXXXX or cell line YYYY, deposited YYYYYYYY as ATCC accession number PTA-YYYYY.

14. A method for producing antigen-binding molecule which binds to a sarbecovirus spike protein, comprising culturing a cell according to claim 12 or claim 13 under conditions suitable for expression of an antigen-binding molecule by the cell.

15. A composition comprising the antigen-binding molecule according to any one of claims 1 to 9, the nucleic acid or the plurality of nucleic acids according to claim 10, the expression vector or the plurality of expression vectors according to claim 11, or the cell according to claim 12 or claim 13, and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

16. The antigen-binding molecule according to any one of claims 1 to 9, a nucleic acid or a plurality of nucleic acids according to claim 10, an expression vector or a plurality of expression vectors according to claim 11, a cell according to claim 12 or 13, or a composition according to claim 15, for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

17. The antigen-binding molecule according to any one of claims 1 to 9, a nucleic acid or a plurality of nucleic acids according to claim 10, an expression vector or a plurality of expression vectors according to claim 11, a cell according to claim 12 or 13, or a composition according to claim 15, for use according to claim 16, wherein the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

18. Use of the antigen-binding molecule according to any one of claims 1 to 9, a nucleic acid or a plurality of nucleic acids according to claim 10, an expression vector or a plurality of expression vectors according to claim 11, or, a cell according to claim 12 or 13, or a composition according to claim 15, in the manufacture of a medicament for use in treatment or prevention of a disease caused by infection with a sarbecovirus.

19. The use according to claim 18, wherein the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

20. 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 the antigen-binding molecule according to any one of claims 1 to 9, the nucleic acid or a

plurality of nucleic acids according to claim 10, an expression vector or a plurality of expression vectors according to claim 11, a cell according to claim 12 or 13, or a composition according to claim 15.

21. The method or claim 20, wherein the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.

22. Use of the antigen-binding molecule according to any one of claims 1 to 9 to inhibit infection of ACE2-expressing cells by a sarbecovirus.

23. Use of claim 22, wherein the sarbecovirus is selected from the group comprising SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.1.7, SARS-CoV-2 B.1.351, SC2r-CoV RaTG13, and SC2r-CoV GX-P5L.