

ANTI-RESPIRATORY SYNCYTIAL VIRUS ANTIBODIES AND USES THEREOF**CROSS-REFERENCE TO RELATED APPLICATION**

[0001] This application claims priority to U.S. Provisional Application No. 63/598,807, filed November 14, 2023, which is incorporated by reference in its entirety.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] This application contains a Sequence Listing which is submitted electronically via Patent Center. The contents of the electronic Sequence Listing (SPC6267WOPCT1SequenceListing.xml; Size: 189 KB; and Date of Creation: November 8, 2024) is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0003] The present disclosure generally relates to anti-Respiratory Syncytial Virus (RSV) antibodies and functional fragments thereof, nucleic acid sequences encoding such antibodies, and methods and reagents for their production and uses.

BACKGROUND OF THE INVENTION

[0004] Respiratory Syncytial Virus (RSV) is a common cold virus belonging to the family of paramyxovirus. RSV is virulent, easily transmissible, and infects both children and adults. Two subtypes of RSV have been identified: subtype A and subtype B. RSV has two major surface glycoproteins, the fusion protein (F protein) and the attachment protein (G protein). The F protein of RSV is a viral membrane protein and responsible for fusion of the virion with a host cell after attachment. In addition, infection of neighboring cells through the formation of syncytia is promoted by the F protein and its function is thought to depend on the original oligomeric structure of the protein. The G protein is a 89 kD protein which is also known as the attachment protein. The G protein differs considerably between the two RSV subtypes, whereas the F protein is more conserved as, for instance, only approximately 53% homology is present within a G protein from subtypes A and B.

[0005] Although both RSV F and G proteins have been shown to induce protective neutralizing antibody responses, RSV F protein is instrumental in infection and is the target for

the majority of neutralizing activity in human serum (Magro, M., et al., *Proc Natl Acad Sci USA* 109, 3089-3094 (2012); Johnson, S., et al., *J Infect Dis* 176, 1215-1224 (1997); Beeler, J.A., et al., *J Virol* 63, 2941-2950 (1989); Karron, R.A., *Proc Natl Acad Sci USA* 94, 13961-13966 (1997); Ngwuta, J.O., *Sci Transl Med* 7, 309ra162 (2015)). RSV F protein is also the target of the monoclonal antibody palivizumab, which is used to passively protect high-risk infants from severe disease (T. I.-R. S. Group, *Pediatrics* 102, 531-537 (1998)).

[0006] The mature RSV F glycoprotein initially exists in a metastable prefusion conformation (preF) (McLellan, J.S., *Science* 340, 1113-1117 (2013)), before undergoing a conformational change that leads to insertion of the hydrophobic fusion peptide into the host-cell membrane. Subsequent refolding of the F protein into a stable, elongated postfusion conformation (postF) (McLellan, J.S., *J Virol* 85, 7788-7796 (2011); Swanson, K.A., *Proc Natl Acad Sci USA* 108, 9619-9624 (2011)) results in fusion of the viral and host-cell membranes. Due to its inherent instability, the preF protein has the propensity to prematurely trigger into postF, both in solution and on the viral surface (Liljeroos, L., *Proc Natl Acad Sci USA* 110, 11133-11138 (2013)). Recently, stabilization of preF has been achieved by protein engineering (Krarup, A., *Nat Commun* 6, 8143 (2015); McLellan, J.S., *Science* 342, 592-598 (2013)), and stabilized preF has been shown to induce higher titers of neutralizing antibodies than postF in animal models (McLellan, J.S., *Science* 342, 592-598 (2013)).

[0007] Despite the advances in RSV research, treatment options for established RSV disease are limited. Severe forms of the disease of the lower respiratory tract often require considerable supportive care, including administration of humidified oxygen and respiratory assistance (Fields et al., eds, 1990, *Fields Virology*, 2nd ed., Vol. 1, Raven Press, New York at pages 1045-1072).

[0008] Ribavirin, which is the only drug approved for treatment of infection, has been shown to be effective in the treatment of pneumonia and bronchiolitis associated with RSV infection, and has been shown to modify the course of severe RSV disease in immunocompetent children (Smith et al., *New Engl. J. Med.* 325:24-29 (1991)). The use of ribavirin is limited due to concerns surrounding its potential risk to pregnant women who may be exposed to the aerosolized drug while it is being administered in a hospital environment.

[0009] While commercially available vaccines have been developed, Arexvy (GlaxoSmithKline; Middlesex, United Kingdom) for the elderly, and Abrysvo (Pfizer; New

York, NY) for maternal immunization, several vaccine candidates have been abandoned and others are under development (Murphy et al., *Virus Res.* 32: 13-36 (1994)). The development of a vaccine has proven to be challenging. In particular, immunization may be required in the immediate neonatal period since the peak incidence of lower respiratory tract disease occurs at 2-5 months of age. However, it is known that the neonatal immune response is immature at that time. Plus, the infant at that point in time still has high titers of maternally acquired RSV antibody, which might reduce vaccine immunogenicity (Murphy et al., *J. Virol.* 62:3907-3910 (1988); and Murphy et al., *Vaccine* 9:185-189 (1991)).

[0010] Currently, an approved approach to prophylaxis of RSV disease is passive immunization. For example, the humanized antibody, palivizumab (SYNAGIS®), which is specific for an epitope on the F protein, is approved for intramuscular administration to pediatric patients for prevention of serious lower respiratory tract disease caused by RSV at recommended monthly doses of 15 mg/kg of body weight throughout the RSV season (November through April in the northern hemisphere). SYNAGIS® is a composite of human (95%) and murine (5%) antibody sequences. (Johnson et al., *J. Infect. Diseases* 176:1215-1224 (1997) and U.S. Pat. No. 5,824,307).

[0011] Although SYNAGIS® has been successfully used for the prevention of RSV infection in pediatric patients, multiple intramuscular doses of 15 mg/kg of SYNAGIS® are required to achieve a prophylactic effect. The necessity for the administration of multiple intramuscular doses of antibody requires repeated visits to the doctor's office, which is not only inconvenient for the patient but can also result in missed doses.

[0012] Efforts were made to improve on the therapeutic profile of an anti-RSV-F antibody, and this led to the identification and development of motavizumab, also referred to as NUMAX™. However, clinical testing revealed that certain of the patients being administered motavizumab were having severe hypersensitivity reactions. Further development of this humanized anti-RSV-F antibody was then discontinued.

[0013] Other antibodies to RSV-F protein have been described and can be found in U.S. Pat. Nos. 6,656,467; 5,824,307, 7,786,273; 7,670,600; 7,083,784; 6,818,216; 7,700,735; 7,553,489; 7,323,172; 7,229,619; 7,425,618; 7,740,851; 7,658,921; 7,704,505; 7,635,568; 6,855,493; 6,565,849; 7,582,297; 7,208,162; 7,700,720; 6,413,771; 5,811,524; 6,537,809; 5,762,905; 7,070,786; 7,364,742; 7,879,329; 7,488,477; 7,867,497 ; 5,534,411 6,835,372; 7,482,024;

7,691,603; 8,562,996; 8,568,726; 9,447,173; US20100015596; WO2009088159A1; and WO2014159822. To date, SYNAGIS® and BEYFORTUS® (MedImmune LLC; Gaithersburg, MD) have been approved by a regulatory agency and CLESROVIMAB® (Merck; Rahway, NJ) is currently in phase 3 clinical trials for use in preventing an RSV infection.

[0014] As such, there remains a need for the provision of highly specific, high affinity, and highly potent anti-RSV antibodies and antigen-binding fragments thereof that can be used to treat and/or neutralize at least one, but preferably both, of subtype A and subtype B RSV viral strains, or at least one symptom associated with subtype A and subtype B RSV viral strains.

SUMMARY OF THE INVENTION

[0015] Provided herein are isolated or recombinant anti-Respiratory Syncytial Virus (RSV) F protein (F) antibody or antigen binding fragments thereof that specifically binds to a Respiratory Syncytial Virus (RSV) F protein (F). The anti-RSV F antibody or antigen binding fragment thereof comprises a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs:1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs:19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs:27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs:35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs:43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs:51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs:59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs:67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs:75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs:83, 84, 85, 86, 87, and 88, respectively.

[0016] In certain embodiments, the anti-RSV F antibody or antigen binding fragment thereof comprises a V_H having an amino acid sequence at least 90% identical to SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89, or a V_L having an amino acid sequence at least 90% identical to SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

[0017] The anti-RSV F antibody or antigen binding fragment thereof can, for example, comprise (1) a V_H having the amino acid sequence of SEQ ID NO:7, and a V_L having the amino acid sequence of SEQ ID NO:8; (2) a V_H having the amino acid sequence of SEQ ID NO:25, and a V_L having the amino acid sequence of SEQ ID NO:26; (3) a V_H having the amino acid

sequence of SEQ ID NO:33, and a V_L having the amino acid sequence of SEQ ID NO:34; (4) a V_H having the amino acid sequence of SEQ ID NO:41, and a V_L having the amino acid sequence of SEQ ID NO:42; (5) a V_H having the amino acid sequence of SEQ ID NO:49, and a V_L having the amino acid sequence of SEQ ID NO:50; (6) a V_H having the amino acid sequence of SEQ ID NO:57, and a V_L having the amino acid sequence of SEQ ID NO:58; (7) a V_H having the amino acid sequence of SEQ ID NO:65, and a V_L having the amino acid sequence of SEQ ID NO:66; (8) a V_H having the amino acid sequence of SEQ ID NO:73, and a V_L having the amino acid sequence of SEQ ID NO:74; (9) a V_H having the amino acid sequence of SEQ ID NO:81, and a V_L having the amino acid sequence of SEQ ID NO:82; or (10) a V_H having the amino acid sequence of SEQ ID NO:89, and a V_L having the amino acid sequence of SEQ ID NO:90.

[0018] In certain embodiments, the antibody or antigen binding fragment comprises an antigen binding fragment comprising a heavy chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99. The antibody or antigen binding fragment can, for example, comprise the antigen binding fragment comprising the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99.

[0019] In certain embodiments, the antibody or antigen binding fragment comprises an antigen binding fragment comprising a light chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108. The antibody or antigen binding fragment can, for example, comprise the antigen binding fragment comprising the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108.

[0020] In certain embodiments, the antibody or antigen binding fragment comprises the antigen binding fragment comprising (1) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13; (2) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:91 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:100; (3) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:92 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:101; (4) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:93 and the light chain polypeptide sequence having the amino acid

sequence of SEQ ID NO:102; (5) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:94 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:103; (6) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:95 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:104; (7) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:96 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:105; (8) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:97 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:106; (9) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:98 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:107; or (10) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:99 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:108.

[0021] In certain embodiments, the antibody or antigen binding fragment comprises the heavy chain polypeptide having the amino acid sequence selected from the group consisting of (1) SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:15; (2) SEQ ID NO:91, SEQ ID NO:109, or SEQ ID NO:118; (3) SEQ ID NO:92, SEQ ID NO:110, or SEQ ID NO:119; (4) SEQ ID NO:93, SEQ ID NO:111, or SEQ ID NO:120; (5) SEQ ID NO:94, SEQ ID NO:112, or SEQ ID NO:121; (6) SEQ ID NO:95, SEQ ID NO:113, or SEQ ID NO:122; (7) SEQ ID NO:96, SEQ ID NO:114, or SEQ ID NO:123; (8) SEQ ID NO:97, SEQ ID NO:115, or SEQ ID NO:124; (9) SEQ ID NO:98, SEQ ID NO:116, or SEQ ID NO:125; or (10) SEQ ID NO:99, SEQ ID NO:117, or SEQ ID NO:126. In certain embodiments, the antibody or antigen binding fragment thereof comprises the light chain polypeptide having the amino acid sequence of SEQ ID NO: 10, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, or SEQ ID NO:108. In certain embodiments, the antibody or antigen binding fragment thereof comprises the heavy chain polypeptide and the light chain polypeptide, respectively, selected from: (1) SEQ ID NO:15 and SEQ ID NO: 10, SEQ ID NO: 9 and SEQ ID NO: 10, or SEQ ID NO: 11 and SEQ ID NO: 10; (2) SEQ ID NO:91 and SEQ ID NO:100, SEQ ID NO:109 and SEQ ID NO:100, SEQ ID NO:118 and SEQ ID NO:100; (3) SEQ ID NO:92 and SEQ ID NO:101, SEQ ID NO:110 and SEQ ID NO:101, or SEQ ID NO:119 and SEQ ID NO:101; (4) SEQ ID NO:93 and SEQ ID NO:102, SEQ ID

NO:111 and SEQ ID NO:102, or SEQ ID NO:120 and SEQ ID NO:102; (5) SEQ ID NO:94 and SEQ ID NO:103, SEQ ID NO:112 and SEQ ID NO:103, or SEQ ID NO:121 and SEQ ID NO:103; (6) SEQ ID NO:95 and SEQ ID NO:104, SEQ ID NO:113 and SEQ ID NO:104, or SEQ ID NO:122 and SEQ ID NO:104; (7) SEQ ID NO:96 and SEQ ID NO:105, SEQ ID NO:114 and SEQ ID NO:105, or SEQ ID NO:123 and SEQ ID NO:105; (8) SEQ ID NO:97 and SEQ ID NO:106, SEQ ID NO:115 and SEQ ID NO:106, or SEQ ID NO:124 and SEQ ID NO:106; (9) SEQ ID NO:98 and SEQ ID NO:107, SEQ ID NO:116 and SEQ ID NO:107, or SEQ ID NO:125 and SEQ ID NO:107; or (10) SEQ ID NO:99 and SEQ ID NO:108, SEQ ID NO:117 and SEQ ID NO:108, or SEQ ID NO:126 and SEQ ID NO:108.

[0022] In certain embodiments, the antibody or antigen binding fragment thereof is capable of neutralizing or blocking RSV-F activity by inhibition of at least one biological activity of RSV-F. In certain embodiments, the antibody or antigen binding fragment thereof is capable of binding to the PreF conformation of RSV-F with a higher binding affinity relative to the PostF conformation of RSV-F.

[0023] In certain embodiments, the antibody or antigen binding fragment is a human antibody, is a humanized antibody, is a chimeric antibody, or is a bispecific or multi-specific antibody. The antibody or antigen binding fragment can, for example, be a human antibody.

[0024] In certain embodiments, the antibody or antigen binding fragment is conjugated to polyethylene glycol (PEG) or to a therapeutic agent or to a diagnostic agent.

[0025] Also provided are isolated nucleic acid molecules comprising a nucleic acid sequence encoding the anti-RSV F antibody or antigen-binding fragment thereof according to the invention.

[0026] Also provided are expression vectors comprising the isolated nucleic acid sequences according to the invention.

