

HUMAN MONOCLONAL ANTIBODIES TO SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-CoV-2)

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PRIORITY

This application claims benefit of priority to U.S. Provisional Application Serial Nos. 62/972,877, filed February 11, 2020 and 62/994,627, filed March 25, 2020, the entire contents of both applications being hereby incorporated by reference.

The sequence listing that is contained in the file named “VBLTP0307WO1_ST25.txt”, which is 4,165 KB (as measured in Microsoft Windows®) and was created on February 10, 2021, is filed herewith by electronic submission and is incorporated by reference herein.

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BACKGROUND

1. Field of the Disclosure

The present disclosure relates generally to the fields of medicine, infectious disease, and immunology. More particular, the disclosure relates to human antibodies binding to a novel coronavirus designated SARS-CoV-2 and methods of use therefor.

2. Background

An epidemic of a novel coronavirus (SARS-CoV-2) affected mainland China, along with cases in 179 other countries and territories. It was identified in Wuhan, the capital of China's Hubei province, after 41 people developed pneumonia without a clear cause. The virus, which causes acute respiratory disease designated coronavirus disease 2019 (COVID-19), is capable of spreading from person to person. The incubation period (time from exposure to onset of symptoms) ranges from 0 to 24 days, with a mean of 3-5 days, but it may be contagious

during this period and after recovery. Symptoms include fever, coughing and breathing difficulties. An estimate of the death rate in February 2020 was 2% of confirmed cases, higher among those who require admission to hospital.

As of 10 February 2020, 40,627 cases have been confirmed (6,495 serious), including
5 in every province-level division of China. A larger number of people may have been infected, but not detected (especially mild cases). As of 10 February 2020, 910 deaths have been attributed to the virus since the first confirmed death on 9 January, with 3,323 recoveries. The first local transmission outside China occurred in Vietnam between family members, while the first international transmission not involving family occurred in Germany on 22 January. The
10 first death outside China was in the Philippines, where a man from Wuhan died on 1 February. As of 10 February 2020, the death toll from this virus had surpassed the global SARS outbreak in 2003.

As of early February 2020, there is no licensed vaccine and no specific treatment, although several vaccine approaches and antivirals are being investigated. The outbreak has
15 been declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO), based on the possible effects the virus could have if it spreads to countries with weaker healthcare systems. Thus, there is an urgent need to explore the biology and pathology of SARS-CoV-2 and well as the human immune response to this virus.

SUMMARY

Thus, in accordance with the present disclosure, there is provided a method of detecting COVID-19 infection with SARS-CoV-2 in a subject comprising (a) contacting a sample from said subject with an antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively; and (b) detecting SARS-CoV-2 in said sample by binding of said antibody or antibody fragment to a SARS-CoV-2 antigen in said sample. The sample may be a body fluid, such as blood, sputum, tears, saliva, mucous or serum, semen, cervical or vaginal secretions, amniotic fluid, placental tissues, urine, exudate, transudate, tissue scrapings or feces. Detection may comprise ELISA, RIA, lateral flow assay or western blot. The method may further comprise performing steps (a) and (b) a second time and determining a change in SARS-CoV-2 antigen levels as compared to the first assay. The antibody or antibody fragment may be encoded by clone-paired variable sequences as set forth in Table 1. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired sequences from Table 2. The antibody or antibody fragment may bind to a SARS-CoV-2 surface spike protein. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

In another embodiment, there is provided a method of treating a subject infected with SARS-CoV-2 or reducing the likelihood of infection of a subject at risk of contracting SARS-CoV-2, comprising delivering to said subject an antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired

sequences from Table 2. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The antibody may be a chimeric antibody or a bispecific antibody. The antibody may be an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS, YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern. The antibody or antibody fragment may bind to a SARS-CoV-2 antigen such as a surface spike protein. The antibody or antibody fragment may be administered prior to infection or after infection. The subject may be of age 60 or older, may be immunocompromised, or may suffer from a respiratory and/or cardiovascular disorder. Delivering may comprise antibody or antibody fragment administration, or genetic delivery with an RNA or DNA sequence or vector encoding the antibody or antibody fragment. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

In yet another embodiment, there is provided a monoclonal antibody, wherein the antibody or antibody fragment is characterized by clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired sequences from Table 2. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The antibody may be a chimeric antibody, is bispecific antibody, or is an intrabody. The antibody may be an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS, YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern. The

antibody or antibody fragment may bind to a SARS-CoV-2 surface spike protein. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

5 A hybridoma or engineered cell encoding an antibody or antibody fragment wherein the antibody or antibody fragment is characterized by clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired sequences from Table 2. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The antibody may be a chimeric antibody, a bispecific antibody, or an intrabody. The antibody may be an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS, YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern. The antibody or antibody fragment may bind to a SARS-CoV-2 surface spike protein. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

25 In still yet another embodiment, there is provided a vaccine formulation comprising one or more antibodies or antibody fragments characterized by clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The at least one of said antibodies or antibody fragments may be encoded by light and heavy chain variable sequences according to clone-paired sequences from Table 1, by light and heavy chain variable sequences having at least 70%, 80%, or 90% identity to clone-paired sequences from Table 1, or by light and heavy chain variable sequences having at least 95% identity to clone-paired sequences from Table 1. The at least one of said antibodies or antibody fragments may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or may comprise light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-

paired sequences from Table 2. The at least one of said antibody fragments is a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The at least one of said antibodies may be a chimeric antibody, a bispecific antibody or an intrabody. The antibody may be an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern. The antibody or antibody fragment may bind to a SARS-CoV-2 antigen surface spike protein. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

In a further embodiment, there is provided a vaccine formulation comprising one or more expression vectors encoding a first antibody or antibody fragment as described herein. The expression vector(s) may be Sindbis virus or VEE vector(s). The vaccine may be formulated for delivery by needle injection, jet injection, or electroporation. The vaccine formulation may further comprise one or more expression vectors encoding for a second antibody or antibody fragment, such as a distinct antibody or antibody fragment as described herein.

In yet a further embodiment, there is provided a method of protecting the health of a subject of age 60 or older, an immunocompromised, subject or a subject suffering from a respiratory and/or cardiovascular disorder that is infected with or at risk of infection with SARS-CoV-2 comprising delivering to said subject an antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired sequences from Table 2. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The antibody may be an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion

mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS, YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern. The antibody may be a chimeric antibody or a bispecific antibody. The said antibody or antibody fragment may be administered prior to infection or after infection. The antibody or antibody fragment may bind to a SARS-CoV-2 antigen such as a surface spike protein. Delivering may comprise antibody or antibody fragment administration, or genetic delivery with an RNA or DNA sequence or vector encoding the antibody or antibody fragment.

5 The antibody or antibody fragment may improve the subject's respiration as compared to an untreated control and/or may reduce viral load as compared to an untreated control. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

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In still yet a further embodiment, there is provided a method of determining the antigenic integrity, correct conformation and/or correct sequence of a SARS-CoV-2 surface spike protein comprising (a) contacting a sample comprising said antigen with a first antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively; and (b) determining antigenic integrity, correct conformation and/or correct sequence of said antigen by detectable binding of said first antibody or antibody fragment to said antigen. The sample may comprise recombinantly produced antigen or a vaccine formulation or vaccine production batch. Detection may comprise ELISA, RIA, western blot, a biosensor using surface plasmon resonance or biolayer interferometry, or flow cytometric staining. The first antibody or antibody fragment may be encoded by clone-paired variable sequences as set forth in Table 1, by light and heavy chain variable sequences having at least 70%, 80%, or 90% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having at least 95% identity to clone-paired sequences as set forth in Table 1. The first antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, may comprise light and heavy chain variable sequences having at least 70%, 80% or 90% identity to clone-paired sequences from Table 2, or may comprise light and heavy chain variable sequences having at least 95% identity to clone-paired sequences from Table 2. The first antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The method may further comprise performing

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steps (a) and (b) a second time to determine the antigenic stability of the antigen over time. Alternatively, any of the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

The method may further comprise (c) contacting a sample comprising said antigen with
5 a second antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively; and (d) determining antigenic integrity of said antigen by detectable binding of said second antibody or antibody fragment to said antigen. The second antibody or antibody fragment may be encoded by clone-paired variable sequences as set forth in Table 1, by light and heavy chain variable sequences having at least 70%, 80%,
10 or 90% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having at least 95% identity to clone-paired sequences as set forth in Table 1. The second antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, may comprise light and heavy chain variable sequences having at least 70%, 80% or 90% identity to clone-paired
15 sequences from Table 2, or may comprise light and heavy chain variable sequences having at least 95% identity to clone-paired sequences from Table 2. The second first antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment. The method may further comprise performing steps (c) and (d) a second time to determine the antigenic stability of the antigen over time. Alternatively, any of
20 the embodiments in this paragraph may employ an antibody having a sequence or encoded by a sequence found in SEQ ID NOS: 1-9151.

Also provided is human monoclonal antibody or antibody fragment, or hybridoma or engineered cell producing the same, wherein said antibody binds to a SARS-CoV-2 antigen surface spike protein.

25 The use of the word “a” or “an” when used in conjunction with the term “comprising” in the claims and/or the specification may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.” The word “about” means plus or minus 5% of the stated number.

It is contemplated that any method or composition described herein can be implemented
30 with respect to any other method or composition described herein. Other objects, features and advantages of the present disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the disclosure, are given by way of

illustration only, since various changes and modifications within the spirit and scope of the disclosure will become apparent to those skilled in the art from this detailed description.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

5 As discussed above, SARS-CoV-2 is a major health concern with active cases increasing daily. Therefore, understanding the biology of this virus and the nature and extent of the human immune response to the virus is of paramount importance. The inventors have identified the sequences of human antibodies to SARS-CoV-2. Those sequences and uses for such antibodies are disclosed herein.

10 These and other aspects of the disclosure are described in detail below.

I. Coronavirus 2019 (SARS-CoV-2)

SARS-CoV-2 is a contagious virus that causes the acute respiratory disease designated coronavirus disease 2019 (COVID-19), a respiratory infection. It is the cause of the ongoing
15 2019–20 coronavirus outbreak, a global health emergency. Genomic sequencing has shown that it is a positive-sense, single-stranded RNA coronavirus.

During the ongoing outbreak, the virus has often been referred to in common parlance as "the coronavirus", "the new coronavirus" and "the Wuhan coronavirus", while the WHO recommends the designation "SARS-CoV-2". The International Committee on Taxonomy of
20 Viruses (ICTV) announced that the official name for the virus is SARS-CoV-2.

Many early cases were linked to a large seafood and animal market in the Chinese city of Wuhan, and the virus is thought to have a zoonotic origin. Comparisons of the genetic sequences of this virus and other virus samples have shown similarities to SARS-CoV (79.5%) and bat coronaviruses (96%). This finding makes an ultimate origin in bats likely, although an
25 intermediate host, such as a pangolin, cannot be ruled out. The virus could be a recombinant virus formed from two or more coronaviruses.

Human-to-human transmission of the virus has been confirmed. Coronaviruses are primarily spread through close contact, in particular through respiratory droplets from coughs and sneezes within a range of about 6 feet (1.8 m). Viral RNA has also been found in stool
30 samples from infected patients. It is possible that the virus can be infectious even during the incubation period.

Animals sold for food were originally suspected to be the reservoir or intermediary hosts of SARS-CoV-2 because many of the first individuals found to be infected by the virus

were workers at the Huanan Seafood Market. A market selling live animals for food was also blamed in the SARS outbreak in 2003; such markets are considered to be incubators for novel pathogens. The outbreak has prompted a temporary ban on the trade and consumption of wild animals in China. However, some researchers have suggested that the Huanan Seafood Market
5 may not be the original source of viral transmission to humans.

With a sufficient number of sequenced genomes, it is possible to reconstruct a phylogenetic tree of the mutation history of a family of viruses. Research into the origin of the 2003 SARS outbreak has resulted in the discovery of many SARS-like bat coronaviruses, most originating in the *Rhinolophus* genus of horseshoe bats. SARS-CoV-2 falls into this category
10 of SARS-related coronaviruses. Two genome sequences from *Rhinolophus sinicus* published in 2015 and 2017 show a resemblance of 80% to SARS-CoV-2. A third virus genome from *Rhinolophus affinis*, "RaTG13" collected in Yunnan province, has a 96% resemblance to SARS-CoV-2.^{[28][29]} For comparison, this amount of variation among viruses is similar to the amount of mutation observed over ten years in the H3N2 human influenza virus strain.

15 SARS-CoV-2 belongs to the broad family of viruses known as coronaviruses; "nCoV" is the standard term used to refer to novel coronaviruses until the choice of a more specific designation. It is a positive-sense single-stranded RNA (+ssRNA) virus. Other coronaviruses are capable of causing illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome (MERS) and Severe acute respiratory syndrome (SARS).
20 It is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HKU1, MERS-CoV, and SARS-CoV.

Like SARS-CoV, SARS-CoV-2 is a member of the subgenus *Sarbecovirus* (Beta-CoV lineage B). Its RNA sequence is approximately 30,000 bases in length. By 12 January, five genomes of SARS-CoV-2 had been isolated from Wuhan and reported by the Chinese Center
25 for Disease Control and Prevention (CCDC) and other institutions; the number of genomes increased to 28 by 26 January. Except for the earliest GenBank genome, the genomes are under an embargo at GISAID. A phylogenetic analysis for the samples is available through Nextstrain.

Publication of the SARS-CoV-2 genome led to several protein modeling experiments on the receptor binding protein (RBD) of the spike (S) protein of the virus. Results suggest that
30 the S protein retains sufficient affinity to the Angiotensin converting enzyme 2 (ACE2) receptor to use it as a mechanism of cell entry. On 22 January, a group in China working with the full virus and a group in the U.S. working with reverse genetics independently and experimentally demonstrated human ACE2 as the receptor for SARS-CoV-2.

To look for potential protease inhibitors, the viral 3C-like protease M(pro) from the ORF1a polyprotein has also been modeled for drug docking experiments. Innophore has produced two computational models based on SARS protease, and the Chinese Academy of Sciences has produced an unpublished experimental structure of a recombinant SARS-CoV-2 protease. In addition, researchers at the University of Michigan have modeled the structures of all mature peptides in the SARS-CoV-2 genome using I-TASSER.

The first known human infection occurred in early December 2019. An outbreak of SARS-CoV-2 was first detected in Wuhan, China, in mid-December 2019, likely originating from a single infected animal. The virus subsequently spread to all provinces of China and to more than two dozen other countries in Asia, Europe, North America, and Oceania. Human-to-human spread of the virus has been confirmed in all of these regions. On 30 January 2020, SARS-CoV-2 was designated a global health emergency by the WHO.

As of 10 February 2020 (17:15 UTC), there were 40,645 confirmed cases of infection, of which 40,196 were within mainland China. Initially, nearly all cases outside China occurred in people who either traveled from Wuhan, or were in direct contact with someone who traveled from the area. Later, spread from travelers to other countries resulted in transmission in many countries in the world. While the proportion of infections that result in confirmed infection or progress to diagnosable SARS-CoV-2 acute respiratory disease remains unclear, the total number of deaths attributed to the virus was over 19,000 as of 25 March 2020.

The basic reproduction number (R-zero) of the virus has been estimated to be between 1.4 and 3.9. This means that, when unchecked, the virus typically results in 1.4 to 3.9 new cases per established infection. It has been established that the virus is able to transmit along a chain of at least four people.

In January 2020, multiple organizations and institutions began work on creating vaccines for SARS-CoV-2 based on the published genome. In China, the Chinese Center for Disease Control and Prevention is developing a vaccine against the novel coronavirus. The University of Hong Kong has also announced that a vaccine is under development there. Shanghai East Hospital is also developing a vaccine in partnership with the biotechnology company Stemirna Therapeutics.

Elsewhere, three vaccine projects are being supported by the Coalition for Epidemic Preparedness Innovations (CEPI), including projects by the biotechnology companies Moderna and Inovio Pharmaceuticals and another by the University of Queensland. The United States National Institutes of Health (NIH) is cooperating with Moderna to create an RNA vaccine matching a spike of the coronavirus surface; Phase I clinical trials began in March 2020. Inovio

Pharmaceuticals is developing a DNA-based vaccination and collaborating with a Chinese firm in order to speed its acceptance by regulatory authorities in China, hoping to perform human trials of the vaccine in the summer of 2020. In Australia, the University of Queensland is investigating the potential of a molecular clamp vaccine that would genetically modify viral proteins to make them mimic the coronavirus and stimulate an immune reaction.

In an independent project, the Public Health Agency of Canada has granted permission to the International Vaccine Centre (VIDO-InterVac) at the University of Saskatchewan to begin work on a vaccine. VIDO-InterVac aims to start production and animal testing in March 2020, and human testing in 2021. The Imperial College Faculty of Medicine in London is now at the stage of testing a vaccine on animals.

COVID-19 acute respiratory disease is a viral respiratory disease caused by SARS-CoV-2. It was first detected during the 2019–20 Wuhan coronavirus outbreak. Symptoms may include fever, dry cough, and shortness of breath. There is no specific licensed treatment available as of March 2020, with efforts focused on lessening symptoms and supporting functioning.

Those infected may either be asymptomatic or have mild to severe symptoms, like fever, cough, shortness of breath. Diarrhoea or upper respiratory symptoms (*e.g.*, sneezing, runny nose, sore throat) are less frequent. Cases of severe infection can progress to severe pneumonia, multi-organ failure, and death. The time from exposure to onset of symptoms is estimated at 2 to 10 days by the World Health Organization, and 2 to 14 days by the US Centers for Disease Control and Prevention (CDC).

Global health organizations have published preventive measures individuals can take to reduce the chances of SARS-CoV-2 infection. Recommendations are similar to those previously published for other coronaviruses and include: frequent washing of hands with soap and water; not touching the eyes, nose, or mouth with unwashed hands; and practicing good respiratory hygiene.

The WHO has published several testing protocols for SARS-CoV-2. Testing uses real time reverse transcription-polymerase chain reaction (rRT-PCR). The test can be done on respiratory or blood samples. Results are generally available within a few hours to days.

Research into potential treatments for the disease were initiated in January 2020. The Chinese Center for Disease Control and Prevention started testing existing pneumonia treatments in coronavirus-related pneumonia in late January. There has also been examination of the RNA polymerase inhibitor remdesivir, and interferon beta. In late January 2020, Chinese medical researchers expressed an intent to start clinical testing on remdesivir, chloroquine, and

lopinavir/ritonavir, all of which seemed to have "fairly good inhibitory effects" on SARS-CoV-2 at the cellular level in exploratory research. On 5 February 2020, China started patenting use of remdesivir for the disease.

Overall mortality and morbidity rates due to infection with SARS-CoV-2 are unknown, both because the case fatality rate may be changing over time in the current outbreak, and because the proportion of infections that progress to diagnosable disease remains unclear. However, preliminary research into SARS-CoV-2 acute respiratory disease has yielded case fatality rate numbers between 2% and 3%, and in January 2020 the WHO suggested that the case fatality rate was approximately 3%. An unreviewed Imperial College preprint study among 55 fatal cases noted that early estimates of mortality may be too high as asymptomatic infections are missed. They estimated a mean infection fatality ratio (the mortality among infected) ranging from 0.8% when including asymptomatic carriers to 18% when including only symptomatic cases from Hubei province.

Early data indicates that among the first 41 confirmed cases admitted to hospitals in Wuhan, 13 (32%) individuals required intensive care, and 6 (15%) individuals died. Of those who died, many were in unsound health to begin with, exhibiting conditions like hypertension, diabetes, or cardiovascular disease that impaired their immune systems. In early cases of SARS-CoV-2 acute respiratory disease that resulted in death, the median time of disease was found to be 14 days, with a total range from six to 41 days.

II. Monoclonal Antibodies and Production Thereof

An "isolated antibody" is one that has been separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In particular embodiments, the antibody is purified: (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most particularly more than 99% by weight; (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator; or (3) to homogeneity by SDS-PAGE under reducing or non-reducing conditions using Coomassie blue or silver stain. Isolated antibody includes the antibody *in situ* within recombinant cells since at least one component of the antibody's natural

environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The basic four-chain antibody unit is a heterotetrameric glycoprotein composed of two identical light (L) chains and two identical heavy (H) chains. An IgM antibody consists of 5 basic heterotetramer units along with an additional polypeptide called J chain, and therefore contain 10 antigen binding sites, while secreted IgA antibodies can polymerize to form polyvalent assemblages comprising 2-5 of the basic 4-chain units along with J chain. In the case of IgGs, the 4-chain unit is generally about 150,000 daltons. Each L chain is linked to an H chain by one covalent disulfide bond, while the two H chains are linked to each other by one or more disulfide bonds depending on the H chain isotype. Each H and L chain also has regularly spaced intrachain disulfide bridges. Each H chain has at the N-terminus, a variable region (V_H) followed by three constant domains (C_H) for each of the alpha and gamma chains and four C_H domains for mu and isotypes. Each L chain has at the N-terminus, a variable region (V_L) followed by a constant domain (C_L) at its other end. The V_L is aligned with the V_H and the C_L is aligned with the first constant domain of the heavy chain (C_{H1}). Particular amino acid residues are believed to form an interface between the light chain and heavy chain variable regions. The pairing of a V_H and V_L together forms a single antigen-binding site. For the structure and properties of the different classes of antibodies, see, *e.g.*, Basic and Clinical Immunology, 8th edition, Daniel P. Stites, Abba I. Terr and Tristram G. Parslow (eds.), Appleton & Lange, Norwalk, Conn., 1994, page 71, and Chapter 6.

The L chain from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda based on the amino acid sequences of their constant domains (C_L). Depending on the amino acid sequence of the constant domain of their heavy chains (C_H), immunoglobulins can be assigned to different classes or isotypes. There are five classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, having heavy chains designated alpha, delta, epsilon, gamma and mu, respectively. They gamma and alpha classes are further divided into subclasses on the basis of relatively minor differences in C_H sequence and function, humans express the following subclasses: IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

The term "variable" refers to the fact that certain segments of the V domains differ extensively in sequence among antibodies. The V domain mediates antigen binding and defines specificity of a particular antibody for its particular antigen. However, the variability is not evenly distributed across the 110-amino acid span of the variable regions. Instead, the V regions consist of relatively invariant stretches called framework regions (FRs) of 15-30 amino acids separated by shorter regions of extreme variability called "hypervariable regions" that are each

9-12 amino acids long. The variable regions of native heavy and light chains each comprise four FRs, largely adopting a beta-sheet configuration, connected by three hypervariable regions, which form loops connecting, and in some cases forming part of, the beta-sheet structure. The hypervariable regions in each chain are held together in close proximity by the FRs and, with the hypervariable regions from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), antibody-dependent neutrophil phagocytosis (ADNP), and antibody-dependent complement deposition (ADCD).

The term "hypervariable region" when used herein refers to the amino acid residues of an antibody that are responsible for antigen binding. The hypervariable region generally comprises amino acid residues from a "complementarity determining region" or "CDR" (*e.g.*, around about residues 24-34 (L1), 50-56 (L2) and 89-97 (L3) in the V_L, and around about 31-35 (H1), 50-65 (H2) and 95-102 (H3) in the V_H when numbered in accordance with the Kabat numbering system; Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)); and/or those residues from a "hypervariable loop" (*e.g.*, residues 24-34 (L1), 50-56 (L2) and 89-97 (L3) in the V_L, and 26-32 (H1), 52-56 (H2) and 95-101 (H3) in the V_H when numbered in accordance with the Chothia numbering system; Chothia and Lesk, J. Mol. Biol. 196:901-917 (1987)); and/or those residues from a "hypervariable loop"/CDR (*e.g.*, residues 27-38 (L1), 56-65 (L2) and 105-120 (L3) in the V_L, and 27-38 (H1), 56-65 (H2) and 105-120 (H3) in the V_H when numbered in accordance with the IMGT numbering system; Lefranc, M. P. *et al.* Nucl. Acids Res. 27:209-212 (1999), Ruiz, M. *et al.* Nucl. Acids Res. 28:219-221 (2000)). Optionally the antibody has symmetrical insertions at one or more of the following points 28, 36 (L1), 63, 74-75 (L2) and 123 (L3) in the V_L, and 28, 36 (H1), 63, 74-75 (H2) and 123 (H3) in the V_{subH} when numbered in accordance with AHO; Honneger, A. and Plunkthun, A. J. Mol. Biol. 309:657-670 (2001)).

By "germline nucleic acid residue" is meant the nucleic acid residue that naturally occurs in a germline gene encoding a constant or variable region. "Germline gene" is the DNA found in a germ cell (*i.e.*, a cell destined to become an egg or in the sperm). A "germline mutation" refers to a heritable change in a particular DNA that has occurred in a germ cell or the zygote at the single-cell stage, and when transmitted to offspring, such a mutation is

incorporated in every cell of the body. A germline mutation is in contrast to a somatic mutation which is acquired in a single body cell. In some cases, nucleotides in a germline DNA sequence encoding for a variable region are mutated (*i.e.*, a somatic mutation) and replaced with a different nucleotide.

5 The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to polyclonal antibody preparations that include
10 different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they may be synthesized uncontaminated by other antibodies. The modifier "monoclonal" is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies useful in the
15 present disclosure may be prepared by the hybridoma methodology first described by Kohler *et al.*, Nature, 256:495 (1975), or may be made using recombinant DNA methods in bacterial, eukaryotic animal or plant cells (see, *e.g.*, U.S. Patent 4,816,567) after single cell sorting of an antigen specific B cell, an antigen specific plasmablast responding to an infection or immunization, or capture of linked heavy and light chains from single cells in a bulk sorted
20 antigen specific collection. The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson *et al.*, Nature, 352:624-628 (1991) and Marks *et al.*, J. Mol. Biol., 222:581-597 (1991), for example.

A. General Methods

25 It will be understood that monoclonal antibodies binding to SARS-CoV-2 will have several applications. These include the production of diagnostic kits for use in detecting and diagnosing SARS-CoV-2 infection, as well as for treating the same. In these contexts, one may link such antibodies to diagnostic or therapeutic agents, use them as capture agents or competitors in competitive assays, or use them individually without additional agents being
30 attached thereto. The antibodies may be mutated or modified, as discussed further below. Methods for preparing and characterizing antibodies are well known in the art (see, *e.g.*, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988; U.S. Patent 4,196,265).

The methods for generating monoclonal antibodies (MAbs) generally begin along the same lines as those for preparing polyclonal antibodies. The first step for both these methods is immunization of an appropriate host or identification of subjects who are immune due to prior natural infection or vaccination with a licensed or experimental vaccine. As is well known in the art, a given composition for immunization may vary in its immunogenicity. It is often necessary therefore to boost the host immune system, as may be achieved by coupling a peptide or polypeptide immunogen to a carrier. Exemplary and preferred carriers are keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA). Other albumins such as ovalbumin, mouse serum albumin or rabbit serum albumin can also be used as carriers. Means for conjugating a polypeptide to a carrier protein are well known in the art and include glutaraldehyde, m-maleimidobencoyl-N-hydroxysuccinimide ester, carbodiimide and bis-biazotized benzidine. As also is well known in the art, the immunogenicity of a particular immunogen composition can be enhanced by the use of non-specific stimulators of the immune response, known as adjuvants. Exemplary and preferred adjuvants in animals include complete Freund's adjuvant (a non-specific stimulator of the immune response containing killed *Mycobacterium tuberculosis*), incomplete Freund's adjuvants and aluminum hydroxide adjuvant and in humans include alum, CpG, MF59 and combinations of immunostimulatory molecules ("Adjuvant Systems", such as AS01 or AS03). Additional experimental forms of inoculation to induce SARS-CoV-2-specific B cells is possible, including nanoparticle vaccines, or gene-encoded antigens delivered as DNA or RNA genes in a physical delivery system (such as lipid nanoparticle or on a gold biolistic bead), and delivered with needle, gene gun, transcutaneous electroporation device. The antigen gene also can be carried as encoded by a replication competent or defective viral vector such as adenovirus, adeno-associated virus, poxvirus, herpesvirus, or alphavirus replicon, or alternatively a virus like particle.

In the case of human antibodies against natural pathogens, a suitable approach is to identify subjects that have been exposed to the pathogens, such as those who have been diagnosed as having contracted the disease, or those who have been vaccinated to generate protective immunity against the pathogen or to test the safety or efficacy of an experimental vaccine. Circulating anti-pathogen antibodies can be detected, and antibody encoding or producing B cells from the antibody-positive subject may then be obtained.

The amount of immunogen composition used in the production of polyclonal antibodies varies upon the nature of the immunogen as well as the animal used for immunization. A variety of routes can be used to administer the immunogen (subcutaneous, intramuscular, intradermal, intravenous and intraperitoneal). The production of polyclonal antibodies may be monitored

by sampling blood of the immunized animal at various points following immunization. A second, booster injection, also may be given. The process of boosting and titering is repeated until a suitable titer is achieved. When a desired level of immunogenicity is obtained, the immunized animal can be bled and the serum isolated and stored, and/or the animal can be used to generate MAbs.

Following immunization, somatic cells with the potential for producing antibodies, specifically B lymphocytes (B cells), are selected for use in the MAb generating protocol. These cells may be obtained from biopsied spleens, lymph nodes, tonsils or adenoids, bone marrow aspirates or biopsies, tissue biopsies from mucosal organs like lung or GI tract, or from circulating blood. The antibody-producing B lymphocytes from the immunized animal or immune human are then fused with cells of an immortal myeloma cell, generally one of the same species as the animal that was immunized or human or human/mouse chimeric cells. Myeloma cell lines suited for use in hybridoma-producing fusion procedures preferably are non-antibody-producing, have high fusion efficiency, and enzyme deficiencies that render them incapable of growing in certain selective media which support the growth of only the desired fused cells (hybridomas). Any one of a number of myeloma cells may be used, as are known to those of skill in the art (Goding, pp. 65-66, 1986; Campbell, pp. 75-83, 1984). HMM2.5 cells or MFP-2 cells are particularly useful examples of such cells.

Methods for generating hybrids of antibody-producing spleen or lymph node cells and myeloma cells usually comprise mixing somatic cells with myeloma cells in a 2:1 proportion, though the proportion may vary from about 20:1 to about 1:1, respectively, in the presence of an agent or agents (chemical or electrical) that promote the fusion of cell membranes. In some cases, transformation of human B cells with Epstein Barr virus (EBV) as an initial step increases the size of the B cells, enhancing fusion with the relatively large-sized myeloma cells. Transformation efficiency by EBV is enhanced by using CpG and a Chk2 inhibitor drug in the transforming medium. Alternatively, human B cells can be activated by co-culture with transfected cell lines expressing CD40 Ligand (CD154) in medium containing additional soluble factors, such as IL-21 and human B cell Activating Factor (BAFF), a Type II member of the TNF superfamily. Fusion methods using Sendai virus have been described by Kohler and Milstein (1975; 1976), and those using polyethylene glycol (PEG), such as 37% (v/v) PEG, by Gefter *et al.* (1977). The use of electrically induced fusion methods also is appropriate (Goding, pp. 71-74, 1986) and there are processes for better efficiency (Yu *et al.*, 2008). Fusion procedures usually produce viable hybrids at low frequencies, about 1×10^{-6} to 1×10^{-8} , but with optimized procedures one can achieve fusion efficiencies close to 1 in 200 (Yu *et al.*,

2008). However, relatively low efficiency of fusion does not pose a problem, as the viable, fused hybrids are differentiated from the parental, infused cells (particularly the infused myeloma cells that would normally continue to divide indefinitely) by culturing in a selective medium. The selective medium is generally one that contains an agent that blocks the *de novo* synthesis of nucleotides in the tissue culture medium. Exemplary and preferred agents are aminopterin, methotrexate, and azaserine. Aminopterin and methotrexate block *de novo* synthesis of both purines and pyrimidines, whereas azaserine blocks only purine synthesis. Where aminopterin or methotrexate is used, the medium is supplemented with hypoxanthine and thymidine as a source of nucleotides (HAT medium). Where azaserine is used, the medium is supplemented with hypoxanthine. Ouabain is added if the B cell source is an EBV-transformed human B cell line, in order to eliminate EBV-transformed lines that have not fused to the myeloma.

The preferred selection medium is HAT or HAT with ouabain. Only cells capable of operating nucleotide salvage pathways are able to survive in HAT medium. The myeloma cells are defective in key enzymes of the salvage pathway, *e.g.*, hypoxanthine phosphoribosyl transferase (HPRT), and they cannot survive. The B cells can operate this pathway, but they have a limited life span in culture and generally die within about two weeks. Therefore, the only cells that can survive in the selective media are those hybrids formed from myeloma and B cells. When the source of B cells used for fusion is a line of EBV-transformed B cells, as here, ouabain may also be used for drug selection of hybrids as EBV-transformed B cells are susceptible to drug killing, whereas the myeloma partner used is chosen to be ouabain resistant.