[0027] Also provided are host cells comprising the expression vectors according to the invention.

[0028] Also provided are methods of preparing the anti-RSV F antibody or antigen-binding fragment thereof. The methods comprise culturing the host cells of the invention under conditions to produce the anti-RSV F antibody or antigen-binding fragment thereof and recovering the anti-RSV F antibody or antigen-binding fragment thereof from the cell or cell culture.

[0029] Also provided are pharmaceutical compositions comprising one or more of the anti-RSV F antibodies or antigen-binding fragments thereof according to the invention, and a pharmaceutically acceptable carrier and/or excipient. Also provided are pharmaceutical compositions comprising one or more nucleic acid sequences according to the invention, or one or more the expression vectors according to the invention, and a pharmaceutically acceptable carrier and/or excipient.

[0030] Also provided are methods of inhibiting at least one biological activity of RSV-F. The methods comprise administering to a subject in need thereof or suspected of being in need thereof: (a) one or more antibodies or antigen-binding fragments thereof according to the invention; (b) the nucleic acid molecule according to the invention; (c) the expression vector according to the invention; (d) the host cell according to the invention; or (e) a pharmaceutical composition according to the invention. In certain embodiments, the subject is in need of treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection. In certain embodiments, the method reduces lung viral titers in the subject. In certain embodiments, any one of (a)-(e) are administered in a therapeutically effective amount.

[0031] Also provided are uses of one or more of the anti-RSV F antibodies or antigen-binding fragments thereof provided herein in the manufacture of a medicament for inhibiting at least one biological activity of RSV-F in a subject.

[0032] Also provided are uses of one or more of the anti-RSV F antibodies or antigen-binding fragments thereof provided herein in the manufacture of a medicament for treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection in a subject.

[0033] Other aspects, features and advantages of the invention will be apparent from the following disclosure, including the detailed description of the invention and its preferred embodiments and the appended claims.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

[0034] FIG. 1 presents a graphical representation of an *in vitro* antiviral activity of RSV antibody 1 analyzed in a 3-day neutralization assay using 25 RSV A and 18 RSV B viruses, four of which (17-058221, MEP-OUT-13-D1, MEP-OUT-01-D1 and 18-002094) contain the F

mutations I206M and Q209R, in accordance with Example 6. In FIG. 1, IC₅₀ denotes 50% inhibitory concentration; and RSV denotes respiratory syncytial virus.

[0035] FIGs. 2A-2C present graphical representations of data related to the prophylactic efficacy of RSV antibody 1 non-YTE in cotton rat models of RSV infection in accordance with Example 7. FIG. 2A presents the lung viral titers determined by a plaque assay on Day 4 post infection with RSV A Long. FIG. 2B presents the lung viral titers determined by plaque assay on Day 4 post infection with RSV B9320. FIG. 2C presents the lung viral titers determined by plaque assay on Day 4 post infection with RSV B 18537. In FIGs. 2A-2C, IM denotes intramuscular; RSV denotes respiratory syncytial virus; SD denotes standard deviation; error bars indicate mean values with SD (n=5-6); the dotted line indicates the lower limit of detection; and the asterisk indicates statistically significant difference (alpha-level 0.05) relative to vehicle control based on Tobit regression with Bonferroni multiplicity correction.

[0036] FIGs. 3A-3C present graphical representations of the correlations between serum concentration of RSV antibody 1 non-YTE and the relative reduction in log lung viral titer on Day 4 post infection in RSV-infected cotton rats in accordance with Example 8. FIG. 3A presents results related to RSV A Long. FIG. 3B presents results related to RSV B 9320. FIG. 3C presents results related to RSV B 18537. In FIG. 3A-FIG. 3C: EC₉₀, 90% effective concentration; RSV, respiratory syncytial virus.

[0037] FIGs. 4A-4B present graphical representations of the activation of Jurkat/NFAT luc effector cells expressing FcγRIIa (FIG. 4A) or FcγRIIIa (FIG. 4B) by RSV antibody 1 Fc variants bound to RSV-infected A549 target cells in accordance with Example 9. In FIGs. 4A-4B: Fc denotes fragment crystallizable; FcγR denotes Fc gamma receptor; LALA denotes L234A/L235A; RSV denotes respiratory syncytial virus; mAb denotes monoclonal antibody; RLU denotes relative light units; SD denotes standard deviation; and YTE denotes M252Y/S254T/T256E.

[0038] FIGs. 5A-5C present graphical representations of the correlation between serum concentration of RSV antibody 1 (FIG. 5A), RSV antibody 1 non-YTE (FIG. 5B), and RSV antibody 1 non-YTE LALA (FIG. 5C), and the relative log lung viral titer reduction on Day 4 post infection in RSV-A2-infected BALB/c mice in accordance with Example 9. Referring to FIGs. 5A-5C: EC₉₀ denotes 90% effective concentration; LALA denotes L234A/L235A; RSV denotes respiratory syncytial virus; mAb denotes monoclonal antibody; RSV denotes respiratory

syncytial virus; YTE denotes M252Y/S254T/T256E; and the dotted line in each graph indicates the EC₉₀ for viral reduction.

[0039] FIG. 6 presents a graphical representation of PK fittings of RSV antibody 1 (n=4) and nirsevimab (n=2) dosed 5 mg/kg IV in cynomolgus monkeys in accordance with Example 11. Referring to FIG. 5: IV, intravenous; PK, pharmacokinetics. Further referring to FIG. 5: study data points are in solid symbols and the model fitting is represented by a solid line.

DETAILED DESCRIPTION OF THE INVENTION

[0040] Various publications, articles and patents are cited or described in the background and throughout the specification; each of these references is herein incorporated by reference in its entirety. Discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is for the purpose of providing context for the invention. Such discussion is not an admission that any or all of these matters form part of the prior art with respect to any inventions disclosed or claimed.

[0041] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this invention pertains. Otherwise, certain terms used herein have the meanings as set in the specification. All patents, published patent applications, and publications cited herein are incorporated by reference as if set forth fully herein.

[0042] It must be noted that as used herein and in the appended claims, the singular forms “a,” “an,” and “the” include plural reference unless the context clearly dictates otherwise.

[0043] Unless otherwise stated, any numerical value, such as a % sequence identity or a % sequence identity range described herein, are to be understood as being modified in all instances by the term “about.” Thus, a numerical value typically includes $\pm 10\%$ of the recited value. For example, a dosage of 10 mg includes 9 mg to 11 mg. As used herein, the use of a numerical range expressly includes all possible subranges, all individual numerical values within that range, including integers within such ranges and fractions of the values unless the context clearly indicates otherwise.

[0044] As used herein, the conjunctive term “and/or” between multiple recited elements is understood as encompassing both individual and combined options. For instance, where two elements are conjoined by “and/or,” a first option refers to the applicability of the first element

without the second. A second option refers to the applicability of the second element without the first. A third option refers to the applicability of the first and second elements together. Any one of these options is understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or” as used herein. Concurrent applicability of more than one of the options is also understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or.”

[0045] Unless otherwise indicated, the term “at least” preceding a series of elements is to be understood to refer to every element in the series. Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the invention.

[0046] Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise,” and variations such as “comprises” and “comprising,” will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integer or step. When used herein the term “comprising” can be substituted with the term “containing” or “including” or sometimes when used herein with the term “having.”

[0047] When used herein “consisting of” excludes any element, step, or ingredient not specified in the claim element. When used herein, “consisting essentially of” does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim. Any of the aforementioned terms of “comprising,” “containing,” “including,” and “having,” whenever used herein in the context of an aspect or embodiment of the invention can be replaced with the term “consisting of” or “consisting essentially of” to vary scopes of the disclosure.

[0048] “Polynucleotide” or “nucleic acid,” as used interchangeably herein, refers to polymers of nucleotides of any length and includes DNA and RNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a polymer by DNA or RNA polymerase or by a synthetic reaction. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and their analogs. “Oligonucleotide,” as used herein, refers to short, generally single-stranded, synthetic polynucleotides that are generally, but not necessarily, fewer than about 200 nucleotides in length. The terms “oligonucleotide” and “polynucleotide” are not mutually exclusive. The description above for polynucleotides is equally and fully applicable to

oligonucleotides. Unless specified otherwise, the left-hand end of any single-stranded polynucleotide sequence disclosed herein is the 5' end; the left-hand direction of double-stranded polynucleotide sequences is referred to as the 5' direction. The direction of 5' to 3' addition of nascent RNA transcripts is referred to as the transcription direction; sequence regions on the DNA strand having the same sequence as the RNA transcript that are 5' to the 5' end of the RNA transcript are referred to as "upstream sequences"; sequence regions on the DNA strand having the same sequence as the RNA transcript that are 3' to the 3' end of the RNA transcript are referred to as "downstream sequences."

[0049] The terms "polypeptide" and "peptide" and "protein" are used interchangeably herein and refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification. Also included within the definition are, for example, polypeptides containing one or more analogs of an amino acid, including but not limited to, unnatural amino acids, as well as other modifications known in the art. It is understood that, because the polypeptides of this disclosure may be based upon antibodies or other members of the immunoglobulin superfamily, in certain embodiments, a "polypeptide" can occur as a single chain or as two or more associated chains.

[0050] The phrases "percent (%) sequence identity" or "% identity" or "% identical to" when used with reference to an amino acid sequence describe the number of matches ("hits") of identical amino acids of two or more aligned amino acid sequences as compared to the number of amino acid residues making up the overall length of the amino acid sequences. In other terms, using an alignment, for two or more sequences the percentage of amino acid residues that are the same (*e.g.* 90%, 91%, 92%, 93%, 94%, 95%, 97%, 98%, 99%, or 100% identity over the full-length of the amino acid sequences) may be determined, when the sequences are compared and aligned for maximum correspondence as measured using a sequence comparison algorithm as known in the art, or when manually aligned and visually inspected. The same determination may be made for nucleotide sequences. The sequences which are compared to determine sequence identity may thus differ by substitution(s), addition(s) or deletion(s) of amino acids. Suitable programs for aligning protein sequences are known to the skilled person. The percentage

sequence identity of protein sequences can, for example, be determined with programs such as CLUSTALW, Clustal Omega, FASTA or BLAST, *e.g.*, using the NCBI BLAST algorithm (Altschul SF, et al (1997), *Nucleic Acids Res.* 25:3389-3402).

[0051] As used herein, the terms and phrases “in combination,” “in combination with,” “co-delivery,” and “administered together with” in the context of the administration of two or more therapies or components to a subject refers to simultaneous administration of two or more therapies or components, or a therapeutic composition and an adjuvant. “Simultaneous administration” can be administration of the two components at least within the same day. When two components are “administered together with” or “administered in combination with,” they can be administered in separate compositions sequentially within a short time period, such as, for example, 24, 20, 16, 12, 8 or 4 hours, or within 1 hour, or they can be administered in a single composition at the same time. The use of the term “in combination with” does not restrict the order in which therapies or components are administered to a subject. For example, a first therapy or component can be administered prior to, concomitantly with or simultaneously with, or subsequent to the administration of a second therapy or component. In some embodiments, a first therapy or component and a second therapy or component are administered in the same composition. In other embodiments, a first therapy or component and a second therapy or component are administered in separate compositions.

[0052] As used herein, a “non-naturally occurring” nucleic acid or polypeptide refers to a nucleic acid or polypeptide that does not occur in nature. A “non-naturally occurring” nucleic acid or polypeptide can be synthesized, treated, fabricated, and/or otherwise manipulated in a laboratory and/or manufacturing setting. In some cases, a non-naturally occurring nucleic acid or polypeptide can comprise a naturally-occurring nucleic acid or polypeptide that is treated, processed, or manipulated to exhibit properties that were not present in the naturally-occurring nucleic acid or polypeptide, prior to treatment. As used herein, a “non-naturally occurring” nucleic acid or polypeptide can be a nucleic acid or polypeptide isolated or separated from the natural source in which it was discovered, and it lacks covalent bonds to sequences with which it was associated in the natural source. A “non-naturally occurring” nucleic acid or polypeptide can be made recombinantly or via other methods, such as chemical synthesis. A “non-naturally occurring” polypeptide can be a “non-naturally occurring” antibody, such as a recombinantly produced antibody.

[0053] As used herein, the term “operably linked” refer to a linkage or a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. For example, a regulatory sequence operably linked to a nucleic acid sequence of interest is capable of directing the transcription of the nucleic acid sequence of interest, or a signal sequence operably linked to an amino acid sequence of interest is capable of secreting or translocating the amino acid sequence of interest over a membrane.

[0054] As used herein, the terms “subject” and “patient” are used interchangeably and refer to any animal, preferably a mammal, most preferably a human, to whom will be or has been treated by a method and/or with an anti-RSV F antibody or antigen binding fragment thereof as described herein. The term “mammal” as used herein, encompasses any mammal. Examples of mammals include, but are not limited to, cows, horses, sheep, pigs, cats, dogs, mice, rats, rabbits, guinea pigs, non-human primates (NHPs) such as monkeys or apes, humans, etc., more preferably a human. A human subject can include a patient.

[0055] By “optional” or “optionally” is meant that the subsequently described event or circumstance may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not.

[0056] The term “pharmaceutically acceptable carrier” or “pharmaceutically acceptable excipient” includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in pharmaceutical compositions is contemplated. Supplementary active ingredients can also be incorporated into the pharmaceutical compositions.

[0057] The term “pharmaceutically acceptable salt” refers to a salt of any of the compounds herein which are known to be non-toxic and are commonly used in the pharmaceutical literature. In some embodiments, the pharmaceutically acceptable salt of a compound retains the biological effectiveness of the compounds described herein and are not biologically or otherwise undesirable. Examples of pharmaceutically acceptable salts can be found in Berge et al., *Pharmaceutical Salts*, *J. Pharmaceutical Sciences*, January 1977, 66(1), 1-19. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid,

sulfuric acid, nitric acid, and phosphoric acid. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, pyruvic acid, lactic acid, oxalic acid, malic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 2-hydroxyethylsulfonic acid, p-toluenesulfonic acid, stearic acid and salicylic acid.

Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases.

Inorganic bases from which salts can be derived include, for example, sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, and aluminum.

Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines; substituted amines including naturally occurring substituted amines; cyclic amines; and basic ion exchange resins. Examples of organic bases include isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine. In some embodiments, the pharmaceutically acceptable base addition salt is selected from ammonium, potassium, sodium, calcium, and magnesium salts.

[0058] As used herein, the term “antibody” is meant in a broad sense and includes immunoglobulin molecules including polyclonal antibodies, monoclonal antibodies including murine, human, humanized and chimeric monoclonal antibodies, antigen-binding fragments, bispecific or multispecific antibodies, dimeric, tetrameric or multimeric antibodies, Fv, Fab and F(ab')₂, bifunctional hybrid (e.g., Lanzavecchia et al., *Eur. J. Immunol.* 17:105 (1987)), single-chain (Huston et al., *Proc. Natl. Acad. Sci. USA* 85:5879 (1988); Bird et al., *Science* 242:423 (1988)), antibodies with altered constant regions (e.g., U.S. Pat. No. 5,624,821), domain antibodies and any other modified configuration of the immunoglobulin molecule that comprises an antigen binding site of the required specificity. Immunoglobulin molecules can be assigned to five major classes, IgA, IgD, IgE, IgG and IgM, depending on the heavy chain constant domain amino acid sequence. IgA and IgG are further sub-classified as the isotypes IgA1, IgA2, IgG1, IgG2, IgG3 and IgG4. Antibody light chains of any vertebrate species may be assigned to one of two clearly distinct types, namely kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains. General principles of antibody molecule structure and various techniques relevant to the production of antibodies are provided in, e.g., Harlow and Lane, *ANTIBODIES: A LABORATORY MANUAL*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N. Y., (1988).

[0059] An isolated protein or construct of the application can also comprise an antibody derivative. The term “antibody derivative” as used herein refers to a molecule comprising a full-length antibody or an antigen-binding fragment thereof, wherein one or more amino acids are chemically modified or substituted. Chemical modifications that can be used in antibody derivative includes, e.g., alkylation, PEGylation, acylation, ester formation or amide formation or the like, e.g., for linking the antibody to a second molecule. Exemplary modifications include PEGylation (e.g., cysteine- PEGylation), biotinylation, radiolabeling, and conjugation with a second agent (such as a cytotoxic agent).

[0060] The term “human antibody,” as used herein, is intended to include antibodies having variable and constant regions derived from human germline immunoglobulin sequences. The human mAbs of the disclosure can include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*), for example in the CDRs and/or in framework regions and/or in the Fc region. However, the term “human antibody,” as used herein, is not intended to include mAbs in which CDR sequences derived from the germline of another mammalian species (e.g., mouse), have been grafted onto human FR sequences.

[0061] The term “humanized antibody” refers to human antibody in which one or more CDRs of such antibody have been replaced with one or more corresponding CDRs obtained a non-human derived (e.g., mouse, rat, rabbit, primate) antibody. Humanized antibodies can also include certain non-CDR sequences or residues derived from such non-human antibodies as well as the one or more non-human CDR sequence. Such antibodies can also be referred to as “chimeric antibodies.”

[0062] The term “recombinant” generally refers to any protein, polypeptide, or cell expressing a gene of interest that is produced by genetic engineering methods. The term “recombinant” as used with respect to a protein or polypeptide, means a polypeptide produced by expression of a recombinant polynucleotide. The proteins used in the immunogenic compositions of the disclosure can be isolated from a natural source or produced by genetic engineering methods.

[0063] The antibodies of the present disclosure can, in some embodiments, be recombinant human antibodies. The term “recombinant human antibody”, as used herein, is intended to include all antibodies, including human or humanized antibodies, that are prepared, expressed,

created or isolated by recombinant means, such as antibodies expressed using a recombinant expression vector transfected into a host cell (described further below), antibodies isolated from a recombinant, combinatorial human antibody library (described further below), antibodies isolated from an animal (e.g., a mouse) that is transgenic for human immunoglobulin genes (see e.g., Taylor et al. *Nucl. Acids Res.* 20:6287-6295 (1992)) or antibodies prepared, expressed, created or isolated by any other means that involves splicing of human immunoglobulin gene sequences to other DNA sequences. Such recombinant human antibodies have variable and constant regions derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies are subjected to *in vitro* mutagenesis (or, when an animal transgenic for human Ig sequences is used, *in vivo* somatic mutagenesis) and thus the amino acid sequences of the V_H and V_L regions of the recombinant antibodies are sequences that, while derived from and related to human germline V_H and V_L sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

[0064] “Complementarity determining regions” (CDR) are antibody regions that bind an antigen. There are three CDRs in the V_H (HCDR1, HCDR2, HCDR3) and three CDRs in the V_L (LCDR1, LCDR2, LCDR3). CDRs may be defined using various delineations such as Kabat (Wu et al. *J Exp Med* 132:211:50 (1970) ; Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., (1991)), Chothia (Chothia et al. *J Mol Biol* 196: 901-17 (1987)), IMGT (Lefranc et al. *Dev Comp Immunol* 27: 55-77 (2003)) and AbM (Martin and Thornton, *J Biol Biol* 263: 800-15 (1996)). The correspondence between the various delineations and variable region numbering is described (see e.g., Lefranc et al., *Dev Comp Immunol* 27: 55-77 (2003); Honegger and Pluckthun, *J Mol Biol* 309:657-70 (2001); International ImMunoGeneTics (IMGT) database; Web resources, http://www_imgt_org). Available programs such as abYsis by UCL Business PLC may be used to delineate CDRs. The terms “CDR”, “HCDR1”, “HCDR2”, “HCDR3”, “LCDR1”, “LCDR2” and “LCDR3” as used herein include CDRs defined by any of the methods described *supra*, Kabat, Chothia, IMGT or AbM, unless otherwise explicitly stated in the specification. Correspondence between the numbering system, including, for example, the Kabat numbering and the IMGT unique numbering system, is well known to one skilled in the art (see, e.g., Kabat, *supra*; Chothia, *supra*; Martin, *supra*; Lefranc et al., *supra*).

[0065] Table 1

	IMGT	Kabat	AbM	Chothia
V _H CDR1	27-38	31-35	26-35	26-32
V _H CDR2	56-65	50-65	50-58	53-55
V _H CDR3	105-117	95-102	95-102	96-101
V _L CDR1	27-38	24-34	24-34	26-32
V _L CDR2	56-65	50-56	50-56	50-52
V _L CDR3	105-117	89-97	89-97	91-96

[0066] As used herein, the terms “treat,” “treatment” and “treating” refer to the reduction or amelioration of the progression, severity, and/or duration of an upper and/or lower respiratory tract RSV infection, otitis media, or a symptom or respiratory condition related thereto (such as asthma, wheezing, or a combination thereof) resulting from the administration of one or more therapies (including, but not limited to, the administration of one or more prophylactic or therapeutic agents). In certain embodiments, such terms refer to the reduction or inhibition of the replication of RSV, the inhibition or reduction in the spread of RSV to other tissues or subjects (e.g., the spread to the lower respiratory tract), the inhibition or reduction of infection of a cell with RSV, or the amelioration of one or more symptoms associated with an upper and/or lower respiratory tract RSV infection or otitis media.

[0067] As used herein, the terms “prevent,” “preventing,” and “prevention” refer to the prevention or inhibition of the development or onset of an upper and/or lower respiratory tract RSV infection, otitis media or a symptom or respiratory condition related thereto in a subject, the prevention or inhibition of the progression of an upper respiratory tract RSV infection to a lower respiratory tract RSV infection, otitis media or a symptom or respiratory condition related thereto resulting from the administration of a therapy (e.g., a prophylactic or therapeutic agent), the prevention of a symptom of an upper and/or lower tract RSV infection, otitis media or a respiratory condition related thereto, or the administration of a combination of therapies (e.g., a combination of prophylactic or therapeutic agents). As used herein, the terms “ameliorate” and “alleviate” refer to a reduction or diminishment in the severity a condition or any symptoms thereof.

[0068] The term “reduces” is a relative term, such that an agent reduces a response or condition if the response or condition is quantitatively diminished following administration of a treatment, or if it is diminished following administration of the treatment, as compared to a reference treatment. Thus, a treatment that reduces or prevents an infection or a response, such as a pathological response, e.g., vaccine enhanced viral disease, can, but does not necessarily

completely eliminate such an infection or response, so long as the infection or response is measurably diminished, for example, by at least about 5%, by at least about 10%, by at least about 15%, by at least about 20%, by at least about 30%, by at least about 40%, by at least about 50%, by at least about 60%, by at least about 70%, or about 80%, or even by about 90% of (that is to 10% or less than) the infection or response in the absence of the treatment, or in comparison to a reference treatment.

[0069] A “prophylactic” treatment is a treatment administered to a subject who does not exhibit signs of a disease or exhibits only early signs for the purpose of decreasing the risk of developing pathology.

[0070] By the phrase “therapeutically effective amount” is meant an amount that produces the desired effect for which it is administered. The exact amount will depend on the purpose of the treatment and will be ascertainable by one skilled in the art using known techniques (see, for example, Lloyd (1999) *The Art, Science and Technology of Pharmaceutical Compounding*) in view of the present disclosure.

[0071] As used herein with reference to anti-RSV antibodies or antigen-binding fragments thereof, a therapeutically effective amount means an amount of the anti-RSV antibody or antigen-binding fragment thereof that results in treatment of a disease, disorder, or condition; prevents or slows the progression of the disease, disorder, or condition; or reduces or completely alleviates symptoms associated with the disease, disorder, or condition.

[0072] According to particular embodiments, a therapeutically effective amount refers to the amount of therapy which is sufficient to achieve one, two, three, four, or more of the following effects: (i) reduce or ameliorate the severity of the disease, disorder or condition to be treated or a symptom associated therewith; (ii) reduce the duration of the disease, disorder or condition to be treated, or a symptom associated therewith; (iii) prevent the progression of the disease, disorder or condition to be treated, or a symptom associated therewith; (iv) cause regression of the disease, disorder or condition to be treated, or a symptom associated therewith; (v) prevent the development or onset of the disease, disorder or condition to be treated, or a symptom associated therewith; (vi) prevent the recurrence of the disease, disorder or condition to be treated, or a symptom associated therewith; (vii) reduce hospitalization of a subject having the disease, disorder or condition to be treated, or a symptom associated therewith; (viii) reduce hospitalization length of a subject having the disease, disorder or condition to be treated, or a

symptom associated therewith; (ix) increase the survival of a subject with the disease, disorder or condition to be treated, or a symptom associated therewith; (xi) inhibit or reduce the disease, disorder or condition to be treated, or a symptom associated therewith in a subject; and/or (xii) enhance or improve the prophylactic or therapeutic effect(s) of another therapy.

[0073] The term “specifically binds,” or “binds specifically to”, or the like, means that an antibody or antigen-binding fragment thereof forms a complex with an antigen that is relatively stable under physiologic conditions. Specific binding can be characterized by an equilibrium dissociation constant of at least about 1×10^{-6} M or less (e.g., a smaller K_D denotes a tighter binding). Methods for determining whether two molecules specifically bind are well known in the art and include, for example, equilibrium dialysis, surface plasmon resonance, and the like. As described herein, antibodies have been identified by surface plasmon resonance, e.g., BIACORE™, biolayer interferometry measurements using, e.g., a ForteBio Octet HTX instrument (Pall Life Sciences), which bind specifically to RSV-F. Moreover, multi-specific antibodies that bind to RSV-F protein and one or more additional antigens, or a bi-specific that binds to two different regions of RSV-F, are nonetheless considered antibodies that “specifically bind,” as used herein. In some aspects, the antibodies disclosed herein display equilibrium dissociation constants (and hence specificities) of about 1×10^{-6} M; about 1×10^{-7} M; about 1×10^{-8} M; about 1×10^{-9} M; about 1×10^{-10} M; between about 1×10^{-6} M and about 1×10^{-7} M; between about 1×10^{-7} M and about 1×10^{-8} M; between about 1×10^{-8} M and about 1×10^{-9} M; or between about 1×10^{-9} M and about 1×10^{-10} M.

[0074] The terms “antigen-binding portion” of an antibody, “antigen-binding fragment” of an antibody, and the like, as used herein, include any naturally occurring, enzymatically obtainable, synthetic, or genetically engineered polypeptide or glycoprotein that specifically binds an antigen to form a complex. In certain embodiments, the terms “antigen-binding portion” of an antibody, or “antibody fragment,” as used herein, refers to one or more fragments of an antibody that retains the ability to bind to RSV-F.

[0075] An “isolated antibody,” as used herein, is intended to refer to an antibody that is substantially free of other antibodies (Abs) having different antigenic specificities (e.g., an isolated antibody that specifically binds RSV-F, or a fragment thereof, is substantially free of Abs that specifically bind antigens other than RSV-F).

[0076] A “blocking antibody” or a “neutralizing antibody”, as used herein (or an “antibody that neutralizes RSV-F activity”), is intended to refer to an antibody whose binding to RSV-F results in inhibition of at least one biological activity of RSV-F. For example, an antibody of the present disclosure can aid in blocking the fusion of RSV to a host cell, or prevent syncytia formation, or prevent the primary disease caused by RSV. Alternatively, an antibody of the present disclosure can demonstrate the ability to ameliorate at least one symptom of the RSV infection. This inhibition of the biological activity of RSV-F can be assessed by measuring one or more indicators of RSV-F biological activity by one or more of several standard *in vitro* assays (such as, for example, a neutralization assay as described herein) or *in vivo* assays known in the art (for example, animal models to look at protection from challenge with RSV following administration of one or more of the antibodies described herein) in view of the present disclosure.

[0077] As used herein, a “therapeutic antibody” refers to any antibody or antigen-binding fragment thereof that is administered for treatment or prophylaxis of an animal, including a human. Such antibodies can be prepared by any known methods for the production of polypeptides in view of the present disclosure, and hence, include, but are not limited to, recombinantly produced antibodies, synthetically produced antibodies, and therapeutic antibodies extracted from cells or tissues and other sources. As isolated from any sources or as produced, therapeutic antibodies can be heterogeneous in length or differ in post-translational modification, such as glycosylation (i.e., carbohydrate content). Heterogeneity of therapeutic antibodies also can differ depending on the source of the therapeutic antibodies. Hence, reference to therapeutic antibodies refers to the heterogeneous population as produced or isolated. References to therapeutic antibodies herein are to their monomeric, dimeric or other multimeric forms, as appropriate.

[0078] The term “epitope” refers to an antigenic determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. The term “epitope” also refers to a site on an antigen to which B and/or T cells respond. It also refers to a region of an antigen that is bound by an antibody. Epitopes can be defined as structural or functional. Functional epitopes are generally a subset of the structural epitopes and have those residues that directly contribute to

the affinity of the interaction. Epitopes can also be conformational, that is, composed of non-linear amino acids. In certain embodiments, epitopes can include determinants that are chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain embodiments, can have specific three-dimensional structural characteristics, and/or specific charge characteristics. In some aspects, an anti-RSV F antibody or antigen binding fragment as described herein binds to SEQ ID NO: 16.

[0079] The term “effective dose 90” or “ED₉₀” refers to the dosage of an agent that produces a desired effect of 90% reduction of, for instance, viral forming plaques relative to the negative control.