Culturing provides a population of hybridomas from which specific hybridomas are selected. Typically, selection of hybridomas is performed by culturing the cells by single-clone dilution in microtiter plates, followed by testing the individual clonal supernatants (after about two to three weeks) for the desired reactivity. The assay should be sensitive, simple and rapid, such as radioimmunoassays, enzyme immunoassays, cytotoxicity assays, plaque assays dot immunobinding assays, and the like. The selected hybridomas are then serially diluted or single-cell sorted by flow cytometric sorting and cloned into individual antibody-producing cell lines, which clones can then be propagated indefinitely to provide mAbs. The cell lines may be exploited for MAb production in two basic ways. A sample of the hybridoma can be injected (often into the peritoneal cavity) into an animal (*e.g.*, a mouse). Optionally, the animals are primed with a hydrocarbon, especially oils such as pristane (tetramethylpentadecane) prior to injection. When human hybridomas are used in this way, it is optimal to inject immunocompromised mice, such as SCID mice, to prevent tumor rejection. The injected

animal develops tumors secreting the specific monoclonal antibody produced by the fused cell hybrid. The body fluids of the animal, such as serum or ascites fluid, can then be tapped to provide MAbs in high concentration. The individual cell lines could also be cultured *in vitro*, where the MAbs are naturally secreted into the culture medium from which they can be readily
5 obtained in high concentrations. Alternatively, human hybridoma cells lines can be used *in vitro* to produce immunoglobulins in cell supernatant. The cell lines can be adapted for growth in serum-free medium to optimize the ability to recover human monoclonal immunoglobulins of high purity.

MAbs produced by either means may be further purified, if desired, using filtration,
10 centrifugation and various chromatographic methods such as FPLC or affinity chromatography. Fragments of the monoclonal antibodies of the disclosure can be obtained from the purified monoclonal antibodies by methods which include digestion with enzymes, such as pepsin or papain, and/or by cleavage of disulfide bonds by chemical reduction. Alternatively, monoclonal antibody fragments encompassed by the present disclosure can be
15 synthesized using an automated peptide synthesizer.

It also is contemplated that a molecular cloning approach may be used to generate monoclonal antibodies. Single B cells identified as responding to infection or vaccination because of plasmablast or activated B cell markers, or memory B cells labelled with the antigen of interest, can be sorted physically using paramagnetic bead selection or flow
20 cytometric sorting, then RNA can be isolated from the single cells and antibody genes amplified by RT-PCR. Various single-cell RNA-seq methods are available to obtain antibody variable genes from single cells. Alternatively, antigen-specific bulk sorted populations of cells can be segregated into microvesicles and the matched heavy and light chain variable genes recovered from single cells using physical linkage of heavy and light chain amplicons, or
25 common barcoding of heavy and light chain genes from a vesicle. Matched heavy and light chain genes from single cells also can be obtained from populations of antigen specific B cells by treating cells with cell-penetrating nanoparticles bearing RT-PCR primers and barcodes for marking transcripts with one barcode per cell. The antibody variable genes also can be isolated by RNA extraction of a hybridoma line and the antibody genes obtained by RT-PCR and cloned
30 into an immunoglobulin expression vector. Alternatively, combinatorial immunoglobulin phagemid libraries are prepared from RNA isolated from the cell lines and phagemids expressing appropriate antibodies are selected by panning using viral antigens. The advantages of this approach over conventional hybridoma techniques are that approximately 10^4 times as many antibodies can be produced and screened in a single round, and that new specificities are

generated by H and L chain combination which further increases the chance of finding appropriate antibodies.

Other U.S. patents, each incorporated herein by reference, that teach the production of antibodies useful in the present disclosure include U.S. Patent 5,565,332, which describes the production of chimeric antibodies using a combinatorial approach; U.S. Patent 4,816,567 which describes recombinant immunoglobulin preparations; and U.S. Patent 4,867,973 which describes antibody-therapeutic agent conjugates.

B. Antibodies of the Present Disclosure

Antibodies according to the present disclosure may be defined, in the first instance, by their binding specificity. Those of skill in the art, by assessing the binding specificity/affinity of a given antibody using techniques well known to those of skill in the art, can determine whether such antibodies fall within the scope of the instant claims. For example, the epitope to which a given antibody bind may consist of a single contiguous sequence of 3 or more (*e.g.*, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20) amino acids located within the antigen molecule (*e.g.*, a linear epitope in a domain). Alternatively, the epitope may consist of a plurality of non-contiguous amino acids (or amino acid sequences) located within the antigen molecule (*e.g.*, a conformational epitope).

Two main categories of SARS-CoV-2 antigens are the surface spike (S) protein and the internal proteins, especially the nucleocapsid (N) protein. Antibodies to the S protein will be useful for prophylaxis, or therapy, or diagnostics, or for characterizing vaccines. S protein antibodies will have additional binding specificity with that protein, with particular antibodies binding to the full-length ectodomain of the SARS-CoV-2 S protein (presented as a monomer or oligomer such as a trimer; with or without conformation stabilizing mutations such as introduction of prolines at critical sites ("2P mutation")) and (a) anti-S protein antibodies that binds to the receptor binding domain (RBD), (b) anti-S protein antibodies that bind to domains other than the RBD. Some of the subset that bind to domains other than the RBD bind to the N terminal domain (NTD), while others bind to an epitope other than the NTD or RBD), and (c) S protein antibodies may further be found to neutralize SARS-CoV-2 by blocking binding of the SARS-CoV-2 S protein to its receptor, human angiotensin-converting enzyme 2 (hACE2), with others that neutralize but do not block receptor binding. Finally, antibodies can cross-react with both SARS-CoV-2 S protein and the S protein of other coronaviruses such as SARS-CoV,

MERS-CoV, HCoV-229E, HCoV-OC43, HCoV-NL63 and/or HCoV-HKU1, as well as cross-neutralize both SARS-CoV-2 and these other coronaviruses.

Another specificity will be antibodies that bind to N antibodies (or other internal targets) that will have primarily diagnostics uses. For example, antibodies to N or other internal proteins of SARS-CoV-2 that specifically recognize SARS-CoV-2 or that cross-reactively recognize SARS-CoV-2 and other coronaviruses such as SARS-CoV, MERS-CoV, HCoV-229E, HCoV-OC43, HCoV-NL63 and/or HCoV-HKU1.

Various techniques known to persons of ordinary skill in the art can be used to determine whether an antibody "interacts with one or more amino acids" within a polypeptide or protein. Exemplary techniques include, for example, routine cross-blocking assays, such as that described in Antibodies, Harlow and Lane (Cold Spring Harbor Press, Cold Spring Harbor, N.Y.). Cross-blocking can be measured in various binding assays such as ELISA, biolayer interferometry, or surface plasmon resonance. Other methods include alanine scanning mutational analysis, peptide blot analysis (Reineke, Methods Mol. Biol. 248: 443-63, 2004), peptide cleavage analysis, high-resolution electron microscopy techniques using single particle reconstruction, cryoEM, or tomography, crystallographic studies and NMR analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer Prot. Sci. 9: 487-496, 2000). Another method that can be used to identify the amino acids within a polypeptide with which an antibody interacts is hydrogen/deuterium exchange detected by mass spectrometry. In general terms, the hydrogen/deuterium exchange method involves deuterium-labeling the protein of interest, followed by binding the antibody to the deuterium-labeled protein. Next, the protein/antibody complex is transferred to water and exchangeable protons within amino acids that are protected by the antibody complex undergo deuterium-to-hydrogen back-exchange at a slower rate than exchangeable protons within amino acids that are not part of the interface. As a result, amino acids that form part of the protein/antibody interface may retain deuterium and therefore exhibit relatively higher mass compared to amino acids not included in the interface. After dissociation of the antibody, the target protein is subjected to protease cleavage and mass spectrometry analysis, thereby revealing the deuterium-labeled residues which correspond to the specific amino acids with which the antibody interacts. See, *e.g.*, Ehring, Analytical Biochemistry 267: 252-259 (1999); Engen and Smith, Anal. Chem. 73: 256A-265A (2001). When the antibody neutralizes SARS-CoV-2, antibody escape mutant variant organisms can be isolated by propagating SARS-CoV-2 *in vitro* or in animal models in the presence of high concentrations of the antibody. Sequence analysis of the SARS-CoV-2 gene encoding the antigen targeted by

the antibody reveals the mutation(s) conferring antibody escape, indicating residues in the epitope or that affect the structure of the epitope allosterically.

The term "epitope" refers to a site on an antigen to which B and/or T cells respond. B-cell epitopes can be formed both from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents, whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

Modification-Assisted Profiling (MAP), also known as Antigen Structure-based Antibody Profiling (ASAP) is a method that categorizes large numbers of monoclonal antibodies (mAbs) directed against the same antigen according to the similarities of the binding profile of each antibody to chemically or enzymatically modified antigen surfaces (see U.S. Patent Publication 2004/0101920, herein specifically incorporated by reference in its entirety). Each category may reflect a unique epitope either distinctly different from or partially overlapping with epitope represented by another category. This technology allows rapid filtering of genetically identical antibodies, such that characterization can be focused on genetically distinct antibodies. When applied to hybridoma screening, MAP may facilitate identification of rare hybridoma clones that produce mAbs having the desired characteristics. MAP may be used to sort the antibodies of the disclosure into groups of antibodies binding different epitopes.

The present disclosure includes antibodies that may bind to the same epitope, or a portion of the epitope. Likewise, the present disclosure also includes antibodies that compete for binding to a target or a fragment thereof with any of the specific exemplary antibodies described herein. One can easily determine whether an antibody binds to the same epitope as, or competes for binding with, a reference antibody by using routine methods known in the art. For example, to determine if a test antibody binds to the same epitope as a reference, the reference antibody is allowed to bind to target under saturating conditions. Next, the ability of a test antibody to bind to the target molecule is assessed. If the test antibody is able to bind to the target molecule following saturation binding with the reference antibody, it can be concluded that the test antibody binds to a different epitope than the reference antibody. On the other hand, if the test antibody is not able to bind to the target molecule following saturation binding with the reference antibody, then the test antibody may bind to the same epitope as the epitope bound by the reference antibody.

To determine if an antibody competes for binding with a reference anti-SARS-CoV-2 antibody, the above-described binding methodology is performed in two orientations: In a first orientation, the reference antibody is allowed to bind to the SARS-CoV-2 antigen under saturating conditions followed by assessment of binding of the test antibody to the SARS-CoV-2 molecule. In a second orientation, the test antibody is allowed to bind to the SARS-CoV-2 antigen molecule under saturating conditions followed by assessment of binding of the reference antibody to the SARS-CoV-2 molecule. If, in both orientations, only the first (saturating) antibody is capable of binding to SARS-CoV-2, then it is concluded that the test antibody and the reference antibody compete for binding to SARS-CoV-2. As will be appreciated by a person of ordinary skill in the art, an antibody that competes for binding with a reference antibody may not necessarily bind to the identical epitope as the reference antibody but may sterically block binding of the reference antibody by binding an overlapping or adjacent epitope.

Two antibodies bind to the same or overlapping epitope if each competitively inhibits (blocks) binding of the other to the antigen. That is, a 1-, 5-, 10-, 20- or 100-fold excess of one antibody inhibits binding of the other by at least 50% but preferably 75%, 90% or even 99% as measured in a competitive binding assay (see, *e.g.*, Junghans *et al.*, Cancer Res. 1990 50:1495-1502). Alternatively, two antibodies have the same epitope if essentially all amino acid mutations in the antigen that reduce or eliminate binding of one antibody reduce or eliminate binding of the other. Two antibodies have overlapping epitopes if some amino acid mutations that reduce or eliminate binding of one antibody reduce or eliminate binding of the other.

Additional routine experimentation (*e.g.*, peptide mutation and binding analyses) can then be carried out to confirm whether the observed lack of binding of the test antibody is in fact due to binding to the same epitope as the reference antibody or if steric blocking (or another phenomenon) is responsible for the lack of observed binding. Experiments of this sort can be performed using ELISA, RIA, surface plasmon resonance, flow cytometry or any other quantitative or qualitative antibody-binding assay available in the art. Structural studies with EM or crystallography also can demonstrate whether or not two antibodies that compete for binding recognize the same epitope.

In another aspect, there are provided monoclonal antibodies having clone-paired CDRs from the heavy and light chains as illustrated in Tables 3 and 4, respectively. Such antibodies may be produced by the clones discussed below in the Examples section using methods described herein.

In another aspect, the antibodies may be defined by their variable sequence, which include additional "framework" regions. Furthermore, the antibodies sequences may vary from these sequences, optionally using methods discussed in greater detail below. For example, nucleic acid sequences may vary from those set out above in that (a) the variable regions may be segregated away from the constant domains of the light and heavy chains, (b) the nucleic acids may vary from those set out above while not affecting the residues encoded thereby, (c) the nucleic acids may vary from those set out above by a given percentage, *e.g.*, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homology, (d) the nucleic acids may vary from those set out above by virtue of the ability to hybridize under high stringency conditions, as exemplified by low salt and/or high temperature conditions, such as provided by about 0.02 M to about 0.15 M NaCl at temperatures of about 50°C to about 70°C, (e) the amino acids may vary from those set out above by a given percentage, *e.g.*, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homology, or (f) the amino acids may vary from those set out above by permitting conservative substitutions (discussed below). Each of the foregoing applies to the nucleic acid sequences and the amino acid sequences.

When comparing polynucleotide and polypeptide sequences, two sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, Wis.), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M. O. (1978) A model of evolutionary change in proteins--Matrices for detecting distant relationships. In Dayhoff, M. O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington D.C. Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogeny pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, Calif.; Higgins, D. G. and Sharp, P. M. (1989) CABIOS 5:151-153; Myers, E. W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E. D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P. H. A. and Sokal, R. R. (1973) Numerical Taxonomy--the Principles and

Practice of Numerical Taxonomy, Freeman Press, San Francisco, Calif.; Wilbur, W. J. and Lipman, D. J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) Add. APL. Math 2:482, by the identity
5 alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443, by the search for similarity methods of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. USA 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, Wis.), or by inspection.

10 One particular example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.* (1977) Nucl. Acids Res. 25:3389-3402 and Altschul *et al.* (1990) J. Mol. Biol. 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example, with the parameters described herein, to determine percent sequence identity for the polynucleotides
15 and polypeptides of the disclosure. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. The rearranged nature of an antibody sequence and the variable length of each gene requires multiple rounds of BLAST searches for a single antibody sequence. Also, manual assembly of different genes is difficult and error-prone. The sequence analysis tool IgBLAST (world-wide-web at
20 ncbi.nlm.nih.gov/igblast/) identifies matches to the germline V, D and J genes, details at rearrangement junctions, the delineation of Ig V domain framework regions and complementarity determining regions. IgBLAST can analyze nucleotide or protein sequences and can process sequences in batches and allows searches against the germline gene databases and other sequence databases simultaneously to minimize the chance of missing possibly the
25 best matching germline V gene.

In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its
30 maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and

Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residues occur in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Yet another way of defining an antibody is as a "derivative" of any of the below-described antibodies and their antigen-binding fragments. The term "derivative" refers to an antibody or antigen-binding fragment thereof that immunospecifically binds to an antigen but which comprises, one, two, three, four, five or more amino acid substitutions, additions, deletions or modifications relative to a "parental" (or wild-type) molecule. Such amino acid substitutions or additions may introduce naturally occurring (*i.e.*, DNA-encoded) or non-naturally occurring amino acid residues. The term "derivative" encompasses, for example, as variants having altered CH1, hinge, CH2, CH3 or CH4 regions, so as to form, for example, antibodies, *etc.*, having variant Fc regions that exhibit enhanced or impaired effector or binding characteristics. The term "derivative" additionally encompasses non-amino acid modifications, for example, amino acids that may be glycosylated (*e.g.*, have altered mannose, 2-N-acetylglucosamine, galactose, fucose, glucose, sialic acid, 5-N-acetylneuraminic acid, 5-glycolneuraminic acid, *etc.* content), acetylated, pegylated, phosphorylated, amidated, derivatized by known protecting/blocking groups, proteolytic cleavage, linked to a cellular ligand or other protein, *etc.* In some embodiments, the altered carbohydrate modifications modulate one or more of the following: solubilization of the antibody, facilitation of subcellular

transport and secretion of the antibody, promotion of antibody assembly, conformational integrity, and antibody-mediated effector function. In a specific embodiment, the altered carbohydrate modifications enhance antibody mediated effector function relative to the antibody lacking the carbohydrate modification. Carbohydrate modifications that lead to altered antibody mediated effector function are well known in the art (for example, see Shields, R. L. *et al.* (2002) “*Lack Of Fucose On Human IgG N-Linked Oligosaccharide Improves Binding To Human Fcγ₃ RIII And Antibody-Dependent Cellular Toxicity*,” J. Biol. Chem. 277(30): 26733-26740; Davies J. *et al.* (2001) “*Expression Of GnTIII In A Recombinant Anti-CD20 CHO Production Cell Line: Expression Of Antibodies With Altered Glycoforms Leads To An Increase In ADCC Through Higher Affinity For FC γ₃ RIII*,” Biotechnology & Bioengineering 74(4): 288-294). Methods of altering carbohydrate contents are known to those skilled in the art, see, *e.g.*, Wallick, S. C. *et al.* (1988) “*Glycosylation Of A VH Residue Of A Monoclonal Antibody Against Alpha (1---6) Dextran Increases Its Affinity For Antigen*,” J. Exp. Med. 168(3): 1099-1109; Tao, M. H. *et al.* (1989) “*Studies Of Aglycosylated Chimeric Mouse-Human IgG. Role of Carbohydrate in The Structure And Effector Functions Mediated By The Human IgG Constant Region*,” J. Immunol. 143(8): 2595-2601; Routledge, E. G. *et al.* (1995) “*The Effect of Aglycosylation on The Immunogenicity of A Humanized Therapeutic CD3 Monoclonal Antibody*,” Transplantation 60(8):847-53; Elliott, S. *et al.* (2003) “*Enhancement Of Therapeutic Protein In Vivo Activities Through Glycoengineering*,” Nature Biotechnol. 21:414-21; Shields, R. L. *et al.* (2002) “*Lack of Fucose on Human IgG N-Linked Oligosaccharide Improves Binding to Human Fcγ₃ RIII And Antibody-Dependent Cellular Toxicity*,” J. Biol. Chem. 277(30): 26733-26740).

A derivative antibody or antibody fragment can be generated with an engineered sequence or glycosylation state to confer preferred levels of activity in antibody dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), antibody-dependent neutrophil phagocytosis (ADNP), or antibody-dependent complement deposition (ADCD) functions as measured by bead-based or cell-based assays or *in vivo* studies in animal models.

A derivative antibody or antibody fragment may be modified by chemical modifications using techniques known to those of skill in the art, including, but not limited to, specific chemical cleavage, acetylation, formulation, metabolic synthesis of tunicamycin, *etc.* In one embodiment, an antibody derivative will possess a similar or identical function as the parental antibody. In another embodiment, an antibody derivative will exhibit an altered activity relative

to the parental antibody. For example, a derivative antibody (or fragment thereof) can bind to its epitope more tightly or be more resistant to proteolysis than the parental antibody.

C. Engineering of Antibody Sequences

5 In various embodiments, one may choose to engineer sequences of the identified antibodies for a variety of reasons, such as improved expression, improved cross-reactivity or diminished off-target binding. Modified antibodies may be made by any technique known to those of skill in the art, including expression through standard molecular biological techniques, or the chemical synthesis of polypeptides. Methods for recombinant expression are addressed
10 elsewhere in this document. The following is a general discussion of relevant goals techniques for antibody engineering.

Hybridomas may be cultured, then cells lysed, and total RNA extracted. Random hexamers may be used with RT to generate cDNA copies of RNA, and then PCR performed using a multiplex mixture of PCR primers expected to amplify all human variable gene
15 sequences. PCR product can be cloned into pGEM-T Easy vector, then sequenced by automated DNA sequencing using standard vector primers. Assay of binding and neutralization may be performed using antibodies collected from hybridoma supernatants and purified by FPLC, using Protein G columns.

Recombinant full-length IgG antibodies can be generated by subcloning heavy and light
20 chain Fv DNAs from the cloning vector into an IgG plasmid vector, transfected into 293 (*e.g.*, Freestyle) cells or CHO cells, and antibodies can be collected and purified from the 293 or CHO cell supernatant. Other appropriate host cells systems include bacteria, such as *E. coli*, insect cells (S2, Sf9, Sf29, High Five), plant cells (*e.g.*, tobacco, with or without engineering for human-like glycans), algae, or in a variety of non-human transgenic contexts, such as mice,
25 rats, goats or cows.

Expression of nucleic acids encoding antibodies, both for the purpose of subsequent antibody purification, and for immunization of a host, is also contemplated. Antibody coding sequences can be RNA, such as native RNA or modified RNA. Modified RNA contemplates certain chemical modifications that confer increased stability and low immunogenicity to
30 mRNAs, thereby facilitating expression of therapeutically important proteins. For instance, N1-methyl-pseudouridine (N1mΨ) outperforms several other nucleoside modifications and their combinations in terms of translation capacity. In addition to turning off the immune/eIF2α phosphorylation-dependent inhibition of translation, incorporated N1mΨ nucleotides dramatically alter the dynamics of the translation process by increasing ribosome pausing and

density on the mRNA. Increased ribosome loading of modified mRNAs renders them more permissive for initiation by favoring either ribosome recycling on the same mRNA or de novo ribosome recruitment. Such modifications could be used to enhance antibody expression *in vivo* following inoculation with RNA. The RNA, whether native or modified, may be

5 delivered as naked RNA or in a delivery vehicle, such as a lipid nanoparticle.

Alternatively, DNA encoding the antibody may be employed for the same purposes. The DNA is included in an expression cassette comprising a promoter active in the host cell for which it is designed. The expression cassette is advantageously included in a replicable vector, such as a conventional plasmid or minivector. Vectors include viral vectors, such as

10 poxviruses, adenoviruses, herpesviruses, adeno-associated viruses, and lentiviruses are contemplated. Replicons encoding antibody genes such as alphavirus replicons based on VEE virus or Sindbis virus are also contemplated. Delivery of such vectors can be performed by needle through intramuscular, subcutaneous, or intradermal routes, or by transcutaneous electroporation when *in vivo* expression is desired.

15 The rapid availability of antibody produced in the same host cell and cell culture process as the final cGMP manufacturing process has the potential to reduce the duration of process development programs. Lonza has developed a generic method using pooled transfectants grown in CDACF medium, for the rapid production of small quantities (up to 50 g) of antibodies in CHO cells. Although slightly slower than a true transient system, the advantages

20 include a higher product concentration and use of the same host and process as the production cell line. Example of growth and productivity of GS-CHO pools, expressing a model antibody, in a disposable bioreactor: in a disposable bag bioreactor culture (5 L working volume) operated in fed-batch mode, a harvest antibody concentration of 2 g/L was achieved within 9 weeks of transfection.

25 Antibody molecules will comprise fragments (such as F(ab'), F(ab')₂) that are produced, for example, by the proteolytic cleavage of the mAbs, or single-chain immunoglobulins producible, for example, via recombinant means. F(ab') antibody derivatives are monovalent, while F(ab')₂ antibody derivatives are bivalent. In one embodiment, such fragments can be combined with one another, or with other antibody fragments or receptor ligands to form

30 "chimeric" binding molecules. Significantly, such chimeric molecules may contain substituents capable of binding to different epitopes of the same molecule.

In related embodiments, the antibody is a derivative of the disclosed antibodies, *e.g.*, an antibody comprising the CDR sequences identical to those in the disclosed antibodies (*e.g.*,

a chimeric, or CDR-grafted antibody). Alternatively, one may wish to make modifications, such as introducing conservative changes into an antibody molecule. In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like.

It also is understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U.S. Patent 4,554,101, incorporated herein by reference, states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein. As detailed in U.S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: basic amino acids: arginine (+3.0), lysine (+3.0), and histidine (-0.5); acidic amino acids: aspartate (+3.0 $\pm$ 1), glutamate (+3.0 $\pm$ 1), asparagine (+0.2), and glutamine (+0.2); hydrophilic, nonionic amino acids: serine (+0.3), asparagine (+0.2), glutamine (+0.2), and threonine (-0.4), sulfur containing amino acids: cysteine (-1.0) and methionine (-1.3); hydrophobic, nonaromatic amino acids: valine (-1.5), leucine (-1.8), isoleucine (-1.8), proline (-0.5 $\pm$ 1), alanine (-0.5), and glycine (0); hydrophobic, aromatic amino acids: tryptophan (-3.4), phenylalanine (-2.5), and tyrosine (-2.3).

It is understood that an amino acid can be substituted for another having a similar hydrophilicity and produce a biologically or immunologically modified protein. In such changes, the substitution of amino acids whose hydrophilicity values are within $\pm$ 2 is preferred, those that are within $\pm$ 1 are particularly preferred, and those within $\pm$ 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions generally are based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take into consideration the various foregoing characteristics are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

The present disclosure also contemplates isotype modification. By modifying the Fc region to have a different isotype, different functionalities can be achieved. For example,

changing to IgG₁ can increase antibody dependent cell cytotoxicity, switching to class A can improve tissue distribution, and switching to class M can improve valency.

Alternatively or additionally, it may be useful to combine amino acid modifications with one or more further amino acid modifications that alter C1q binding and/or the complement dependent cytotoxicity (CDC) function of the Fc region of an IL-23p19 binding molecule. The binding polypeptide of particular interest may be one that binds to C1q and displays complement dependent cytotoxicity. Polypeptides with pre-existing C1q binding activity, optionally further having the ability to mediate CDC may be modified such that one or both of these activities are enhanced. Amino acid modifications that alter C1q and/or modify its complement dependent cytotoxicity function are described, for example, in WO/0042072, which is hereby incorporated by reference.

One can design an Fc region of an antibody with altered effector function, *e.g.*, by modifying C1q binding and/or FcγR binding and thereby changing CDC activity and/or ADCC activity. “Effector functions” are responsible for activating or diminishing a biological activity (*e.g.*, in a subject). Examples of effector functions include, but are not limited to: C1q binding; complement dependent cytotoxicity (CDC); Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (*e.g.*, B cell receptor; BCR), *etc.* Such effector functions may require the Fc region to be combined with a binding domain (*e.g.*, an antibody variable domain) and can be assessed using various assays (*e.g.*, Fc binding assays, ADCC assays, CDC assays, *etc.*).

For example, one can generate a variant Fc region of an antibody with improved C1q binding and improved FcγRIII binding (*e.g.*, having both improved ADCC activity and improved CDC activity). Alternatively, if it is desired that effector function be reduced or ablated, a variant Fc region can be engineered with reduced CDC activity and/or reduced ADCC activity. In other embodiments, only one of these activities may be increased, and, optionally, also the other activity reduced (*e.g.*, to generate an Fc region variant with improved ADCC activity, but reduced CDC activity and *vice versa*).

FcRn binding. Fc mutations can also be introduced and engineered to alter their interaction with the neonatal Fc receptor (FcRn) and improve their pharmacokinetic properties. A collection of human Fc variants with improved binding to the FcRn have been described (Shields *et al.*, (2001). High resolution mapping of the binding site on human IgG1 for FcγRI, FcγRII, FcγRIII, and FcRn and design of IgG1 variants with improved binding to the FcγR, (J. Biol. Chem. 276:6591-6604). A number of methods are known that can result in increased half-life (Kuo and Aveson, (2011)), including amino acid modifications may be generated through

techniques including alanine scanning mutagenesis, random mutagenesis and screening to assess the binding to the neonatal Fc receptor (FcRn) and/or the *in vivo* behavior. Computational strategies followed by mutagenesis may also be used to select one of amino acid mutations to mutate.

5 The present disclosure therefore provides a variant of an antigen binding protein with optimized binding to FcRn. In a particular embodiment, the said variant of an antigen binding protein comprises at least one amino acid modification in the Fc region of said antigen binding protein, wherein said modification is selected from the group consisting of 226, 227, 228, 230, 231, 233, 234, 239, 241, 243, 246, 250, 252, 256, 259, 264, 265, 267, 269, 270, 276, 284, 285,
10 288, 289, 290, 291, 292, 294, 297, 298, 299, 301, 302, 303, 305, 307, 308, 309, 311, 315, 317, 320, 322, 325, 327, 330, 332, 334, 335, 338, 340, 342, 343, 345, 347, 350, 352, 354, 355, 356, 359, 360, 361, 362, 369, 370, 371, 375, 378, 380, 382, 384, 385, 386, 387, 389, 390, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 403, 404, 408, 411, 412, 414, 415, 416, 418, 419, 420, 421, 422, 424, 426, 428, 433, 434, 438, 439, 440, 443, 444, 445, 446 and 447 of the Fc region
15 as compared to said parent polypeptide, wherein the numbering of the amino acids in the Fc region is that of the EU index in Kabat. In a further aspect of the disclosure the modifications are M252Y/S254T/T256E.

 Additionally, various publications describe methods for obtaining physiologically active molecules whose half-lives are modified, see for example Kontermann (2009) either by
20 introducing an FcRn-binding polypeptide into the molecules or by fusing the molecules with antibodies whose FcRn-binding affinities are preserved but affinities for other Fc receptors have been greatly reduced or fusing with FcRn binding domains of antibodies.

 Derivatized antibodies may be used to alter the half-lives (*e.g.*, serum half-lives) of parental antibodies in a mammal, particularly a human. Such alterations may result in a half-
25 life of greater than 15 days, preferably greater than 20 days, greater than 25 days, greater than 30 days, greater than 35 days, greater than 40 days, greater than 45 days, greater than 2 months, greater than 3 months, greater than 4 months, or greater than 5 months. The increased half-lives of the antibodies of the present disclosure or fragments thereof in a mammal, preferably a human, results in a higher serum titer of said antibodies or antibody fragments in the mammal,
30 and thus reduces the frequency of the administration of said antibodies or antibody fragments and/or reduces the concentration of said antibodies or antibody fragments to be administered. Antibodies or fragments thereof having increased *in vivo* half-lives can be generated by techniques known to those of skill in the art. For example, antibodies or fragments thereof with increased *in vivo* half-lives can be generated by modifying (*e.g.*, substituting, deleting or

adding) amino acid residues identified as involved in the interaction between the Fc domain and the FcRn receptor.

Beltramello *et al.* (2010) previously reported the modification of neutralizing mAbs, due to their tendency to enhance dengue virus infection, by generating in which leucine residues at positions 1.3 and 1.2 of CH2 domain (according to the IMGT unique numbering for C-domain) were substituted with alanine residues. This modification, also known as “LALA” mutation, abolishes antibody binding to FcγRI, FcγRII and FcγRIIIa, as described by Hessel *et al.* (2007). The variant and unmodified recombinant mAbs were compared for their capacity to neutralize and enhance infection by the four dengue virus serotypes. LALA variants retained the same neutralizing activity as unmodified mAb but were completely devoid of enhancing activity. LALA mutations of this nature are therefore contemplated in the context of the presently disclosed antibodies.

Altered Glycosylation. A particular embodiment of the present disclosure is an isolated monoclonal antibody, or antigen binding fragment thereof, containing a substantially homogeneous glycan without sialic acid, galactose, or fucose. The monoclonal antibody comprises a heavy chain variable region and a light chain variable region, both of which may be attached to heavy chain or light chain constant regions respectively. The aforementioned substantially homogeneous glycan may be covalently attached to the heavy chain constant region.

Another embodiment of the present disclosure comprises a mAb with a novel Fc glycosylation pattern. The isolated monoclonal antibody, or antigen binding fragment thereof, is present in a substantially homogenous composition represented by the GNGN or G1/G2 glycoform. Fc glycosylation plays a significant role in anti-viral and anti-cancer properties of therapeutic mAbs. The disclosure is in line with a recent study that shows increased anti-lentivirus cell-mediated viral inhibition of a fucose free anti-HIV mAb *in vitro*. This embodiment of the present disclosure with homogenous glycans lacking a core fucose, showed increased protection against specific viruses by a factor greater than two-fold. Elimination of core fucose dramatically improves the ADCC activity of mAbs mediated by natural killer (NK) cells but appears to have the opposite effect on the ADCC activity of polymorphonuclear cells (PMNs).

The isolated monoclonal antibody, or antigen binding fragment thereof, comprising a substantially homogenous composition represented by the GNGN or G1/G2 glycoform exhibits increased binding affinity for Fc gamma RI and Fc gamma RIII compared to the same antibody without the substantially homogeneous GNGN glycoform and with G0, G1F, G2F, GNF,

GNGNF or GNGNFX containing glycoforms. In one embodiment of the present disclosure, the antibody dissociates from Fc gamma RI with a K_d of 1×10^{-8} M or less and from Fc gamma RIII with a K_d of 1×10^{-7} M or less.

Glycosylation of an Fc region is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side chain of an asparagine residue. O-linked glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used. The recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain peptide sequences are asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline. Thus, the presence of either of these peptide sequences in a polypeptide creates a potential glycosylation site.

The glycosylation pattern may be altered, for example, by deleting one or more glycosylation site(s) found in the polypeptide, and/or adding one or more glycosylation site(s) that are not present in the polypeptide. Addition of glycosylation sites to the Fc region of an antibody is conveniently accomplished by altering the amino acid sequence such that it contains one or more of the above-described tripeptide sequences (for N-linked glycosylation sites). An exemplary glycosylation variant has an amino acid substitution of residue Asn 297 of the heavy chain. The alteration may also be made by the addition of, or substitution by, one or more serine or threonine residues to the sequence of the original polypeptide (for O-linked glycosylation sites). Additionally, a change of Asn 297 to Ala can remove one of the glycosylation sites.

In certain embodiments, the antibody is expressed in cells that express beta (1,4)-N-acetylglucosaminyltransferase III (GnT III), such that GnT III adds GlcNAc to the IL-23p19 antibody. Methods for producing antibodies in such a fashion are provided in WO/9954342, WO/03011878, patent publication 20030003097A1, and Umana *et al.*, Nature Biotechnology, 17:176-180, February 1999. Cell lines can be altered to enhance or reduce or eliminate certain post-translational modifications, such as glycosylation, using genome editing technology such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). For example, CRISPR technology can be used to eliminate genes encoding glycosylating enzymes in 293 or CHO cells used to express recombinant monoclonal antibodies.