[0080] The term “IC₅₀” refers to the “half maximal inhibitory concentration”, which value measures the effectiveness of compound (e.g., anti-RSV F antibody) inhibition towards a biological or biochemical utility. This quantitative measure indicates the quantity required for a particular inhibitor to inhibit a given biological process by half. In certain embodiments, RSV virus neutralization potencies for anti-RSV antibodies disclosed herein are expressed as neutralization IC₅₀ values.

[0081] A “conservative amino acid substitution” is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art in view of the present disclosure. (See, e.g., Pearson (1994) *Methods Mol. Biol.* 24: 307-331). Examples of groups of amino acids that have side chains with similar chemical properties include 1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; 2) aliphatic-hydroxyl side chains: serine and threonine; 3) amide-containing side chains: asparagine and glutamine; 4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; 5) basic side chains: lysine, arginine, and histidine; 6) acidic side chains: aspartate and glutamate, and 7) sulfur-containing side chains: cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a

positive value in the PAM250 log-likelihood matrix disclosed in Gonnet et al. (1992) Science 256: 1443-45. A “moderately conservative” replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

[0082] In an attempt to help the reader of the present disclosure, the description has been separated in various paragraphs or sections or is directed to various embodiments of the present disclosure. These separations should not be considered as disconnecting the substance of a paragraph or section or embodiments from the substance of another paragraph or section or embodiments. To the contrary, one skilled in the art will understand that the description has broad application and encompasses all the combinations of the various sections, paragraphs and sentences that can be contemplated. The discussion of any embodiment is meant only to be exemplary and is not intended to suggest that the scope of the disclosure, including the claims, is limited to these examples.

RSV Antibodies and Antigen Binding Fragments Thereof

[0083] Despite decades of research, the development of a safe and effective vaccines or therapeutic, prophylactic, preventative, and/or blocking antibodies against RSV has remained elusive, highlighting the need for novel strategies that induce or provide protective immune responses. (Rogovik, A. L., et al., *Can Fam Physician* 56, 769-772 (2010); Graham, B. S., *Immunol Rev* 239, 149-166 (2011); J. R. Groothuis, E. A. Simoes, V. G. Hemming, *Pediatrics* 95, 463-467 (1995)). Indeed, to date there are only two commercially available vaccines (Arexvy for the elderly and Abrysvo for maternal immunization), and passive prophylaxis with the monoclonal antibody palivizumab (marketed as Synagis®) is restricted to high-risk infants in part due to its modest efficacy.

[0084] As such, the present disclosure generally relates to anti-RSV F antibodies or antigen binding fragments thereof that specifically bind to Respiratory Syncytial Virus (RSV) F protein (F), and which anti-RSV F antibodies and antigen binding fragments thereof can be used in methods of treating, preventing, ameliorating, inhibiting, and/or neutralizing RSV or at least one symptom associated with RSV. In one aspect, the present disclosure generally relates to an antibody or antigen binding fragment thereof that competes for binding to Respiratory Syncytial Virus (RSV) F protein (F) with an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising a heavy chain complementarity

determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. In one aspect, the present disclosure generally relates to an isolated or recombinant anti-Respiratory Syncytial Virus (RSV) F protein (F) antibody or antigen binding fragment thereof that specifically binds to a Respiratory Syncytial Virus (RSV) F protein (F), wherein the anti-RSV F antibody or antigen binding fragment thereof comprises a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. Moreover, the present disclosure generally relates to an antibody or antigen binding fragment thereof that binds to the same epitope of Respiratory Syncytial Virus (RSV) F protein (F) as an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and

48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. In some instances, the epitope comprises SEQ ID NO: 16. Furthermore, the present disclosure generally relates to antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) and has the same complementarity determining regions (CDRs) as an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising the amino acid sequence of SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89, and a variable light chain region (V_L) comprising the amino acid sequence of SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

[0085] RSV

[0086] Human RSV is a member of the Pneumovirus subfamily of the family Paramyxoviridae. There are two distinct subgroups of human RSV, group A and group B. Additionally, each subtype is further divided into two strains, A1 and A2, and B1 and B2. RSV is an enveloped, non-segmented, negative-sense RNA virus with a genome of composed of approximately 15,000 nucleotides that encode eleven viral proteins.

[0087] Respiratory syncytial virus (RSV) infection is a major cause of lower respiratory tract disease in infants and children. RSV infection also is the most common cause of bronchiolitis, or inflammation of the small airways in the lung, and pneumonia in children under 1 year of age in the United States. In addition, RSV infection also is recognized as an important cause of respiratory illness in older adults. Symptoms and conditions associated with RSV infection include, for example, asthma, wheezing, reactive airway disease (RAD), and chronic obstructive pulmonary disease (COPD). Accordingly, as described herein, the anti-RSV F antibodies and antigen binding fragments thereof provided herein can be employed for the prophylaxis of RSV and/or one or more symptoms thereof, for treatment of RSV infection and/or one or more symptoms thereof, and/or for alleviation of one or more symptoms of such RSV-mediated diseases.

[0088] RSV F Protein

[0089] RSV encodes two major surface glycoproteins, glycoprotein G and glycoprotein F. Glycoprotein G, or the attachment protein, mediates virus binding to the cell receptor while

glycoprotein F, or the fusion protein, promotes fusion of the viral and cell membranes, allowing penetration of the viral ribonucleoprotein into the cell cytoplasm (Lopez et al. *J. Virology* 72:6922-6928 (1998)). Glycoprotein F also promotes fusion of the membranes of infected cells with those of adjacent cells leading to the formation of syncytia.

[0090] The RSV F protein exhibits over 91% similarity across the RSV A and B subgroups, while the RSV G protein exhibit only 53% amino acid similarity between the RSV A and RSV B subgroups (Sullender *Clin. Microbiol. Rev.* 13:1-15 (2000)). Because A and B virus subtypes co-circulate in most RSV epidemics, an antibody that neutralizes A and B subtypes of RSV, such as the anti-RSV F antibodies or antigen-binding fragments provided herein, is desirable.

[0091] “Respiratory Syncytial Virus-F protein,” also referred to as “RSV-F,” “RSV F,” “RSV Fusion protein,” or “RSV F glycoprotein” is a type I transmembrane surface protein, which has an N terminal cleaved signal peptide and a membrane anchor near the C terminus (Collins, P. L. et al., *PNAS (USA)* 81 :7683-7687 (1984)). The RSV-F protein is synthesized as an inactive 67 KDa precursor denoted as F0 (Calder, L. J.; et al., *Virology* 277,122-131 (2000)). The F0 protein is activated proteolytically in the Golgi complex by a furin-like protease at two sites, yielding two disulfide linked polypeptides, F2 and F1, from the N and C terminal, respectively. There is a 27 amino acid peptide released called “pep27.” There are furin cleavage sites (FCS) on either side of the pep27 (Collins, P. L.; Mottet, G., *J. Gen. Virol.* 72: 3095-3101 (1991); Sugrue, R. J, et al., *J. Gen. Virol.*, 82, 1375-1386 (2001)). The F2 subunit consists of the Heptad repeat C (HRC), while the F1 contains the fusion polypeptide (FP), heptad repeat A (HRA), domain I, domain II, heptad repeat B (HRB), transmembrane (TM) and cytoplasmic domain (CP) (See Sun, Z. et al., *Viruses* 5:21 1-225 (2013)). The RSV-F protein plays a role in fusion of the virus particle to the cell membrane, and is expressed on the surface of infected cells, thus playing a role in cell to cell transmission of the virus and syncytia formation. The amino acid sequence of the RSV-F protein is provided in GenBank as accession number AAX23994.

[0092] RSV F protein prefusion conformation: A structural conformation adopted by the RSV F protein prior to triggering of the fusogenic event that leads to transition of RSV F to the postfusion conformation and following processing into a mature RSV F protein in the secretory system. In the prefusion state, the RSV F protein includes an antigenic site at the membrane distal apex (“antigenic site Ø,” *see*, for instance, Example 1 of WO2011020079, the disclosure of

which is herein incorporated by reference in its entirety), that includes RSV F residues 62-69 and 196-209. As used herein, an RSV F protein in a prefusion conformation can be specifically bound by an anti-RSV F antibody or antigen binding fragment thereof that is specific for the prefusion conformation of the RSV F protein, such as an antibody that specifically binds within antigenic site Ø, such as, for example, one or more the anti-RSV F antibodies and antigen binding fragments described herein. In some aspects, the anti-RSV F antibody or antigen binding fragment as described herein binds an epitope comprising SEQ ID NO:16.

[0093] RSV F protein postfusion conformation: A structural conformation adopted by the RSV F protein that is not the prefusion conformation, and in which the N- and C- termini of the RSV F protein are proximal in a stable coil-coil. The post fusion conformation of RSV F protein has been described at the atomic level (see, e.g., McLellan et al., J. Virol., 85, 7788, 2011; Swanson et al., Proc. Natl. Acad. Sci. U.S.A., 108, 9619, 2011; and structural coordinates deposited PDB Accession No. 3RRR; each of which is incorporated by reference herein). In the post-fusion conformation, the RSV F protein does not include antigenic site Ø. The RSV postfusion conformation occurs, for example, following fusion of the F protein with the cell membrane.

[0094] Antibodies and Antigen Binding Fragments

[0095] As discussed above, provided herein are anti-RSV F antibodies or antigen-binding fragments thereof that can be employed for therapeutic, prophylactic, and diagnostic use. The anti-RSV F antibodies or antigen-binding fragments thereof provided herein can be used, for example, for passive immunization of a subject against RSV or for treatment of a subject with a viral infection. In some aspects, the anti-RSV F antibodies or antigen-binding fragments thereof provided herein are used for prophylaxis, i.e., the prevention of RSV infection. In some instances, the anti-RSV F antibodies or antigen-binding fragments thereof provided herein are used as therapeutic antibodies, i.e., for treatment of a RSV viral infection. In yet other instances, the anti-RSV F antibodies or antigen-binding fragments thereof provided herein are used for passive immunization of a subject against RSV. The provided anti-RSV F antibodies or antigen-binding fragments thereof also can be used for detection of a RSV infection or for monitoring RSV infection *in vitro* and *in vivo*.

[0096] As such, in one aspect, the present disclosure generally relates to an antibody or antigen binding fragment thereof that competes for binding to Respiratory Syncytial Virus (RSV)

F protein (F) with an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. In one aspect, the present disclosure generally relates to an isolated or recombinant anti-Respiratory Syncytial Virus (RSV) F protein (F) antibody or antigen binding fragment thereof that specifically binds to a Respiratory Syncytial Virus (RSV) F protein (F), wherein the anti-RSV F antibody or antigen binding fragment thereof comprises a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. Moreover, the present disclosure generally relates to an antibody or antigen binding fragment thereof that binds to the same epitope of Respiratory Syncytial Virus (RSV) F protein (F) as an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino

acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively. In some instances, the epitope comprises SEQ ID NO: 16. Furthermore, the present disclosure generally relates to antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) and has the same complementarity determining regions (CDRs) as an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising the amino acid sequence of SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89, and a variable light chain region (V_L) comprising the amino acid sequence of SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

[0097] In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises a V_H having an amino acid sequence at least 90%, at least 91%, at least 92%, at least 94%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises the V_H having an amino acid sequence of SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises a V_L having an amino acid sequence at least 90%, at least 91%, at least 92%, at least 94%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises the V_L having an amino acid sequence of SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises: (1) a V_H having the amino acid sequence of SEQ ID NO:7, and a V_L having the amino acid sequence of SEQ ID NO:8; (2) a V_H having the amino acid sequence of SEQ ID NO:25, and a V_L having the amino acid sequence of SEQ ID NO:26; (3) a V_H having the amino acid sequence of SEQ ID NO:33, and a V_L having the amino acid sequence of SEQ ID NO:34; (4) a V_H having the amino acid sequence of SEQ ID NO:41, and a V_L having the amino acid sequence of SEQ ID NO:42; (5) a

V_H having the amino acid sequence of SEQ ID NO:49, and a V_L having the amino acid sequence of SEQ ID NO:50; (6) a V_H having the amino acid sequence of SEQ ID NO:57, and a V_L having the amino acid sequence of SEQ ID NO:58; (7) a V_H having the amino acid sequence of SEQ ID NO:65, and a V_L having the amino acid sequence of SEQ ID NO:66; (8) a V_H having the amino acid sequence of SEQ ID NO:73, and a V_L having the amino acid sequence of SEQ ID NO:74; (9) a V_H having the amino acid sequence of SEQ ID NO:81, and a V_L having the amino acid sequence of SEQ ID NO:82; or (10) a V_H having the amino acid sequence of SEQ ID NO:89, and a V_L having the amino acid sequence of SEQ ID NO:90.

[0098] In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises an antigen binding fragment comprising a heavy chain polypeptide sequence having an amino acid sequence at least 90%, at least 91%, at least 92%, at least 94%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to SEQ ID NO:12, 91, 92, 93, 94, 95, 96, 97, 98, or 99. In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises the antigen binding fragment comprising the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:12, 91, 92, 93, 94, 95, 96, 97, 98, or 99. In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises an antigen binding fragment comprising a light chain polypeptide sequence having an amino acid sequence at least 90%, at least 91%, at least 92%, at least 94%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to SEQ ID NO:13, 100, 101, 102, 103, 104, 105, 106, 107, or 108. In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises the antigen binding fragment comprising the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:13, 100, 101, 102, 103, 104, 105, 106, 107, or 109. In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises the antigen binding fragment comprising: (1) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:12, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:13; (2) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:91, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:100; (3) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:92, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:101; (4) the heavy chain polypeptide sequence having the amino acid

sequence of SEQ ID NO:93, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:102; (5) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:94, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:103; (6) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:95, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:104; (7) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:96, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:105; (8) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:97, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:106; (9) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:98, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:107; or (10) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:99, and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:108.

[0099] In some aspects, the isolated or recombinant anti-RSV F antibody or antigen binding fragment comprises the heavy chain polypeptide having the amino acid sequence selected from (1) SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:15; (2) SEQ ID NO:91, SEQ ID NO:109, or SEQ ID NO:118; (3) SEQ ID NO:92, SEQ ID NO:110, or SEQ ID NO:119; (4) SEQ ID NO:93, SEQ ID NO:111, or SEQ ID NO:120; (5) SEQ ID NO:94, SEQ ID NO:112, or SEQ ID NO:121; (6) SEQ ID NO:95, SEQ ID NO:113, or SEQ ID NO:122; (7) SEQ ID NO:96, SEQ ID NO:114, or SEQ ID NO:123; (8) SEQ ID NO:97, SEQ ID NO:115, or SEQ ID NO:124; (9) SEQ ID NO:98, SEQ ID NO:116, or SEQ ID NO:125; or (10) SEQ ID NO:99, SEQ ID NO:117, or SEQ ID NO:126. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises the light chain polypeptide having the amino acid sequence of SEQ ID NO: 10, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, or SEQ ID NO:108. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof comprises the heavy chain polypeptide and the light chain polypeptide, respectively, selected from: (1) SEQ ID NO:15 and SEQ ID NO: 10, SEQ ID NO: 9 and SEQ ID NO: 10, or SEQ ID NO: 11 and SEQ ID NO: 10; (2) SEQ ID NO:91 and SEQ ID NO:100, SEQ ID NO:109 and SEQ ID NO:100, SEQ ID NO:118 and SEQ ID NO:100; (3) SEQ ID NO:92 and SEQ ID NO:101, SEQ ID NO:110 and SEQ ID NO:101, or

SEQ ID NO:119 and SEQ ID NO:101; (4) SEQ ID NO:93 and SEQ ID NO:102, SEQ ID NO:111 and SEQ ID NO:102, or SEQ ID NO:120 and SEQ ID NO:102; (5) SEQ ID NO:94 and SEQ ID NO:103, SEQ ID NO:112 and SEQ ID NO:103, or SEQ ID NO:121 and SEQ ID NO:103; (6) SEQ ID NO:95 and SEQ ID NO:104, SEQ ID NO:113 and SEQ ID NO:104, or SEQ ID NO:122 and SEQ ID NO:104; (7) SEQ ID NO:96 and SEQ ID NO:105, SEQ ID NO:114 and SEQ ID NO:105, or SEQ ID NO:123 and SEQ ID NO:105; (8) SEQ ID NO:97 and SEQ ID NO:106, SEQ ID NO:115 and SEQ ID NO:106, or SEQ ID NO:124 and SEQ ID NO:106; (9) SEQ ID NO:98 and SEQ ID NO:107, SEQ ID NO:116 and SEQ ID NO:107, or SEQ ID NO:125 and SEQ ID NO:107; or (10) SEQ ID NO:99 and SEQ ID NO:108, SEQ ID NO:117 and SEQ ID NO:108, or SEQ ID NO:126 and SEQ ID NO:108.

[0100] In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of binding to the PreF form of RSV-F with a higher binding affinity relative to the PostF form of RSV-F. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing or blocking RSV-F activity by inhibition of at least one biological activity of RSV-F. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of binding to the RSV A preF form of RSV-F with a K_D of 1.00×10^{-7} M or less, 1.00×10^{-8} M or less, 1.00×10^{-9} M or less, 7.50×10^{-10} M or less, 5.00×10^{-10} M or less, 2.50×10^{-10} M or less, 2.00×10^{-10} M or less, 1.75×10^{-10} M or less, 1.50×10^{-10} M or less, 1.25×10^{-10} M or less, or 1.24×10^{-10} M or less. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of binding to the RSV B preF form of RSV-F with a K_D of 1.00×10^{-7} M or less, 1.00×10^{-8} M or less, 1.00×10^{-9} M or less, 7.50×10^{-10} M or less, 5.00×10^{-10} M or less, 2.50×10^{-10} M or less, 2.00×10^{-10} M or less, 1.75×10^{-10} M or less, 1.70×10^{-10} M or less, 1.65×10^{-10} M or less, or 1.59×10^{-10} M or less.

[0101] In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing RSV A. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing RSV B. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of binding to antigenic site Ø of the preF form of RSV-F. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing RSV A with IC_{50} value ranging from 26 to 390 pM and RSV B with IC_{50} value ranging from 150 to 1000 pM. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing RSV A or RSV B with an IC_{50} value of about 1500

pM or less, 1250 pM or less, 1000 pM or less, 900 pM or less, 800 pM or less, 700 pM or less, 600 pM or less, 500 pM or less, 400 pM or less, 300 pM or less, 200 pM or less, 100 pM or less, 75 pM or less, 50 pM or less, 40 pM or less, 30 pM or less, 25 pM or less, 20 pM or less, 15 pM or less, 10 pM or less, 9 pM or less, 8 pM or less, or 7 pM or less. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of neutralizing RSV A or RSV B with an IC₅₀ value of about 20 pM to about 1500 pM, about 40 pM to about 1250 pM, about 50 pM to about 1000 pM, about 75 pM to about 900 pM, about 100 pM to about 800 pM, about 200 pM to about 700 pM, about 300 pM to about 600 pM, about 400 pM to about 500 pM, or any range in between these ranges. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of reducing lung viral titers in an RSV infected subject. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of reducing lung viral titers by about 2 fold, about 3 fold, about 4 fold, about 5 fold, about 6 fold, about 7 fold, about 8 fold, about 9 fold, about 10 fold, about 20 fold, about 30 fold, about 40 fold, about 50 fold, about 60 fold, about 70 fold, about 80 fold, or about 88 fold as compared to a vehicle control. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of exhibiting an EC₉₀ value for neutralizing of RSV of about 22.5 µg/mL or less, 22.0 µg/mL or less, 21.0 µg/mL or less, 20.0 µg/mL or less, 19.0 µg/mL or less, 18.0 µg/mL or less, 17.0 µg/mL or less, 16.0 µg/mL or less, 15.0 µg/mL or less, 14.0 µg/mL or less, 13.0 µg/mL or less, 12.0 µg/mL or less, 11.0 µg/mL or less, 10.0 µg/mL or less, 9.0 µg/mL or less, 8.0 µg/mL or less, 7.0 µg/mL or less, 6.0 µg/mL or less, 5.0 µg/mL or less, 4.0 µg/mL or less, 3.0 µg/mL or less, 2.8 µg/mL or less, 2.6 µg/mL or less, 2.4 µg/mL or less, 2.2 µg/mL or less, 2.0 µg/mL or less, 1.9 or less, 1.8 µg/mL or less, 1.7 or less, 1.6 or less, 1.5 or less, 1.4 or less, 1.3 or less, or 1.2 or less. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of activating FcγRIIa and/or FcγRIIIa. In some aspects, the anti-RSV F antibody or antigen binding fragment thereof is capable of avoiding off-target interactions, such as can be measured by a protein array-based techniques, such as the Retrogenix technique of Example 10.

[0102] In some aspects, the binding specificity, or epitope, of the anti-RSV F antibodies or antigen binding fragments thereof provided herein can be determined by any assay known to one of skill in the art in view of the present disclosure, including, but not limited to surface plasmon resonance assays, competition assays and virus neutralization assays. The epitope can be in the isolated protein, i.e., the isolated F protein, or in the protein in the virus. The ability of two

antibodies to bind to the same epitope can be determined by known assays in the art such as, for example, surface plasmon resonance assays and antibody competition assays. Typically, antibodies that immunospecifically bind to the same epitope can compete for binding to the epitope, which can be measured, for example, by an *in vitro* binding competition assay (e.g. competition ELISA), using techniques known the art. Typically, a first antibody that immunospecifically binds to the same epitope as a second antibody can compete for binding to the epitope by about or 30 %, 35 %, 40 %, 45 %, 50 %, 55 %, 60 %, 65 %, 70 %, 75 %, 80 %, 85 %, 90 %, 95 %, 100 %, where the percentage competition is measured ability of the second antibody to displace binding of the first antibody to the epitope. In some competition assays, the antigen is incubated in the presence a predetermined limiting dilution of a labeled antibody (e.g., 50-70 % saturation concentration), and serial dilutions of an unlabeled competing antibody. Competition is determined by measuring the binding of the labeled antibody to the antigen for any decreases in binding in the presence of the competing antibody.

[0103] In some aspects, the anti-RSV F antibodies and antigen binding fragments thereof described herein have subnanomolar affinity to an epitope in antigenic site Ø of RSV. In some aspects, the anti-RSV F antibodies and antigen binding fragments thereof described herein display broad and potent *in vitro* activity against RSV A and B, including recent RSV B strains with I206M and Q209R mutations. In some aspects, the anti-RSV F antibodies and antigen binding fragments thereof described herein also show strong prophylactic efficacy against RSV A and B in cotton rats, with *in vivo* EC₉₀ values of, respectively, 2.0 and 2.5 µg/mL. In some aspects, although the anti-RSV F antibodies and antigen binding fragments thereof described herein can engage and activate FcγRs *in vitro*, Fc-mediated effector functions do not contribute to its prophylactic efficacy in RSV-infected mice.

[0104] The anti-RSV antibodies F or antigen-binding fragments thereof provided herein can be analyzed by any suitable method known in the art for the detection of viral neutralization. Methods for detection of viral neutralization include, but are not limited to, plaque assays and assays for inhibition of syncytium formation. Such assays can be employed to assess, for example, inhibition of viral attachment, viral entry and cell-to-cell spread of the virus (see, e.g., Burioni et al., *Proc. Natl. Acad. Sci. U.S.A.* 91 :355-359 (1994); Sanna et al., *Virology* 270:386-396 (2000); and De Logu et al., *J CHn Microbiol* 36:3198-3204 (1998)). One of skill in the art can identify any assay capable of measuring viral neutralization.

[0105] Standard plaque assays include, for example, plaque reduction assays, plaque size reduction assays, neutralization assays and neutralization kinetic assays. Plaque reduction assays can be used to measure the ability of the anti-RSV antibody or antigen-binding fragment thereof to effect viral neutralization in solution. Plaque size reduction assays can be used to measure the ability of the anti-RSV antibody or antigen-binding fragment thereof to inhibit of viral cell-to-cell spread.

[0106] Virus neutralization assays can be used to measure the ability of the anti-RSV antibody or antigen-binding fragment thereof to effect viral neutralization at the target cell surface by association of the antibody or antigen-binding fragment thereof with the target cell prior to virus exposure.

[0107] *In vivo* studies using animal models can be performed to assess the efficacy of the anti-RSV F antibodies or antigen-binding fragments thereof provided herein. *In vivo* studies using animal models can be performed to assess any toxicity of administration of such antibodies or antigen-binding fragments thereof. A variety of assays, such as those employing *in vivo* animal models, are available to those of skill in the art for evaluating the ability of the anti-RSV F antibodies to inhibit or treat RSV virus infection and for assaying any toxicity. The therapeutic effect of the anti-RSV F antibodies can be assessed using animal models of the pathogenic infection, including animal models of viral infection. Such animal models are known in the art, and include, but are not limited to, animal models for RSV infection, such as but not limited to cotton rat, inbred mouse, calf, ferret, hamster, guinea pig, chimpanzee, owl monkey, rhesus monkey, African green monkey, cebus monkey, squirrel monkey, bonnet monkey, baboon, (see, e.g., Prince et al., *Am. J. Pathol.* 93:771-791 (1978); Prince et al. *Infect. Immunol.* 26:764-766 (1979); Byrd and Prince, *Clinical Infectious Diseases* 25:1363-1368 (1997), including references cited therein, for exemplary models of RSV infection). For *in vivo* testing of an antibody or antigen-binding fragment or composition's toxicity, any animal model system known in the art can be used, including, but not limited to, rats, mice, cows, monkeys, and rabbits.

[0108] In certain embodiments, the anti-RSV F antibody or antibody fragment for use in the method of the invention may be mono-specific, bi-specific, or multi-specific. Multi-specific antibodies may be specific for different epitopes of one target polypeptide or may contain antigen-binding domains specific for epitopes of more than one target polypeptide.

[0109] As used herein, the term “multi-specific antibody” refers to an antibody that comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment, the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment, the first and second epitopes overlap or substantially overlap. In an embodiment, the first and second epitopes do not overlap or do not substantially overlap. In an embodiment, the first and second epitopes are on different antigens, *e.g.*, different proteins (or different subunits of a multimeric protein). In an embodiment, a multi-specific antibody comprises a third, fourth, or fifth immunoglobulin variable domain. In an embodiment, a multi-specific antibody is a bispecific antibody molecule, a tri-specific antibody molecule, or a tetra-specific antibody molecule.

[0110] As used herein, the term “bispecific antibody” refers to a multi-specific antibody that binds no more than two epitopes or two antigens. A bispecific antibody is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment, the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment, the first and second epitopes overlap or substantially overlap. In an embodiment, the first and second epitopes are on different antigens, *e.g.*, different proteins (or different subunits of a multimeric protein). In an embodiment, a bispecific antibody comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment, a bispecific antibody comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment, a bispecific antibody comprises a scFv, or fragment thereof, having binding specificity for a first epitope, and a scFv, or fragment thereof, having binding specificity for a second epitope. In an embodiment, the first epitope is located on RSV F glycoprotein of this invention and the second epitope is located on other RSV antigens or other respiratory antigen binding domains, *e.g.*, a

respiratory antigen binding domain from coronavirus or influenza. In an embodiment, the first and the second epitopes are located on the same RSV F glycoprotein of this invention.

[0111] In some aspects, the anti-RSV F antibody or antigen binding fragment is a human antibody, is a humanized antibody, is a chimeric antibody, or is a bispecific or multi-specific antibody. In some aspects, the anti-RSV F antibody or antigen binding fragment is a human antibody. In some aspects, the anti-RSV F antibody or antigen binding fragment is a recombinant human antibody or antigen binding fragment thereof. In some aspects, the antibody or antigen binding fragment is conjugated to polyethylene glycol (PEG) or to a therapeutic agent or to a diagnostic agent.

[0112] Fc Modifications

[0113] In some aspects, the anti RSV-F antibody and antigen binding fragments thereof provided herein can comprise a wild-type Fc region or a modified Fc region. For instance, in some aspects, the anti-RSV F antibody or antigen binding fragment comprises a heavy chain polypeptide having a heavy chain constant region comprising the substitutions M252Y, S254T, and T256E, according to EU numbering, of an IgG1 heavy chain polypeptide. For example, in some aspects, the anti-RSV F antibody or antigen binding fragment comprises the heavy chain polypeptide having a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:14, wherein SEQ ID NO:14 comprises substitutions M252Y, S254T, and T256E substitutions, i.e., SEQ ID NO:171 to produce a heavy chain of SEQ ID NO:15. In some aspects, the anti-RSV F antibody or antigen binding fragment comprises a heavy chain polypeptide having a heavy chain constant region comprising the substitutions L234A and L235A, according to EU numbering, of an IgG1 heavy chain polypeptide. In some aspects, the anti-RSV F antibody or antigen binding fragment comprises the heavy chain polypeptide of SEQ ID NO: 11, that is, the heavy chain polypeptide comprises the substitutions L234A and L235A, according to EU numbering, of an IgG1 heavy chain polypeptide. Similar substitutions can be made for SEQ ID NOs:91-99 to produce SEQ ID NOs:118-126 and 109-117, respectively.