Elimination of monoclonal antibody protein sequence liabilities. It is possible to engineer the antibody variable gene sequences obtained from human B cells to enhance their manufacturability and safety. Potential protein sequence liabilities can be identified by searching for sequence motifs associated with sites containing:

- 1) Unpaired Cys residues,
- 2) N-linked glycosylation,
- 3) Asn deamidation,
- 4) Asp isomerization,
- 5 5) SYE truncation,
- 6) Met oxidation,
- 7) Trp oxidation,
- 8) N-terminal glutamate,
- 9) Integrin binding,
- 10 10) CD11c/CD18 binding, or
- 11) Fragmentation

Such motifs can be eliminated by altering the synthetic gene for the cDNA encoding recombinant antibodies.

Protein engineering efforts in the field of development of therapeutic antibodies clearly
 15 reveal that certain sequences or residues are associated with solubility differences (Fernandez-Escamilla *et al.*, *Nature Biotech.*, 22 (10), 1302-1306, 2004; Chennamsetty *et al.*, *PNAS*, 106 (29), 11937-11942, 2009; Voynov *et al.*, *Biocon. Chem.*, 21 (2), 385-392, 2010) Evidence from solubility-altering mutations in the literature indicate that some hydrophilic residues such as aspartic acid, glutamic acid, and serine contribute significantly more favorably to protein
 20 solubility than other hydrophilic residues, such as asparagine, glutamine, threonine, lysine, and arginine.

Stability. Antibodies can be engineered for enhanced biophysical properties. One can use elevated temperature to unfold antibodies to determine relative stability, using average apparent melting temperatures. Differential Scanning Calorimetry (DSC) measures the heat
 25 capacity, C_p , of a molecule (the heat required to warm it, per degree) as a function of temperature. One can use DSC to study the thermal stability of antibodies. DSC data for mAbs is particularly interesting because it sometimes resolves the unfolding of individual domains within the mAb structure, producing up to three peaks in the thermogram (from unfolding of the Fab, C_H2 , and C_H3 domains). Typically unfolding of the Fab domain produces the strongest
 30 peak. The DSC profiles and relative stability of the Fc portion show characteristic differences for the human IgG₁, IgG₂, IgG₃, and IgG₄ subclasses (Garber and Demarest, *Biochem. Biophys. Res. Commun.* 355, 751-757, 2007). One also can determine average apparent melting temperature using circular dichroism (CD), performed with a CD spectrometer. Far-UV CD spectra will be measured for antibodies in the range of 200 to 260 nm at increments of 0.5 nm.

The final spectra can be determined as averages of 20 accumulations. Residue ellipticity values can be calculated after background subtraction. Thermal unfolding of antibodies (0.1 mg/mL) can be monitored at 235 nm from 25-95 °C and a heating rate of 1 °C/min. One can use dynamic light scattering (DLS) to assess for propensity for aggregation. DLS is used to characterize size of various particles including proteins. If the system is not disperse in size, the mean effective diameter of the particles can be determined. This measurement depends on the size of the particle core, the size of surface structures, and particle concentration. Since DLS essentially measures fluctuations in scattered light intensity due to particles, the diffusion coefficient of the particles can be determined. DLS software in commercial DLS instruments displays the particle population at different diameters. Stability studies can be done conveniently using DLS. DLS measurements of a sample can show whether the particles aggregate over time or with temperature variation by determining whether the hydrodynamic radius of the particle increases. If particles aggregate, one can see a larger population of particles with a larger radius. Stability depending on temperature can be analyzed by controlling the temperature *in situ*.

Capillary electrophoresis (CE) techniques include proven methodologies for determining features of antibody stability. One can use an iCE approach to resolve antibody protein charge variants due to deamidation, C-terminal lysines, sialylation, oxidation, glycosylation, and any other change to the protein that can result in a change in pI of the protein. Each of the expressed antibody proteins can be evaluated by high throughput, free solution isoelectric focusing (IEF) in a capillary column (cIEF), using a Protein Simple Maurice instrument. Whole-column UV absorption detection can be performed every 30 seconds for real time monitoring of molecules focusing at the isoelectric points (pIs). This approach combines the high resolution of traditional gel IEF with the advantages of quantitation and automation found in column-based separations while eliminating the need for a mobilization step. The technique yields reproducible, quantitative analysis of identity, purity, and heterogeneity profiles for the expressed antibodies. The results identify charge heterogeneity and molecular sizing on the antibodies, with both absorbance and native fluorescence detection modes and with sensitivity of detection down to 0.7 µg/mL.

Solubility. One can determine the intrinsic solubility score of antibody sequences. The intrinsic solubility scores can be calculated using CamSol Intrinsic (Sormanni *et al.*, *J Mol Biol* 427, 478-490, 2015). The amino acid sequences for residues 95-102 (Kabat numbering) in HCDR3 of each antibody fragment such as a scFv can be evaluated via the online program to calculate the solubility scores. One also can determine solubility using laboratory techniques. Various techniques exist, including addition of lyophilized protein to a solution until the

solution becomes saturated and the solubility limit is reached, or concentration by ultrafiltration in a microconcentrator with a suitable molecular weight cut-off. The most straightforward method is induction of amorphous precipitation, which measures protein solubility using a method involving protein precipitation using ammonium sulfate (Trevino *et al.*, *J Mol Biol*, 366: 449-460, 2007). Ammonium sulfate precipitation gives quick and accurate information on relative solubility values. Ammonium sulfate precipitation produces precipitated solutions with well-defined aqueous and solid phases and requires relatively small amounts of protein. Solubility measurements performed using induction of amorphous precipitation by ammonium sulfate also can be done easily at different pH values. Protein solubility is highly pH dependent, and pH is considered the most important extrinsic factor that affects solubility.

Autoreactivity. Generally, it is thought that autoreactive clones should be eliminated during ontogeny by negative selection, however it has become clear that many human naturally occurring antibodies with autoreactive properties persist in adult mature repertoires, and the autoreactivity may enhance the antiviral function of many antibodies to pathogens. It has been noted that HCDR3 loops in antibodies during early B cell development are often rich in positive charge and exhibit autoreactive patterns (Wardemann *et al.*, *Science* 301, 1374-1377, 2003). One can test a given antibody for autoreactivity by assessing the level of binding to human origin cells in microscopy (using adherent HeLa or HEP-2 epithelial cells) and flow cytometric cell surface staining (using suspension Jurkat T cells and 293S human embryonic kidney cells). Autoreactivity also can be surveyed using assessment of binding to tissues in tissue arrays.

Preferred residues (“Human Likeness”). B cell repertoire deep sequencing of human B cells from blood donors is being performed on a wide scale in many recent studies. Sequence information about a significant portion of the human antibody repertoire facilitates statistical assessment of antibody sequence features common in healthy humans. With knowledge about the antibody sequence features in a human recombined antibody variable gene reference database, the position specific degree of “Human Likeness” (HL) of an antibody sequence can be estimated. HL has been shown to be useful for the development of antibodies in clinical use, like therapeutic antibodies or antibodies as vaccines. The goal is to increase the human likeness of antibodies to reduce potential adverse effects and anti-antibody immune responses that will lead to significantly decreased efficacy of the antibody drug or can induce serious health implications. One can assess antibody characteristics of the combined antibody repertoire of three healthy human blood donors of about 400 million sequences in total and created a novel “relative Human Likeness” (rHL) score that focuses on the hypervariable region of the antibody.

The rHL score allows one to easily distinguish between human (positive score) and non-human sequences (negative score). Antibodies can be engineered to eliminate residues that are not common in human repertoires.

5 **D. Single Chain Antibodies**

A single chain variable fragment (scFv) is a fusion of the variable regions of the heavy and light chains of immunoglobulins, linked together with a short (usually serine, glycine) linker. This chimeric molecule retains the specificity of the original immunoglobulin, despite removal of the constant regions and the introduction of a linker peptide. This modification
10 usually leaves the specificity unaltered. These molecules were created historically to facilitate phage display where it is highly convenient to express the antigen binding domain as a single peptide. Alternatively, scFv can be created directly from subcloned heavy and light chains derived from a hybridoma or B cell. Single chain variable fragments lack the constant Fc region found in complete antibody molecules, and thus, the common binding sites (*e.g.*, protein A/G)
15 used to purify antibodies. These fragments can often be purified/immobilized using Protein L since Protein L interacts with the variable region of kappa light chains.

Flexible linkers generally are comprised of helix- and turn-promoting amino acid residues such as alanine, serine and glycine. However, other residues can function as well. Tang *et al.* (1996) used phage display as a means of rapidly selecting tailored linkers for single-
20 chain antibodies (scFvs) from protein linker libraries. A random linker library was constructed in which the genes for the heavy and light chain variable domains were linked by a segment encoding an 18-amino acid polypeptide of variable composition. The scFv repertoire (approx. 5×10^6 different members) was displayed on filamentous phage and subjected to affinity selection with hapten. The population of selected variants exhibited significant increases in
25 binding activity but retained considerable sequence diversity. Screening 1054 individual variants subsequently yielded a catalytically active scFv that was produced efficiently in soluble form. Sequence analysis revealed a conserved proline in the linker two residues after the V_H C terminus and an abundance of arginines and prolines at other positions as the only common features of the selected tethers.

30 The recombinant antibodies of the present disclosure may also involve sequences or moieties that permit dimerization or multimerization of the receptors. Such sequences include those derived from IgA, which permit formation of multimers in conjunction with the J-chain. Another multimerization domain is the Gal4 dimerization domain. In other embodiments, the

chains may be modified with agents such as biotin/avidin, which permit the combination of two antibodies.

In a separate embodiment, a single-chain antibody can be created by joining receptor light and heavy chains using a non-peptide linker or chemical unit. Generally, the light and heavy chains will be produced in distinct cells, purified, and subsequently linked together in an appropriate fashion (*i.e.*, the N-terminus of the heavy chain being attached to the C-terminus of the light chain via an appropriate chemical bridge).

Cross-linking reagents are used to form molecular bridges that tie functional groups of two different molecules, *e.g.*, a stabilizing and coagulating agent. However, it is contemplated that dimers or multimers of the same analog or heteromeric complexes comprised of different analogs can be created. To link two different compounds in a step-wise manner, hetero-bifunctional cross-linkers can be used that eliminate unwanted homopolymer formation.

An exemplary hetero-bifunctional cross-linker contains two reactive groups: one reacting with primary amine group (*e.g.*, N-hydroxy succinimide) and the other reacting with a thiol group (*e.g.*, pyridyl disulfide, maleimides, halogens, *etc.*). Through the primary amine reactive group, the cross-linker may react with the lysine residue(s) of one protein (*e.g.*, the selected antibody or fragment) and through the thiol reactive group, the cross-linker, already tied up to the first protein, reacts with the cysteine residue (free sulfhydryl group) of the other protein (*e.g.*, the selective agent).

It is preferred that a cross-linker having reasonable stability in blood will be employed. Numerous types of disulfide-bond containing linkers are known that can be successfully employed to conjugate targeting and therapeutic/preventative agents. Linkers that contain a disulfide bond that is sterically hindered may prove to give greater stability *in vivo*, preventing release of the targeting peptide prior to reaching the site of action. These linkers are thus one group of linking agents.

Another cross-linking reagent is SMPT, which is a bifunctional cross-linker containing a disulfide bond that is "sterically hindered" by an adjacent benzene ring and methyl groups. It is believed that steric hindrance of the disulfide bond serves a function of protecting the bond from attack by thiolate anions such as glutathione which can be present in tissues and blood, and thereby help in preventing decoupling of the conjugate prior to the delivery of the attached agent to the target site.

The SMPT cross-linking reagent, as with many other known cross-linking reagents, lends the ability to cross-link functional groups such as the SH of cysteine or primary amines (*e.g.*, the epsilon amino group of lysine). Another possible type of cross-linker includes the

hetero-bifunctional photoreactive phenylazides containing a cleavable disulfide bond such as sulfosuccinimidyl-2-(p-azido salicylamido) ethyl-1,3'-dithiopropionate. The N-hydroxy-succinimidyl group reacts with primary amino groups and the phenylazide (upon photolysis) reacts non-selectively with any amino acid residue.

5 In addition to hindered cross-linkers, non-hindered linkers also can be employed in accordance herewith. Other useful cross-linkers, not considered to contain or generate a protected disulfide, include SATA, SPDP and 2-iminothiolane (Wawrzynczak & Thorpe, 1987). The use of such cross-linkers is well understood in the art. Another embodiment involves the use of flexible linkers.

10 U.S. Patent 4,680,338, describes bifunctional linkers useful for producing conjugates of ligands with amine-containing polymers and/or proteins, especially for forming antibody conjugates with chelators, drugs, enzymes, detectable labels and the like. U.S. Patents 5,141,648 and 5,563,250 disclose cleavable conjugates containing a labile bond that is cleavable under a variety of mild conditions. This linker is particularly useful in that the agent
15 of interest may be bonded directly to the linker, with cleavage resulting in release of the active agent. Particular uses include adding a free amino or free sulfhydryl group to a protein, such as an antibody, or a drug.

 U.S. Patent 5,856,456 provides peptide linkers for use in connecting polypeptide constituents to make fusion proteins, *e.g.*, single chain antibodies. The linker is up to about 50
20 amino acids in length, contains at least one occurrence of a charged amino acid (preferably arginine or lysine) followed by a proline, and is characterized by greater stability and reduced aggregation. U.S. Patent 5,880,270 discloses aminooxy-containing linkers useful in a variety of immunodiagnostic and separative techniques.

25 **E. Multispecific Antibodies**

 In certain embodiments, antibodies of the present disclosure are bispecific or multispecific. Bispecific antibodies are antibodies that have binding specificities for at least two different epitopes. Exemplary bispecific antibodies may bind to two different epitopes of a single antigen. Other such antibodies may combine a first antigen binding site with a binding
30 site for a second antigen. Alternatively, an anti-pathogen arm may be combined with an arm that binds to a triggering molecule on a leukocyte, such as a T-cell receptor molecule (*e.g.*, CD3), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and Fc gamma RIII (CD16), so as to focus and localize cellular defense mechanisms to the infected cell. Bispecific antibodies may also be used to localize cytotoxic agents to infected cells. These

antibodies possess a pathogen-binding arm and an arm that binds the cytotoxic agent (*e.g.*, saporin, anti-interferon- α , vinca alkaloid, ricin A chain, methotrexate or radioactive isotope hapten). Bispecific antibodies can be prepared as full-length antibodies or antibody fragments (*e.g.*, F(ab')₂ bispecific antibodies). WO 96/16673 describes a bispecific anti-ErbB2/anti-Fc gamma RIII antibody and U.S. Patent 5,837,234 discloses a bispecific anti-ErbB2/anti-Fc gamma RI antibody. A bispecific anti-ErbB2/Fc alpha antibody is shown in WO98/02463. U.S. Patent 5,821,337 teaches a bispecific anti-ErbB2/anti-CD3 antibody.

Methods for making bispecific antibodies are known in the art. Traditional production of full-length bispecific antibodies is based on the co-expression of two immunoglobulin heavy chain-light chain pairs, where the two chains have different specificities (Millstein *et al.*, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. Purification of the correct molecule, which is usually done by affinity chromatography steps, is rather cumbersome, and the product yields are low. Similar procedures are disclosed in WO 93/08829, and in Traunecker *et al.*, EMBO J., 10:3655-3659 (1991).

According to a different approach, antibody variable regions with the desired binding specificities (antibody-antigen combining sites) are fused to immunoglobulin constant domain sequences. Preferably, the fusion is with an Ig heavy chain constant domain, comprising at least part of the hinge, C_{H2}, and C_{H3} regions. It is preferred to have the first heavy-chain constant region (C_{H1}) containing the site necessary for light chain bonding, present in at least one of the fusions. DNAs encoding the immunoglobulin heavy chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host cell. This provides for greater flexibility in adjusting the mutual proportions of the three polypeptide fragments in embodiments when unequal ratios of the three polypeptide chains used in the construction provide the optimum yield of the desired bispecific antibody. It is, however, possible to insert the coding sequences for two or all three polypeptide chains into a single expression vector when the expression of at least two polypeptide chains in equal ratios results in high yields or when the ratios have no significant effect on the yield of the desired chain combination.

In a particular embodiment of this approach, the bispecific antibodies are composed of a hybrid immunoglobulin heavy chain with a first binding specificity in one arm, and a hybrid immunoglobulin heavy chain-light chain pair (providing a second binding specificity) in the

other arm. It was found that this asymmetric structure facilitates the separation of the desired bispecific compound from unwanted immunoglobulin chain combinations, as the presence of an immunoglobulin light chain in only one half of the bispecific molecule provides for a facile way of separation. This approach is disclosed in WO 94/04690. For further details of generating
5 bispecific antibodies see, for example, Suresh *et al.*, Methods in Enzymology, 121:210 (1986).

According to another approach described in U.S. Patent 5,731,168, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers that are recovered from recombinant cell culture. The preferred interface comprises at least a part of the C_{H3} domain. In this method, one or more small amino acid side
10 chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.*, tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.*, alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such
15 as homodimers.

Bispecific antibodies include cross-linked or "heteroconjugate" antibodies. For example, one of the antibodies in the heteroconjugate can be coupled to avidin, the other to biotin. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent 4,676,980), and for treatment of HIV infection (WO 91/00360,
20 WO 92/200373, and EP 03089). Heteroconjugate antibodies may be made using any convenient cross-linking methods. Suitable cross-linking agents are well known in the art, and are disclosed in U.S. Patent 4,676,980, along with a number of cross-linking techniques.

Techniques for generating bispecific antibodies from antibody fragments have also been described in the literature. For example, bispecific antibodies can be prepared using
25 chemical linkage. Brennan *et al.*, Science, 229: 81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent, sodium arsenite, to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then
30 reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The

bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Techniques exist that facilitate the direct recovery of Fab'-SH fragments from *E. coli*, which can be chemically coupled to form bispecific antibodies. Shalaby *et al.*, J. Exp. Med., 175: 217-225 (1992) describe the production of a humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described (Merchant *et al.*, *Nat. Biotechnol.* **16**, 677-681 (1998). doi:10.1038/nbt0798-677pmid:9661204). For example, bispecific antibodies have been produced using leucine zippers (Kostelny *et al.*, J. Immunol., 148(5):1547-1553, 1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a V_H connected to a V_L by a linker that is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See Gruber *et al.*, J. Immunol., 152:5368 (1994).

In a particular embodiment, a bispecific or multispecific antibody may be formed as a DOCK-AND-LOCK™ (DNL™) complex (see, *e.g.*, U.S. Patents 7,521,056; 7,527,787; 7,534,866; 7,550,143 and 7,666,400, the Examples section of each of which is incorporated herein by reference.) Generally, the technique takes advantage of the specific and high-affinity binding interactions that occur between a dimerization and docking domain (DDD) sequence of the regulatory (R) subunits of cAMP-dependent protein kinase (PKA) and an anchor domain (AD) sequence derived from any of a variety of AKAP proteins (Baillie *et al.*, *FEBS Letters*. 2005; 579: 3264; Wong and Scott, *Nat. Rev. Mol. Cell Biol.* 2004; 5: 959). The DDD and AD peptides may be attached to any protein, peptide or other molecule. Because the DDD

sequences spontaneously dimerize and bind to the AD sequence, the technique allows the formation of complexes between any selected molecules that may be attached to DDD or AD sequences.

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared (Tutt *et al.*, J. Immunol. 147: 60, 1991; Xu *et al.*, *Science*, 358(6359):85-90, 2017). A multivalent antibody may be internalized (and/or catabolized) faster than a bivalent antibody by a cell expressing an antigen to which the antibodies bind. The antibodies of the present disclosure can be multivalent antibodies with three or more antigen binding sites (*e.g.*, tetravalent antibodies), which can be readily produced by recombinant expression of nucleic acid encoding the polypeptide chains of the antibody. The multivalent antibody can comprise a dimerization domain and three or more antigen binding sites. The preferred dimerization domain comprises (or consists of) an Fc region or a hinge region. In this scenario, the antibody will comprise an Fc region and three or more antigen binding sites amino-terminal to the Fc region. The preferred multivalent antibody herein comprises (or consists of) three to about eight, but preferably four, antigen binding sites. The multivalent antibody comprises at least one polypeptide chain (and preferably two polypeptide chains), wherein the polypeptide chain(s) comprise two or more variable regions. For instance, the polypeptide chain(s) may comprise VD1-(X1)_n-VD2-(X2)_n-Fc, wherein VD1 is a first variable region, VD2 is a second variable region, Fc is one polypeptide chain of an Fc region, X1 and X2 represent an amino acid or polypeptide, and n is 0 or 1. For instance, the polypeptide chain(s) may comprise: VH-CH1-flexible linker-VH-CH1-Fc region chain; or VH-CH1-VH-CH1-Fc region chain. The multivalent antibody herein preferably further comprises at least two (and preferably four) light chain variable region polypeptides. The multivalent antibody herein may, for instance, comprise from about two to about eight light chain variable region polypeptides. The light chain variable region polypeptides contemplated here comprise a light chain variable region and, optionally, further comprise a C_L domain.

Charge modifications are particularly useful in the context of a multispecific antibody, where amino acid substitutions in Fab molecules result in reducing the mispairing of light chains with non-matching heavy chains (Bence-Jones-type side products), which can occur in the production of Fab-based bi-/multispecific antigen binding molecules with a VH/VL exchange in one (or more, in case of molecules comprising more than two antigen-binding Fab molecules) of their binding arms (see also PCT publication no. WO 2015/150447, particularly the examples therein, incorporated herein by reference in its entirety).

Accordingly, in particular embodiments, an antibody comprised in the therapeutic agent comprises

- (a) a first Fab molecule which specifically binds to a first antigen
 - (b) a second Fab molecule which specifically binds to a second antigen, and wherein the variable domains VL and VH of the Fab light chain and the Fab heavy chain are replaced by each other,
- wherein the first antigen is an activating T cell antigen and the second antigen is a target cell antigen, or the first antigen is a target cell antigen and the second antigen is an activating T cell antigen; and
- wherein
- i) in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted by a positively charged amino acid (numbering according to Kabat), and wherein in the constant domain CH1 of the first Fab molecule under a) the amino acid at position 147 or the amino acid at position 213 is substituted by a negatively charged amino acid (numbering according to Kabat EU index); or
 - ii) in the constant domain CL of the second Fab molecule under b) the amino acid at position 124 is substituted by a positively charged amino acid (numbering according to Kabat), and wherein in the constant domain CH1 of the second Fab molecule under b) the amino acid at position 147 or the amino acid at position 213 is substituted by a negatively charged amino acid (numbering according to Kabat EU index).

The antibody may not comprise both modifications mentioned under i) and ii). The constant domains CL and CH1 of the second Fab molecule are not replaced by each other (*i.e.*, remain unexchanged).

In another embodiment of the antibody, in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) (in one preferred embodiment independently by lysine (K) or arginine (R)), and in the constant domain CH1 of the first Fab molecule under a) the amino acid at position 147 or the amino acid at position 213 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).

In a further embodiment, in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat), and in the constant domain CH1 of the first Fab

molecule under a) the amino acid at position 147 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).

In a particular embodiment, in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) (in one preferred embodiment independently by lysine (K) or arginine (R)) and the amino acid at position 123 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) (in one preferred embodiment independently by lysine (K) or arginine (R)), and in the constant domain CH1 of the first Fab molecule under a) the amino acid at position 147 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index) and the amino acid at position 213 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).

In a more particular embodiment, in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted by lysine (K) (numbering according to Kabat) and the amino acid at position 123 is substituted by lysine (K) or arginine (R) (numbering according to Kabat), and in the constant domain CH1 of the first Fab molecule under a) the amino acid at position 147 is substituted by glutamic acid (E) (numbering according to Kabat EU index) and the amino acid at position 213 is substituted by glutamic acid (E) (numbering according to Kabat EU index).

In an even more particular embodiment, in the constant domain CL of the first Fab molecule under a) the amino acid at position 124 is substituted by lysine (K) (numbering according to Kabat) and the amino acid at position 123 is substituted by arginine (R) (numbering according to Kabat), and in the constant domain CH1 of the first Fab molecule under a) the amino acid at position 147 is substituted by glutamic acid (E) (numbering according to Kabat EU index) and the amino acid at position 213 is substituted by glutamic acid (E) (numbering according to Kabat EU index).

F. Chimeric Antigen Receptors

Artificial T cell receptors (also known as chimeric T cell receptors, chimeric immunoreceptors, chimeric antigen receptors (CARs)) are engineered receptors, which graft an arbitrary specificity onto an immune effector cell. Typically, these receptors are used to graft the specificity of a monoclonal antibody onto a T cell, with transfer of their coding sequence facilitated by retroviral vectors. In this way, a large number of target-specific T cells

can be generated for adoptive cell transfer. Phase I clinical studies of this approach show efficacy.

The most common form of these molecules are fusions of single-chain variable fragments (scFv) derived from monoclonal antibodies, fused to CD3-zeta transmembrane and endodomain. Such molecules result in the transmission of a zeta signal in response to recognition by the scFv of its target. An example of such a construct is 14g2a-Zeta, which is a fusion of a scFv derived from hybridoma 14g2a (which recognizes disialoganglioside GD2). When T cells express this molecule (usually achieved by oncoretroviral vector transduction), they recognize and kill target cells that express GD2 (*e.g.*, neuroblastoma cells). To target malignant B cells, investigators have redirected the specificity of T cells using a chimeric immunoreceptor specific for the B-lineage molecule, CD19.

The variable portions of an immunoglobulin heavy and light chain are fused by a flexible linker to form a scFv. This scFv is preceded by a signal peptide to direct the nascent protein to the endoplasmic reticulum and subsequent surface expression (this is cleaved). A flexible spacer allows to the scFv to orient in different directions to enable antigen binding. The transmembrane domain is a typical hydrophobic alpha helix usually derived from the original molecule of the signaling endodomain which protrudes into the cell and transmits the desired signal.

Type I proteins are in fact two protein domains linked by a transmembrane alpha helix in between. The cell membrane lipid bilayer, through which the transmembrane domain passes, acts to isolate the inside portion (endodomain) from the external portion (ectodomain). It is not so surprising that attaching an ectodomain from one protein to an endodomain of another protein results in a molecule that combines the recognition of the former to the signal of the latter.

Ectodomain. A signal peptide directs the nascent protein into the endoplasmic reticulum. This is essential if the receptor is to be glycosylated and anchored in the cell membrane. Any eukaryotic signal peptide sequence usually works fine. Generally, the signal peptide natively attached to the amino-terminal most component is used (*e.g.*, in a scFv with orientation light chain - linker - heavy chain, the native signal of the light-chain is used

The antigen recognition domain is usually an scFv. There are however many alternatives. An antigen recognition domain from native T-cell receptor (TCR) alpha and beta single chains have been described, as have simple ectodomains (*e.g.*, CD4 ectodomain to recognize HIV infected cells) and more exotic recognition components such as a linked cytokine (which leads to recognition of cells bearing the cytokine receptor). In fact, almost

anything that binds a given target with high affinity can be used as an antigen recognition region.

A spacer region links the antigen binding domain to the transmembrane domain. It should be flexible enough to allow the antigen binding domain to orient in different directions to facilitate antigen recognition. The simplest form is the hinge region from IgG1. Alternatives include the CH₂CH₃ region of immunoglobulin and portions of CD3. For most scFv based constructs, the IgG1 hinge suffices. However, the best spacer often has to be determined empirically.

Transmembrane domain. The transmembrane domain is a hydrophobic alpha helix that spans the membrane. Generally, the transmembrane domain from the most membrane proximal component of the endodomain is used. Interestingly, using the CD3-zeta transmembrane domain may result in incorporation of the artificial TCR into the native TCR a factor that is dependent on the presence of the native CD3-zeta transmembrane charged aspartic acid residue. Different transmembrane domains result in different receptor stability. The CD28 transmembrane domain results in a brightly expressed, stable receptor.

Endodomain. This is the "business-end" of the receptor. After antigen recognition, receptors cluster and a signal is transmitted to the cell. The most commonly used endodomain component is CD3-zeta which contains 3 ITAMs. This transmits an activation signal to the T cell after antigen is bound. CD3-zeta may not provide a fully competent activation signal and additional co-stimulatory signaling is needed.

"First-generation" CARs typically had the intracellular domain from the CD3 ξ -chain, which is the primary transmitter of signals from endogenous TCRs. "Second-generation" CARs add intracellular signaling domains from various costimulatory protein receptors (e.g., CD28, 41BB, ICOS) to the cytoplasmic tail of the CAR to provide additional signals to the T cell. Preclinical studies have indicated that the second generation of CAR designs improves the antitumor activity of T cells. More recent, "third-generation" CARs combine multiple signaling domains, such as CD3z-CD28-41BB or CD3z-CD28-OX40, to further augment potency.

G. ADCs

Antibody Drug Conjugates or ADCs are a new class of highly potent biopharmaceutical drugs designed as a targeted therapy for the treatment of people with infectious disease. ADCs are complex molecules composed of an antibody (a whole mAb or an antibody fragment such as a single-chain variable fragment, or scFv) linked, via a stable chemical linker with labile

bonds, to a biological active cytotoxic/anti-viral payload or drug. Antibody Drug Conjugates are examples of bioconjugates and immunoconjugates.

By combining the unique targeting capabilities of monoclonal antibodies with the cancer-killing ability of cytotoxic drugs, antibody-drug conjugates allow sensitive discrimination between healthy and diseased tissue. This means that, in contrast to traditional systemic approaches, antibody-drug conjugates target and attack the infected cell so that healthy cells are less severely affected.

In the development ADC-based anti-tumor therapies, an anticancer drug (*e.g.*, a cell toxin or cytotoxin) is coupled to an antibody that specifically targets a certain cell marker (*e.g.*, a protein that, ideally, is only to be found in or on infected cells). Antibodies track these proteins down in the body and attach themselves to the surface of cancer cells. The biochemical reaction between the antibody and the target protein (antigen) triggers a signal in the tumor cell, which then absorbs or internalizes the antibody together with the cytotoxin. After the ADC is internalized, the cytotoxic drug is released and kills the cell or impairs viral replication. Due to this targeting, ideally the drug has lower side effects and gives a wider therapeutic window than other agents.

A stable link between the antibody and cytotoxic/anti-viral agent is a crucial aspect of an ADC. Linkers are based on chemical motifs including disulfides, hydrazones or peptides (cleavable), or thioethers (noncleavable) and control the distribution and delivery of the cytotoxic agent to the target cell. Cleavable and noncleavable types of linkers have been proven to be safe in preclinical and clinical trials. Brentuximab vedotin includes an enzyme-sensitive cleavable linker that delivers the potent and highly toxic antimicrotubule agent Monomethyl auristatin E or MMAE, a synthetic antineoplastic agent, to human specific CD30-positive malignant cells. Because of its high toxicity MMAE, which inhibits cell division by blocking the polymerization of tubulin, cannot be used as a single-agent chemotherapeutic drug. However, the combination of MMAE linked to an anti-CD30 monoclonal antibody (cAC10, a cell membrane protein of the tumor necrosis factor or TNF receptor) proved to be stable in extracellular fluid, cleavable by cathepsin and safe for therapy. Trastuzumab emtansine, the other approved ADC, is a combination of the microtubule-formation inhibitor mertansine (DM-1), a derivative of the Maytansine, and antibody trastuzumab (Herceptin®/Genentech/Roche) attached by a stable, non-cleavable linker.

The availability of better and more stable linkers has changed the function of the chemical bond. The type of linker, cleavable or noncleavable, lends specific properties to the cytotoxic (anti-cancer) drug. For example, a non-cleavable linker keeps the drug within the cell. As a result,

the entire antibody, linker and cytotoxic agent enter the targeted cancer cell where the antibody is degraded to the level of an amino acid. The resulting complex – amino acid, linker and cytotoxic agent – now becomes the active drug. In contrast, cleavable linkers are catalyzed by enzymes in the host cell where it releases the cytotoxic agent.

- 5 Another type of cleavable linker, currently in development, adds an extra molecule between the cytotoxic/anti-viral drug and the cleavage site. This linker technology allows researchers to create ADCs with more flexibility without worrying about changing cleavage kinetics. Researchers are also developing a new method of peptide cleavage based on Edman degradation, a method of sequencing amino acids in a peptide. Future direction in the
10 development of ADCs also include the development of site-specific conjugation (TDCs) to further improve stability and therapeutic index and α emitting immunoconjugates and antibody-conjugated nanoparticles.

H. BiTES

- 15 Bi-specific T-cell engagers (BiTEs) are a class of artificial bispecific monoclonal antibodies that are investigated for the use as anti-cancer drugs. They direct a host's immune system, more specifically the T cells' cytotoxic activity, against infected cells. *BiTE* is a registered trademark of Micromet AG.

- 20 BiTEs are fusion proteins consisting of two single-chain variable fragments (scFvs) of different antibodies, or amino acid sequences from four different genes, on a single peptide chain of about 55 kilodaltons. One of the scFvs binds to T cells via the CD3 receptor, and the other to an infected cell via a specific molecule.

- 25 Like other bispecific antibodies, and unlike ordinary monoclonal antibodies, BiTEs form a link between T cells and target cells. This causes T cells to exert cytotoxic/anti-viral activity on infected cells by producing proteins like perforin and granzymes, independently of the presence of MHC I or co-stimulatory molecules. These proteins enter infected cells and initiate the cell's apoptosis. This action mimics physiological processes observed during T cell attacks against infected cells.