[0114] In some aspects, the anti RSV-F antibody can be modified to alter the heavy chain constant region by incorporating an IgG allotype. By way of an example, the anti RSV-F antibody can be modified to contain the IgG1_G1m(17) allotype (SEQ ID NO:170). By way of another example, the anti RSV-F antibody can be modified to contain any IgG allotype, including, but not limited to an IgG1_G1m(z,a) allotype, an IgG1_G1m(f) allotype, an IgG_G1m(f,a) allotype, an IgG_G1m(z,a,x) allotype, an IgG_G1m(z,a,v) allotype, an IgG2_G2m allotype, an IGG2_G2m(n) allotype, an IgG_G4m(a) allotype, and an IgG_G4m(b) allotype. IgG allotypes are known in the art, see, e.g., Vidarsson et al., *Front. Immunol.* 5:1-17 (2014) and Jefferis et al., *MAbs* 1(4):332-8 (2009).

[0115] In some aspects, the Fc region can be modified to alter one or more properties of the Fc polypeptide. For example, the Fc region can be modified to alter (i.e., more or less) effector functions compared to the effector function of an Fc region of a wild-type immunoglobulin heavy chain. The Fc regions of an antibody interacts with a number of Fc receptors, and ligands, imparting an array of important functional capabilities referred to as effector functions. Fc

effector functions include, for example, Fc receptor binding, complement fixation, and T cell depleting activity (see e.g., U.S. Patent No. 6,136,310). Methods of assaying T cell depleting activity, Fc effector function, and antibody stability are known in the art. For example, the Fc region of an IgG molecule interacts with the Fc γ Rs. These receptors are expressed in a variety of immune cells, including for example, monocytes, macrophages, neutrophils, dendritic cells, eosinophils, mast cells, platelets, B cells, large granular lymphocytes, Langerhans' cells, natural killer (NK) cells, and $\gamma\delta$ T cells. Formation of the Fc/Fc γ R complex recruits these effector cells to sites of bound antigen, typically resulting in signaling events within the cells and important subsequent immune responses such as release of inflammation mediators, B cell activation, endocytosis, phagocytosis, and cytotoxic attack. The ability to mediate cytotoxic and phagocytic effector functions is a potential mechanism by which antibodies destroy targeted cells.

Recognition of and lysis of bound antibody on target cells by cytotoxic cells that express Fc γ Rs is referred to as antibody dependent cell-mediated cytotoxicity (ADCC). Other Fc receptors for various antibody isotypes include Fc ϵ Rs (IgE), Fc α Rs (IgA), and Fc μ Rs (IgM).

[0116] Thus, in some aspects, a modified Fc domain can have altered affinity, including but not limited to, increased or low or no affinity for the Fc receptor. For example, the different IgG subclasses have different affinities for the Fc γ Rs, with IgG1 and IgG3 typically binding substantially better to the receptors than IgG2 and IgG4. In addition, different Fc γ Rs mediate different effector functions. Fc γ R1, Fc γ RIIa/c, and Fc γ RIIIa are positive regulators of immune complex triggered activation, characterized by having an intracellular domain that has an immunoreceptor tyrosine-based activation motif (ITAM). Fc γ RIIb, however, has an immunoreceptor tyrosine-based inhibition motif (ITIM) and is therefore inhibitory. Thus, altering the affinity of an Fc region for a receptor can modulate the effector functions induced by the Fc domain.

[0117] In some aspects, an Fc region is used that is modified for optimized binding to certain Fc γ Rs to better mediate effector functions, such as for example, antibody-dependent cellular cytotoxicity, ADCC. Such modified Fc regions can contain modifications at one or more of amino acid residues (according to the Kabat numbering scheme, Kabat et al. (1991) Sequences of Proteins of Immunological Interest, U.S. Department of Health and Human Services), including, but not limited to, amino acid positions 249, 252, 259, 262, 268, 271, 273, 277, 280, 281, 285, 287, 296, 300, 317, 323, 343, 345, 346, 349, 351, 352, 353, and 424. For example modifications

in an Fc region can be made corresponding to any one or more of G119S, G119A, S122D, S122E, S122N, S122Q, S122T, K129H, K129Y, D132Y, R138Y, E141Y, T143H, V147I, S150E, H151D, E155Y, E155I, E155H, K157E, G164D, E166L, E166H, S181A, S181D, S187T, S207G, S307I, K209T, K209E, K209D, A210D, A213Y, A213L, A213I, I215D, I215E, I215N, I215Q, E216Y, E216A, K217T, K217F, K217A, and P279L of an exemplary IgG1 sequence set forth in SEQ ID NO:1601 of WO 2011/020079 (SEQ ID NO: 14 of the instant application). A modified Fc containing these mutations can have enhanced binding to an FcR such as, for example, the activating receptor FcγRIIIa and/or can have reduced binding to the inhibitory receptor FcγRIIb (see e.g., US 2006/0024298). Fc regions modified to have increased binding to FcRs can be more effective in facilitating the destruction of viral (e.g., RSV) infected cells in patients.

[0118] In some examples, the anti-RSV F antibodies or antigen-binding fragments provided herein can be further modified to improve the interaction of the antibody or antigen-binding fragment thereof with the FcRn receptor in order to increase the *in vivo* half-life and pharmacokinetics of the antibody or antigen-binding fragment thereof (see, e.g., U.S. Patent No. 7,217,797, U.S. Pat. Pub. Nos. 2006/0198840 and 2008/0287657). FcRn is the neonatal FcR, the binding of which recycles endocytosed antibody or antigen-binding fragment thereof from the endosomes back to the bloodstream. This process, coupled with preclusion of kidney filtration due to the large size of the full length molecule, results in favorable antibody serum half-lives ranging from one to three weeks. Binding of Fc to FcRn also plays a role in antibody transport.

[0119] In some aspects, modifications of the Fc region include but are not limited to, mutation of the Fc described in U.S. Patent No. 7,217,797; U.S. Pat. Pub. Nos. 2006/0198840, 2006/0024298 and 2008/0287657, and International Patent Pub. No. WO 2005/063816, such as mutations at one or more of amino acid residues (Kabat numbering, Kabat et al. (1991)) 251-256, 285-90, 308-314, in the CH2 domain and/or amino acids residues 385-389, and 428-436 in the CH3 domain of the Fc heavy chain constant region, where the modification alters Fc receptor binding affinity and/or serum half-life relative to unmodified antibody or antigen-binding fragment thereof. In some examples, the IgG constant domain is modified in the Fc region at one or Phe124, Leu125, Phe126, Thr133, Pro174, Arg175, Glu177, Gln178, and Asn180 in the CH2 domain and amino acids Gln245, Val246, Ser247, Thr249, Ser283, Gly285, Ser286, Phe288, and Met31 in the CH3 domain in an exemplary IgG1 sequence set forth in SEQ ID NO:1601 of WO

2011/020079, SEQ ID NO: 14 of the present application. In some examples, the modification is at one or more surface-exposed residues, and the modification is a substitution with a residue of similar charge, polarity or hydrophobicity to the residue being substituted.

[0120] In some aspects, a Fc heavy chain constant region is modified at one or more of amino acid positions 251, 252, 254, 255, and 256 (Kabat numbering), where position 251 is substituted with Leu or Arg, position 252 is substituted with Tyr, Phe, Ser, Trp or Thr, position 254 is substituted with Thr or Ser, position 255 is substituted with Leu, Gly, He or Arg, and/or position 256 is substituted with Ser, Arg, Gln, Glu, Asp, Ala, Asp or Thr. In some examples, a Fc heavy chain constant region is modified at one or more of amino acid positions 308, 309, 311, 312, and 314, where position 308 is substituted with Thr or He, position 309 is substituted with Pro, position 311 is substituted with serine or Glu, position 312 is substituted with Asp, and/or position 314 is substituted with Leu. In some examples, a Fc heavy chain constant region is modified at one or more of amino acid positions 428, 433, 434, and 436, where position 428 is substituted with Met, Thr, Leu, Phe, or Ser, position 433 is substituted with Lys, Arg, Ser, He, Pro, Gln, or His, position 434 is substituted with Phe, Tyr, or His, and/or position 436 is substituted with His, Asn, Asp, Thr, Lys, Met, or Thr. In some examples, a Fc heavy chain constant region is modified at one or more of amino acid positions 263 and 459, where position 263 is substituted with Gln or Glu and/or position 459 is substituted with Leu or Phe.

[0121] In some aspects, a Fc heavy chain constant region can be modified to enhance binding to the complement protein C1q. In addition to interacting with FcRs, Fc also interact with the complement protein C1q to mediate complement dependent cytotoxicity (CDC). C1q forms a complex with the serine proteases C1r and C1s to form the C1 complex. C1q is capable of binding six antibodies, although binding to two IgGs is sufficient to activate the complement cascade. Similar to Fc interaction with FcRs, different IgG subclasses have different affinity for C1q, with IgG1 and IgG3 typically binding substantially better than IgG2 and IgG4. Thus, a modified Fc having increased binding to C1q can mediate enhanced CDC, and can enhance destruction of viral (e.g., RSV) infected cells. Exemplary modifications in an Fc region that increase binding to C1q include, but are not limited to, amino acid modifications at positions 345 and 353 (Kabat numbering). Exemplary modifications include those corresponding to K209W, K209Y, and E216S.

[0122] Furthermore, a variety of Fc mutants with substitutions to reduce or ablate binding with FcγRs also are known. Such muteins are useful in instances where there is a need for reduced or eliminated effector function mediated by Fc. This is often the case where antagonism, but not killing of the cells bearing a target antigen is desired. Exemplary of such an Fc is an Fc mutein described in U.S. Patent No. 5,457,035, which is modified at amino acid positions 248, 249 and 251 (Kabat numbering). In an exemplary IgG1 sequence, amino acid 117 is modified from Leu to Ala, amino acid 118 is modified from Leu to Glu, and amino acid 120 is modified from Gly to Ala. Similar mutations can be made in any Fc sequence such as, for example, the exemplary Fc sequence. This mutein exhibits reduced affinity for Fc receptors.

[0123] In some aspects, the anti-RSV F antibodies or antigen-binding fragments thereof provided herein can be engineered to contain modified Fc regions. For example, methods for fusing or conjugating polypeptides to the constant regions of antibodies (i.e., making Fc fusion proteins) are known in the art and described in, for example, U.S. Pat. Nos. 5,336,603, 5,622,929, 5,359,046, 5,349,053, 5,447,851, 5,723,125, 5,783,181, 5,908,626, 5,844,095, and 5,112,946; EP 307,434; EP 367,166; EP 394,827; PCT publications WO 91/06570, WO 96/04388, WO 96/22024, WO 97/34631, and WO 99/04813; Ashkenazi et al. (1991) Proc. Natl. Acad. Sci. USA 88:10535-10539; Traunecker et al. (1988) Nature 331:84-86; Zheng et al (1995) J. Immunol. 154:5590-5600; and ViI et al. (1992) Proc. Natl. Acad. Sci. USA 89:11337-1 1341 (1992) and described elsewhere herein. In some examples, a modified Fc region having one or more modifications that increases the FcγRn binding affinity and/or improves half-life can be fused to an anti-RSV antibody or antigen-binding fragment thereof provided herein.

[0124] In some aspects, the anti-RSV F antibodies or antigen-binding fragments thereof provided herein can be engineered to contain modified Fc regions to enhance ADCP activity. In particular, the Fc substitutions can comprise a G236A, A330L, and I332E substitution, see, e.g., Yamin et al., Nature 599:465-70 (2021) and Bournazos et al., Nature 588:485-490 (2020). Additional Fc substitutions for improved antiviral antibody response and induction of vaccine effects that are considered for anti-RSV F antibodies and antigen-binding fragments thereof are disclosed in Nawab, Human Vaccines & Immunotherapeutics 17(12):5532-45 (2021).

[0125] *Further Modifications*

[0126] In some aspects, the anti-RSV F antibodies and antibody fragments provided herein can be further modified by conjugation to a detectable moiety. The detectable moieties can be

detected directly or indirectly. Methods of labeling antibodies with detectable moieties are known in the art and include, for example, recombinant and chemical methods. In some aspects, the anti-RSV antibodies and antibody fragments provided herein can be further modified by conjugation to a therapeutic moiety.

[0127] Nucleic Acid Molecules, Polynucleotides, and Host Cells

[0128] The present disclosure further generally relates to an isolated nucleic acid molecule comprising a nucleic acid sequence encoding an anti-RSV F antibody or antigen-binding fragment thereof as described herein.

[0129] As used herein, a “vector” is a nucleic acid molecule used to carry genetic material into another cell, where it can be replicated and/or expressed. Any vector known to those skilled in the art in view of the present disclosure can be used. Examples of vectors include, but are not limited to, plasmids, viral vectors (bacteriophage, animal viruses, and plant viruses), cosmids, and artificial chromosomes (*e.g.*, YACs). Preferably, a vector is a DNA plasmid. A vector can be a DNA vector or an RNA vector. One of ordinary skill in the art can construct a vector of the application through standard recombinant techniques in view of the present disclosure. A vector of the application can be an expression vector. As used herein, the term “expression vector” refers to any type of genetic construct comprising a nucleic acid coding for an RNA capable of being transcribed. Expression vectors include, but are not limited to, vectors for recombinant protein expression, such as a DNA plasmid or a viral vector, and vectors for delivery of nucleic acid into a subject for expression in a tissue of the subject, such as a DNA plasmid or a viral vector. It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc.

[0130] Vectors of the application can contain a variety of regulatory sequences. As used herein, the term “regulatory sequence” refers to any sequence that allows, contributes or modulates the functional regulation of the nucleic acid molecule, including replication, duplication, transcription, splicing, translation, stability and/or transport of the nucleic acid or one of its derivative (*i.e.*, mRNA) into the host cell or organism. In the context of the disclosure, this term encompasses promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals and elements that affect mRNA stability).