I. Intrabodies

30 In a particular embodiment, the antibody is a recombinant antibody that is suitable for action inside of a cell – such antibodies are known as “intrabodies.” These antibodies may interfere with target function by a variety of mechanism, such as by altering intracellular protein trafficking, interfering with enzymatic function, and blocking protein-protein or

protein-DNA interactions. In many ways, their structures mimic or parallel those of single chain and single domain antibodies, discussed above. Indeed, single-transcript/single-chain is an important feature that permits intracellular expression in a target cell, and also makes protein transit across cell membranes more feasible. However, additional features are required.

5 The two major issues impacting the implementation of intrabody therapeutic are delivery, including cell/tissue targeting, and stability. With respect to delivery, a variety of approaches have been employed, such as tissue-directed delivery, use of cell-type specific promoters, viral-based delivery and use of cell-permeability/membrane translocating peptides. With respect to the stability, the approach is generally to either screen by brute force, including
10 methods that involve phage display and may include sequence maturation or development of consensus sequences, or more directed modifications such as insertion stabilizing sequences (*e.g.*, Fc regions, chaperone protein sequences, leucine zippers) and disulfide replacement/modification.

 An additional feature that intrabodies may require is a signal for intracellular targeting.
15 Vectors that can target intrabodies (or other proteins) to subcellular regions such as the cytoplasm, nucleus, mitochondria and ER have been designed and are commercially available (Invitrogen Corp.; Persic *et al.*, 1997).

 By virtue of their ability to enter cells, intrabodies have additional uses that other types of antibodies may not achieve. In the case of the present antibodies, the ability to interact with
20 the MUC1 cytoplasmic domain in a living cell may interfere with functions associated with the MUC1 CD, such as signaling functions (binding to other molecules) or oligomer formation. In particular, it is contemplated that such antibodies can be used to inhibit MUC1 dimer formation.

J. Purification

25 In certain embodiments, the antibodies of the present disclosure may be purified. The term “purified,” as used herein, is intended to refer to a composition, isolatable from other components, wherein the protein is purified to any degree relative to its naturally-obtainable state. A purified protein therefore also refers to a protein, free from the environment in which it may naturally occur. Where the term “substantially purified” is used, this designation will
30 refer to a composition in which the protein or peptide forms the major component of the composition, such as constituting about 50%, about 60%, about 70%, about 80%, about 90%, about 95% or more of the proteins in the composition.

 Protein purification techniques are well known to those of skill in the art. These techniques involve, at one level, the crude fractionation of the cellular milieu to polypeptide

and non-polypeptide fractions. Having separated the polypeptide from other proteins, the polypeptide of interest may be further purified using chromatographic and electrophoretic techniques to achieve partial or complete purification (or purification to homogeneity). Analytical methods particularly suited to the preparation of a pure peptide are ion-exchange chromatography, exclusion chromatography; polyacrylamide gel electrophoresis; isoelectric focusing. Other methods for protein purification include, precipitation with ammonium sulfate, PEG, antibodies and the like or by heat denaturation, followed by centrifugation; gel filtration, reverse phase, hydroxylapatite and affinity chromatography; and combinations of such and other techniques.

10 In purifying an antibody of the present disclosure, it may be desirable to express the polypeptide in a prokaryotic or eukaryotic expression system and extract the protein using denaturing conditions. The polypeptide may be purified from other cellular components using an affinity column, which binds to a tagged portion of the polypeptide. As is generally known in the art, it is believed that the order of conducting the various purification steps may be
15 changed, or that certain steps may be omitted, and still result in a suitable method for the preparation of a substantially purified protein or peptide.

Commonly, complete antibodies are fractionated utilizing agents (*i.e.*, protein A) that bind the Fc portion of the antibody. Alternatively, antigens may be used to simultaneously purify and select appropriate antibodies. Such methods often utilize the selection agent bound
20 to a support, such as a column, filter or bead. The antibodies are bound to a support, contaminants removed (*e.g.*, washed away), and the antibodies released by applying conditions (salt, heat, *etc.*).

Various methods for quantifying the degree of purification of the protein or peptide will be known to those of skill in the art in light of the present disclosure. These include, for example,
25 determining the specific activity of an active fraction, or assessing the amount of polypeptides within a fraction by SDS/PAGE analysis. Another method for assessing the purity of a fraction is to calculate the specific activity of the fraction, to compare it to the specific activity of the initial extract, and to thus calculate the degree of purity. The actual units used to represent the amount of activity will, of course, be dependent upon the particular assay technique chosen to
30 follow the purification and whether or not the expressed protein or peptide exhibits a detectable activity.

It is known that the migration of a polypeptide can vary, sometimes significantly, with different conditions of SDS/PAGE (Capaldi *et al.*, 1977). It will therefore be appreciated that

under differing electrophoresis conditions, the apparent molecular weights of purified or partially purified expression products may vary.

5 **III. Active/Passive Immunization and Treatment/Prevention of SARS-CoV-2 Infection**

A. Formulation and Administration

 The present disclosure provides pharmaceutical compositions comprising anti-SARS-CoV-2 virus antibodies and antigens for generating the same. Such compositions comprise a prophylactically or therapeutically effective amount of an antibody or a fragment thereof, or a peptide immunogen, and a pharmaceutically acceptable carrier. In a specific embodiment, the term “pharmaceutically acceptable” means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term “carrier” refers to a diluent, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a particular carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Other suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like.

 The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. Oral formulations can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, *etc.* Examples of suitable pharmaceutical agents are described in “Remington's Pharmaceutical Sciences.” Such compositions will contain a prophylactically or therapeutically effective amount of the antibody or fragment thereof, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration, which can be oral, intravenous, intraarterial, intrabuccal, intranasal, nebulized, bronchial inhalation, intra-rectal, vaginal, topical or delivered by mechanical ventilation.

Active vaccines are also envisioned where antibodies like those disclosed are produced *in vivo* in a subject at risk of SARS-CoV-2 infection. Such vaccines can be formulated for parenteral administration, *e.g.*, formulated for injection *via* the intradermal, intravenous, intramuscular, subcutaneous, or even intraperitoneal routes. Administration by intradermal and intramuscular routes are contemplated. The vaccine could alternatively be administered by a topical route directly to the mucosa, for example, by nasal drops, inhalation, by nebulizer, or via intrarectal or vaginal delivery. Pharmaceutically acceptable salts include the acid salts and those which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

Passive transfer of antibodies, known as artificially acquired passive immunity, generally will involve the use of intravenous or intramuscular injections. The forms of antibody can be human or animal blood plasma or serum, as pooled human immunoglobulin for intravenous (IVIG) or intramuscular (IG) use, as high-titer human IVIG or IG from immunized or from donors recovering from disease, and as monoclonal antibodies (MAb). Such immunity generally lasts for only a short period of time, and there is also a potential risk for hypersensitivity reactions, and serum sickness, especially from gamma globulin of non-human origin. However, passive immunity provides immediate protection. The antibodies will be formulated in a carrier suitable for injection, *i.e.*, sterile and syringeable.

Generally, the ingredients of compositions of the disclosure are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compositions of the disclosure can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, *etc.*, and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, *etc.*

2. ADCC

Antibody-dependent cell-mediated cytotoxicity (ADCC) is an immune mechanism leading to the lysis of antibody-coated target cells by immune effector cells. The target cells are cells to which antibodies or fragments thereof comprising an Fc region specifically bind, generally via the protein part that is N-terminal to the Fc region. By “antibody having increased/reduced antibody dependent cell-mediated cytotoxicity (ADCC)” is meant an antibody having increased/reduced ADCC as determined by any suitable method known to those of ordinary skill in the art.

As used herein, the term “increased/reduced ADCC” is defined as either an increase/reduction in the number of target cells that are lysed in a given time, at a given concentration of antibody in the medium surrounding the target cells, by the mechanism of ADCC defined above, and/or a reduction/increase in the concentration of antibody, in the medium surrounding the target cells, required to achieve the lysis of a given number of target cells in a given time, by the mechanism of ADCC. The increase/reduction in ADCC is relative to the ADCC mediated by the same antibody produced by the same type of host cells, using the same standard production, purification, formulation and storage methods (which are known to those skilled in the art), but that has not been engineered. For example, the increase in ADCC mediated by an antibody produced by host cells engineered to have an altered pattern of glycosylation (*e.g.*, to express the glycosyltransferase, GnTIII, or other glycosyltransferases) by the methods described herein, is relative to the ADCC mediated by the same antibody produced by the same type of non-engineered host cells.

3. CDC

Complement-dependent cytotoxicity (CDC) is a function of the complement system. It is the processes in the immune system that kill pathogens by damaging their membranes without the involvement of antibodies or cells of the immune system. There are three main processes. All three insert one or more membrane attack complexes (MAC) into the pathogen which cause lethal colloid-osmotic swelling, *i.e.*, CDC. It is one of the mechanisms by which antibodies or antibody fragments have an anti-viral effect.

IV. Antibody Conjugates

Antibodies of the present disclosure may be linked to at least one agent to form an antibody conjugate. In order to increase the efficacy of antibody molecules as diagnostic or therapeutic agents, it is conventional to link or covalently bind or complex at least one desired

molecule or moiety. Such a molecule or moiety may be, but is not limited to, at least one effector or reporter molecule. Effector molecules comprise molecules having a desired activity, *e.g.*, cytotoxic activity. Non-limiting examples of effector molecules which have been attached to antibodies include toxins, anti-tumor agents, therapeutic enzymes, radionuclides, antiviral agents, chelating agents, cytokines, growth factors, and oligo- or polynucleotides. By contrast, a reporter molecule is defined as any moiety which may be detected using an assay. Non-limiting examples of reporter molecules which have been conjugated to antibodies include enzymes, radiolabels, haptens, fluorescent labels, phosphorescent molecules, chemiluminescent molecules, chromophores, photoaffinity molecules, colored particles or ligands, such as biotin.

Antibody conjugates are generally preferred for use as diagnostic agents. Antibody diagnostics generally fall within two classes, those for use in *in vitro* diagnostics, such as in a variety of immunoassays, and those for use *in vivo* diagnostic protocols, generally known as "antibody-directed imaging." Many appropriate imaging agents are known in the art, as are methods for their attachment to antibodies (see, for *e.g.*, U.S. Patents 5,021,236, 4,938,948, and 4,472,509). The imaging moieties used can be paramagnetic ions, radioactive isotopes, fluorochromes, NMR-detectable substances, and X-ray imaging agents.

In the case of paramagnetic ions, one might mention by way of example ions such as chromium (III), manganese (II), iron (III), iron (II), cobalt (II), nickel (II), copper (II), neodymium (III), samarium (III), ytterbium (III), gadolinium (III), vanadium (II), terbium (III), dysprosium (III), holmium (III) and/or erbium (III), with gadolinium being particularly preferred. Ions useful in other contexts, such as X-ray imaging, include but are not limited to lanthanum (III), gold (III), lead (II), and especially bismuth (III).

In the case of radioactive isotopes for therapeutic and/or diagnostic application, one might mention astatine²¹¹, ¹⁴carbon, ⁵¹chromium, ³⁶chlorine, ⁵⁷cobalt, ⁵⁸cobalt, copper⁶⁷, ¹⁵²Eu, gallium⁶⁷, ³hydrogen, iodine¹²³, iodine¹²⁵, iodine¹³¹, indium¹¹¹, ⁵⁹iron, ³²phosphorus, rhenium¹⁸⁶, rhenium¹⁸⁸, ⁷⁵selenium, ³⁵sulphur, technetium^{99m} and/or yttrium⁹⁰. ¹²⁵I is often being preferred for use in certain embodiments, and technetium^{99m} and/or indium¹¹¹ are also often preferred due to their low energy and suitability for long range detection. Radioactively labeled monoclonal antibodies of the present disclosure may be produced according to well-known methods in the art. For instance, monoclonal antibodies can be iodinated by contact with sodium and/or potassium iodide and a chemical oxidizing agent such as sodium hypochlorite, or an enzymatic oxidizing agent, such as lactoperoxidase. Monoclonal antibodies according to the disclosure may be labeled with technetium^{99m} by ligand exchange process, for example, by

reducing pertechnetate with stannous solution, chelating the reduced technetium onto a Sephadex column and applying the antibody to this column. Alternatively, direct labeling techniques may be used, *e.g.*, by incubating pertechnetate, a reducing agent such as SnCl_2 , a buffer solution such as sodium-potassium phthalate solution, and the antibody. Intermediary functional groups
5 which are often used to bind radioisotopes which exist as metallic ions to antibody are diethylenetriaminepentaacetic acid (DTPA) or ethylene diaminetetracetic acid (EDTA).

Among the fluorescent labels contemplated for use as conjugates include Alexa 350, Alexa 430, AMCA, BODIPY 630/650, BODIPY 650/665, BODIPY-FL, BODIPY-R6G, BODIPY-TMR, BODIPY-TRX, Cascade Blue, Cy3, Cy5, 6-FAM, Fluorescein Isothiocyanate,
10 HEX, 6-JOE, Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, REG, Rhodamine Green, Rhodamine Red, Renographin, ROX, TAMRA, TET, Tetramethylrhodamine, and/or Texas Red.

Additional types of antibodies contemplated in the present disclosure are those intended primarily for use *in vitro*, where the antibody is linked to a secondary binding ligand and/or to
15 an enzyme (an enzyme tag) that will generate a colored product upon contact with a chromogenic substrate. Examples of suitable enzymes include urease, alkaline phosphatase, (horseradish) hydrogen peroxidase or glucose oxidase. Preferred secondary binding ligands are biotin and avidin and streptavidin compounds. The use of such labels is well known to those of skill in the art and are described, for example, in U.S. Patents 3,817,837, 3,850,752,
20 3,939,350, 3,996,345, 4,277,437, 4,275,149 and 4,366,241.

Yet another known method of site-specific attachment of molecules to antibodies comprises the reaction of antibodies with hapten-based affinity labels. Essentially, hapten-based affinity labels react with amino acids in the antigen binding site, thereby destroying this site and blocking specific antigen reaction. However, this may not be advantageous since it
25 results in loss of antigen binding by the antibody conjugate.

Molecules containing azido groups may also be used to form covalent bonds to proteins through reactive nitrene intermediates that are generated by low intensity ultraviolet light (Potter and Haley, 1983). In particular, 2- and 8-azido analogues of purine nucleotides have been used as site-directed photoprobes to identify nucleotide binding proteins in crude cell
30 extracts (Owens & Haley, 1987; Atherton *et al.*, 1985). The 2- and 8-azido nucleotides have also been used to map nucleotide binding domains of purified proteins (Khatoon *et al.*, 1989; King *et al.*, 1989; Dholakia *et al.*, 1989) and may be used as antibody binding agents.

Several methods are known in the art for the attachment or conjugation of an antibody to its conjugate moiety. Some attachment methods involve the use of a metal chelate complex

employing, for example, an organic chelating agent such a diethylenetriaminepentaacetic acid anhydride (DTPA); ethylenetriaminetetraacetic acid; N-chloro-p-toluenesulfonamide; and/or tetrachloro-3 α -6 α -diphenylglycouril-3 attached to the antibody (U.S. Patents 4,472,509 and 4,938,948). Monoclonal antibodies may also be reacted with an enzyme in the presence of a coupling agent such as glutaraldehyde or periodate. Conjugates with fluorescein markers are prepared in the presence of these coupling agents or by reaction with an isothiocyanate. In U.S. Patent 4,938,948, imaging of breast tumors is achieved using monoclonal antibodies and the detectable imaging moieties are bound to the antibody using linkers such as methyl-p-hydroxybenzimidate or N-succinimidyl-3-(4-hydroxyphenyl)propionate.

In other embodiments, derivatization of immunoglobulins by selectively introducing sulfhydryl groups in the Fc region of an immunoglobulin, using reaction conditions that do not alter the antibody combining site are contemplated. Antibody conjugates produced according to this methodology are disclosed to exhibit improved longevity, specificity and sensitivity (U.S. Patent 5,196,066, incorporated herein by reference). Site-specific attachment of effector or reporter molecules, wherein the reporter or effector molecule is conjugated to a carbohydrate residue in the Fc region have also been disclosed in the literature (O'Shannessy *et al.*, 1987). This approach has been reported to produce diagnostically and therapeutically promising antibodies which are currently in clinical evaluation.

V. Immunodetection Methods

In still further embodiments, the present disclosure concerns immunodetection methods for binding, purifying, removing, quantifying and otherwise generally detecting SARS-CoV-2 and its associated antigens. While such methods can be applied in a traditional sense, another use will be in quality control and monitoring of vaccine and other virus stocks, where antibodies according to the present disclosure can be used to assess the amount or integrity (*i.e.*, long term stability) of antigens in viruses. Alternatively, the methods may be used to screen various antibodies for appropriate/desired reactivity profiles.

Other immunodetection methods include specific assays for determining the presence of SARS-CoV-2 in a subject. A wide variety of assay formats are contemplated, but specifically those that would be used to detect SARS-CoV-2 in a fluid obtained from a subject, such as saliva, blood, plasma, sputum, semen or urine. In particular, semen has been demonstrated as a viable sample for detecting SARS-CoV-2 (Purpura *et al.*, 2016; Mansuy *et al.*, 2016; Barzon *et al.*, 2016; Gornet *et al.*, 2016; Duffy *et al.*, 2009; CDC, 2016; Halfon *et*

al., 2010; Elder *et al.* 2005). The assays may be advantageously formatted for non-healthcare (home) use, including lateral flow assays (see below) analogous to home pregnancy tests. These assays may be packaged in the form of a kit with appropriate reagents and instructions to permit use by the subject of a family member.

5 Some immunodetection methods include enzyme linked immunosorbent assay (ELISA), radioimmunoassay (RIA), immunoradiometric assay, fluoroimmunoassay, chemiluminescent assay, bioluminescent assay, and Western blot to mention a few. In particular, a competitive assay for the detection and quantitation of SARS-CoV-2 antibodies directed to specific parasite epitopes in samples also is provided. The steps of various useful
10 immunodetection methods have been described in the scientific literature, such as, *e.g.*, Doolittle and Ben-Zeev (1999), Gulbis and Galand (1993), De Jager *et al.* (1993), and Nakamura *et al.* (1987). In general, the immunobinding methods include obtaining a sample suspected of containing SARS-CoV-2, and contacting the sample with a first antibody in accordance with the present disclosure, as the case may be, under conditions effective to allow
15 the formation of immunocomplexes.

 These methods include methods for purifying SARS-CoV-2 or related antigens from a sample. The antibody will preferably be linked to a solid support, such as in the form of a column matrix, and the sample suspected of containing the SARS-CoV-2 or antigenic component will be applied to the immobilized antibody. The unwanted components will be
20 washed from the column, leaving the SARS-CoV-2 antigen immunocomplexed to the immobilized antibody, which is then collected by removing the organism or antigen from the column.

 The immunobinding methods also include methods for detecting and quantifying the amount of SARS-CoV-2 or related components in a sample and the detection and quantification
25 of any immune complexes formed during the binding process. Here, one would obtain a sample suspected of containing SARS-CoV-2 or its antigens and contact the sample with an antibody that binds SARS-CoV-2 or components thereof, followed by detecting and quantifying the amount of immune complexes formed under the specific conditions. In terms of antigen detection, the biological sample analyzed may be any sample that is suspected of containing
30 SARS-CoV-2 or SARS-CoV-2 antigen, such as a tissue section or specimen, a homogenized tissue extract, a biological fluid, including blood and serum, or a secretion, such as feces or urine.

 Contacting the chosen biological sample with the antibody under effective conditions and for a period of time sufficient to allow the formation of immune complexes (primary

immune complexes) is generally a matter of simply adding the antibody composition to the sample and incubating the mixture for a period of time long enough for the antibodies to form immune complexes with, *i.e.*, to bind to SARS-CoV-2 or antigens present. After this time, the sample-antibody composition, such as a tissue section, ELISA plate, dot blot or Western blot, will generally be washed to remove any non-specifically bound antibody species, allowing only those antibodies specifically bound within the primary immune complexes to be detected.

In general, the detection of immunocomplex formation is well known in the art and may be achieved through the application of numerous approaches. These methods are generally based upon the detection of a label or marker, such as any of those radioactive, fluorescent, biological and enzymatic tags. Patents concerning the use of such labels include U.S. Patents 3,817,837, 3,850,752, 3,939,350, 3,996,345, 4,277,437, 4,275,149 and 4,366,241. Of course, one may find additional advantages through the use of a secondary binding ligand such as a second antibody and/or a biotin/avidin ligand binding arrangement, as is known in the art.

The antibody employed in the detection may itself be linked to a detectable label, wherein one would then simply detect this label, thereby allowing the amount of the primary immune complexes in the composition to be determined. Alternatively, the first antibody that becomes bound within the primary immune complexes may be detected by means of a second binding ligand that has binding affinity for the antibody. In these cases, the second binding ligand may be linked to a detectable label. The second binding ligand is itself often an antibody, which may thus be termed a "secondary" antibody. The primary immune complexes are contacted with the labeled, secondary binding ligand, or antibody, under effective conditions and for a period of time sufficient to allow the formation of secondary immune complexes. The secondary immune complexes are then generally washed to remove any non-specifically bound labeled secondary antibodies or ligands, and the remaining label in the secondary immune complexes is then detected.

Further methods include the detection of primary immune complexes by a two-step approach. A second binding ligand, such as an antibody that has binding affinity for the antibody, is used to form secondary immune complexes, as described above. After washing, the secondary immune complexes are contacted with a third binding ligand or antibody that has binding affinity for the second antibody, again under effective conditions and for a period of time sufficient to allow the formation of immune complexes (tertiary immune complexes). The third ligand or antibody is linked to a detectable label, allowing detection of the tertiary immune complexes thus formed. This system may provide for signal amplification if this is desired.

One method of immunodetection uses two different antibodies. A first biotinylated antibody is used to detect the target antigen, and a second antibody is then used to detect the biotin attached to the complexed biotin. In that method, the sample to be tested is first incubated in a solution containing the first step antibody. If the target antigen is present, some of the antibody binds to the antigen to form a biotinylated antibody/antigen complex. The antibody/antigen complex is then amplified by incubation in successive solutions of streptavidin (or avidin), biotinylated DNA, and/or complementary biotinylated DNA, with each step adding additional biotin sites to the antibody/antigen complex. The amplification steps are repeated until a suitable level of amplification is achieved, at which point the sample is incubated in a solution containing the second step antibody against biotin. This second step antibody is labeled, for example, with an enzyme that can be used to detect the presence of the antibody/antigen complex by histoenzymology using a chromogen substrate. With suitable amplification, a conjugate can be produced which is macroscopically visible.

Another known method of immunodetection takes advantage of the immuno-PCR (Polymerase Chain Reaction) methodology. The PCR method is similar to the Cantor method up to the incubation with biotinylated DNA, however, instead of using multiple rounds of streptavidin and biotinylated DNA incubation, the DNA/biotin/streptavidin/antibody complex is washed out with a low pH or high salt buffer that releases the antibody. The resulting wash solution is then used to carry out a PCR reaction with suitable primers with appropriate controls. At least in theory, the enormous amplification capability and specificity of PCR can be utilized to detect a single antigen molecule.

A. ELISAs

Immunoassays, in their most simple and direct sense, are binding assays. Certain preferred immunoassays are the various types of enzyme linked immunosorbent assays (ELISAs) and radioimmunoassays (RIA) known in the art. Immunohistochemical detection using tissue sections is also particularly useful. However, it will be readily appreciated that detection is not limited to such techniques, and western blotting, dot blotting, FACS analyses, and the like may also be used.

In one exemplary ELISA, the antibodies of the disclosure are immobilized onto a selected surface exhibiting protein affinity, such as a well in a polystyrene microtiter plate. Then, a test composition suspected of containing the SARS-CoV-2 or SARS-CoV-2 antigen is added to the wells. After binding and washing to remove non-specifically bound immune complexes, the bound antigen may be detected. Detection may be achieved by the addition of

another anti-SARS-CoV-2 antibody that is linked to a detectable label. This type of ELISA is a simple “sandwich ELISA.” Detection may also be achieved by the addition of a second anti-SARS-CoV-2 antibody, followed by the addition of a third antibody that has binding affinity for the second antibody, with the third antibody being linked to a detectable label.

5 In another exemplary ELISA, the samples suspected of containing the SARS-CoV-2 or SARS-CoV-2 antigen are immobilized onto the well surface and then contacted with the anti-SARS-CoV-2 antibodies of the disclosure. After binding and washing to remove non-specifically bound immune complexes, the bound anti-SARS-CoV-2 antibodies are detected. Where the initial anti-SARS-CoV-2 antibodies are linked to a detectable label, the immune
10 complexes may be detected directly. Again, the immune complexes may be detected using a second antibody that has binding affinity for the first anti-SARS-CoV-2 antibody, with the second antibody being linked to a detectable label.

 Irrespective of the format employed, ELISAs have certain features in common, such as coating, incubating and binding, washing to remove non-specifically bound species, and
15 detecting the bound immune complexes. These are described below.

 In coating a plate with either antigen or antibody, one will generally incubate the wells of the plate with a solution of the antigen or antibody, either overnight or for a specified period of hours. The wells of the plate will then be washed to remove incompletely adsorbed material. Any remaining available surfaces of the wells are then “coated” with a nonspecific protein that
20 is antigenically neutral with regard to the test antisera. These include bovine serum albumin (BSA), casein or solutions of milk powder. The coating allows for blocking of nonspecific adsorption sites on the immobilizing surface and thus reduces the background caused by nonspecific binding of antisera onto the surface.

 In ELISAs, it is probably more customary to use a secondary or tertiary detection means
25 rather than a direct procedure. Thus, after binding of a protein or antibody to the well, coating with a non-reactive material to reduce background, and washing to remove unbound material, the immobilizing surface is contacted with the biological sample to be tested under conditions effective to allow immune complex (antigen/antibody) formation. Detection of the immune complex then requires a labeled secondary binding ligand or antibody, and a secondary binding
30 ligand or antibody in conjunction with a labeled tertiary antibody or a third binding ligand.

 “Under conditions effective to allow immune complex (antigen/antibody) formation” means that the conditions preferably include diluting the antigens and/or antibodies with solutions such as BSA, bovine gamma globulin (BGG) or phosphate buffered saline

(PBS)/Tween. These added agents also tend to assist in the reduction of nonspecific background.

The “suitable” conditions also mean that the incubation is at a temperature or for a period of time sufficient to allow effective binding. Incubation steps are typically from about 1 to 2 to 4 hours or so, at temperatures preferably on the order of 25°C to 27°C, or may be overnight at about 4°C or so.

Following all incubation steps in an ELISA, the contacted surface is washed so as to remove non-complexed material. A preferred washing procedure includes washing with a solution such as PBS/Tween, or borate buffer. Following the formation of specific immune complexes between the test sample and the originally bound material, and subsequent washing, the occurrence of even minute amounts of immune complexes may be determined.

To provide a detecting means, the second or third antibody will have an associated label to allow detection. Preferably, this will be an enzyme that will generate color development upon incubating with an appropriate chromogenic substrate. Thus, for example, one will desire to contact or incubate the first and second immune complex with a urease, glucose oxidase, alkaline phosphatase or hydrogen peroxidase-conjugated antibody for a period of time and under conditions that favor the development of further immune complex formation (*e.g.*, incubation for 2 hours at room temperature in a PBS-containing solution such as PBS-Tween).

After incubation with the labeled antibody, and subsequent to washing to remove unbound material, the amount of label is quantified, *e.g.*, by incubation with a chromogenic substrate such as urea, or bromocresol purple, or 2,2'-azino-di-(3-ethyl-benzthiazoline-6-sulfonic acid (ABTS), or H₂O₂, in the case of peroxidase as the enzyme label. Quantification is then achieved by measuring the degree of color generated, *e.g.*, using a visible spectra spectrophotometer.

In another embodiment, the present disclosure contemplates the use of competitive formats. This is particularly useful in the detection of SARS-CoV-2 antibodies in sample. In competition-based assays, an unknown amount of analyte or antibody is determined by its ability to displace a known amount of labeled antibody or analyte. Thus, the quantifiable loss of a signal is an indication of the amount of unknown antibody or analyte in a sample.

Here, the inventor proposes the use of labeled SARS-CoV-2 monoclonal antibodies to determine the amount of SARS-CoV-2 antibodies in a sample. The basic format would include contacting a known amount of SARS-CoV-2 monoclonal antibody (linked to a detectable label) with SARS-CoV-2 antigen or particle. The SARS-CoV-2 antigen or organism is preferably attached to a support. After binding of the labeled monoclonal antibody to the support, the

sample is added and incubated under conditions permitting any unlabeled antibody in the sample to compete with, and hence displace, the labeled monoclonal antibody. By measuring either the lost label or the label remaining (and subtracting that from the original amount of bound label), one can determine how much non-labeled antibody is bound to the support, and thus how much antibody was present in the sample.

B. Western Blot

The Western blot (alternatively, protein immunoblot) is an analytical technique used to detect specific proteins in a given sample of tissue homogenate or extract. It uses gel electrophoresis to separate native or denatured proteins by the length of the polypeptide (denaturing conditions) or by the 3-D structure of the protein (native/ non-denaturing conditions). The proteins are then transferred to a membrane (typically nitrocellulose or PVDF), where they are probed (detected) using antibodies specific to the target protein.

Samples may be taken from whole tissue or from cell culture. In most cases, solid tissues are first broken down mechanically using a blender (for larger sample volumes), using a homogenizer (smaller volumes), or by sonication. Cells may also be broken open by one of the above mechanical methods. However, it should be noted that bacteria, virus or environmental samples can be the source of protein and thus Western blotting is not restricted to cellular studies only. Assorted detergents, salts, and buffers may be employed to encourage lysis of cells and to solubilize proteins. Protease and phosphatase inhibitors are often added to prevent the digestion of the sample by its own enzymes. Tissue preparation is often done at cold temperatures to avoid protein denaturing.

The proteins of the sample are separated using gel electrophoresis. Separation of proteins may be by isoelectric point (pI), molecular weight, electric charge, or a combination of these factors. The nature of the separation depends on the treatment of the sample and the nature of the gel. This is a very useful way to determine a protein. It is also possible to use a two-dimensional (2-D) gel which spreads the proteins from a single sample out in two dimensions. Proteins are separated according to isoelectric point (pH at which they have neutral net charge) in the first dimension, and according to their molecular weight in the second dimension.

In order to make the proteins accessible to antibody detection, they are moved from within the gel onto a membrane made of nitrocellulose or polyvinylidene difluoride (PVDF). The membrane is placed on top of the gel, and a stack of filter papers placed on top of that. The entire stack is placed in a buffer solution which moves up the paper by capillary action, bringing

the proteins with it. Another method for transferring the proteins is called electroblotting and uses an electric current to pull proteins from the gel into the PVDF or nitrocellulose membrane. The proteins move from within the gel onto the membrane while maintaining the organization they had within the gel. As a result of this blotting process, the proteins are exposed on a thin surface layer for detection (see below). Both varieties of membrane are chosen for their non-specific protein binding properties (*i.e.*, binds all proteins equally well). Protein binding is based upon hydrophobic interactions, as well as charged interactions between the membrane and protein. Nitrocellulose membranes are cheaper than PVDF but are far more fragile and do not stand up well to repeated probings. The uniformity and overall effectiveness of transfer of protein from the gel to the membrane can be checked by staining the membrane with Coomassie Brilliant Blue or Ponceau S dyes. Once transferred, proteins are detected using labeled primary antibodies, or unlabeled primary antibodies followed by indirect detection using labeled protein A or secondary labeled antibodies binding to the Fc region of the primary antibodies.

15

C. Lateral Flow Assays

Lateral flow assays, also known as lateral flow immunochromatographic assays, are simple devices intended to detect the presence (or absence) of a target analyte in sample (matrix) without the need for specialized and costly equipment, though many laboratory-based applications exist that are supported by reading equipment. Typically, these tests are used as low resources medical diagnostics, either for home testing, point of care testing, or laboratory use. A widely spread and well-known application is the home pregnancy test.

The technology is based on a series of capillary beds, such as pieces of porous paper or sintered polymer. Each of these elements has the capacity to transport fluid (*e.g.*, urine) spontaneously. The first element (the sample pad) acts as a sponge and holds an excess of sample fluid. Once soaked, the fluid migrates to the second element (conjugate pad) in which the manufacturer has stored the so-called conjugate, a dried format of bio-active particles (see below) in a salt-sugar matrix that contains everything to guarantee an optimized chemical reaction between the target molecule (*e.g.*, an antigen) and its chemical partner (*e.g.*, antibody) that has been immobilized on the particle's surface. While the sample fluid dissolves the salt-sugar matrix, it also dissolves the particles and in one combined transport action the sample and conjugate mix while flowing through the porous structure. In this way, the analyte binds to the particles while migrating further through the third capillary bed. This material has one or more areas (often called stripes) where a third molecule has been immobilized by the

manufacturer. By the time the sample-conjugate mix reaches these strips, analyte has been bound on the particle and the third 'capture' molecule binds the complex. After a while, when more and more fluid has passed the stripes, particles accumulate and the stripe-area changes color. Typically there are at least two stripes: one (the control) that captures any particle and thereby shows that reaction conditions and technology worked fine, the second contains a specific capture molecule and only captures those particles onto which an analyte molecule has been immobilized. After passing these reaction zones, the fluid enters the final porous material – the wick – that simply acts as a waste container. Lateral Flow Tests can operate as either competitive or sandwich assays. Lateral flow assays are disclosed in U.S. Patent 6,485,982.

D. Immunohistochemistry

The antibodies of the present disclosure may also be used in conjunction with both fresh-frozen and/or formalin-fixed, paraffin-embedded tissue blocks prepared for study by immunohistochemistry (IHC). The method of preparing tissue blocks from these particulate specimens has been successfully used in previous IHC studies of various prognostic factors and is well known to those of skill in the art (Brown *et al.*, 1990; Abbondanzo *et al.*, 1990; Allred *et al.*, 1990).

Briefly, frozen-sections may be prepared by rehydrating 50 ng of frozen “pulverized” tissue at room temperature in phosphate buffered saline (PBS) in small plastic capsules; pelleting the particles by centrifugation; resuspending them in a viscous embedding medium (OCT); inverting the capsule and/or pelleting again by centrifugation; snap-freezing in -70°C isopentane; cutting the plastic capsule and/or removing the frozen cylinder of tissue; securing the tissue cylinder on a cryostat microtome chuck; and/or cutting 25-50 serial sections from the capsule. Alternatively, whole frozen tissue samples may be used for serial section cuttings.

Permanent-sections may be prepared by a similar method involving rehydration of the 50 mg sample in a plastic microfuge tube; pelleting; resuspending in 10% formalin for 4 hours fixation; washing/pelleting; resuspending in warm 2.5% agar; pelleting; cooling in ice water to harden the agar; removing the tissue/agar block from the tube; infiltrating and/or embedding the block in paraffin; and/or cutting up to 50 serial permanent sections. Again, whole tissue samples may be substituted.

E. Immunodetection Kits

In still further embodiments, the present disclosure concerns immunodetection kits for use with the immunodetection methods described above. As the antibodies may be used to

detect SARS-CoV-2 or SARS-CoV-2 antigens, the antibodies may be included in the kit. The immunodetection kits will thus comprise, in suitable container means, a first antibody that binds to SARS-CoV-2 or SARS-CoV-2 antigen, and optionally an immunodetection reagent.

5 In certain embodiments, the SARS-CoV-2 antibody may be pre-bound to a solid support, such as a column matrix and/or well of a microtiter plate. The immunodetection reagents of the kit may take any one of a variety of forms, including those detectable labels that are associated with or linked to the given antibody. Detectable labels that are associated with or attached to a secondary binding ligand are also contemplated. Exemplary secondary ligands are those secondary antibodies that have binding affinity for the first antibody.

10 Further suitable immunodetection reagents for use in the present kits include the two-component reagent that comprises a secondary antibody that has binding affinity for the first antibody, along with a third antibody that has binding affinity for the second antibody, the third antibody being linked to a detectable label. As noted above, a number of exemplary labels are known in the art and all such labels may be employed in connection with the present disclosure.

15 The kits may further comprise a suitably aliquoted composition of the SARS-CoV-2 or SARS-CoV-2 antigens, whether labeled or unlabeled, as may be used to prepare a standard curve for a detection assay. The kits may contain antibody-label conjugates either in fully conjugated form, in the form of intermediates, or as separate moieties to be conjugated by the user of the kit. The components of the kits may be packaged either in aqueous media or in
20 lyophilized form.

The container means of the kits will generally include at least one vial, test tube, flask, bottle, syringe or other container means, into which the antibody may be placed, or preferably, suitably aliquoted. The kits of the present disclosure will also typically include a means for containing the antibody, antigen, and any other reagent containers in close confinement for
25 commercial sale. Such containers may include injection or blow-molded plastic containers into which the desired vials are retained.

F. Vaccine and Antigen Quality Control Assays

30 The present disclosure also contemplates the use of antibodies and antibody fragments as described herein for use in assessing the antigenic integrity of a viral antigen in a sample. Biological medicinal products like vaccines differ from chemical drugs in that they cannot normally be characterized molecularly; antibodies are large molecules of significant complexity and have the capacity to vary widely from preparation to preparation. They are also administered to healthy individuals, including children at the start of their lives, and thus a

strong emphasis must be placed on their quality to ensure, to the greatest extent possible, that they are efficacious in preventing or treating life-threatening disease, without themselves causing harm.

5 The increasing globalization in the production and distribution of vaccines has opened new possibilities to better manage public health concerns but has also raised questions about the equivalence and interchangeability of vaccines procured across a variety of sources. International standardization of starting materials, of production and quality control testing, and the setting of high expectations for regulatory oversight on the way these products are manufactured and used, have thus been the cornerstone for continued success. But it remains a
10 field in constant change, and continuous technical advances in the field offer a promise of developing potent new weapons against the oldest public health threats, as well as new ones - malaria, pandemic influenza, and HIV, to name a few - but also put a great pressure on manufacturers, regulatory authorities, and the wider medical community to ensure that products continue to meet the highest standards of quality attainable.

15 Thus, one may obtain an antigen or vaccine from any source or at any point during a manufacturing process. The quality control processes may therefore begin with preparing a sample for an immunoassay that identifies binding of an antibody or fragment disclosed herein to a viral antigen. Such immunoassays are disclosed elsewhere in this document, and any of these may be used to assess the structural/antigenic integrity of the antigen. Standards for
20 finding the sample to contain acceptable amounts of antigenically correct and intact antigen may be established by regulatory agencies.

Another important embodiment where antigen integrity is assessed is in determining shelf-life and storage stability. Most medicines, including vaccines, can deteriorate over time. Therefore, it is critical to determine whether, over time, the degree to which an antigen, such
25 as in a vaccine, degrades or destabilizes such that it is no longer antigenic and/or capable of generating an immune response when administered to a subject. Again, standards for finding the sample to contain acceptable amounts of antigenically intact antigen may be established by regulatory agencies.

In certain embodiments, viral antigens may contain more than one protective epitope.
30 In these cases, it may prove useful to employ assays that look at the binding of more than one antibody, such as 2, 3, 4, 5 or even more antibodies. These antibodies bind to closely related epitopes, such that they are adjacent or even overlap each other. On the other hand, they may represent distinct epitopes from disparate parts of the antigen. By examining the integrity of

multiple epitopes, a more complete picture of the antigen's overall integrity, and hence ability to generate a protective immune response, may be determined.

- Antibodies and fragments thereof as described in the present disclosure may also be used in a kit for monitoring the efficacy of vaccination procedures by detecting the presence of protective SARS-CoV-2 antibodies. Antibodies, antibody fragment, or variants and derivatives thereof, as described in the present disclosure may also be used in a kit for monitoring vaccine manufacture with the desired immunogenicity.
- 5

TABLE 1 - NUCLEOTIDE SEQUENCES FOR ANTIBODY VARIABLE REGION

Clone	Seq ID	Chain	Variable Sequence Region
COV2-166	9152	heavy	CAGGTGACAGCTGGTGCAATCTGGGTCTGAGTTGCAGAAGCCTGGGGCCTCAGTGAAGGTTTC CTGTAAGGCTTCTGGAAACACCTTCCCTACTTATGATATGAATTGGGTGGGACAGGCCCTTG GACAAGGGCTTGAGTGGATGGGATGGATCAACACCAACACTGGGAGGCCAACGTATGCCAG GGCTTACCAGGACGGTTTGTCTTCTCTCTGGACACATCTGTCAGCAGGCATATCTGGAGAT CAGCAGCCTAAAGGCTGAGGACACTGCCGTGTATTACTGTGCGAGAGAGGGGTATCACTACG GTATGGACGTCTGGGGCCAGGGACCACGGTCACCGTCTCCTCA
	9153	light	GACATCCAGATGACCCAGTCTCCATCCTCACTGTCTGCCTCTGTAGGAGACAGAGTCACCAT CACTTGTGCGGGCAGTCAGGACATTAAACAATTATTTAGCCTGGTTTCAGCAGAAACCAGGTA AAGCCCCCTAAGTCCCTGATCTATTCTGCGTCCAGTTTGCAAAGTGGGGTCCCCTCGAGGTTT AGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGACGCCTGAAGATTT TGCAACTTATTATTGCCAACAGTATCGTAGTTACCCCTCGGACTTTTGCCAGGGGACCAAGC TGGAGATCAAAC
COV2-167	9154	heavy	CAGGCACACCTGGTGACGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGAAGGTCTC CTGCAAGGCTTCTGGAGGCACCTTCAACAGTCATGCCATCGGCTGGGTGGGACAGGCCCTTG GACAAGGCCCTTGAGTGGATGGGAAGGATCGTCCCTATCCGGAAGACCACACTAGCCACCG CAGTTACAGGGCAGACTCAGCGTGACCGCGGACACATCCAGGACACACTGTACATGGAAC GAGTAGCCTGCGATCCGAGGACTCGGCCCGGTATTACTGTGCGAGAGTCATTCTGTCTGGGA GGGGCTTTGACATCTGGGGCCAGGGATCCCTGGTGGCGCTCTCCTCAG
	9155	light	TCCTATGAGCTGACACAGCCACCTCAGTGTGAGTGTCCCAGGACAGAGGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCGTGTGTTGGTGATATTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAAAGCAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCTCTAG
COV2-168	9156	heavy	GAGGTGACAGTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTAGTAACCTTTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAAGAACTCACTGTATCTGCAAA GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9157	light	TCCTATGAGCTGACACAGCCACCTCAGTGTGAGTGTCCCAGGACAGAGGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCGTGTGTTGGTGATATTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAAAGCAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCTCTAG
COV2-169	9158	heavy	GAGGTGACAGTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTAGTAACCTTTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAAGAACTCACTGTATCTGCAAA GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9159	light	GACATCCAGATGACCCAGTCTCCATCCTCACTGTCTGCCTCTGTAGGAGACAGAGTCACCAT CACTTGTGCGGGCAGTCAGGACATTAAACAATTATTTAGCCTGGTTTCAGCAGAAACCAGGTA AAGCCCCCTAAGTCCCTGATCTATTCTGCGTCCAGTTTGCAAAGTGGGGTCCCCTCGAGGTTT AGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGACGCCTGAAGATTT TGCAACTTATTATTGCCAACAGTATCGTAGTTACCCCTCGGACTTTTGCCAGGGGACCAAGC TGGAGATCAAAC
COV2-170	9160	heavy	GAGGTGACAGTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTAGCAGCTATGCCGTGTACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTCTCATTATTAGTGGTGGTGGTGAACACACAGACTACGCAGAC TCCGTGAAGGGCCGGTTACCATCTCCAGAGACAATTCCAAGAACACGTTGTATCTGCAAA GAACGGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAATCCCCGGACGCAACAT TTCTGTGGTTCCGGGAGCCCTTCGGCTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCA G
	9161	light	GAAATTTGTGTGACGACAGTCTCCAGGCACCTGTCTTTGTCTCCAGGGGAAAGAGCCACCT CTCCTGCAGGGCCAGTGAGAGTGTCAAGTAGTAAGTACTAGCCTGGTACCAGCAGAAAGCCTG GCCAGGCTCCAGGCTCCTCATCTACGATGCATCCAGCAGGGCCACTGGCATCCAGACAGG TTCAAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAAACTGGAGCCTGAAGA

			TTTTGCAGTATATTACTGTGACAGTATGCTCGGGCCCCGGACACCTTCGCCCAAGGGACAC GACTGGAGATTAAAC
COV2- 171	9162	heavy	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTCAGTAGCTATGCTATGCACCTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGCAATAAATACTACGCAGAC TCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTCCAAGAACACGGTGTATCTGCAAAAT GAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGAGATCCTAACCAATGG TTTTGGCCTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9163	light	CAGACTGTGGTGACCCAGGAGCCATCGTTCTCAGTGTCCCCTGGAGGGACAGTCACACTCAC TTGTGGCTTGAGCTCTGGCTCAGTCTCTACTAGTTACTACCCAGCTGGTACCAGCAGACCC CAGGCCAGGCTCCACGCACGCTCATCTACAGCACAAACACTCGCTCTTCTGGGGTCCCTGAT CGCTTCTCTGGCTCCATCCTTGGGAACAAAGCTGCCCTCACCATCAGGGGGGCCAGGCAGA TGATGAATCTGATTATTACTGTGTGCTGTATATGGGTAGTGGCATTTGGGTGTTCGGCGGAG GGACCAAGCTGACCGTCTCTAG
COV2- 172	9164	heavy	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTTAGCAGCTATGCCGTGTACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTCTCATTATTAGTGGTGGTGGTGAACACACAGACTACGCAGAC TCCGTGAAGGGCCGTTTACCATCTCCAGAGACAATTCCAAGAACACGTGTATCTGCAAAAT GAACGGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAATCCCGGAGCAACAT TTCTGTGGTTCGGGGAGCCCTTCGGCTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCA G
	9165	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTGAGTGTCCCAGGACAGACGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAACAGCCAGGCAGG CCCCGTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAAAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTTCGGCGGAGGGACCA AGCTGACCGTCTCTAG
COV2- 173	9166	heavy	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC GTGTGCAGCCTCTGGTTTAAACCTCAGCAACTATGCTATGCACCTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGTCACTTATATCATACGATGGAAGTATTAAATATTACACAGAC TCCGTGAAGGGCCGATTACCGTCTCCGGGGACAATTCCAAGAACACACTGTTTCTGCAAAAT GAACAGCCTGCGACCTGACGACTCGGCTCTTTATTACTGTGTGAGGGGGCGGTGTAGTGGCC CAAAATCTTTTGATATGTGGGGCCAAGGGACAACGGTCACCGTCTCTCTC
	9167	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTGAGTGTCCCAGGACAGACGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAACAGCCAGGCAGG CCCCGTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAAAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTTCGGCGGAGGGACCA AGCTGACCGTCTCTAG
COV2- 174	9168	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCACATGGAAGAAGTGAAGTGAGAAAACTATGTGGAC TCTGTGAAGGGCCGATTTCATCATCTCCAGAGACGACGCCAAGAAGTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTCTGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9169	light	GAAATAGTGTGACGCAGTCTCCAGCCACCCCTGTCTGTGTCTCCAGGGGAAAGGGTCACCCCT CTCCTGCAGGGCCAGTCAGACTGTAAACAACAACCTTAACTGGCTCCAGCACAAACCGGGCC AGGCTCCAGGCTCGTCATCATTGGTACATCTACCAGGGCCTCTGGTGTCCAGCCAGGTTTC AGTGGCAGTGGGTGGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTCTGAGGATTA TGCAATTTATTACTGTCAACAGTATTATGAGTGGCCTCCGATCACCTACGCCCAAGGGACAC GACTGGAGATTA
COV2- 175	9170	heavy	CAAGTGCAGCTCCAGCAGTCCGGGCCAGGACTGGTGAGGCCTTCGGGGACCCCTGTCCCTCAC GTGCGGTGTCTCTGGTGGCTCCATCAGCAGTCTTAATTGGTGGAGTTGGGTCCGCCAGGCCC CAGGGAAAGGACTGGAGTGGATTGGCGAAGTCTATCCTACTGGGAACACCTACTACAACCCG TCCCTCAAGAGTTCAGTCAACATTTCAATAGAGGAGTGAAGAACGAGTTCTCCCTGAACTT GAGCTCTGTGACCGCCGACAGATGGGCATTTATTACTGTGCGAGAGGCGCTCGTGGGAGCAA GCGACTTCTATTATTACGGTATGGACGTCTGGGGCCAAGGGACCGCGGTACCGTCTCCTCA
	9171	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTTCCAACAATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTGAGCCTCCTAAGTTGCTCTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACGATTCCGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTCTGTGACAGTATTTTAGTCTCCGTATACTT TTGGCCAGGGGACCAAGCTGGAGATCAAC
COV2- 176	9172	heavy	CAGGTGCAGCTGCAGGAGTCCGGGCCAGGACTGGTGAAGCCTTCACAGACCCCTGTCCCTCAA CTGCTCTGTCTGGAGACTCCATCAGCAGAAGTGATTATCACTGGAGTTGGATCCGCCAGC ACCCGGGAAAGGGCCTGGAGTGGATTGGCTATATATAATAATGGCGACACATATTATAAT CCGTCCCTCAAGAGTCTGTGTACCATGTGAGTACACGCTAAGAACGAGTTCTCCCTGAA

			GCTGACCTCTGTGACTGCCGCGGACACGGCCGTCTATTACTGTGCGAGAGACGGTTACGCTG GTAACCTCCGAGGCTCTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTC
	9173	light	GAAATTGTGTTGACACAGTCTCCAGCCTCCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAGAGTGTACCAACTACTTAGCCTGGTACCAACAGAGACCTGGCC AGGCTCCCAGGCTCCTCATCTATCAAACATCCAACAGGGCCACTGGCATCCCAGCCAGGTTT AGTGGCAGTGGGTCTGGGACAGACTTCACACTCACCATCAGCAGCCTAGAGCCTGAAGATTT TGCATTTTATTACTGTGAGCAGCGCAGCCACCGGCCCGGGGGATCAGCTTCGCCCAAGGGA CAGACTGGAGATTAAAC
COV2- 177	9174	heavy	GAGGTGCACTTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTGAGACTCTC CTGTGCAGCCTCTGGATTCTCTTTAGTAACTTTTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9175	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCAGGCGAGTCAGGACATTAGCAACTATTTAAATTTGGTATCAGCAGAAACAGGGGA AAGCCCCCTAAGCTCCTGATCTACGATGTCATCCAATTTGAAACAGGGGTCCCATCAAGGTTT AGCGGCAGTGGATCTGGGACAGATTTTACTTTACCATCAGCAGCCTGCAGCCTGAAGATAT TGCAACATATTACTGTCAACAGATATGATAATCTCCCTCTCACTTTCGGCCCTGGGACCAAAG TGGATATCAAAC
COV2- 178	9176	heavy	GAGGTGCACTTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTGAGACTCTC CTGTGCAGCCTCTGGATTCTCTTTAGTAACTTTTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9177	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTTCCAAACATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTCAGCCTCCTAAGTTGCTCTTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACCGATTCCGGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTTCTGTGACAGTATTTTAGTCTCCGTATACTTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2- 179	9178	heavy	GAGGTGCAATTAGTGGAGTCTGGGGGAGGCTGGTCAAGCCTGGGGAGTCCCTGAGACTCTC CTGTGCGGCCTCTAAATTCACCTTCAGTACCTATCATATGAACCTGGATTGCGCAGGCTCCAG GAAAGGGGCTAGAGTGGGTCTCAGCCATCAGTGTGACAGTACGGTCACAACATATGCAGAC TCAGTGAGGGGCGGATTTCATCTTTCTAGAGACAACGACAAGAATTCAGTGTATCTGCAAAAT GAATGGCCTGAGAGTGGACGACCTGGCTGTATATTACTGTGCGAGGGGGCTGCGGCTGGTA GTGATCATACTGGATTTGACTCCTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9179	light	GATATTGTGATGACTCAGTCTCCACTCTCCCTGTCCGTACCCCTGGAGAGCCGGCTCCAT CTCCTGCAGGTCAGTCCAGGCTCCTGCATCGTAATGGATACAACTATTTGGATTGGTACC TGCAAGGCCAGGGCAGTCTCCAACTCCTGATCTATTGGGTTCTAATCGGGCTCCGGG GTCCCTGACAGGTTTCACTGGCAGTGGATCGGGCAGGACTTTACATTGAAATCAGCAGAGT GGAGGCTGAGGATGTGGGGTTTACTACTGCTATGCAAGGCTACAGACTCCTCCGTACACTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2- 180	9180	heavy	GAGGTGCACTTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTGAGACTCTC CTGTGCAGCCTCTGGATTCTCTTTAGTAACTTTTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9181	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTACCACTATTTAAATTTGGTATCAGCAGAAAGCAGGGGA AAGCCCCCTAAGCTCCTGATCTATGCTCCATCCAATTTGCAAAAGTGGGGTCCCATCAAGATT AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTT TGGAACTTACTACTGTGAGCAGAGTTACAGTAGTCCGTTCACTTTCGGCCCTGGGACCAAAG TGGATATCAAAC
COV2- 181	9182	heavy	GAGGTGCACTTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTGAGACTCTC CTGTGCAGCCTCTGGATTCTCTTTAGTAACTTTTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACTATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9183	light	GAAATAGTGTGACGCACTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGGGTCACCCCT CTCCTGCAGGGCCAGTCAGACTGTAACACAACTTAACTGGGTCAGCAGACAACCGGGGCC AGGCTCCAGGCTCGTCATATTGGTACATCTACCAGGGCCTCTGGTGTCCAGCCAGGTTT AGTGGCAGTGGGTGGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTCTGAGGATTA

			TGCAATTTATTACTGTCAACAGTATTATGAGTGGCCTCCGATCACCTACGGCCAAGGGACAC GACTGGAGATTA
COV2- 182	9184	heavy	CAAGTGCAGCTCCAGCAGTCGGGCCAGGACTGGTGAGGCCTTCGGGGACCCTGTCCCTCAC GTGCGGTGTCTCTGGTGGCTCCATCAGCAGTCCTAATTGGTGGAGTTGGGTCCGCCAGGCCC CAGGGGAAGGGACTGGAGTGGATTGGCGAAGTCTATCCTACTGGGAACACCTACTACAACCCG TCCCTCAAGAGTCGAGTCACCATTTCAATAGAGGAGTCGAAGAACGAGTTCTCCCTGAACCTT GAGCTCTGTGACCGCCGACAGACATGGGCATTTATTACTGTGCGAGAGGCGTCGTGGGAGCAA GCGACTTCTATTATTACGGTATGGACGTCTGGGGCCAAAGGACCGCGGTACCCGTCTCCTCA
	9185	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTCTGAGTGTCCCCAGGACAGACGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCGTGTGTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACCAACAGTTCAGTTGACCATCAGTGGAGTCCAGGCAGAAAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCTTAG
COV2- 183	9186	heavy	CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC CTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACTGGAGCTGGATCCGGCAGCCCCAG GGAAGGGACTGGAGTACATTGGCTATATCTATTACAGTGGGAGCACCACTACAACCCCTCC CTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTATCCCTGAAGCTGAG GTCTGTGACCGCTCGGCACACGGCCGTGTATTACTGTGCGAGGGGTTGACTATTGGGGCC AGGGAACCCCTGGTACCGTCTCCTCAG
	9187	light	GAAATTGTGTGACGACGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAGCTACTAGCCTGGTACCAGCAGAAACCTG GCCAGGCTCCAGGCTCCTCATCTATGGTACATCCAGCAGGGCCACTGGCATCCCAGCAGAG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTCTTACTGTGACGAGTATGGTAACCTCCGTGGACGTTCCGGCAAGGGACCA AGGTGGAATCAAAC
COV2- 184	9188	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAAACTATTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAACATATGTGGAC TCTGTGAAGGGCCGATTATCATCTCCAGAGACGACGCCAAGAACCTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9189	light	GAAATTGTGTGACACAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCTACTAGCCTGGTACCACAGAAACCTGGCC AGGCTCCAGGCTCCTCATTTTGTATGCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTT AGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTT TGCAGTTTATTTCTGTGACGAGCTAGCAGCTGGCAGGGGATCACTTTCGGCGGAGGGACCA AGGTGGAGATCAAAC
COV2- 185	9190	heavy	GAGGTGCAGTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTTAGTAACCTTTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAAATACATATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAACCTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACCAACCGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCCCTGGTCAACCGTCTCCTCAG
	9191	light	GAAATTGTGTGACACAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCTACTAGCCTGGTACCACAGAAACCTGGCC AGGCTCCAGGCTCCTCATTTTGTATGCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTT AGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTT TGCAGTTTATTTCTGTGACGAGCTAGCAGCTGGCAGGGGATCACTTTCGGCGGAGGGACCA AGGTGGAGATCAAAC
COV2- 186	9192	heavy	CAAGTGCAGCTCCAGCAGTCGGGCCAGGACTGGTGAGGCCTTCGGGGACCCTGTCCCTCAC GTGCGGTGTCTCTGGTGGCTCCATCAGCAGTCCTAATTGGTGGAGTTGGGTCCGCCAGGCCC CAGGGGAAGGGACTGGAGTGGATTGGCGAAGTCTATCCTACTGGGAACACCTACTACAACCCG TCCCTCAAGAGTCGAGTCACCATTTCAATAGAGGAGTCGAAGAACGAGTTCTCCCTGAACCTT GAGCTCTGTGACCGCCGACAGACATGGGCATTTATTACTGTGCGAGAGGCGTCGTGGGAGCAA GCGACTTCTATTATTACGGTATGGACGTCTGGGGCCAAAGGACCGCGGTACCCGTCTCCTCA
	9193	light	GAAATTGTGTGACACAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCTACTAGCCTGGTACCACAGAAACCTGGCC AGGCTCCAGGCTCCTCATTTTGTATGCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTT AGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGCCTGAGAGCTGAAGATTT TGGAACTTATTACTGTGACGAGTATAATCACTGGCGGACGTTCCGGCAAGGACCAAGGTGG AAATCAAAC
COV2- 187	9194	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAAACTATTGGATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAACATATGTGGAC TCTGTGAAGGGCCGATTATCATCTCCAGAGACGACGCCAAGAACCTCACTATATCTACAAAT

			GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9195	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTCCCAACAATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTCAGCCTCCTAAGTTGCTCTTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACCGATTCCGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTCTGTGAGCAGTATTTAGTCTCCGTATACTTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2- 188	9196	heavy	GAGGTGCAGTTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTAGTAACTTTTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAAATACATATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCGTGGTACCCTCTCCTCAG
	9197	light	GAAATTGTGTTGACGCAGTCTCCAGGCACCCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCCT CTCCTGCAGGGCCAGTGAGAGTGTGAGTAGTAACACTTAGCCTGGTACCAGCAGAAAGCCTG GCCAGGCTCCAGGCTCCTCATCTACGATGCATCCAGCAGGGCCACTGGCATCCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAAACTGGAGCCTGAAGA TTTTCAGTATATTACTGTGAGCAGTATGCTCGGGCCCCGACACCTTCGCCCAAGGGACAC GACTGGAGATTAAAC
COV2- 189	9198	heavy	CAAAATGCAGCTGGTGCAGTCTGGGGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGAAGGTCTC CTGCAAGGCTTCTGGAGGCCACCTTCATCAATTATGCTATCAACTGGGTGCGACAGGCCCTCG GACAACGACTTGAGTACATGGGAGGGATCATCCCTCTTCTTGGTGTTCGCAAACTACACACAG CGATTCCAGGGCAGAGTACGATGACCGCGGACAGATCTACGAGCAGAGCCTACATGGAGCT GAGTAATCTGCAATTGAAGACACGGCCGTGTATTACTGTGCGAGAGAGTATAGCAGCAGCC GGCCCTTATTTTACACCTACAACCTACGGTATGGACGTCTGGGGCCAAAGGACACCGGTACCC GTCTCCTCA
	9199	light	GATATTGTGATGACCCAGACTCCACTCTCTGTGTCCTGACCCCTGGACAGCCGGCCTCCAT CTCCTGCAAGTCTAGTCAGGGCCTCCTGCATGGTGTGGGAAGACCTATTGTATTGGTTCT TGCAGAAGGCCAGGCCAGCCTCCACAACCTCCTGATCATGAAGTTTCAAACCGCTTCTCCGGA GTGCCAGATAGATTACGCGGACGCGGTGAGGACAGATTTCACTGAAAATCAGCCGGGT GGAGGCTGAGGATGTTGGGATTTATTATTGCATGCAAAGTGTACACCTTCGTACACTTTTG GCCAGGGGACCAAGTTGGAGATCAAAC
COV2- 190	9200	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAAACTATGTGGAC TCTGTGAAGGGCCGATTCACTCATCTCCAGAGACGACGCCAAGAAGTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9201	light	TCCTATGAGCTGACTCAGCCACCCCTCAGTGTCCGTGTCCCCAGGACAGACAGCCAGCATCAC CTGCTCTGGAGATAAAATTGGGGGAGAAATATGCTTGGTGGTATCAGCAGAAGCCAGGCGAGT CCCCGTGTGTTGGTCATTATCAAGATACCAAGCGGCCCTCAGGGATCCCTGAGCGATTCTCT GGCTCCAACCTCTGGGAACACAGCCACGCTGACCATCAGCGGGACCCAGGCTGTGGATGAGGC TGACTATTACTGTGAGCGTGGGACTACACCACCGTGATATTCCGGCGAGGGACCAAGCTGA CCGTCTCAG
COV2- 191	9202	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAAACTATGTGGAC TCTGTGAAGGGCCGATTCACTCATCTCCAGAGACGACGCCAAGAAGTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9203	light	GAAATTGTGTTGACGCAGTCTCCAGGCACCCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTG GCCAGGCTCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGAGCAGTATGGTAGCTCTTACACTTTTGGCCAGGGGACCAAGC TGGAGATCAAAC
COV2- 192	9204	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAAACTATGTGGAC TCTGTGAAGGGCCGATTCACTCATCTCCAGAGACGACGCCAAGAAGTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9205	light	GAAATTGTGTTGACACAGTCTCCAGGCACCCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCTACTTAGCCTGGTACCAACAGAAACCTGGCC AGGCTCCAGGCTCCTCATTTTGTATGCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTT AGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATT

			TGCAACTTATTATTGCCAACAGTATCGTAGTTACCCCTCGGACTTTTGGCCAGGGGACCAAGC TGGAGATCAAAC
COV2- 193	9206	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGCAGCCTCTGGTTTGACCATTAGAACTATTGGATGAACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAACTATGTGGAC TCTGTGAAGGGCCGATTCAATCATCTCCAGAGACGACGCCAAGAACTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9207	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTACCACCTATTAAATTGGTATCAGCAGAAAGCAGGGA AAGCCCCTAACCTCCTGATCTATGCTCCATCCAATTTGCAAAGTGGGGTCCCATCAAGATTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTT TGGAACTTACTACTGTCTCAGCAGAGTTACAGTAGTCCGTTCACTTTCGGCCCTGGGACCAAG TGGATATCAAAC
COV2- 194	9208	heavy	CAGGTGCAGCTGGAGCAGTCTGGGGCTGAGGTGAAGAGGCCCTGGGTCTTCGGTGAAGGTCTC CTGCAAGGGTGGATGGGACACATTAGCAGACATATGCCATCACCTGGGTGGCAGGCGCCCTG GACAAGGGCTTGAGTGGATGGGAGGATCATCCCTGGCCTTGACCTGGTGGATAATCAACAG AAGTTTCAGGACAGACTGACAATTACCGCGGACAAATCCACGACCACAGCTACATGGAGCT GAGAAGCCTCAGATCTGAAGACACGGCCGTATATTATTGTGCGAGAGGTAGACGTTACCAATT TTTTGGATGGTCAATATACGTCATGGTACTTCGACATTTGGGGCCGTGGCACCCCTGGTCACT GTCTCCTCAG
	9209	light	AATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCTCCAT GTCTGCAAGTCTAATCAGAGCCTCCTGTATGGTAATGGATACAACATTATTGGATTGGTACC TGCAGAGACCAGGGCAGTCTCCACAGCTCCTAATCTTTTGGGTTCTAATCGGGCTCCGGG GTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGATTTTACACTGAAAAATCAACAGAGT GGAGGCTGAGGATGTGGGAATTTATTACTGCATGCAAGGTCAAGAGAATCCTCCAACTTTGG GCCCTGGGACCAAAGTGGAGATCAAAC
COV2- 195	9210	heavy	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTTAGCAGCTATGCCGTGTACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGTCTCATTATTAGTGGTGGTGGTGAACACACAGACTACGCAGAC TCCGTGAAGGGCCGGTTACCATCTCCAGAGACAATCCAAGAACAGTTGTATCTGCAAAAT GAACGGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAATCCCGGACGCAACAT TTCTGTGGTTCCGGGAGCCCTTCGGCTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCA G
	9211	light	GAAATAGTGATGACGCAGTCTCCAGCCACCTGTCTGTGTCTCCAGGGGAAAGAGCCACCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAACTTAGCCTGGTACCAGCAGAAACCTGGCC AGGCTCCCAGGCTCCTCATCTATGGTGCATCCACAGGGCCACTGGTATCCAGCCAGGTTT AGTGGCATTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGCCTGCAGTCTGAAGATTT TGCAGTTTATTACTGTCTCAGCAGTATAATAACTGGCGGACGTTCCGCCAAGGGACCAAGGTGG AAATCAAAC
CR302 2	9212	heavy	CAGATGCAACTGGTGCAGAGCGGGACCGAGGTGAAAAAACCCGGCGAGTCTTGAAGATTAG TTGCAAGGGTTAGGTTATGGATTATTACCTACTGGATAGGATGGGTAAAGACAAATGCCAG GTAAGGGTTGGAGTGGATGGGGATAATATACCCCTGGGGATTCTGAGACAAGATACTCCCC AGCTTCCAGGGTCAGGTAACATATATCTGCAGATAAAAGTATAAACACTGGCTATCTTCAGTG GTCCTCACTGAAAGCATCTGACACTGCTATCTACTACTGTGCCGGAGGTAGTGGCATATCAA CTCCAATGGACGTATGGGGTCAAGGGACAACGTGTACCGCTCTCC
	9213	light	TCTGTACTCTACAGCAGCATCAATAAAAAATTACCTCGCATGGTATCAGCAAAAGCCAGGACA ACCCCCAAAACTTCTCATATATTGGGCAAGTACACGGGAGTCTGGCGTCCCCGATAGGTTTT CTGGTAGTGGGAGTGGTACTGACTTTACCTTACCATATCATCACTTCAAGCCGAGGATGTC GCTGTGTACTACTGCCAACATATTTATTCAACCCCTTATACATTCCGCCAGGGCACAAGGT AGAAATTAAA
COV2- 122	9214	heavy	CAGGTGCAGCTGCAGGAGTCCGGCCAGGACTGGTGAAGCCTTCACAGACCTGTCCCTCAC CTGCACTGTCTCTGGTGGCTCCATCAGCAGTGGTAGTCACTACTGGAGCTGGATTCCGGCAGC CCGCCGAAAGGGACTGGAGTGGGTCCGGCGTATCTATACCACTGGGAGCACCACACTACAAC CCCTCCCTCGAGCGTCGAGTCACCATATCACTAGGCAGTCCAAGAACCAGTTCTACCTTGA TCTGACCTCTGTGACCGCCGACAGACCGGCCGTGTATTACTGTGCGAGAGATTCCCTGAGTG GTTCTTACCCTACTACTACGGTATGGACGTCTGGGGCCAAGGACCTCGGTACCGCTCTCC TCA
	9215	light	CAGTCTGTGCTGACTCAGCCACCTCAGCGTCTGGGACCCCGGGCAGAGGGTCACCATCTC TTGTTCTGGAAGCAGTTCCAAACATCGGAAGTAATTATGTTTACTGGTACCAGCACCTCCAG GAACGGCCCCCAAACCTCCTCATCTATAGGAATTATCAGCGGCCCTCAGGGGCTCCAGCCGA TTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGA TGAGGGTGATTATTATTGTGCAGTTTGGGATGACAGCCTGAGTGGTGGGTGTTTCGGCGGAG GGACCAAGCTGACCGTCTTAG
	9216	heavy	CAGGTGCAACTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTCATTAGCTATACTATGCACCTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGGCACTTATATCATATGATGGATACAATAAGTAGTATGCAGAC