[0131] In some embodiments of the application, a vector is a non-viral vector. Examples of non-viral vectors include, but are not limited to, DNA plasmids, bacterial artificial chromosomes, yeast artificial chromosomes, bacteriophages, etc. Examples of non-viral vectors include, but are not limited to, RNA replicon, mRNA replicon, modified mRNA replicon or self-amplifying mRNA, closed linear deoxyribonucleic acid, *e.g.*, a linear covalently closed DNA, *e.g.*, a linear covalently closed double stranded DNA molecule. Preferably, a non-viral vector is a DNA plasmid. A “DNA plasmid,” which is used interchangeably with “DNA plasmid vector,” “plasmid DNA” or “plasmid DNA vector,” refers to a double-stranded and generally circular DNA sequence that is capable of autonomous replication in a suitable host cell. DNA plasmids used for expression of an encoded polynucleotide typically comprise an origin of replication, a multiple cloning site, and a selectable marker, which for example, can be an antibiotic resistance gene. Examples of suitable DNA plasmids that can be used include, but are not limited to, commercially available expression vectors for use in well-known expression systems (including both prokaryotic and eukaryotic systems), such as pSE420 (Invitrogen, San Diego, Calif.), which can be used for production and/or expression of protein in *Escherichia coli* pYES2 (Invitrogen, Thermo Fisher Scientific), which can be used for production and/or expression in *Saccharomyces cerevisiae* strains of yeast; MAXBAC® complete baculovirus expression system (Thermo Fisher Scientific), which can be used for production and/or expression in insect cells; pcDNA™ or pcDNA3™ (Life Technologies, Thermo Fisher Scientific), which can be used for high level constitutive protein expression in mammalian cells; and pVAX or pVAX-1 (Life Technologies, Thermo Fisher Scientific), which can be used for high-level transient expression of a protein of interest in most mammalian cells. The backbone of any commercially available DNA plasmid can be modified to optimize protein expression in the host cell, such as to reverse the orientation of certain elements (*e.g.*, origin of replication and/or antibiotic resistance cassette), replace a promoter endogenous to the plasmid (*e.g.*, the promoter in the antibiotic resistance cassette), and/or replace the polynucleotide sequence encoding transcribed proteins (*e.g.*, the coding sequence of the antibiotic resistance gene), by using routine techniques and readily available starting materials. (See *e.g.*, Sambrook et al., *Molecular Cloning a Laboratory Manual*, Second Ed. Cold Spring Harbor Press (1989)).

[0132] A vector of the application, *e.g.*, a DNA plasmid or a viral vector, can comprise any regulatory elements to establish conventional function(s) of the vector. Regulatory elements

include, but are not limited to, a promoter, an enhancer, a polyadenylation signal, translation stop codon, a ribosome binding element, a transcription terminator, selection markers, origin of replication, etc. A vector can comprise one or more expression cassettes. An “expression cassette” is part of a vector that directs the cellular machinery to make RNA and protein. An expression cassette typically comprises three components: a promoter sequence, an open reading frame, and a 3'-untranslated region (UTR) optionally comprising a polyadenylation signal. An open reading frame (ORF) is a reading frame that contains a coding sequence of a protein of interest from a start codon to a stop codon. As used herein, the term “operably linked” is to be taken in its broadest reasonable context and refers to a linkage of polynucleotide elements in a functional relationship. A polynucleotide is “operably linked” when it is placed into a functional relationship with another polynucleotide. For instance, a promoter is operably linked to a coding sequence if it affects the transcription of the coding sequence. Any components suitable for use in an expression cassette described herein can be used in any combination and in any order to prepare vectors of the application.

[0133] A vector can comprise a promoter sequence, preferably within an expression cassette, to control expression. The term “promoter” is used in its conventional sense and refers to a nucleotide sequence that initiates the transcription of an operably linked nucleotide sequence. A promoter is located on the same strand near the nucleotide sequence it transcribes. Promoters can be a constitutive, inducible, or repressible. Promoters can be naturally occurring or synthetic. A promoter can be derived from sources including viral, bacterial, fungal, plants, insects, and animals. A promoter can be a homologous promoter (i.e., derived from the same genetic source as the vector) or a heterologous promoter (i.e., derived from a different vector or genetic source). For example, if the vector to be employed is a DNA plasmid, the promoter can be endogenous to the plasmid (homologous) or derived from other sources (heterologous).

[0134] Examples of promoters that can be used include, but are not limited to, a promoter from simian virus 40 (SV40), a mouse mammary tumor virus (MMTV) promoter, a human immunodeficiency virus (HIV) promoter such as the bovine immunodeficiency virus (BIV) long terminal repeat (LTR) promoter, a Moloney virus promoter, an avian leukosis virus (ALV) promoter, a cytomegalovirus (CMV) promoter such as the CMV immediate early promoter (CMV-IE), Epstein Barr virus (EBV) promoter, or a Rous sarcoma virus (RSV) promoter. A promoter can also be a promoter from a human gene such as human actin, human myosin, human

hemoglobin, human muscle creatine, or human metallothionein. A promoter can also be a tissue specific promoter, such as a muscle or skin specific promoter, natural or synthetic.

[0135] Furthermore, the present disclosure generally relates to a host cell comprising a nucleic acid molecule, plasmid, and/or vector as described herein. The host cell of the present disclosure can be any prokaryotic cell or eukaryotic cell, including but not limited to bacterial cells (e.g., *Escherichia coli*, *Bacillus subtilis*), insect cells (e.g., using baculovirus expression systems), yeast or mammalian cells (e.g., CHO or BHK cell line). Other suitable host cells are known to those skilled in the art.

[0136] Moreover, the present disclosure generally relates to a method of preparing an anti-RSV F antibody or antigen-binding fragment thereof as described herein, comprising culturing a host cell as described herein under conditions to produce the anti-RSV F antibody or antigen-binding fragment thereof, and recovering the anti-RSV F antibody or antigen-binding fragment thereof from the cell or cell culture. Moreover, the present disclosure generally relates to a transgenic organism comprising a nucleic acid sequence as described herein; or an expression vector as described herein.

[0137] Pharmaceutical Compositions

[0138] The present disclosure further generally relates to a pharmaceutical composition comprising: one or more of the isolated anti-RSV F antibodies or antigen-binding fragments thereof as described herein; and a pharmaceutically acceptable carrier and/or excipient. Moreover, the present disclosure further generally relates to a pharmaceutical composition comprising: one or more nucleic acid sequences as described herein; or one or more the expression vectors as described herein; and a pharmaceutically acceptable carrier and/or excipient, wherein said nucleic acid sequences and/or expression vectors encode for one or more anti-RSV F antibodies as described herein.

[0139] Typically, the administration of pharmaceutical compositions and therapeutic combinations of the present disclosure will have a therapeutic aim to treat or prevent a disease, disorder, or condition (e.g., an RSV infection) in a subject in need thereof. A therapeutically effective amount can be an amount sufficient to achieve one, two, three, four, or more of the following effects: (i) reduce or ameliorate the severity of the disease, disorder or condition to be treated or a symptom associated therewith; (ii) reduce the duration of the disease, disorder or condition to be treated, or a symptom associated therewith; (iii) prevent the progression of the

disease, disorder or condition to be treated, or a symptom associated therewith; (iv) cause regression of the disease, disorder or condition to be treated, or a symptom associated therewith; (v) prevent the development or onset of the disease, disorder or condition to be treated, or a symptom associated therewith; (vi) prevent the recurrence of the disease, disorder or condition to be treated, or a symptom associated therewith; (vii) reduce hospitalization of a subject having the disease, disorder or condition to be treated, or a symptom associated therewith; (viii) reduce hospitalization length of a subject having the disease, disorder or condition to be treated, or a symptom associated therewith; (ix) increase the survival of a subject with the disease, disorder or condition to be treated, or a symptom associated therewith; (xi) inhibit or reduce the disease, disorder or condition to be treated, or a symptom associated therewith in a subject; and/or (xii) enhance or improve the prophylactic or therapeutic effect(s) of another therapy.

[0140] The therapeutically effective amount or dosage can vary according to various factors, such as the disease, disorder or condition to be treated, the means of administration, the target site, the physiological state of the subject (including, e.g., age, body weight, health), whether the subject is a human or an animal, other medications administered, and whether the treatment is prophylactic or therapeutic. Treatment dosages are optimally titrated to optimize safety and efficacy.

[0141] Compositions and therapeutic combinations of the present disclosure, such as anti-RSV F antibodies or antigen binding fragments thereof in combination with one or more therapeutic agents, can also comprise a pharmaceutically acceptable carrier. A pharmaceutically acceptable carrier is non-toxic and should not interfere with the efficacy of the active ingredient. Pharmaceutically acceptable carriers can include one or more excipients such as binders, disintegrants, swelling agents, suspending agents, emulsifying agents, wetting agents, lubricants, flavorants, sweeteners, preservatives, dyes, solubilizers and coatings. Pharmaceutically acceptable carriers can include vehicles, such as lipid (nano)particles. The precise nature of the carrier or other material can depend on the route of administration, *e.g.*, intramuscular, intradermal, subcutaneous, oral, intravenous, cutaneous, intramucosal (*e.g.*, gut), intranasal or intraperitoneal routes. For liquid injectable preparations, for example, suspensions and solutions, suitable carriers and additives include water, glycols, oils, alcohols, preservatives, coloring agents and the like. For solid oral preparations, for example, powders, capsules, caplets, gelcaps and tablets, suitable carriers and additives include starches, sugars, diluents, granulating agents,

lubricants, binders, disintegrating agents and the like. For nasal spray s/inhalant mixtures, the aqueous solution/suspension can comprise water, glycols, oils, emollients, stabilizers, wetting agents, preservatives, aromatics, flavors, and the like as suitable carriers and additives.

[0142] Compositions and therapeutic combinations of the application, that is, those comprising an anti-RSV F antibody or antigen binding fragment thereof, can be formulated in any matter suitable for administration to a subject to facilitate administration and improve efficacy, including, but not limited to, oral (enteral) administration and parenteral injections. The parenteral injections include intravenous injection or infusion, subcutaneous injection, intradermal injection, and intramuscular injection. Compositions of the application can also be formulated for other routes of administration including transmucosal, ocular, rectal, long acting implantation, sublingual administration, under the tongue, from oral mucosa bypassing the portal circulation, inhalation, or intranasal.

[0143] According to aspects of the present disclosure, compositions and therapeutic combinations for administration will typically comprise a buffered solution in a pharmaceutically acceptable carrier, *e.g.*, an aqueous carrier such as buffered saline and the like, *e.g.*, phosphate buffered saline (PBS). The compositions and therapeutic combinations can also contain pharmaceutically acceptable substances as required to approximate physiological conditions such as pH adjusting and buffering agents. For example, a composition or therapeutic combination of the application comprising plasmid DNA can contain phosphate buffered saline (PBS) as the pharmaceutically acceptable carrier.

[0144] Pharmaceutical compositions and therapeutic combinations of the present disclosure can be administered to a subject by any method known in the art in view of the present disclosure, including, but not limited to, parenteral administration (*e.g.*, intramuscular, subcutaneous, intravenous, or intradermal injection), oral administration, transdermal administration, and nasal administration. Preferably, pharmaceutical compositions and therapeutic combinations are administered parenterally (*e.g.*, by intramuscular injection or intradermal injection) or transdermally.

[0145] Methods of Use

[0146] The present disclosure generally relates to a method of inhibiting at least one biological activity of RSV-F, comprising administering to a subject in need thereof or suspected of being in need thereof: (a) one or more antibodies or antigen-binding fragments thereof as

described herein; (b) a nucleic acid molecule as described herein; (c) an expression vector as described herein; (d) a host cell as described herein; or (e) a pharmaceutical composition as described herein. Furthermore, the present disclosure further generally relates to a method of treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection, comprising administering to a patient in need thereof or suspected of being in need thereof: (a) one or more anti-RSV F antibodies or antigen-binding fragments thereof as described herein; (b) a nucleic acid molecule as described herein; (c) an expression vector as described herein; (d) a host cell according as described herein; or (e) a pharmaceutical composition as described herein; such that the RSV infection is treated, prevented, or ameliorated, and/or the at least one symptom associated with RSV infection is treated, ameliorated, or reduced in severity, or prevented. Examples of symptoms of RSV can include, but is not limited to, mild-cold like signs and symptoms, congested or runny nose, dry cough, low-grade fever, sore throat, sneezing, headache. In severe cases, the symptoms can include, but are not limited to, spreading to the lower respiratory tract causing pneumonia or bronchiolitis (inflammation of small airway passages entering the lungs), fever, severe cough, wheezing (a high pitched noise that is usually heard on breathing out), rapid breathing or difficulty breathing, and bluish color of skin due to lack of oxygen. In infants, symptoms of RSV can include, but are not limited to, short, shallow, and rapid breathing; struggling to breathe; coughing; poor feeding; unusual tiredness (lethargy), and irritability. In some aspects, any one of (a)-(e) is administered in a therapeutically effective amount.

[0147] In some aspects, the method inhibits of at least one biological activity of RSV-F. In some aspects, the method reduces lung viral titers in an RSV infected subject. In some aspects, the method reduces lung viral titers by about 2 fold, about 3 fold, about 4 fold, about 5 fold, about 6 fold, about 7 fold, about 8 fold, about 9 fold, about 10 fold, about 20 fold, about 30 fold, about 40 fold, about 50 fold, about 60 fold, about 70 fold, about 80 fold, or about 88 fold as compared to a vehicle control. In some aspects, the method activates FcγRIIa and/or FcγRIIIa. In some aspects, the subject is in need of treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection. In some aspects, the method neutralizes or blocks RSV-F activity

by inhibition of at least one biological activity of RSV-F. In some aspects, the method neutralizes RSV A. In some aspects, the method neutralizes RSV B.

[0148] Diagnostic Uses

[0149] The anti-RSV F antibodies or antigen-binding fragments thereof provided herein can be used in diagnostic assays for the detection, purification, and/or neutralization of RSV.

Exemplary diagnostic assays include *in vitro* and *in vivo* detection of RSV. For example, assays using the anti-RSV F antibodies or antigen-binding fragments thereof provided herein for qualitatively and quantitatively measuring levels of RSV in an isolated biological sample (e.g., sputum) or *in vivo* are provided. In some aspects, the anti-RSV F antibodies or antigen-binding fragments thereof can be used as a companion diagnostic, i.e., they can be used to qualitatively and quantitatively measure levels of RSV in an isolated biological sample from a subject being treated for RSV to determine the drug's efficacy. In some aspects, the RSV F protein is detected using an anti-RSV F antibody or antigen binding fragment as described herein. In some aspects, the RSV is detected during the diagnostic use by detecting the RSV preF conformation of the RSV F protein using an anti-RSV F antibody or antigen binding fragment as described herein.