COV2-123			TCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTCCAAGAACACGCTGTATGTGCAAAATGAACAGCCTGAGAGCTGAGGACACGGCTCTGTATTACTGTGCGAGAGAAGGGAGCCCGGAGGCCTTTGACTACTGGGGCCAGGGAACCCCTGGTCACCGTCTCCTCAG
	9217	light	GAAATAGTGTGACGCGAGTCTCCAGCCACCCCTGTCTGTGTCTCCAGGGGAAAGGGTCACCCCTCTCCTGCAAGGGCCAGTCACTGTAAACAACAACCTAAACTGGCTCCAGCACAAACCGGGCCAGGCTCCCAGGCTCGTCATCATTGGTACATCTACCAGGGCCCTCTGGTGTCCAGCCAGGTTCTAGTGGCAGTGGGTGGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTCTGAGGATTA TGCAATTTATTACTGTCAACAGTATTATGAGTGGCCTCCGATCACCTACGGCCAAGGGACACGACTGGAGATTA
COV2-124	9218	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCGGGGGGTCCCGGAGACTCTCTGTGGAGCCTCTGGATTACCTTTACTAATCATTGGATGAGCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAGCATAAAGCAAGATGGAGCTGAGAAATCTATGTGGAC TATCTGAAGGGCCGATTACCATCTCCAGAGACAACGCCAAGAATTCAGTGTATCTGCAAAAT GAACAGCCTGAGAGTCGAGGACACGGCTGTTTATTACTGTGCGAGAGCTATCAGATGGCAC TGGCTGGTTGGGGTGGGGTATGGACGTCTGGGGCCAAGGGACCACGGTCAGAGTCTCCTCA
	9219	light	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCCTCCAT CTCCTGCAGGTCTAGTCGGAGTCTCTTGTCTAGGAATGGATACAACCTATTGGATGGTACC TGCAGAGGCCAGGGCAGTCTCCACAGCTCGTGATCTATTGGGTCTTAATCGGGCCTCCGGG GTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGATTTACACTGAAAAATCAGCAGAGT GGAGGCTGAGGATGTTGGGCTTTATTACTGCATGCAAGCTATGCAAGCTCCTCTCACTTTTCG GCCCCGGGACCAAAGTGGAAATCAAAC
COV2-125	9220	heavy	CAGGTGCAGCTGGTACAATCTGGGTCTGAATTGAAGAAGCCTGGGGCCTCAGTGAAGGTTTC CTGCAAGAGCTTCTGGATACACCTTCACTAGTTATGCTATAAATTGGGTGCGACAGGCCCTG GACAAGGGCTTGAGTGGATCGGATGGATCAACATCAACACTGGGAAACCAACGATGCCCCAG GGCTTCACAGGACGGGTGACTTCTCCTTGGACACCTCTGTCAGCACGGCATATCTGCAGAT CAGAAGCCTAAAGGCTGAGGACACTGCTGTGTATTACTGTGCGAGAGATCGGGGTATAGCAG CTGTCGGGGATACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC TCCTCA
	9221	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTGAGTGTCCCCAGGACAGAGCGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCCTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCAAGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCCTAG
COV2-126	9222	heavy	CAGGTGCAGCTGGAGCAGTCTGGGGCTGAGGTGAAGAGCCTGGGTCTTCGGTGAAGGTCTC CTGCAAGGGTGATGGGGACACATTCAAGCAGATATGCCATCACCTGGGTGCGACAGGCCCTTG GACAAGGGCTTGAGTGGATGGGGAGGATCATCCCTGGCCTTGACCTGGTGGATAATCAACAG AAGTTTCAGGACAGACTGACAATTACCGCGGACAAATCCACGACCAACAGCCTACATGGAGCT GAGAAGCCTCAGATCTGAAGACACGGCCGTATATTATTGTGCGAGAGGTAGACGTTACGATT TTTTGGATGGTCAATATACGTCAATGGTACTTCGACATTTGGGGCCGTGGACACCTGGTCACT GTCTCCTCAG
	9223	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTGAGTGTCCCCAGGACAGAGCGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCCTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCAAGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCCTAG
COV2-127	9224	heavy	CAGGTGCAGCTGCAGGAGTGGGGCCAGGACTGGTGAAGCCTTCGGAGACCCCTGTCCCTCAC CTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACTGGAGCTGGATCCGGCAGCCCCCAG GGAAGGGACTGGAGTACATTGGCTATATCTATTACAGTGGGAGCACCAACTACAACCCCTCC CTCAGAGTCGAGTCACCATATCAGTAGACAGCTCCAAGAACCAGTTATCCCTGAAGCTGAG GTCTGTGACCGCTGCGGACACGGCCGTGTTACTGTGCGAGGGGGTTGACTATTGGGGCC AGGGAACCCCTGGTCACCGTCTCCTCAG
	9225	light	TCCTATGAGCTGACACAGCCACCCCTCAGTGTGAGTGTCCCCAGGACAGAGCGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCCTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCAAGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCCTAG
COV2-128	9226	heavy	CAGGTGCAGCTTCAAGCAGTGGGGCGCAGGACTTTTGAAGCCTTCGGAAACCCCTGTCCCTCAC CTGCGCTGTCCACGGTGGGTCTTCACTGGTCCCTACTGGACCTGGATCCGGCAGTCGCCAA GTACAGGGCTGGAGTGGATTGGAGAAATCGGTCCTCGTGGGATCACCTACTACAGCCCGTCC CTCGAGAGTCGAGTCACCATATCAGCAGACAGCTCCAGGAATCAGTTCTCCCTGAGGCTGAC GTCTGTGACCCCGCGGACACGGCTGTCTATTACTGTGCGAGAGGCTTGGTTATTGGAAGAA GCAGCCTAAACTTTGACTCTTGGGGCCAGGGAACCCCTGGTCACCGTCTCCTCAG
	9227	light	GAAATGTGTTGACGCGAGTCTCCAGGCACCCCTGTCTTGTCTCCAGGGGAAAGAGCCACCCCT CTCCTGCAAGGGCCAGTGAAGTGTGAGTAGTAACCTACTAGCCTGGTACCAGCAGAAGCCTG

			GCCAGGCTCCAGGCTCCTCATCTACGATGCATCCAGCAGGGCCACTGGCATCCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACCTCTCACCATCAGCAAACCTGGAGCCTGAAGA TTTTGCAGTATATTACTGTGACGAGTATGCTCGGGCCCCGGACACCTTCGCCCCAAGGGACAC GACTGGAGATTAAAC
COV2- 129	9228	heavy	GAGGTGCAACTGGTGGAGGCTGGGGGAGGCCTGGTCAAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTCAGTGGCTATGCCATAAACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTCTCGTCCATTAGTGGGAATAAATGATATGTACTACGCAGAC TCAGTGAAGGGCCGATTACCATCTCCAGAGACAACGCCAAGAGCTCAGTGTCTTCTGCAAAAT GAACAGCCTGAGAGTCCAGGACACGGCTATCTATTACTGTGCGAGAGATAACTTAGCACTGG CTGGGGAGGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9229	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTTCACAACATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTACAGCCTCCTTAAGTTGCTCTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACCGATTCCGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTCTGTGACGAGTATTTAGTCTCCGTATACTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2- 130	9230	heavy	GAGGTGCAGCTGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTTAGCAGCTATGCCGTGTACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGTCTCATTTATTAGTGGTGGTGGTGAACACACAGATACGCAGAC TCCGTGAAGGGCCGGTTACCATCTCCAGAGACAATTCCAAGAACAGCTGTATCTGCAAAAT GAACGGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAATCCCGGACGCAACAT TTCTGTGGTTCTGGGGAGCCCTTCGGCTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCA G
	9231	light	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGAGTCAACCT CTCCTGCAGGGCCAGTCAAGTGTAGCAGCAACGTAGCCTGGTACCAGCAGAAACCTGGCC AGGCTCCCAGCCTCCTCATCTATGGTGCATCCACCAGGGCCACTGGTACCCAGCAGGTTTC AGTGGCAGTGGGTCTGGGACAGGGTTCACTCTCACCATCACCAGCCTGCAGTCTGAAGATTT TGGAGTTTATTACTGTGACCAATATAATAACTGGCGATTCACTTTCGGCCCTGGGACCAAG TGGAGATCAAAC
COV2- 131	9232	heavy	GAGGTGCAGTGTGGAGTCTGGGGGAGGCTTGGTGCAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTCTGTCTTTAGCAGCTATTCATGAATGGGTCCGCCTGGCTCCAG GAAAGGGGCTGGCCTGGGTCTCTGTGTGGTGTGTAGTCCCGTCAACAAATCTATGAAGAC TCCGTGAAGGGCCGGTTACCATTTCCAGAGACAACCTCCAAGAACACGATATATCTGCAAAAT GAACAACCTGAGAGCCGAAGACACGGCCGTATATCACTGTGCGAAAAGTCAGCCGGTGTCTC GCATGGGTGCGTTCTTCGTGGTTGGACGTCTGGGGCCAGGGACACGGTCACCGTCTCC TCA
	9233	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTTCACAACATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTACAGCCTCCTAAGTTGCTCTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACCGATTCCGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTCTGTGACGAGTATTTAGTCTCCGTATACTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2- 132	9234	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCAAGCCTGGGGGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTCAGTAGTTATAGCATGAACCTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTCTCATCCATTAGTAGTACTAGTAGTTACATATACAGCAGAC TCAGTGAAGGGCCGATTACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTGCGAGACGTAGGGCGGCAACTG GTACGGAGTTCTACTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9235	light	CAGTCTGTGTGACGCAGCCGCCCTCAGTGTCTGCGGGCCAGGACAGAAGGTCAACATCTC CTGCTCTGGAAGCAGCTCCAACATTGGGAATAATTATGTATCCTGGTACCAGCAGCTCCCAG GAACAGCCCCCAACTCCTCATTTATGACAATAATAAGCGACCCCTCAGGGATTCTGACCGA TTCTCTGGCTCCAAGTCTGGCAGTCAAGCACCCTGGGCATCACCAGACTCCAGACTGGGGA CGAGGCCGATTATTACTGCGGAACATGGGATAGCAGCCTGAGTGTGTGTATTCTGCGCGAG GGACCAAGCTACCGTCTCAG
COV2- 133	9236	heavy	CAGGCACACCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCCTGGTGAAGGTCTC CTGCAAGGCTTCTGGAGGCACCTTCAACAGTCAATGCCATCGGCTGGGTGCGACAGGCCCTCG GACAAGGCCCTTGGTGGATGGGAAGGATCGTCCCTATCCGGAAGACCACAACCTACGCACCG CAGTTACAGGGCAGACTACGCTGACCGCGGACACATCCACGAGCACACTGTACATGGAACT GAGTAGCCTGCGATCCGAGGACTCGGCCCGGTATTACTGTGCGAGAGTCACTTGTCTGGGA GGGGCTTTGACATCTGGGGCCAGGGATCCCTGGTGGCGCTCTCCTCAG
	9237	light	GACATCCAAATGACCAATCTCCTTCCGCCCTGGCTGCATCTCTGGGAGACAGAGTCATCAT CACTTGCCAGGCGAGTCACGACATTGGTCACAATTTAAATGGTATCAGCAGAGACAGGGG AAGCCCCCTCAGCTCCTGATCTACGATGTATCCAATTTGCAACAGGGGTCCCATCAAGGTT AGTGGCTTTGGATTGGGACAAATTTACTTTCAACATCAGCGGCCTGCAGTCTGAAGATAT CGGAACATATTACTGTCAACAGTATGATAGTATTTTGGCCCGAGGGACCAAGTTGGAGATCA AAC

COV2-134	9238	heavy	CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGAAGGTCTC CTGCAAGGCTTCTGGAGGCACCTTTAGCAGCTATGCTTTCAGTTGGGTGCGACAGGCCCTG GACAAAGGCTTGAAGGATGGGAAGGATCATCCTTATTCTTGGTATAACAGACTACGCACCG AAGTTCCAGGGCAGAGTCACGATTACCGCGGACAAATCCACGAGCAGAGTGTACATGGAGGT GAGCAGCCTGAGATCGGACGACACGGCCGTGTATTACTGTGCGAGAGAAAGGCCAAGAGACC CCTCCAGTAACACGTTGCCTACTACGCTATGGACGTCTGGGGCCAAGGACCTCGGTCAAC GTCTCGTCA
	9239	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCAGAGCATTACCACCTATTAAATTGGTATCAGCAGAAAGCAGGGA AAGCCCCCTAACCTCCTGATCTATGCTCCATCCAATTGCAAAGTGGGGTCCCATCAAGATT AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATT TGGAACTTACTACTGTGTCAGCAGATTACAGTAGTCCGTTCACTTTCGGCCCTGGGACCAAG TGGATATCAAAC
COV2-135	9240	heavy	CAAGTGCAGCTCCAGCAGTGGGGCCAGGACTGGTGAGGCCTTCGGGGACCCCTGTCCCTCAC GTGCGGTGTCTCTGGTGGCTCCATCAGCAGTCTTAATTGGTGGAGTTGGGTCCGCCAGGCC CAGGGAAGGGACTGGAGTGGATTGGCGAAGTCTATCCTACTGGGAACACCTACTACAACCCG TCCCTCAAGAGTCGAGTCACCATTTCAATAGAGGAGTGAAGAAGCAGGTTCTCCCTGAACCT GAGCTCTGTGACCGCCGACAGATGGGCATTTATTACTGTGCGAGAGGCGTCGTGGGAGCAA GCGACTTCTATTATTACGGTATGGACGTCTGGGGCCAAGGACCGCGGTACCGTCTCCTCA
	9241	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGGACAGAGTCACCAT CACTTGCCGGGCAAGTGAAACCATTAGTAATTTTAAATTGGTATCTCCAACGACCCAGGGA AAGCCCCCTCAGGTCCTCATCTATTCTGACGCCGTTTACAAAGTGGGGTCCCATCAAGGTT CGTGCCAGTGGATCTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACTTGAAGATT TGGAGTTTATTACTGTCAACAGAGTTTCAATACCCCTCGGACGTTCCGCCAAGGGACCCAGG TGGAGATCAAA
COV2-136	9242	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGACACTCTC CTGTGACGCCTCTGGTTTGACCATTAGAAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCACATGGAAGAAGATGGAAGTGAGAAAACATATGTGGAC TCTGTGAAGGGCCGATTATCATCTCTCCAGAGACGACGCCAAGAATCACTATATCTACAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGG ATTTTTCTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9243	light	GAAATGTGTGACGCACTCTCCAGGCACCCCTGTCTTGTCTCCAGGGGAAAGAGCCACCT CTCCTGCAGGGCCAGTGAGAGTGTCTAGTAACCTACTAGCCTGGTACCAGCAGAAGCCTG GCCAGGCTCCAGGCTCCTCATCTACGATGCATCCAGCAGGGCCACTGGCATCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAAACTGGAGCCTGAAGA TTTTGCACTATATTACTGTGTCAGCAGTATGCTCGGGCCCCGACACCTTCGCCCAAGGGACAC GACTGGAGATTAAAC
COV2-137	9244	heavy	CAGGTGCAGCTACAGCAGTGGGGCCAGGACTCTTGAAGCCTGCGGAGACCCCTGTCCCTCAC CTGCGCTGTCCATGGTGGGTCTTCACTGATTCTCACTGGAGTTGGATCCGCCAGACCCCGG GGCAGGGACTGGAGTGGCTTGGGGAAGTCAATCATAGTGGAAAGCACCACCTACAGCCGCTC CTCAAGACTCGAGTCGCCATATCAATAGACACGTCGAAGAACCAGGTCTCCCTCAGGCTGAC CTCTGTGAGCGCCCGGACACGGCTGTCTATTATTGTGCGAGAGGAATGGCCGTTCCGGGG GACAGCTCTACTTACTCGGGGGCTATGACCTCTGGGGCCAGGGAACCTGGTCAACCGTCTCC TCAG
	9245	light	GAAGTTGTGATGACGCACTCTCCAGCCACCCCTGTCTGTCTCCAGGGGAAAGAGCCACCT CTCCTGCAGGGCCAGTCAGAGTGTCTACATCAACTAGCCTGGTACCAGCAGAAACCTGGCC AGCCTCCAGGCTCCTCATCTATGGTGCATCCACCAGGGCCACTGGTATCCAGCCAGGTT AGTGGCAGTGGGTCTGGGACAGATTCACTCTCACCATCAGCAGCCTGGAGTCTGAAGATT TGGAACTTATTACTGTGTCAGCAGTATAATCACTGGCGGACGTTCCGCCAAGGGACCAAGGTG AAATCAAAC
COV2-138	9246	heavy	TCCCAGCTGCTGCAGGAGTGGGGCCAGGACTCGTGAAGCCTTCGGAGACCCCTGTCCCTCAC GTGCACTGTATTGGTGAATCCATCTATGGTTACTACTGGACTTGGATCCGGCAGCCCCCAG GGAGGGGACTGGAGTGGATTGGGTCTGTCTATCAGAGTGGCAGCACCACCTACAACCCCTCC CTCATGAGTCGAGTCACCATATCAGTGGACACGTCGAGAGCAGTTCTCCCTGAAGGTGAC TTCTGTGACCGGTGCGGACACGGCCGTATATTTTGTGCGAGAGGGGTGGCTGGCGGGGGT ATTTTGACGCTGGGGCCAGGGAACCTGGTCCGCTCTCCTCAG
	9247	light	GACGTCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCGGGCAAGTCGGGCATTAAACACTTATTAGCCTGGTATCAGCAGAAAGCCAGGGC AAGTTCCAGCCTCCTGATCTATGGTGCATCCACCTTGCATCTGGGGTCCCGTCTCGGTTC AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGACAGTCTGAAGATGT TGCAACTTATTACTGTGAGGCTTATTACGTTGGCCTCGGTACTTTCGCCCAAGGGACCAAGG TGGAAATCAAAC
COV2-139	9248	heavy	GAGGTGCAACTGGTGGAGTCTGGGGGAGGAGTGGTACGGCCTGGGGAGTCCCTGAGACTCTC CTGTGTAGGCTCTGGATTCCCTTTGGTGGCTATGGCATGAGTTGGGTCCGCCAAGTTCAG GGAAGGGGCTGGAGTGGGTCTTGGAAATTAATTGGAGTGTGATCGAAGAGTTTATGACAGAC TTTGTGAAGGGCCGATTACCATCTCCAGAGACTACCCCAAGAAGTCTGTCTCTTGCATAAT

			GGACAATCTCAGAGCCGAGGACACGGCCCTCTATTATTGTGCGAGAGAGCGGACCTCTCGCCGTGACTTTGACTTCTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9249	light	TCCTTTGTGCTGACTCAGCCACCCTCAGTGTGAGTGGCTCCAGGACAGACGGCCAGGATTCCCTGTGCGAAAAATTATCGTGAAGTCAGACTGTGCACTGGTACCAGCGGAAGCCAGGCCAGGCCCTGTCTTGGTCATCAATTCTGATGACGACCGGCCCTCAGGGATCTCTGAGCGATTCTCTGGCTCCAACTCTGGGAACACGGCCACCCTGACCATCAGCAGGGTCGAAGCCGGGGATGAGGCGACTATTATTGTGAGGTGTGGATCCCAGTTCTGATCAAAGCGCTATTCGCCGGAGGGACCA CGCTGACCGTCCTA
COV2-140	9250	heavy	GAGGTGCAGCTGGTGGACTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCTGTGCGACCTCTGGATTACCTTTACTAGTTATTGGATGAACCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAAACATAAAGCAAGATGGAAGTGAGAAAAGACTATGTGGACTCTGTGAAGGGACGATTACCATCTCCAGAGACAACGCCAAGAAGTCACTGTATCTGCAAAATGAGCAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGATCTCGGCAGTGGCTCGTACCACCTCTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9251	light	TCCTATGAGCTGACACAGCCACCCTCAGTGTGAGTGTCCCCAGGACAGACGGCCAGGATCATCTGCTCTGGAGATGCATTGCCAAAGCAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGGCCCTGTGTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCTGGCTCCAGCTCGGGGACAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCCGCGGAGGGACCAAGCTGACCGTCCTAG
COV2-141	9252	heavy	CAGGTGCAGCTGGTACAATCTGGGTCTGAATTGAAGAAGCCTGGGGCCTCAGTGAAGGTTCTGCAAGACTTCTGGATACACCTTCACTAGTTATGCTATAAATTGGGTGCGACAGGCCCTGGAACGGGCTTGAAGTGGATCGGATGGATCAACATCAACACTGGGAACCAACCTATGCCAGGGCTTACAGGACGGGTTGACTTCTCCTTGGACACCTCTGTGACGACGGCATACTGTGAGATCAGAAGCCTAAAGGCTGAGGACACTGCTGTGTATTACTGTGCGAGAGATCGGGGTATAGCAGCTCGTGGGATACTACTACTACGGTATGGACGCTCTGGGGCCAAGGGACACGGTCACCGTCTCCTCA
	9253	light	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTACCACCTATTAAATTGGTATCAGCAGAAAGCAGGGGAAGCCCCCTAACCTCCTGATCTATGCTCCATCCAATTGCAAGTGGGGTCCCATCAAGATTAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGGAACTTACTACTGTGAGCAGAGTTACAGTAGTCCGTTCACTTTCGGCCCTGGGACCAAGTGGATATCAAAAC
COV2-142	9254	heavy	GAGGTGCAACTGGTGGAGTCTGGGGGAGGAGTGGTACGGCCTGGGGAGTCCCTGAGACTCTCTGTGTAGGCTCTGGATTCCCCTTTGGTGGCTATGGCATGAGTGGGTCCGCCAAGTTCAGGGAAGGGGCTGGAGTGGGTCTCTGGAATTAATTGGAGTGTGATCGAAGAGTTTATGCGAGACTTGTGAAGGGCCGATTACCATCTCCAGAGACTACCCCAAGAAGTCTGTGCTCTGCAAAATGGACAATCTCAGAGCCGAGGACACGGCCCTCTATTATTGTGCGAGAGAGCGGACCTCTCGCCGTGACTTTGACTTCTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9255	light	TCCTATGAGCTGACACAGCCACCCTCAGTGTGAGTGTCCCCAGGACAGACGGCCAGGATCATCTGCTCTGGAGATGCATTGCCAAAGCAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGGCCCTGTGTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCTGGCTCCAGCTCGGGGACAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCCGCGGAGGGACCAAGCTGACCGTCCTAG
COV2-143	9256	heavy	GAGGTGCAGCTGGTGGACTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCTGTGCGACCTCTGGATTACCTTTACTAGTTATTGGATGAACCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAAACATAAAGCAAGATGGAAGTGAGAAAAGACTATGTGGACTCTGTGAAGGGACGATTACCATCTCCAGAGACAACGCCAAGAAGTCACTGTATCTGCAAAATGAGCAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGATCTCGGCAGTGGCTCGTACCACCTCTTTGACTACTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9257	light	CAGTCTGTGTGACGACGCCGCCCTCAGTGTCTGCGGCCCCAGGACAGAAGTCAACATCTCTGCTCTGGAAGCAGCTCCAAACATTGGGAATAATTATGTATCCTGGTACCAGCAGTCCCGAGAACAGCCCCAACTCCTCATTATGACAATAATAAGCGACCTCAGGGATTCTCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTGAGCCACCCTGGGCATCACCGGACTCCAGACTGGGGAAGGCGGATTTACTGCGGAACATGGGATAACAGCCTGAGTGCCTGGGTGTTCCGCGGAGGGACCAAGCTGACCGTCCTA
COV2-144	9258	heavy	CAGGTGCAGCTGCAGGAGTGGGCCCCAGGACTGGTGAAGCCTTCGGAGACCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGGACTGGAGTACATTGGCTATATCTATTACAGTGGGAGCACCACCTACAACCCCTCCCTAAAGAGTCGAGTACCATATCAGTAGACAGTCCAAGAACCAGTTATCCCTGAAGCTGAGGTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCGAGGGGGTTTACTATTGGGGCCAGGGAACCTGGTCACCGTCTCCTCAG
	9259	light	GAAATTTGTGTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCGAGGGCCAGTCAGAGTGTAGCAGCTACTAGCCTGGTACCACAGAAACCTGGCCAGGCTCCAGGCTCCTCATTTTGTATGCATCCAACAGGGCCACTGGCATCCAGCCAGGTTTCACTGGCAGTGGGTCTGGGACAGACTTCACTCTACCATCAGCAGCCTAGAGCCTGAAGATT

			TGCAGTTTATTTCTGTGACGAGCGTAGCAGCTGGCAGGGGATCACTTTCGGCGGAGGGACCA AGGTGGAGATCAAAC
COV2- 145	9260	heavy	CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAAGAAGCCTGGGGCCTCAGTTAAGATTTC CTGCAAGACTTCTGGATACAATTTCACTAATCATCCTATAAATGGGTGCGACAGGCCCTTG GACAAGGGCTTGAGTGGATGGGATGGATCAACACCAACACTGGGAACCCAACTATGGCCAG GCCTTCACAGGACGATTGTCTTCTCCTTTGACACCTCTGTGCGCACGGCATATCTGCACAT CAGCGGCCTGCAGCCTGGAGACACTGCCTTCTATTACTGTGTGAGAGAGGACCTGAGACTTA GACAGGTGTGGTGGCGGTGGTTGACCCCTGGGGCCAGGGAACCTGGTCACCGTCTCCTCA G
	9261	light	GAGATCCAGATGACCCAGTCACCATCCTCCCTGTCTGCCTCTGTAGGAGACAGAGTCACCAT TTCTTGTGCGGCAAGTCAGAGCGTCGGCGGTCAATTAATTTGGTATCAGCAGAAACCGGGGA AAGCCCCTAAGGTCCTGATCCACGCTGCTCCAGTTTAGAAGGTGGGGTCCCTTCACGGTTC AGTGGCAGTGGATCTGGGACAGATTACACTCTCACCATCACCACCTTCAGCCTGAAGATTT TGCGACTTACTTCTGCCAGCAGAGTCGCAACTCCCTGCGACGTTGCGCCAAGGGACCAAGG TGGAGATGAAAC
COV2- 146	9262	heavy	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC CTGTGACGCTCTGGATTACCTTCAGTAGCTATGCTATGCACTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGCAATAAATACACGACAGAC TCCGTGAAGGGCCGATTACCATCTCCAGAGACAATCCAAGAACACGCTGTATCTGCAAAAT GAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGAGGAAAATGGGGATAG TCGGTGATGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCAG
	9263	light	GACATCCAGATGACCCAGTCCTCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT CACTTGCCAGGCGAGTCAGGACATTAGCAACTATTTAAATTTGGTATCAGCAGAAACCGGGGA AAGCCCCTAAGGTCCTGATCTACGATGCATCCAATTTGGAACAGGGGTCCCATCAAGGTTTC AGTGGAAAGTGGATCTGGGACAGATTTTACTTTTACCATCAGCAGCCTGCAGCCTGAAGATAT TGCAACATATTACTGTCAACAGTATGATAATCTCCCTCTCACTTTCGGCCCTGGGACCAAG TGGATATCAAAC
COV2- 147	9264	heavy	TCCCAGCTGTGTCAGGAGTCTGGGGCCAGGACTCGTGAAGCCTTCGGAGACCCCTGTCCCTCAC GTGCACTGTATTTGGTGACTCCATCTATGGTTACTACTGGACTTGGATCCGGCAGCCCCCAG GGAGGGGACTGGAGTGGATTGGGTCTGTCTATCAGAGTGGCAGCACCAACTACAACCCCTCC CTCATGAGTCGAGTCACCATATCAGTGGACACGTCGAGAGAGCAGTTCTCCCTGAAGGTGAC TTCTGTGACCGGTGCGGACACGGCCGTATATTTTGTGCGAGAGGGCTGGCTGGCGGGGGTT ATTTTGACGCTGGGGCCAGGGAACCTGGTCGCCGTCTCCTCAG
	9265	light	TCCTATGAGCTGACACAGCCACCTCAGTGTGAGTGTCCCAGGACAGAGCGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCGTGTGTTGGTGATTTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAAACAGTCACGTTGACCATCAGTGGAGTCCAGGACAGAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGCTCCTAG
COV2- 148	9266	heavy	CAGGTGCAGCTGGAGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCTTCGGTGAAGGTCTC CTGCAAGGGTGTGGGACACATTACGACATATGCCATCACCTGGGTGCGACAGGCCCTTG GACAAGGGCTTGAGTGGATGGGAGGATCATCCCTGGCCTTGACCTGGTGGATAATCAACAG AAGTTTCAGGACAGACTGACAATTACCGCGGACAAATCCACGACACAGCCTACATGGAGCT GAGAAGCCTCAGATCTGAAGACACGGCCGTATATTTTGTGCGAGAGGTAGACGTTACGATT TTTTGGATGGTCAATATACGTCATGGTACTTCGACATTTGGGGCCGTGGCACCCCTGGTCACT GTCTCCTCAG
	9267	light	GAAATAGTGTGACGCACTCTCCAGCCACCTGTCTGTGTCTCCAGGGGAAAGGGTCACCCCT CTCCTGCAGGGCCAGTCAGACTGTAAACAACAATTAACCTGGCTCCAGCACAAACCGGGCC AGGCTCCCAGGCTCGTCATCATTGGTACATCTACCAGGGCCTCTGGTGTCCAGCCAGGTTTC AGTGGCAGTGGGTGCGGACAGAGTTCACTCTCACCATCAGCAGCCTGCAGTCTGAGGATTA TGCAATTTATTACTGTCAACAGTATTATGAGTGGCCTCCGATCACCTACGGCCAAGGGACAC GACTGGAGATTA
COV2- 149	9268	heavy	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCTACAGTGAAATCTC CTGCAAGGTTTCTGGATACACCTTCACCGACTACTACATGCACTGGGTGCGACAGGCCCTTG GAAAAGGGCTTGAGTGGATGGGACTTGTGATCCTGAAGATGGTGAACAAATATACGCAGAG AAGTTCCAGGGCAGAGTCACCATACCGCGGACACGCTCTACAGACACAGCCTACATGGAGCT GAGCAGCCTGAGATCTGAGGACACGGCCGTGATTACTGTGCAACAGTGTCCAGGTGGTACT ACTACTACTACGATATGACGCTCTGGGGCCAAGGACACGGTCACCGTCTCCTCA
	9269	light	GAAATTTGTTGACGCACTCTCCAGGCACCTGTCTTTGTCTCCAGGGGAAAGAGCCACCT CTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTTG GCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGAGCAGTATGGTAGCTCTTACACTTTTGGCCAGGGGACCAAGC TGGAGATCAAAC
	9270	heavy	CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC GTGTGACGCTCTGGTTTTAACCTCAGCAACTATGCTATGCACTGGGTCCGCCAGGCATCAG GCAAGGGGCTGGAGTGGGTGTCACTTATATCATACGATGGAAGTATTAATATTACACAGAC

COV2-150			TCCGTGAAGGGCCGATTACCCGTCTCCGGGGACAATTCCAAGAACACACTGTTTCTGCAAAATGAACAGCCTGCGACCTGACGACTCGGCTCTTTATTACTGTGTGAGGGGCGGTGTCACTGGCCCAAATTCCTTTTGATATGTGGGGCCAAGGGACAACGGTCACCGTCTCTTC
	9271	light	GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGACAGCGGGCTCCATCTCCTGCAGGTCTAGTCAAAGCCTCGTATACAGTGATGGAACACCTACGTGAATTGGTTTCAGCAGAGGCCAGGCCAATCTCCAAGGCGCCTAATCTATCAGGTTTCTATCCGGGCTCTGGGGTCCCAGACAGATTACAGCGGAGTGGGTGAGGCACTGATTTCCGCACTGAAATCAGCAGGGTGGAGGCTGAGGATGTTGGGATTATATTGTCATGCAAGGTACACACTGGCCGGTGACGTTCCGCCAAGGGACCAAGTGGAAATCAAAC
COV2-151	9272	heavy	GAGGTGCAGTTGTTGGAGTCCGGGGGAGGCTTGGTGCAGCCTGGGGGTCCTCGAGACTCTCTGTGCAGCCTCTGGATTCTGCTTTAGCGACTATTCCATGAATTGGGTCCGCTGGCTCCAGGAAAGGGGCTGGCGTGGGTCTCTGTTGTTGGTGTGATGCCGTCAACAAATTCATGAAGACTCCGTGAAGGGCCGTTTACCAATTTCCAGAGACAACCTCCAAGAACACGATATATCTGCAAAATGAACAACCTGAGAGCCGAAGACACGGCCGTATATCACTGTGCGAAAAGTCAGCCGGTGTCTCGCATGGGTCTGCTTCTGCTCGGTTTGGACGTCTGGGGCCAAGGGACACGGTCACCGTCTCTCA
	9273	light	CAGTCTGCCCTGACTCAGCCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCACTCACCATTCTCTGCACTGGAAGCAGCAATGACGTGGTCTGTATTAATGATGTCTCATGGTACCAACATCAACAGGCAAAGCCCCAGACTCATGATTCTGAGGTCTGTAAGCGGCCCTCAGGGTCCGTGATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCCTCCCTGACCGTCTCTGGACTCCAGGCTGAGATGAGGCTGATTATTACTGCAAGTCAATATGGAGGCAACAACATTTACTATTCCGGCGGAGGGACCAAGCTGACCGTCTCTAG
COV2-152	9274	heavy	CAGGTGCAACTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTCACTTCACTTAGCTATACATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCACTTATATCATATGATGGATACAATAAGTACTATGCAGACTCCGTGAAGGGCCGATTACCAATCTCCAGAGACAATCCAAGAACACGCTGTATGTGCAAAATGAACAGCCTGAGAGCTGAGGACACGGCTCTGTATTACTGTGCGAGAGAAGGGAGCCCGGAGGCCCTTGACTACTGGGGCCAGGGAACCTGGTCAACGCTCTCTCTCAG
	9275	light	TCCTATGAGCTGACACAGCCACCTCAGTGTCACTGTCTCCAGGACAGAGCGGCCAGGATCATCTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCGCAGGCCCTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCTGGCTCCAGCTCGGGGCAACAGTCAAGTTCAGCATCAGTGGAGTCCAGGCAGAGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCAAGCTGACCGTCTCTAG
COV2-153	9276	heavy	GAGATGCAGCTGGTGGAGTCCGGGGGAGGCTTAGTTCAAGCCGGGGGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTCACTTCACTGACTACTACATGTACTGGGTCCGCCAAGCTCCAGGGAAGGGGCTGGTGTGGGTCTCACGTATTAAGCCTGATGGGACTGGCACAAGTTACGCGGACTCCGTGAGGGGCCGATTACCCGTCTCCAGAGACAACGCCAAGAACACGCTGAATCTGCAAAATGAACAGTCTGAGAGCCGAGGACACGGCTGTGTATTATTGTGTGGCTACAACCTGGAACACAGACTTCTGCTGGGGCCAGGGAACCTGGTAACCGTCTCCGCAAG
	9277	light	GATGTTACTGTGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGACAGCGGGCTCCATCTCCTGCAGGTCTAGTCAAAGCCTCGTATACAGTGATGGAACACCTACTTGAATTGGTTTCAGCAGAGGCCAGGCCAATCTCCAAGGCGCCTAATTTATCAGGTTTCTAACCGGACTCTGGGTCCCAGACAGATTACAGCGGAGTGGGTGAGGCACTGATTTACACTGACAATTAGCAGGGTGGAGGCTGAAGATGTTGGGGTTTATTACTGCATGCAAGGTTTCATACTGGCCATTCACTTTCCGCCCTGGGACCAAGTGATATCAAAC
COV2-154	9278	heavy	GAGGTGCAATTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCGGGGGGTCCCTGAGGCTCTCTGTTCAAGCCTCTGGATTCACTTACAGTAATTATTGGATGACTTGGGTCCGACAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAACTAAGACGAGATGGAAGTGTGGAGCACTATGTGGACTCTGTGAGGGGCCGATTACCAATCTCCAGAGACAACGCCAAGAACCTCCCTGTATCTACAAATGGACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGATTAAAGTCCCGGCGTTTGGGGCCATTACGATGTTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCAG
	9279	light	GCCATCCAGATGACCCAGTCTCCATCTCCCTGTCTGCATCTTTGGGAGACAGAATCTCCATCACTTGCCGGGCAAGTCAGGGCATTGGAAATGAGTTGGGCTGGTATCAGCAGAAAACAGGTAAGCCCCCTAGACTCCTCATCTATGCTGGTCCACTTTACAAGGTGGAGTCCCACCAAGGTTACGCGGCTCTGGATCTGGCACAGATTTCACTCTCAACATAAGCAGCCTGCAGGCTGAAGATTTGCAACATATTATTGTCTGCAAGATTACGCCCTACCCCTCGGACGTTCCGGCCAGGGACCAAGGTGGAAGTCAAAC
COV2-155	9280	heavy	GAGGTGCAGTTGTTGGAGTCCGGGGGAGGCTTGGTGCAGCCTGGGGGTCCTCGAGACTCTCTGTGCAGCCTCTGGATTCTGCTTTAGCGACTATTCCATGAATTGGGTCCGCTGGCTCCAGGAAAGGGGCTGGCGTGGGTCTCTGTTGTTGGTGTGATGCCGTCAACAAATTCATGAAGACTCCGTGAAGGGCCGTTTACCAATTTCCAGAGACAACCTCCAAGAACACGATATATCTGCAAAATGAACAACCTGAGAGCCGAAGACACGGCCGTATATCACTGTGCGAAAAGTCAGCCGGTGTCTCGCATGGGTCTGCTTCTGCTCGGTTTGGACGTCTGGGGCCAAGGGACACGGTCACCGTCTCTCA

	9281	light	GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAGCTACTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGACAGTATGGTAGCTCTTACACTTTTGGCCAGGGGACCAAGCTGGAGATCAAAAC
COV2-156	9282	heavy	GAGGTGACAGTGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTACCTTTAGCAGCTATGCCATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGGTAGTGGTGGTAGCACATAGTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAAGATCAACACATGGTTTGGGAGCTATAGGCTTTGACTACTGGGGCCAGGGAACCTGGTACCCTGCTCCTCAG
	9283	light	GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTAGCAGCAACTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCCACTGGTATCCCAGCCAGGTTTCAAGTGGCAGTGGGTCTGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCACTGTGAAGATTTGCACTTTATTACTGTGACAGTATAATAACTGGCGGACGTTCCGCCAAGGGACCAAGGTGGAATCAAAAC
COV2-157	9284	heavy	GAGGTGACAGTGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTCACTTTAGTAACCTTTGGATGAAGTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCACATACAGCAAGATGGAAGTGAGAAATACATATGTGGACTCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAAGAACTCACTGTATCTGCAAAATGAACAGCCTGAGAGCCGAAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACGACTGGTACTTTGACTACTGGGGCCAGGGAACCTGGTACCCTGCTCCTCAG
	9285	light	GACATCCAGATGACCCAGTCTCCATCTTCTGTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGTGGGCGAGTCAGGGTATTAACAGCTGGTTAGCCTGGTATCAGCAGAAACACAGGGAAGCCCCCTAAGCTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTTACGGCCAGTGGATCTGGGACAGATTTCACTCTCACTATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGCTCAGAGTTCCCAATCACCTTCGCCCAAGGGACACGAC TGGAGATTAAAC
COV2-158	9286	heavy	GAGGTGACAGTGTGGAGTCTGGGGGAGGCTTGGTGCAGCCTGGGGGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTCTGTCTTTAGCAGCTATTCATGAATTGGGTCCGCCAGGCTCCAGGAAAGGGGCTGGCCTGGGTCTCTGTGTGTGGTGTGATGCCGTACCAAAATCTATGAAGACTCCGTGAAGGGCCGGTTCACCATTTCCAGAGACAACCTCCAAGAACACGATATATCTGCAAAATGAACAACCTGAGAGCCGAAAGACACGGCCGTATATCACTGTGCGAAAAAGTCAGCCGGTGTCTCGCATGGTCCGCTTCTTCTCGTCCGTTTGGACGTCTGGGGCCAAGGGACACCGTACCGTCTCTCTCA
	9287	light	TCCTATGAGCTGACACAGCCACCCTCAGTGTCACTGTCCCCAGGACAGAGCCGAGGATCATCTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTTGGTACCAGAAGAGCCAGGCCAGGCCCTTGTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCTGGCTCCAGCTCGGGGACAACAGTCACGTTGACCATCAGTGGAGTCCAGGCAGAAAGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGGACCAAGCTGACCGTCTCTAG
COV2-159	9288	heavy	CAGGTGCAACTGGTACAATCCGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCTGTACAGCCTCTGGATTACCTTCAGTAATTATGCTATGCAGTGGGTCCGCCAGGCCCCAGGCAAGGGGCTGGAGTGGGGGCGAGTTATATCATATGACGGAACTATTACACTCTATGAAGACTCCATGAGGGGCGGCTTCACCATCTCCAGAGACAATTCCAGGGACACCCTGTATCTGCAAAATGAATAGTCTGCGACCTGATGACACGGCTGTATATTACTGTGGGAGAGACCTCTCTGGGGGGG GTTTGGACGTCTGGGGCCAAGGGACACCGGTACCCGTCTCTCTCA
	9289	light	CAGTCTGCCCTGACTCAGGCTCGCTCAGTGTCCGGGTCTCCTGGACAGTCACTACCGTCTCTGTGCACTGGAAGCAGCAATGATGTTGGTGGTCATAACTATGTCTCCTGGTACCAGCATAGCCAGGGCAAAGCCCCAAACTCATTATTATGATGTCACTAAACGGCCCTCTGGGGTCCCTGATCGCTTCTCCGGCTCCAAGTCTGGCGACACGGCCCTCCCTGACCATCTCTGGGCTCCAGGCTGACGATGAAGGTGATTATTACTGTGCTGCATATAAGAGTACTTACGACTATGTCTTCGGAAGTGGACCACGGTCTCCGTCTCT
COV2-160	9290	heavy	CAGGTGACAGTGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCTGTGCAGCCTCTGGATTACCTTCAGTATCTATGCTATCCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGATGGCAGTTATATCATATGATGGAATAATCAATACTACGCAGACTCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAATGAACAGCCTGAGAAGTACGACACACGGCTGTCTATTACTGTGCGAGGAGCGAGGGAGGGGGTTACCATGATGCTTTTGATATCTGGGGCCAAGGGACAATGGTACCGTCTCTCTCAG
	9291	light	CAGCTTGTGCTGACTCAATCGCCCTCTGCCTCTGCCTCCCTGGGAGCCTCGGTCAAACCTCACCTGCACTCTGAGCAGTGGGCACAGCAGTACGCCATCGCGTGGCATCAGCAGCAGCCAGAGAGGGCCCTCGGTACTTGATGAAGCTTAACAGTGATGGCAGCCACAACAAGGGGACGGGATCCCTGATCGCTTCTCAGGCTCCAGCTCTGGGGCTGAGCGCTACCTCACCATCTCCAGCCTCCAGTCTGAGGATGAGGCTGACTATTTCTGTGACACCTGGGGCACTGGCATTACGTGTTCCGGCGAGGGACCAAGCTGACCGTCTCTAG

COV2-161	9292	heavy	CAGGTGCAACTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTCATTAGCTATACTATGCAGCTGGGTCCGCCAGGCTCCAG GCAAGGGGCTGGAGTGGGTGGCACTTATATCATATGATGGATACAATAAGTACTATGACAGAC TCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTCCAAGAACACGCTGTATGTGCAAAAT GAACAGCCTGAGAGCTGAGGACACGGCTCTGTATTACTGTGCGAGAGAAGGGAGCCCGGAGG CCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAG
	9293	light	TCCTTTGAGCTGACACAGCCACCCTCGCTGTCTAGTGTCCCCAGGACAGACGGCCAGGATCAC CTGCTCTGGAGATGCATTGTCAAAGCAATTTACTTATTGGTACCAGCAGAGCCAGGCCAGG CCCCTGTGTTGGTGATTATATAAGACAGTGAGCGGCCCTCAGGGATCCCTGAGCGATTCTCT GGCTCCAGCTCAGGGACAACAGTACGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGC TGACTATTACTGTCAATCAGCACACAGCAGTGGTTTTATCGTGTGGTATTCGGCGGAGGGGA CCAAGCTGACCGTCTCTAG
COV2-162	9294	heavy	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGTCCTTGAGACTCTC CTGTGCAGCCTCTGGATTACCTTTAGCAGCTATGCCGTGTACTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGCCTCTCATTTATTAGTGGTGGTGGTGAACCCACAGACTACGCAGAC TCCGTGAAGGGCCGTTTACCATCTCCAGAGACAATTCCAAGAACACGTTGTATCTGCAAAAT GAACGGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAATCCCGGACGCAACAT TTCTGTGGTTCGGGGAGCCCTTCGGCTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA G
	9295	light	GAAATAGTGTGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGGGTCAACCCT CTCCTGCAGGGCCAGTCACTGTAAACACAACCTTAACTGGCTCCAGCACAAACCGGGCC AGGCTCCCAGGCTCGTCATCATTTGGTACATCTACCAGGGCCTCTGGTGTCCAGCCAGGTTTC AGTGGCAGTGGGTCCGGGACAGAGTTCACTCTCACCATCAGCAGCCTGCACTCTGAGGATTA TGCAATTTATTACTGTCAACAGTATTATGAGTGGCCTCCGATCACCTACGGCCAAGGGACAC GACTGGAGATTA
COV2-163	9296	heavy	CAGGTGCAGCTGGAGCAGTCTGGGGCTGAGGTGAAGAGGCCTGGGTCTTCGGTGAAGGTCTC CTGCAAGGGTGATGGGGACACATTACGCACATATGCCATCACCTGGGTGCGACAGGCCCTTG GACAAAGGGCTTGAGTGGATGGGGAGGATCATCCCTGGCCTTGACCTGGTGGATATCAACAG AAGTTTCAGGACAGACTGACAATTACCGGGACAATCCACGACCACAGCCTCATCTGGAGCT GAGAAGCCTCAGATCTGAAGACACGGCCGTATATTATTGTGCGAGAGGTAGACGTTACGATT TTTTGGATGGTCAATATACGTCATGGTACTTCGACATTTGGGGCCGTGGCACCTGTGCTACT GTCTCCTCAG
	9297	light	GAGATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCACCAT CAGCTGCAAGTCCAGCCAGAGTCTTTTATACAGTTCCAACAATAGGGACTACTTAGCTTGGT ACCAACAGAAAGCAGGTCAAGCTCCTAAGTTGCTCTTTTACTGGGCATCTACCCGGGAATCC GGGGTCCCTGACGATTCCGGTGGCAGCGGGTCTGGGACACATTTCACTCTCACCATTCTACAA CCTGCAGCCTGAAGATGTGGCAGTTTATTCTGTGACAGTATTTTAGTCTCCGTATACTTT TTGGCCAGGGGACCAAGCTGGAGATCAAAC
COV2-164	9298	heavy	GAGGTGCAGTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTTGAGACTCTC CTGTGCAGCCTCTGGATTCACTTTTAGTAACCTTTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATACAGCAAGATGGAAGTGAGAAATACATGTGGAC TCTGTGAAGGGCCGATTACCATCTCCACAGACCTCGCCAAGAAGTCACTGTATCTGCAAAAT GAACAGCCTGAGAGCCGAAGACACGGCTGTGTATTACTGTGCGAGACAACACGGTGACTACG ACTGGTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAG
	9299	light	GAAATGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT CTCCTGCAGGGCCAGTCAAGTGTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTTG GCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCCACTGGCATCCAGACAGG TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGACAGTATGGTAGCTCTTACACTTTTGGCCAGGGGACCAAGC TGGAGATCAAAC
COV2-165	9300	heavy	GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGTCCTTGACACTCTC CTGTGCAGCCTCTGGTTTGACCAATTAGAACTATTGGATGAAGTGGGTCCGCCAGGCTCCAG GGAAGGGGCTGGAGTGGGTGGCCAAACATGGAAGAAGATGGAAGTGAGAAAAATATGTGGAC TCTGTGAAGGGCCGATTCAATCATCTCCAGAGACGACGCCAAGAAGTCACTATATCTACAAAT GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTACGAGAGATCCCGGTCCCGGGG ATTTTTCGTGGGGCCAGGGAACCGTGGTAACCGTCTCCTCAG
	9301	light	TCCTATGAGCTGACACAGCCACCCTCAGTGTCTAGTGTCCCCAGGACAGACGGCCAGGATCAT CTGCTCTGGAGATGCATTGCCAAAGCAAAATGCTTATTGGTACCAGAAGAAGCCAGGCCAGG CCCCTGTGTTGGTGATATTTAAAGACAGTGAGAGGCCCTCAGGCATCCCTCAGCGATTCTCT GGCTCCAGCTCGGGGACAACAGTACGTTGACCATCAGTGGAGTCCAGGCAGAGACGAGGC TGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTATGTGGTATTCGGCGGAGGGACCA AGCTGACCGTCTCTAG

TABLE 2 - PROTEIN SEQUENCES FOR ANTIBODY VARIABLE REGION

Clone	Seq ID	Chain	Variable Sequence Region
COV2-166	9302	heavy	QVQLVQSGSEIQKPGASVKVSCASGNTFTPTDMMNWRQAPGQGLEWMGWINTNTGSPTYAQGLPGRFVFSLDTSVSTAYLEISSLKAEDTAVYYCAREGYHYGMDVWGQGTITVTVSS
	9303	light	DIQMTQSPSSLSASVGRVITITCRASQDINNYLAWFQQKPKGAPKSLIYSASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYRSYPRTFGGGTGLEIK
COV2-167	9304	heavy	QAHLVQSGAEVKKPGSSVKVSCASGDTFNHAIQWVRQAPGQGLEWMGRIVPIRKTITTYAPQLQGRRLTLTADTSTSTLYMELSSLSRSEDARYYCARVILSGRGFDIWGQGSLLAVVSS
	9305	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRFSGSSSGTTVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGTGLTVL
COV2-168	9306	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFISSNFWMNWRQAPGKGLEWVANIQDQSEKYYVD SVKGRFTISDIAKNSLYLQMNSLRAEDTAVYYCARQHGDDWYFDYWGQGTITVTVSS
	9307	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRFSGSSSGTTVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGTGLTVL
COV2-169	9308	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFISSNFWMNWRQAPGKGLEWVANIQDQSEKYYVD SVKGRFTISDIAKNSLYLQMNSLRAEDTAVYYCARQHGDDWYFDYWGQGTITVTVSS
	9309	light	DIQMTQSPSSLSASVGRVITITCRASQDINNYLAWFQQKPKGAPKSLIYSASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYRSYPRTFGGGTGLEIK
COV2-170	9310	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAVYVWRQAPGKGLECVSFISGGGETTDYAD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKSPDATFLWFGEPPGYWGQGTITVTVSS
	9311	light	EIVLTQSPGTLSTLSPGERATLSCRASESVSSNYLAWYQQKPGQAPRLLIYDASSRATGIPDR FSGSGSGTDFTLTISKLEPEDFAVYYCQYARAPDTFAQGTGLEIK
COV2-171	9312	heavy	QVQLVESGGGVVQPGRLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAIVSYDGSNKYYAD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARDPNMVLAYFDYWGQGTITVTVSS
	9313	light	QTVVTQEPSPSVSPGGTITLTCLSGSGSVSTSYPPSWYQQTPGQAPRLTIYSTNTRSSGVPDRFSGSILGNKAALTITGAQADESDYYCVLYMGSGIWFVGGGTGLTVL
COV2-172	9314	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAVYVWRQAPGKGLECVSFISGGGETTDYAD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKSPDATFLWFGEPPGYWGQGTITVTVSS
	9315	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRFSGSSSGTTVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGTGLTVL
COV2-173	9316	heavy	QVQLVESGGGVVQPGRLRLSCAASGFNLSNYAMHWVRQASGKGLEWVSLISYDGSIKYYTD SVKGRFTVSGDNTKNTLYLQMNSLRPDDSALEYCVRGVSGPNSFDMWGQGTITVTVSS
	9317	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRFSGSSSGTTVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGTGLTVL
COV2-174	9318	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMNWRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFTISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTITVTVSS
	9319	light	EIVLTQSPATLSVSPGERVTLSCRASQTVNNNLNLQHKPGQAPRLVIIGTSTRASGVPARFSGSGSGTEFTLTISLQSEDIATYYCQYEWPPITYGQGTGLEIK
COV2-175	9320	heavy	QVQLQQSGPGLVPRPGTSLTLCGVSGGSISSPNWWSVWRQAPGKGLEWIGEVYPTGNTYYNP SLKSRVTISIEESKNEFSLNLSVTAADMGIYYCARGVVGASDFYYYGMDVWGQGTAVTVSS
	9321	light	EIVMTQSPDSTLSLGERATISCKSSQSLYSSNNRDYLAWYQQKAGQPPKLLFYWASTRES GVPDRFGGSGSGTHFTLTINLQPEDVAVYFCQQYFSPPYTFGGGTGLEIK
COV2-176	9322	heavy	QVQLQESGPGLVKPSQTLNCSVSGDSISRSDYHWSWIRQHPGKLEWIGIYINNGDTYYN PSLKSRVTMSVDTSKNEFSLKLTSTVTAADTAVYYCARDGYAGNSEALDYWGQGTITVTVSS
	9323	light	EIVLTQSPASLSLSPGERATLSCRASQSVTNLYLAWYQQRPQAPRLLIYQTSNRATGIPARFSGSGSGTDFTLTISLQPEDFAFYYCQQRSHRPGGITFGGTGLEIK
COV2-177	9324	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFISSNFWMNWRQAPGKGLEWVANIQDQSEKYYVD SVKGRFTISDIAKNSLYLQMNSLRAEDTAVYYCARQHGDDWYFDYWGQGTITVTVSS
	9325	light	DIQMTQSPSSLSASVGRVITITCRASQDINNYLAWYQQKPKGAPKSLIYDASNLETGVPSRFSGSGSGTDFTLTISLQPEDIATYYCQYDNLPLTFGGGTGVKDIK

COV2-178	9326	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIISNFWMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNSLRAEDTAVYYCARQHGDYDWYFDYWGQGTILVTVSS
	9327	light	EIVMTQSPDLSLTSLGERATISCKSSQSLYSSNNRDYLAWYQQKAGQPPLLFYWASTRES GVPDRFGSGSGTHFTLTIIYNLQPEDVAVYFCQQYFSPPYTFGQGTGLEIK
COV2-179	9328	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYHNMNWRQAPGKGLEWVSAISADSTVTTYAD SVRGRFTIISRDNDAKNSLYLQMNSLRAEDTAVYYCARGRARGSDHTGFDSWGQGTILVTVSS
	9329	light	DIVMTQSPSLSVTPGEPASISCRSSQSLHNRNGYNILDWYLQKPGQSPQLLIYLGSNRASG VPDRFGSGSGTDFTLKISRVEAEDVGYYCMQGLQTPPYTFGQGTGLEIK
COV2-180	9330	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIISNFWMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNSLRAEDTAVYYCARQHGDYDWYFDYWGQGTILVTVSS
	9331	light	DIQMTQSPSSLSASVGRVITICRASQSITTYLNWYQQKAGKAPNLLIYAPSNLQSGVPSRF SGSGSGTDFTLTISSSLQPEDFGTYICQQSYSSPFTFGPGTKVDIK
COV2-181	9332	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIISNFWMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNSLRAEDTAVYYCARQHGDYDWYFDYWGQGTILVTVSS
	9333	light	EIVLTQSPATLSVSPGERVTLSCRASQTVNNNLNLQHKPGQAPRLVIIGTSTRASGVPARF SGSGSGTEFTLTITISLQSEDTAVYYCQQYEWPPITYGQGTGLEIK
COV2-182	9334	heavy	QVQLQQSGPGLVLRPSGTLSTLCGVSGGSISSPNWWSWVRQAPGKGLEWIGEVYPTGNTYYNP SLKSRVTISIEESKNEFSLNLSVTAADMGIYYCARGVVGASDFYYGMDVWGQGTAVTVSS
	9335	light	SYELTQPPSVSVSPGQTARIICSGDALPKQAYWYQKPGQAPVLVIFKDSERPSPGIPQRF GSSSGTTLTITISGVQAEDEADYYCQSDSSGTYVVFSGGKTLTVL
COV2-183	9336	heavy	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYWSWIRQPPGKLEYIGYIYSGSTNYNPS LKSRTVISVDTSKNLKLSRVTAADTAVYYCARGFDYWGQGTILVTVSS
	9337	light	EIVLTQSPGTLSTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGTSSRATGIPDR FSGSGSGTDFTLTISRLEPEDFAVYFCQQYGNPWTFGQGTKEIK
COV2-184	9338	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMNWRQAPGKGLEWVANMEEDGSEKYYVD SVKGRFTIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9339	light	EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIIFDASNRATGIPARF SGSGSGTDFTLTISSLEPEDFAVYFCQQRSSWQGITFGGKKEIK
COV2-185	9340	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIISNFWMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNSLRAEDTAVYYCARQHGDYDWYFDYWGQGTILVTVSS
	9341	light	EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIIFDASNRATGIPARF SGSGSGTDFTLTISSLEPEDFAVYFCQQRSSWQGITFGGKKEIK
COV2-186	9342	heavy	QVQLQQSGPGLVLRPSGTLSTLCGVSGGSISSPNWWSWVRQAPGKGLEWIGEVYPTGNTYYNP SLKSRVTISIEESKNEFSLNLSVTAADMGIYYCARGVVGASDFYYGMDVWGQGTAVTVSS
	9343	light	EIVLTQSPATPSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIIFDASNRATGIPARF SGSGSGTDFTLTISSLESEDFGTYICQQYNHWRFTFGQGTKEIK
COV2-187	9344	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMNWRQAPGKGLEWVANMEEDGSEKYYVD SVKGRFTIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9345	light	EIVMTQSPDLSLTSLGERATISCKSSQSLYSSNNRDYLAWYQQKAGQPPLLFYWASTRES GVPDRFGSGSGTHFTLTIIYNLQPEDVAVYFCQQYFSPPYTFGQGTGLEIK
COV2-188	9346	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIISNFWMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNSLRAEDTAVYYCARQHGDYDWYFDYWGQGTILVTVSS
	9347	light	EIVLTQSPGTLSTLSPGERATLSCRASESVSNNYLAWYQQKPGQAPRLLIYDASSRATGIPDR FSGSGSGTDFTLTISKLEPEDFAVYICQQYARAPDTFAQGTGLEIK
COV2-189	9348	heavy	QMQLVQSGAEVKKPGSSVKVSKASGGTFINYNWVRQAPGQRLEYMGGIIPLLGVANYTQ RFQGRVTMTADRSTSTAYMELSLNLAIEDTAVYYCAREYSSSRPLFYTYNYGMDVWGQGTIVT VSS
	9349	light	DIVMTQTPSLSVTPGQPASISCKSSQGLHGDGKTYLYWFLQKAGQPPQLLIYEVSNRFSG VPDRFGSGSGTDFTLKISRVEAEDVGYYCMQSVHLPYTFGQGTGLEIK
COV2-190	9350	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMNWRQAPGKGLEWVANMEEDGSEKYYVD SVKGRFTIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9351	light	SYELTQPPSVSVSPGQTASITCSGDKLGEKYACWYQQKPGQSPVLVIYQDTRKPSGIPERFS GNSNGNTATLTISGTQAVDEADYYCQAWDYTTVIFGGGKTLTVL

COV2-191	9352	heavy	EVQLVESGGGLVQPGGSLTISCAASGLTIRNYWMNWVRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFIIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9353	light	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDR FSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSTYFGQGTKLEIK
COV2-192	9354	heavy	EVQLVESGGGLVQPGGSLTISCAASGLTIRNYWMNWVRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFIIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9355	light	EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYFDASNRATGIPARF SGSGSGTDFTLTISLQPEDFATYYCQQYRSYPRTFGQGTKLEIK
COV2-193	9356	heavy	EVQLVESGGGLVQPGGSLTISCAASGLTIRNYWMNWVRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFIIISRDDAKNSLYLQMNSLRAEDTAVYYCTRDPGPGDFSWGQGTIVTVSS
	9357	light	DIQMTQSPSSLSASVGRVITITCRASQSIITYNWYQQKAGKAPNLLIYAPSNLQSGVPSRF SGSGSGTDFTLTISLQPEDFGTYCQQYSSTPFTFGPGTKVDIK
COV2-194	9358	heavy	QVQLQQSGAEVKRPGSSVKVSCKGDGDTFSTYAITWVRQAPGQGLEWMGRIIPGLDLVDNQ KFQDRLTITADKSTTTAYMELRSLRSEDVAVYYCARGRRYDFLDGQYTSWYFDIWGRGTLVT VSS
	9359	light	NIVMTQSPSLPVPVTPGEPASMSCRSNQSLLYNGNYLDWYLQRPQGSPQLLIFLGSNRASG VPDRFSGSGSGTDFTLKINRVEAEDVGIYYCMQGGQENPPTFGPGTKVEIK
COV2-195	9360	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAVYVVRQAPGKGLECVSFISSGGGETTDYAD SVKGRFTISRDNKNTLYLQMNGLRAEDTAVYYCAKSPDATFLWFGEPPFYWGQGLTVTVSS
	9361	light	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARF SGSGSGTDFTLTISLQSEDFAVYYCQQYNNWRTFGQGTKVEIK
CR3022	9362	heavy	QMQLVQSGTEVKKPGESLKIISCKGSGYGFITYWIGWVRQMPGKGLEWMGIIYPGDSETRYSP SFQGGVTTISADKSIINTAYLQWSSLKASDTAIYYCAGGSGISTPMDVWGQGTITVTVS
	9363	light	SVLYSSINKNYLAWYQQKPGQPPKLLIYWASTRESGVDPDRFSGSGSGTDFTLTISLQAEADV AVYYCQQYSTPYTFGQGTKVEIK
COV2-122	9364	heavy	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGSHYWSWIRPAGKGLEWVGRIYTSGSTNYN PSLERRVTISLGTSKNQFYLDLTSVTAADTAVYYCARDLSGSHYHYGMDVWGQGTISVTVS S
	9365	light	QSVLTQPPSASGTPGQRTVITSCSGSSSNIGSNYVYQHLPGTAPKLLIYRNYQRPSGVDPDR FSGSGSGTSASLAIISLRSEDEGDYYCAVWDDSLSGWVFGGGTKLTVL
COV2-123	9366	heavy	QVQLVESGGGVVQPGSRSLRLSCAASGFTFISYTMHWVRQAPGKGLEWVALISYDGNKYAD SVKGRFTISRDNKNTLYVQMNSLRAEDTALYYCAREGSPEAFDYWGQGLTVTVSS
	9367	light	EIVLTQSPATLSVSPGERVTLSCRASQTVNNNLNWLQHKPGQAPRLVIIGTSTRASGVPARF SGSGSGTEFTLTISLQSEDAIYYCQQYYEWPPITYGQGTRELI
COV2-124	9368	heavy	EVQLVESGGGLVQPGGSRRLSCGASGFTFTNHWSWVRQAPGKGLEWVASIKQDGAEKYYVD YLKGRFTISRDNKNSLYLQMNLSLRVEDTAVYYCARRITMALAGWGWGMDVWGQGTIVRVSS
	9369	light	DIVMTQSPSLPVPVTPGEPASISCRSSRLSRNGYNYLDWYLQRPQGSPQLVIYLGSNRASG VPDRFSGSGSGTDFTLKISRVEAEDVGLYYCMQAMQAPLTFGPGTKVEIK
COV2-125	9370	heavy	QVQLVQSGSELKKPGASVKVSCKTSYFTSYAINWVRQAPGQGLEWIGWININTGNPTYAQ GFTGRVDFSLDTSVSTAYLQIRSLKAEDTAVYYCARDRGIAARRGYYYGMDVWGQGTITVTV SS
	9371	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRF SGSSGTTVTLTISGVQAEDEADYYCQADSSGTYVVFVGGGKTLTVL
COV2-126	9372	heavy	QVQLQQSGAEVKRPGSSVKVSCKGDGDTFSTYAITWVRQAPGQGLEWMGRIIPGLDLVDNQ KFQDRLTITADKSTTTAYMELRSLRSEDVAVYYCARGRRYDFLDGQYTSWYFDIWGRGTLVT VSS
	9373	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRF SGSSGTTVTLTISGVQAEDEADYYCQADSSGTYVVFVGGGKTLTVL
COV2-127	9374	heavy	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYWSWIRQPPGKLEYIGYIYSGSTNYNPS LKSRTVTSVDTSKNQLSLKLSVTAADTAVYYCARGFDYWGQGLTVTVSS
	9375	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERPSPGIPQRF SGSSGTTVTLTISGVQAEDEADYYCQADSSGTYVVFVGGGKTLTVL
	9376	heavy	QVQLQQWAGLLKPSSETLSLTCAVHGGSFSGPYWTWIRQSPSQGLEWIGEIGPRGITYYSPS LESRTVTSADTSRNQFSLRLTSVTAADTAVYYCARGLVIGRSSINFDWSGQGLTVTVSS

COV2-128	9377	light	EIVLTQSPGTLISLSPGERATLSCRASESVSSNYLAWYQQKPGQAPRLLIYDASSRATGIPDR FSGSGSGTDFTLTISKLEPEDFAVYYCQYARAPDTFAQGTRLEIK
COV2-129	9378	heavy	EVQLVEAGGGLVLPKPGSLRLSCAASGFTFSGYAINWVRQAPGKGLEWVSSISGNNNDMYAD SVKGRFTISRDNKSSVFLQMNSLRVEDTAIYYCARDNLALAGEDYWGQGTLLTVSS
	9379	light	EIVMTQSPDSTLVSLGERATISCKSSQSLYSSNNRDYLAWYQQKAGQPPLLFYWASTRES GVPDRFGSGSGTHFTLTIIYNLQPEDVAVYFCQQYFSPPYTFGGQGTKLEIK
COV2-130	9380	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAVYVWRQAPGKGLECVSFISGGGETTDYAD SVKGRFTISRDNKNTLYLQMNSLRVEDTAIYYCAKSPDATFLWFGEPFGYWGQGTLLTVSS
	9381	light	EIVMTQSPATLSVSPGERVTLSRASQSVSSNVAWYQQKPGQAPSLLIYGASTRATGTTPARF SGSGSGTGFTLTITSLQSEDFGVYYCQQYNWRTFGPGTKVEIK
COV2-131	9382	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFVFSYDMNWVRQAPGKGLAWVSVVGDAVTKFYED SVKGRFTISRDNKNTIYLQMNSLRVEDTAIYHCAKSPVSRMRGFFVGLDVGWQGTLLTVSS
	9383	light	EIVMTQSPDSTLVSLGERATISCKSSQSLYSSNNRDYLAWYQQKAGQPPLLFYWASTRES GVPDRFGSGSGTHFTLTIIYNLQPEDVAVYFCQQYFSPPYTFGGQGTKLEIK
COV2-132	9384	heavy	EVQLVESGGGLVLPKPGSLRLSCAASGFTFSSYMNWVRQAPGKGLEWVSSISSTSSYIYAD SVKGRFTISRDNKNSLYLQMNSLRVEDTAIYYCARRAATGTEFYFDYWGQGTLLTVSS
	9385	light	QSVLTQPPSVSAAPGQKVTISCSGSSSNIIGNNYVSWYQQLPGTAPKLLIYDNNKRPSPGIPDR FSGSGSGTSATLTIGITGLTGEADYYCGTWDSSL SAVLFGGGTKLTVL
COV2-133	9386	heavy	QAHVLQSGAEVKKPGSSVKVSCASGGTFNSHAIGWVRQAPGQGLEWMGRIVPIRKTITTYAP QLQGRRLTITADTSTSTLYMELSSLRSEDSARYYCARVILSGRGFDIWGQGSILVAVSS
	9387	light	DIQMTQSPSALAASLGDRVITTCQASHDIGHNINWYQQRPGAPQLLIYDVSNLQTVPSRF SGFGFTNFTFTISGLQSEDIGTYCQQYDSIFGPGTKLEIK
COV2-134	9388	heavy	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAFSWVRQAPGQGLEWMGRITILGITDYAP KFQGRVTITADKSTSTVMEVSSLRSDDTAVYYCARERPRDPSNYYVAYAMDVWGQGSVTVSS
	9389	light	DIQMTQSPSSLSASVGDRTITCRASQSIITTYLNWYQQKAGKAPNLLIYAPSNLQSGVPSRF SGSGSGTDFTLTITSLQPEDFGTYCQQYSSSPFTFGPGTKVDIK
COV2-135	9390	heavy	QVQLQQSGPGLVLRPSGTLSTCGVSGGSISPNWWSWVRQAPGKGLEWIGEVYPTGNTYYNP SLKSRVTISIEESKNEFSLNLSVTAADMGIIYCCARGVVGASDFYYGMDVWGQGTAVTVSS
	9391	light	DIQMTQSPSSLSASVGDRTITCRASETISNFINWYLRQPGKAPQVLIYSAARLQSGVPSRF RASGSGTDFTLTITSLQLEDFGVYYCQQSFNTPTFTFGQGTTRVEIK
COV2-136	9392	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMWVRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFTISRDDAKNSLYLQMNSLRVEDTAIYYCTRDPGPGDFSWGQGTVVTVSS
	9393	light	EIVLTQSPGTLISLSPGERATLSCRASESVSSNYLAWYQQKPGQAPRLLIYDASSRATGIPDR FSGSGSGTDFTLTISKLEPEDFAVYYCQYARAPDTFAQGTRLEIK
COV2-137	9394	heavy	QVQLQQWAGLLKPAETLSLTCAVHGGSFDTSYWSWIRQTPGQGLEWLGVEVNHSGSTNYSPS LKRVAISIDTSKNQVSLRLTSVSAADTAIYYCARGMAVRGRQLYLLGGYDLWGQGTLLTVSS
	9395	light	EVVMTQSPATLSVSPGERATLSCRASQSVYINLAWYQQKPGQAPRLLIYGASTRATGTTPARF SGSGSGTEFTLTITSSLESEDFGVYYCQQYNWRTFGQGTKEIK
COV2-138	9396	heavy	SQLLQESGPGILVKPSETLSLTCTVFSDSYGYWTVIRQPPRGLWIGSVYHSGSTNYNPS LMSRVITISVDTSKQFSLKVTSTGADTAIYFCARGLAGGGYFDAGQGQNLVAVSS
	9397	light	DVQMTQSPSSLSASVGDRTITCRASPGINTYLAWYQQKPGQVDPDLIYGASTLRSGVPSRF SGSGSGTDFTLTITSLQLEDAIYCYQAYVGLGTFGGQGTKEIK
COV2-139	9398	heavy	EVQLVESGGGVVRPGEISLRSLSCVSGGFPFGGYGMSWVRQVPGKGLEWVSGINWSADRRVYAD FVKGRFTISRDPKKSLSLQMDNLRAEDTAIYYCARETSRRDFDFWGQGTLLTVSS
	9399	light	SFVLTQPPSVSVAPGQTARIPCAKNYRGSTVHWYQKRPQAPVLVINSDDDRPSGISERFS GSNSGNTATLTISRVEAGDEADYYCQVWDPSDQALFAGGTLLTVL
COV2-140	9400	heavy	EVQLVDSGGGLVQPGGSLRLSCAASGFTFTSYWMWVRQAPGKGLEWVANIKQDGSEKDYVD SVKGRFTISRDNKNSLYLQMSLRVEDTAIYYCARDLGSGSYHLFDYWGQGTLLTVSS
	9401	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKPKGQAPVLVIFKDSERPSPGIPQRF GSSSGTITVTLTISGVQAEADYYCQADSSGTYVVFGGGKTLTVL

COV2-141	9402	heavy	QVQLVQSGSEELKPGASVKVSCKTSGYTFTSYAINWVRQAPQGGLWIGWININTGNPTYAQ GFTGRVDFSLDTSVSTAYLQIRSLKAEDTAVYYCARDRGIAARRGYYYGMDVWGQGTITVTV SS
	9403	light	DIQMTQSPSSLSASVSGDRVITITCRASQSITTYLNWYQQKAGKAPNLLIYAPSNLQSGVPSRF SGSGSGTDFTLTITSSLPEDFGTYTCQQSYSSPFTFGPGTKVDIK
COV2-142	9404	heavy	EVQLVESGGGVVVRPGEISLRSLSCVSGSFPFGGYGMSWVRQVPGKGLEWVSGINWSADRRVYAD FVKGRFTISRDPKKSLSLQMDNLRAEDTALYYCARETSRRDFDFWGQGTITVTVSS
	9405	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERP SGIPQRFS GSSSGTITVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGKTLTVL
COV2-143	9406	heavy	EVQLVDSGGGLVQPGGSLRLSCAASGFTFTSYWMNWVRQAPGKGLEWVANIKQDGSEKDYVD SVKGRFTISRDNKNSLYLQMNLSRAEDTAVYYCARDLGSGSYHLFDYWGQGTITVTVSS
	9407	light	QSVLTQPPSVSAAPGQKVTISCSGSSSNIGNNYVSWYQQLPGTAPKLLIYDNNKRP SGIPDR FSGSGSGTSATLGITGLTQDEADYYCGTWDNLSAWVFGGKTLTVL
COV2-144	9408	heavy	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWIRQPPGKGLYIGYIYSGSTNYNPS LKSRTVISVDTSKNQLSLKRSVTAADTAVYYCARGFDYWGQGTITVTVSS
	9409	light	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIIFDASNRATGIPARF SGSGSGTDFTLTITSSLEPEDFAVYFCQQRSSWQGITFGGKTKVEIK
COV2-145	9410	heavy	QVQLVQSGSEELKPGASVKISCKTSGYNFTNHPINWVRQAPQGGLWGMWINTGNPTYGQ AFTGRVFSFDTSVGTAYLHISGLQPGDTAFYYCVREDLRLRQVWWRWDFPWGQGTITVTVSS
	9411	light	EIQMTQSPSSLSASVSGDRVITISCRASQSVGGHLNWYQQKPGKAPKVLHAASSLEGVPSRF SGSGSGTDYTLTITNLQPEDFATYFCQQSRNSPATFGGKTKVEMK
COV2-146	9412	heavy	QVQLVESGGGVVQPGRLSLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISYDGSNKYYAD SVKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCARGKLGVGDADFIDWGQGTITVTVSS
	9413	light	DIQMTQSPSSLSASVSGDRVITICQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRF SGSGSGTDFTFTITSSLPEDFIATYYCQQYDNLPLTFGPGTKVDIK
COV2-147	9414	heavy	SQLLQESGPGLVKPSSETLSLTCTVFGDSIYGYWTWIRQPPGRLWIGSVYHSGSTNYNPS LMSRVITISVDTSEKQFSLKVTSVTGADTAVYFCARGLAGGGYFDAWGQGNLVAVSS
	9415	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERP SGIPQRFS GSSSGTITVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGKTLTVL
COV2-148	9416	heavy	QVQLQESGAEVKRP GSVKVSCKGDDTFTSYAITWVRQAPQGGLWMMGRIIPGLDLVDNQ KFQDRLTITADKSTTTAYMELRSLRSED TAVYYCARGRRYDFLDGQYTSWYFDIWRGTLVT VSS
	9417	light	EIVLTQSPATLSVSPGERVTLSCRASQTVNNNLNLQHKPGQAPRLVIIGTSTRASGVPARF SGSGSGTEFTLTITSSLSQSEDAIYYCQQYYEWPPIITYGQGTIRLEI
COV2-149	9418	heavy	EVQLVQSGAEVKRPGATVKRISCKVSGYTFDYYMHVWVRQAPGKGLEWMLVDPEDGETIYAE KFQGRVTITADTSTD TAYMELSSLRSED TAVYYCATVSRWYYYYYGMDVWGQGTITVTVSS
	9419	light	EIVLTQSPGTLISLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDR FSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSYTFGGGKTKLEIK
COV2-150	9420	heavy	QVQLVESGGGVVQPGRLSLSCAASGFNLSNYAMHWVRQASGKGLEWVSLISYDGSIKYYTD SVKGRFTVSGDNSKNTLFLQMNLSLRPDDALYYCVRGGVSGPNSFDMWGQGTITVTVSS
	9421	light	DVVMTQSPSLPVTLGQPASISCRSSQSLVYSDGNTYVNWVQRPQSPRRLIYQVSIASG VPDRFSGSGSCTDFALKISRVEAEDVGIIYCMQGTHTPVTFGQGTKEIK
COV2-151	9422	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFVFSYDMNWVRLAPGKGLAWVSVVGDAVTKFYED SVKGRFTISRDNKNTIYLQMNLSRAEDTAVYHCAKSPVSRMGRFFVGLDVWGQGTITVTVS S
	9423	light	QSALTQPPSASGSPGQSVTISCTGSSNDVGRYNYVSWYQHHPGKAPRLMISEVVKRPSGVDP RFSGSKSGNTASLTVSGLQAEDEADYYCSSYGGNNILLFGGKTLTVL
COV2-152	9424	heavy	QVQLVESGGGVVQPGRLSLSCAASGFTFISYTMHWVRQAPGKGLEWVALISYDGYNKYYAD SVKGRFTISRDNKNTLYVQMNLSRAEDTALYYCAREGSPFAFDYWGQGTITVTVSS
	9425	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAWYQKKPGQAPVLVIFKDSERP SGIPQRFS GSSSGTITVTLTISGVQAEDEADYYCQADSSSGTYVVFSGGKTLTVL
	9426	heavy	EMQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMYWVRQAPGKGLVWVSRIPKPDGTGTSYAD SVRGRFTVSRDNKNTLNLQMNLSRAEDTAVYYCVAYNWNVDFCWGQGTITVTVSA

COV2-153	9427	light	DVTVTQSPSLPVTLGQPASISCRSSQSLVYSDGNTYLNWFQQRPQGSPRRLIYQVSNRDSG VPDRFSGSGSGTDFTLTISRVEAEDVGYYCMQGSYWPFTFGPGTKVDIK
COV2-154	9428	heavy	EVQLVESGGGLVQPGGSLRLSCASGFSYSNYWMWVRQAPGKGLEWVANLRDGSVEHYVD SVRGRFTISRDNKNSLYLQMDSLRAEDTAVYYCARDLSPGGGLGAYYDVFDIWQGGMVTVS S
	9429	light	AIQMTQSPSSLSASLGDRISITCRASQGGIGNELGWYQQKPGKAPRLLIYAGSTLQGGVPPRF SGSGSGTDFTLTISLQAEEDFATYYCLQDYAYPRTFGPGTKVEVK
COV2-155	9430	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFVFSYDMNWVRQAPGKGLAWVSVVGVDVTKFYED SVKGRFTISRDNKNTIYLQMNLRRAEDTAVYHCAKSPVSRMGRFFVGLDVGQGTTVTVS S
	9431	light	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDR FSGSGSGTDFTLTISRLEPEDFAVYYCQYQGSSTFGQGTKEIK
COV2-156	9432	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYAD SVKGRFTISRDNKNTIYLQMNLSRAEDTAVYYCAKDHMVRGAIGFDYWGQGTTLTVSS
	9433	light	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARF SGSGSGTEFTLTISLQSEDFAVYYCQYNNWRTFGQGTKEIK
COV2-157	9434	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIFSNEFMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNLSRAEDTAVYYCARQHGDYDWFYDYGQGTTLTVSS
	9435	light	DIQMTQSPSSVSASVGRVITITCRASQGINSLAWYQQKPGKAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISLQPEDFATYYCQQAHSFPIITFGQGTREIK
COV2-158	9436	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFVFSYDMNWVRQAPGKGLAWVSVVGVDVTKFYED SVKGRFTISRDNKNTIYLQMNLRRAEDTAVYHCAKSPVSRMGRFFVGLDVGQGTTVTVS S
	9437	light	SYELTQPPSVSVSPGQTARIICSGDALPKQAYWYQKPGQAPVLVIFKDSERPSPGIPQRF GSSSGTTVTLTISGVQAEDEADYYCQADSSGYVVFVGGGKLTVL
COV2-159	9438	heavy	QVQLVQSGGGVQVQGRSLRLSCTASGFTFSNYAMHWVRQAPGKGLEWGAVISYDGTITLYED SMRGRFTISRDNSTRDLYLQMNLSRPDDTAVYYCGRDLGGGLDVGQGTTVTVSS
	9439	light	QSALTQARSVSGSPGQSVTVSCTGSSNDVGGHNYVSWYQHSFGKAPKLLIYDVKRPSGVPD RFSGSKSGDTASLTISGLQADDEGDYYCCSYKSTYDYVFGSGTTVSVL
COV2-160	9440	heavy	QVQLVESGGGVQVQGRSLRLSCAASGFTFSIYAIHWVRQAPGKGLEWMAVISYDGNQYYAD SVKGRFTISRDNKNTIYLQMNLSRDTDDTAVYYCARSEGGGYHDAFDIWQGGMVTVSS
	9441	light	QVLVLTQSPSASASLGASVKLTCTLSGHSYIAIWHQQPEKGPRIYMKLNSDGSHNKGDGI PDRFSGSSGAERYLTISLQSEDEADYFCQTWGTGIHVFVGGGKLTVL
COV2-161	9442	heavy	QVQLVESGGGVQVQGRSLRLSCAASGFTFISYTMHWVRQAPGKGLEWVALISYDGNKYAD SVKGRFTISRDNKNTIYLQMNLSRAEDTALYYCAREGSPEAFDYWGQGTTLTVSS
	9443	light	SFELTQPPSLSVSPGQTARITCSGDALSKQFTYWYQQKPGQAPVLVIYKDSERPSPGIPERFS GSSSGTTVTLTISGVQAEDEADYYCQSAHSSGFYRVVFGGGTCLTVL
COV2-162	9444	heavy	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAVYVVRQAPGKGLECVSFIGSGGETTDYAD SVKGRFTISRDNKNTIYLQMNGLRAEDTAVYYCAKSPDATFLWFGEPPGYWGQGTTLTVSS
	9445	light	EIVLTQSPATLSVSPGERVTLSCRASQTVNNNLNWLQHKPGQAPRLVIIGTSTRASGVPARF SGSGSGTEFTLTISLQSEDYATYYCQYEWPPITYGQGTREI
COV2-163	9446	heavy	QVQLVQSGAEVVRPGSSVVKVSCKGDGDTFSTYAITWVRQAPGKGLEWVGRIIPGLDLVDNQ KFQDRLTITADKSTTTAYMELRSLRSEDVAVYYCARGRRYDFLDGQYTSWYFDIWRGTLVT VSS
	9447	light	EIVMTQSPDLSLTVSLGERATISCKSSQSLYSSNNRDYLAHYQQKAGQPKLLIFYWASTRES GVPDRFSGSGSGTHFTLTINYLPEDVAVYFCQYFSPPYTFGQGTKEIK
COV2-164	9448	heavy	EVQLVESGGGLVQPGGSLRLSCAASGFIFSNEFMNWVRQAPGKGLEWVANIQQDGSEKYYVD SVKGRFTISTDLAKNSLYLQMNLSRAEDTAVYYCARQHGDYDWFYDYGQGTTLTVSS
	9449	light	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDR FSGSGSGTDFTLTISRLEPEDFAVYYCQYQGSSTFGQGTKEIK
	9450	heavy	EVQLVESGGGLVQPGGSLRLSCAASGLTIRNYWMNWVRQAPGKGLEWVANMEEDGSEKNYVD SVKGRFTISRDDAKNSLYLQMNLSRAEDTAVYYCTRDPGPGDFSWGQGTTVTVSS

COV2-165	9451	light	SYELTQPPSVSVSPGQTARIICSGDALPKQNAVWYQKKPGQAPVLVIFKDSERP SGIPQRFSGSSSGTTVTLTISGVQAEDEADYYCQSADSSGTYVVFGGGKLTVL
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TABLE 3 - HEAVY CHAIN SEQUENCES

Clone	CDRH1	CDRH2	CDRH3
COV2-166	GNTFPTYD	INTNTGSP	AREGYHYGMDV
	9452	9453	9454
COV2-167	GGTFNSHA	IVPIRKTT	ARVILSGRGFDI
	9455	9456	9457
COV2-168	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9458	5459	9460
COV2-169	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9461	9462	9463
COV2-170	GFTFSSYA	ISGGGETT	AKSPDATFLWFGEPPFGY
	9464	9465	9466
COV2-171	GFTFSSYA	ISYDGSNK	ARDPNPMVLAYFDY
	9467	9468	9469
COV2-172	GFTFSSYA	ISGGGETT	AKSPDATFLWFGEPPFGY
	9470	9471	9472
COV2-173	GFNLSNYA	ISYDGSIK	VRGGVSGPNSFDM
	9473	9474	9475
COV2-174	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9476	9477	9478
COV2-175	GGSISSPNW	VYPTGNT	ARGVVGASDFYYYGMDV
	9479	9480	9481
COV2-176	GDSISRSDYH	IYNNGDT	ARDGYAGNSEALDY
	9482	9483	9484

COV2-177	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9485	9486	9487
COV2-178	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9488	9489	9490
COV2-179	KFTFSTYH	ISADSTVT	ARGRARGSDHTGFDS
	9491	9492	9493
COV2-180	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9494	9495	9496
COV2-181	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9497	9498	9499
COV2-182	GGSISSPNW	VYPTGNT	ARGVVGASDFYYYGMDV
	9500	9501	9502
COV2-183	GGSISSYY	IYYSGST	ARGFDY
	9503	9504	9505
COV2-184	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9506	9507	9508
COV2-185	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9509	9510	9511
COV2-186	GGSISSPNW	VYPTGNT	ARGVVGASDFYYYGMDV
	9512	9513	9514
COV2-187	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9515	9516	9517
COV2-188	GFIFSNEW	IQQDGSEK	ARQHGDYDWYFDY
	9518	9519	9520
COV2-189	GGTFINYA	IIPLLGVA	AREYSSSRPLFYTYNYGMDV
	9521	9522	9523

COV2-190	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9524	9525	9526
COV2-191	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9527	9528	9529
COV2-192	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9530	9531	9532
COV2-193	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9533	9534	9535
COV2-194	GDTFSTYA	IIPGLDLV	ARGRRYDFLDGQYTSWYFDI
	9536	9537	9538
COV2-195	GFTFSSYA	ISGGGETT	AKSPDATFLWFGEPPFGY
	9539	9540	9541
CR3022	GYGFITYW	IYPGDSET	AGGSGISTPMDV
	9542	9543	9544
COV2-122	GGSISSGSHY	IYTSGST	ARDSLSGSYHYHYYGMDV
	9545	9546	9547
COV2-123	GFTFISYT	ISYDGYNK	AREGSPEAFDY
	9548	9549	9550
COV2-124	GFTFTNHW	IKQDGAEK	ARRITMALAGWGWGMDV
	9551	9552	9553
COV2-125	GYTFTSYA	ININTGNP	ARDRGIAARRGYHYYGMDV
	9554	9555	9556
COV2-126	GDTFSTYA	IIPGLDLV	ARGRRYDFLDGQYTSWYFDI
	9557	9558	9559
COV2-127	GGSISSYY	IYYSGST	ARGFDY
	9560	9561	9562

COV2-128	GGSFSGPY	IGPRGIT	ARGLVIGRSSLNFD
	9563	9564	9565
COV2-129	GFTFSGYA	ISGNNNDM	ARDNLALAGEDY
	9566	9567	9568
COV2-130	GFTFSSYA	ISGGGETT	AKSPDATFLWFGEFGY
	9569	9570	9571
COV2-131	GFVFS DYS	VGVDATK	AKSQPVSRMGRFFVGLDV
	9572	9573	9574
COV2-132	GFTFSSYS	ISSTSSYI	ARRRAATGTEFYFDY
	9575	9576	9577
COV2-133	GGTFNSHA	IVPIRKT	ARVILSGRGFDI
	9578	9579	9580
COV2-134	GGTFSSYA	IILILGIT	AREPRDPSSNYVAYAMDV
	9581	9582	9583
COV2-135	GGSISSPNW	VYPTGNT	ARGVVGASDFYYYGMDV
	9584	9585	9586
COV2-136	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9587	9588	9589
COV2-137	GGSF TDSY	VNHSGST	ARGMAVRGRQLYLLGGYDL
	9590	9591	9592
COV2-138	GDSIYGY	VYHSGST	ARLAGGGYFDA
	9593	9594	9595
COV2-139	GFPFGGYG	INWSADRR	ARERTSRRDFDF
	9596	9597	9598
COV2-140	GFTFTSYW	IKQDGSEK	ARDLGSGSYHLFDY
	9599	9600	9601

COV2-141	GYTFTSYA	ININTGNP	ARDRGIAARRGYYYGMDV
	9602	9603	9604
COV2-142	GFPFGGYG	INWSADRR	ARERTSRRDFDF
	9605	9606	9607
COV2-143	GFTFTSYW	IKQDGSEK	ARDLGSGSYHLFDY
	9608	9609	9610
COV2-144	GGSISSYY	IYYSGST	ARGFDY
	9611	9612	9613
COV2-145	GYNFTNHP	INTNTGNP	VREDLRLRQVWWRWFDP
	9614	9615	9616
COV2-146	GFTFSSYA	ISYDGSNK	ARGKLGIVGDAFDI
	9617	9618	9619
COV2-147	GDSIYGYY	VYHSGST	ARGLAGGGYFDA
	9620	9621	9622
COV2-148	GDTFSTYA	IIPGLDLV	ARGRRYDFLDGQYTSWYFDI
	9623	9624	9625
COV2-149	GYTFTDYY	VPEDGET	ATVSRWYYYYGMDV
	9626	9627	9628
COV2-150	GFNLSNYA	ISYDGSIK	VRGGVSGPNSFDM
	9629	9630	9631
COV2-151	GFVFS DYS	VGVDVATK	AKSQPVSRMGRFFVGLDV
	9632	9633	9634
COV2-152	GFTFISYT	ISYDGYNK	AREGSPEAFDY
	9635	9636	9637
COV2-153	GFTFSDYY	IKPDGTGT	VAYNWN YDFC
	9638	9639	9640

COV2-154	GFSYSNYW	LRRDGSVE	ARDLSPGGGLGAYYDVFDI
	9641	9642	9643
COV2-155	GFVFSNYS	VGVDVATK	AKSQPVSRMGRFFVGLDV
	9644	9645	9646
COV2-156	GFTFSSYA	ISGSGGST	AKDQHMVRGAIGFDY
	9647	9648	9649
COV2-157	GFIFSNFW	IQQDGSEK	ARQHGDYDWYFDY
	9650	9651	9652
COV2-158	GFVFSNYS	VGVDVATK	AKSQPVSRMGRFFVGLDV
	9653	9654	9655
COV2-159	GFTFSNYA	ISYDGTIT	GRDLSGGGLDV
	9656	9657	9658
COV2-160	GFTFSIYA	ISYDGNNQ	ARSEGGGYHDAFDI
	9659	9660	9661
COV2-161	GFTFISYT	ISYDGYNK	AREGSPEAFDY
	9662	9663	9664
COV2-162	GFTFSSYA	ISGGGETT	AKSPDATFLWFGEPPGY
	9665	9666	9667
COV2-163	GDTFSTYA	IIPGLDLV	ARGRRYDFLDGQYTSWYFDI
	9668	9669	9670
COV2-164	GFIFSNFW	IQQDGSEK	ARQHGDYDWYFDY
	9671	9672	9673
COV2-165	GLTIRNYW	MEEDGSEK	TRDPGPGDFS
	9674	9675	9676

TABLE 4 - LIGHT CHAIN SEQUENCES

Clone	CDRL1	CDRL2	CDRL3
COV2-166	QDINNY	SAS	QQYRSYPRT
	9677	9678	9679
COV2-167	ALPKQN	KDS	QSADSSGTYVV
	9680	9681	9682
COV2-168	ALPKQN	KDS	QSADSSGTYVV
	9683	9684	9685
COV2-169	QDINNY	SAS	QQYRSYPRT
	9686	9687	9688
COV2-170	ESVSSNY	DAS	QQYARAPDT
	9689	9690	9691
COV2-171	SGSVSTSY	STN	VLYMGSGIWV
	9692	9693	9694
COV2-172	ALPKQN	KDS	QSADSSGTYVV
	9695	9696	9697
COV2-173	ALPKQN	KDS	QSADSSGTYVV
	9698	9699	9700
COV2-174	QTVNNN	GTS	QQYYEWPPIIT
	9701	9702	9703
COV2-175	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9704	9705	9706
COV2-176	QSVTNY	QTS	QQRSHRPGGIT
	9707	9708	9709
COV2-177	QDISNY	DAS	QQYDNLPLT
	9710	9711	9712

COV2-178	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9713	9714	9715
COV2-179	QSLLHRNGYNI	LGS	MQGLQTPPYT
	9716	9717	9718
COV2-180	QSITTY	APS	QQSYSSPFT
	9719	9720	9721
COV2-181	QTVNNN	GTS	QQYYEWPPIT
	9722	9723	9724
COV2-182	ALPKQN	KDS	QSADSSGTYVV
	9725	9726	9727
COV2-183	QSVSSSY	GTS	QQYGNSEWT
	9728	9729	9730
COV2-184	QSVSSY	DAS	QQRSSWQGIT
	9731	9732	9733
COV2-185	QSVSSY	DAS	QQRSSWQGIT
	9734	9735	9736
COV2-186	QSVSSY	DAS	QQYNHWRT
	9737	9738	9739
COV2-187	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9740	9741	9742
COV2-188	ESVSSNY	DAS	QQYARAPDT
	9743	9744	9745
COV2-189	QGLLHGDGKTY	EVS	MQSVHLPYT
	9746	9747	9748
COV2-190	KLGEKY	QDT	QAWDYTTVI
	9749	9750	9751

COV2-191	QSVSSSY	GAS	QQYGSSYT
	9752	9753	9754
COV2-192	QSVSSY	DAS	QQYRSYPRT
	9755	9756	9757
COV2-193	QSITTY	APS	QQSYSSPFT
	9758	9759	9760
COV2-194	QSLLYGNGYNY	LGS	MQGQENPPT
	9761	9762	9763
COV2-195	QSVSSN	GAS	QQYNNWRT
	9764	9765	9766
CR3022	SVLYSSINKNY	WAS	QQYYSTPYT
	9767	9768	9769
COV2-122	SSNIGSNY	RNY	AVWDDSLSGWV
	9770	9771	9772
COV2-123	QTVNNN	GTS	QQYYEWPPIT
	9773	9774	9775
COV2-124	RSLLSRNGYNY	LGS	MQAMQAPLT
	9776	9777	9778
COV2-125	ALPKQN	KDS	QSADSSGTYVV
	9779	9780	9781
COV2-126	ALPKQN	KDS	QSADSSGTYVV
	9782	9783	9784
COV2-127	ALPKQN	KDS	QSADSSGTYVV
	9785	9786	9787
COV2-128	ESVSSNY	DAS	QQYARAPDT
	9788	9789	9790

COV2-129	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9791	9792	9793
COV2-130	QSVSSN	GAS	QQYNNWRFT
	9794	9795	9796
COV2-131	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9797	9798	9799
COV2-132	SSNIGNNY	DNN	GTWDSLSAVL
	9800	9801	9802
COV2-133	HDIGHN	DVS	QQYDSI
	9803	9804	9805
COV2-134	QSITTY	APS	QQSYSSPFT
	9806	9807	9808
COV2-135	ETISNF	SAA	QQSFNTPT
	9809	9810	9811
COV2-136	ESVSSNY	DAS	QQYARAPDT
	9812	9813	9814
COV2-137	QSVYIN	GAS	QQYNHWRT
	9815	9816	9817
COV2-138	PGINTY	GAS	QAYYVGLGT
	9818	9819	9820
COV2-139	YRGSQT	SDD	QVWDPSSDQAL
	9821	9822	9823
COV2-140	ALPKQN	KDS	QSADSSGTYVV
	9824	9825	9826
COV2-141	QSITTY	APS	QQSYSSPFT
	9827	9828	9829

COV2-142	ALPKQN	KDS	QSADSSGTYVV
	9830	9831	9832
COV2-143	SSNIGNNY	DNN	GTWDNSLSAWV
	9833	9834	9835
COV2-144	QSVSSY	DAS	QQRSSWQGIT
	9836	9837	9838
COV2-145	QSVGGH	AAS	QQRNSPAT
	9839	9840	9841
COV2-146	QDISNY	DAS	QQYDNLPLT
	9842	9843	9844
COV2-147	ALPKQN	KDS	QSADSSGTYVV
	9845	9846	9847
COV2-148	QTVNNN	GTS	QQYYEWPPIT
	9848	9849	9850
COV2-149	QSVSSSY	GAS	QQYGSSYT
	9851	9852	9853
COV2-150	QSLVYSDGNTY	QVS	MQGTHWPVT
	9854	9855	9856
COV2-151	SNDVGGRYNY	EVV	SSYGNNILL
	9857	9858	9859
COV2-152	ALPKQN	KDS	QSADSSGTYVV
	9860	9861	9862
COV2-153	QSLVYSDGNTY	QVS	MQGSYWPFT
	9863	9864	9865
COV2-154	QGIGNE	AGS	LQDYAYPRT
	9866	9867	9868

COV2-155	QSVSSSY	GAS	QQYGSSYT
	9869	9870	9871
COV2-156	QSVSSN	GAS	QQYNNWRT
	9872	9873	9874
COV2-157	QGINSW	AAS	QQAHSFPIT
	9875	9876	9877
COV2-158	ALPKQN	KDS	QSADSSGTYVV
	9878	9879	9880
COV2-159	SNDVGGHNY	DVT	CSYKSTYDYV
	9881	9882	9883
COV2-160	SGHSSYA	LNSDGSH	QTWGTGIHV
	9884	9885	9886
COV2-161	ALSKQF	KDS	QSAHSSGFYRVV
	9887	9888	9889
COV2-162	QTVNNN	GTS	QQYYEWPPIT
	9890	9891	9892
COV2-163	QSLLYSSNNRDY	WAS	QQYFSPPYT
	9893	9894	9895
COV2-164	QSVSSSY	GAS	QQYGSSYT
	9896	9897	9898
COV2-165	ALPKQN	KDS	QSADSSGTYVV
	9899	9900	9901

* * * * *

5 All of the compositions and methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this disclosure have been described in terms of preferred
embodiments, it will be apparent to those of skill in the art that variations may be applied to
the compositions and methods and in the steps or in the sequence of steps of the method
described herein without departing from the concept, spirit and scope of the disclosure. More
specifically, it will be apparent that certain agents which are both chemically and
physiologically related may be substituted for the agents described herein while the same or
10 similar results would be achieved. All such similar substitutes and modifications apparent to
those skilled in the art are deemed to be within the spirit, scope and concept of the disclosure
as defined by the appended claims.

VII. REFERENCES

The following references, to the extent that they provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference.

U.S. Patent 3,817,837

U.S. Patent 3,850,752

U.S. Patent 3,939,350

U.S. Patent 3,996,345

U.S. Patent 4,196,265

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U.S. Patent 4,366,241

U.S. Patent 4,472,509

U.S. Patent 4,554,101

U.S. Patent 4,680,338

U.S. Patent 4,816,567

U.S. Patent 4,867,973

U.S. Patent 4,938,948

U.S. Patent 5,021,236

U.S. Patent 5,141,648

U.S. Patent 5,196,066

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