[0150] Combination Therapies

[0151] The anti-RSV F antibodies or antigen-binding fragments thereof provided herein can be administered alone or in combination with one or more therapeutic agents or therapies for the prophylaxis and/or treatment of a disease or condition. For example, the provided anti-RSV F antibodies or antigen-binding fragments thereof can be administered in combination with one or more antiviral agents for the prophylaxis and/or treatment of an RSV infection. The antiviral agents can include agents to decrease and/or eliminate the pathogenic infection or agents to alleviate one or more symptoms of a pathogenic infection. In some examples, a plurality of antibodies or antigen-binding fragments thereof (e.g., one or more antiviral antibodies) also can be administered in combination, where at least one of the antibodies is an anti-RSV F antibody or antigen-binding fragment thereof provided herein. In some examples, a plurality of antibodies can be administered in combination for the prophylaxis and/or treatment of a RSV infection or multiple viral infections, where at least one of the antibodies is an anti-RSV F antibody or antigen-binding fragment thereof provided herein. In some examples, the anti-RSV F antibodies provided can be administered in combination with one or more antiviral antibodies, which bind to and neutralize the same virus, i.e., RSV, or a different respiratory virus, such as influenza or

SARS-CoV-2. In some examples, the anti-RSV F antibodies or antigen-binding fragments thereof provided can be administered in combination with one or more antibodies, which can inhibit or alleviate one or more symptoms of RSV infection. In some examples, two or more of the anti-RSV F antibodies or antigen-binding fragments thereof provided herein are administered in combination.

[0152] The one or more additional agents can be administered simultaneously, sequentially or intermittently with the anti-RSV F antibody or antigen-binding fragment thereof.

[0153] Any therapy which is known to be useful, or which is or has been used for the prevention, management, treatment, or amelioration of a RSV infection or one or more symptoms thereof can be used in combination with anti-RSV F antibody or antigen-binding fragment thereof provided herein (see, e.g., Gilman et al., Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 10th ed., McGraw-Hill, New York, 2001; The Merck Manual of Diagnosis and Therapy, Berkow, M. D. et al. (eds.), 17th Ed., Merck Sharp & Dohme Research Laboratories, Rahway, NJ., 1999; Cecil Textbook of Medicine, 20th Ed., Bennett and Plum (eds.), W.B. Saunders, Philadelphia, 1996, for information regarding therapies {e.g., prophylactic or therapeutic agents) which have been or are used for preventing, treating, managing, or ameliorating a RSV infection or one or more symptoms thereof).

[0154] Detection Kit

[0155] The present disclosure also generally relates to a detection kit comprising of an anti-RSV F antibody or antigen binding fragment as described herein, a nucleic acid molecule as described herein, a plasmid as described herein, a host cell as described herein, or a pharmaceutical composition as described herein, wherein the detection kit is optionally used to detect RSV. In some instances, RSV-F can be detected by use of the detection kit, such as detecting the RSV preF form of RSV F.

Embodiments

[0156] Embodiment 1. An antibody or antigen binding fragment thereof that competes for binding to Respiratory Syncytial Virus (RSV) F protein (F) with an isolated or recombinant anti-RSV F antibody or antigen binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F) comprising a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1

(LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively.

[0157] Embodiment 2. An isolated or recombinant anti-Respiratory Syncytial Virus (RSV) F protein (F) antibody or antigen binding fragment thereof that specifically binds to a Respiratory Syncytial Virus (RSV) F protein (F), wherein the anti-RSV F antibody or antigen binding fragment thereof comprises a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of (1) SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively; (2) SEQ ID NOs: 19, 20, 21, 22, 23, and 24, respectively; (3) SEQ ID NOs: 27, 28, 29, 30, 31, and 32, respectively; (4) SEQ ID NOs: 35, 36, 37, 38, 39, and 40, respectively; (5) SEQ ID NOs: 43, 44, 45, 46, 47, and 48, respectively; (6) SEQ ID NOs: 51, 52, 53, 54, 55, and 56, respectively; (7) SEQ ID NOs: 59, 60, 61, 62, 63, and 64, respectively; (8) SEQ ID NOs: 67, 68, 69, 70, 71, and 72, respectively; (9) SEQ ID NOs: 75, 76, 77, 78, 79, and 80, respectively; or (10) SEQ ID NOs: 83, 84, 85, 86, 87, and 88, respectively.

[0158] Embodiment 3. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 1 or embodiment 2, wherein the antibody or antigen binding fragment thereof comprises a V_H having an amino acid sequence at least 90% identical to SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89.

[0159] Embodiment 4. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 3, wherein the antibody or antigen binding fragment thereof comprises the V_H having the amino acid sequence of SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89.

[0160] Embodiment 5. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 4, wherein the antibody or antigen binding fragment thereof comprises a V_L having an amino acid sequence at least 90% identical to SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

[0161] Embodiment 6. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 5, wherein the antibody or antigen binding fragment thereof comprises the V_L having the amino acid sequence of SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

[0162] Embodiment 7. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 6, wherein the antibody or antigen binding fragment thereof comprises:

- (1) a V_H having the amino acid sequence of SEQ ID NO:7, and a V_L having the amino acid sequence of SEQ ID NO:8;
- (2) a V_H having the amino acid sequence of SEQ ID NO:25, and a V_L having the amino acid sequence of SEQ ID NO:26;
- (3) a V_H having the amino acid sequence of SEQ ID NO:33, and a V_L having the amino acid sequence of SEQ ID NO:34;
- (4) a V_H having the amino acid sequence of SEQ ID NO:41, and a V_L having the amino acid sequence of SEQ ID NO:42;
- (5) a V_H having the amino acid sequence of SEQ ID NO:49, and a V_L having the amino acid sequence of SEQ ID NO:50;
- (6) a V_H having the amino acid sequence of SEQ ID NO:57, and a V_L having the amino acid sequence of SEQ ID NO:58;
- (7) a V_H having the amino acid sequence of SEQ ID NO:65, and a V_L having the amino acid sequence of SEQ ID NO:66;
- (8) a V_H having the amino acid sequence of SEQ ID NO:73, and a V_L having the amino acid sequence of SEQ ID NO:74;
- (9) a V_H having the amino acid sequence of SEQ ID NO:81, and a V_L having the amino acid sequence of SEQ ID NO:82; or
- (10) a V_H having the amino acid sequence of SEQ ID NO:89, and a V_L having the amino acid sequence of SEQ ID NO:90.

[0163] Embodiment 8. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 7, wherein the antibody or antigen binding fragment comprises an antigen binding fragment comprising a heavy chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99.

[0164] Embodiment 9. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 8, wherein the antibody or antigen binding fragment comprises the antigen binding fragment comprising the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99.

[0165] Embodiment 10. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 9, wherein the antibody or antigen binding fragment comprises an antigen binding fragment comprising a light chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108.

[0166] Embodiment 11. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 10, wherein the antibody or antigen binding fragment comprises the antigen binding fragment comprising the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108.

[0167] Embodiment 12. The anti-RSV F antibody or antigen binding fragment thereof according to embodiment 1 or embodiment 2, wherein the antibody or antigen binding fragment comprises an antigen binding fragment comprising:

- (1) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13;
- (2) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 91 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 100;
- (3) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 92 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 101;
- (4) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 93 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 102;
- (5) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 94 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 103;

- (6) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:95 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:104;
- (7) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:96 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:105;
- (8) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:97 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:106;
- (9) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:98 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:107; or
- (10) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:99 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:108.

[0168] Embodiment 13. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 12, wherein the antibody or antigen binding fragment comprises the heavy chain polypeptide having the amino acid sequence selected from (1) SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:15; (2) SEQ ID NO:91, SEQ ID NO:109, or SEQ ID NO:118; (3) SEQ ID NO:92, SEQ ID NO:110, or SEQ ID NO:119; (4) SEQ ID NO:93, SEQ ID NO:111, or SEQ ID NO:120; (5) SEQ ID NO:94, SEQ ID NO:112, or SEQ ID NO:121; (6) SEQ ID NO:95, SEQ ID NO:113, or SEQ ID NO:122; (7) SEQ ID NO:96, SEQ ID NO:114, or SEQ ID NO:123; (8) SEQ ID NO:97, SEQ ID NO:115, or SEQ ID NO:124; (9) SEQ ID NO:98, SEQ ID NO:116, or SEQ ID NO:125; or (10) SEQ ID NO:99, SEQ ID NO:117, or SEQ ID NO:126.

[0169] Embodiment 14. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 13, wherein the antibody or antigen binding fragment thereof comprises the light chain polypeptide having the amino acid sequence of SEQ ID NO:10, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, or SEQ ID NO:108.

[0170] Embodiment 15. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 14, wherein the antibody or antigen binding fragment

thereof comprises the heavy chain polypeptide and the light chain polypeptide, respectively, selected from: (1) SEQ ID NO:15 and SEQ ID NO: 10, SEQ ID NO: 9 and SEQ ID NO: 10, or SEQ ID NO: 11 and SEQ ID NO: 10; (2) SEQ ID NO:91 and SEQ ID NO:100, SEQ ID NO:109 and SEQ ID NO:100, SEQ ID NO:118 and SEQ ID NO:100; (3) SEQ ID NO:92 and SEQ ID NO:101, SEQ ID NO:110 and SEQ ID NO:101, or SEQ ID NO:119 and SEQ ID NO:101; (4) SEQ ID NO:93 and SEQ ID NO:102, SEQ ID NO:111 and SEQ ID NO:102, or SEQ ID NO:120 and SEQ ID NO:102; (5) SEQ ID NO:94 and SEQ ID NO:103, SEQ ID NO:112 and SEQ ID NO:103, or SEQ ID NO:121 and SEQ ID NO:103; (6) SEQ ID NO:95 and SEQ ID NO:104, SEQ ID NO:113 and SEQ ID NO:104, or SEQ ID NO:122 and SEQ ID NO:104; (7) SEQ ID NO:96 and SEQ ID NO:105, SEQ ID NO:114 and SEQ ID NO:105, or SEQ ID NO:123 and SEQ ID NO:105; (8) SEQ ID NO:97 and SEQ ID NO:106, SEQ ID NO:115 and SEQ ID NO:106, or SEQ ID NO:124 and SEQ ID NO:106; (9) SEQ ID NO:98 and SEQ ID NO:107, SEQ ID NO:116 and SEQ ID NO:107, or SEQ ID NO:125 and SEQ ID NO:107; or (10) SEQ ID NO:99 and SEQ ID NO:108, SEQ ID NO:117 and SEQ ID NO:108, or SEQ ID NO:126 and SEQ ID NO:108.

[0171] Embodiment 16. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 15, wherein the antibody or antigen binding fragment thereof is capable of neutralizing or blocking RSV-F activity by inhibition of at least one biological activity of RSV-F.

[0172] Embodiment 17. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 16, wherein the antibody or antigen binding fragment thereof is capable of binding to the PreF conformation of RSV-F with a higher binding affinity relative to the PostF conformation of RSV-F.

[0173] Embodiment 18. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 17, wherein the antibody or antigen binding fragment thereof is capable of binding to the RSV A preF conformation of RSV-F with a K_D of 1.00×10^{-7} M or less, 1.00×10^{-8} M or less, 1.00×10^{-9} M or less, 7.50×10^{-10} M or less, 5.00×10^{-10} M or less, 2.50×10^{-10} M or less, 2.00×10^{-10} M or less, 1.75×10^{-10} M or less, 1.50×10^{-10} M or less, 1.25×10^{-10} M or less, or 1.24×10^{-10} M or less.

[0174] Embodiment 19. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 18, wherein the antibody or antigen binding fragment

thereof is capable of binding to the RSV B preF conformation of RSV-F with a K_D of 1.00×10^{-7} M or less, 1.00×10^{-8} M or less, 1.00×10^{-9} M or less, 7.50×10^{-10} M or less, 5.00×10^{-10} M or less, 2.50×10^{-10} M or less, 2.00×10^{-10} M or less, 1.75×10^{-10} M or less, 1.70×10^{-10} M or less, 1.65×10^{-10} M or less, or 1.59×10^{-10} M or less.

[0175] Embodiment 20. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 19, wherein the antibody or antigen binding fragment thereof is capable of neutralizing RSV A.

[0176] Embodiment 21. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 20, wherein the antibody or antigen binding fragment thereof is capable of neutralizing RSV B.

[0177] Embodiment 22. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 21, wherein the antibody or antigen binding fragment thereof is capable of binding to antigenic site Ø of the preF form of RSV-F.

[0178] Embodiment 23. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 22, wherein the antibody or antigen binding fragment thereof is capable of neutralizing RSV with an IC_{50} value ranging from about 26 to about 1000 pM.

[0179] Embodiment 24. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 23, wherein the antibody or antigen binding fragment thereof is capable of neutralizing RSV A with an IC_{50} value of about 400 pM or less, 300 pM or less, 200 pM or less, 100 pM or less, 75 pM or less, 50 pM or less, 40 pM or less, 30 pM or less, 25 pM or less, or 20 pM or less.

[0180] Embodiment 24a. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 23, wherein the antibody or antigen binding fragment thereof is capable of neutralizing RSV B with an IC_{50} value of 1250 pM or less, 1000 pM or less, 900 pM or less, 800 pM or less, 700 pM or less, 600 pM or less, 500 pM or less, 400 pM or less, 300 pM or less, 200 pM or less, or 150 pM or less.

[0181] Embodiment 25. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 24, wherein the antibody or antigen binding fragment thereof is capable of reducing lung viral titers in an RSV infected subject.

[0182] Embodiment 26. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 25, wherein the antibody or antigen binding fragment thereof is capable of reducing lung viral titers by about 2 fold, about 3 fold, about 4 fold, about 5 fold, about 6 fold, about 7 fold, about 8 fold, about 9 fold, about 10 fold, about 20 fold, about 30 fold, about 40 fold, about 50 fold, about 60 fold, about 70 fold, about 80 fold, or about 88 fold as compared to a vehicle control.

[0183] Embodiment 27. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 26, wherein the antibody or antigen binding fragment thereof is capable of exhibiting an EC₉₀ value for neutralizing of RSV of about 22.5 µg/mL or less, 22.0 µg/mL or less, 21.0 µg/mL or less, 20.0 µg/mL or less, 19.0 µg/mL or less, 18.0 µg/mL or less, 17.0 µg/mL or less, 16.0 µg/mL or less, 15.0 µg/mL or less, 14.0 µg/mL or less, 13.0 µg/mL or less, 12.0 µg/mL or less, 11.0 µg/mL or less, 10.0 µg/mL or less, 9.0 µg/mL or less, 8.0 µg/mL or less, 7.0 µg/mL or less, 6.0 µg/mL or less, 5.0 µg/mL or less, 4.0 µg/mL or less, 3.0 µg/mL or less, 2.8 µg/mL or less, 2.6 µg/mL or less, 2.4 µg/mL or less, 2.2 µg/mL or less, 2.0 µg/mL or less, 1.9 or less, 1.8 µg/mL or less, 1.7 or less, 1.6 or less, 1.5 or less, 1.4 or less, 1.3 or less, or 1.2 or less.

[0184] Embodiment 28. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 27, wherein the antibody or antigen binding fragment thereof is capable of activating FcγRIIa and/or FcγRIIIa.

[0185] Embodiment 29. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 28, wherein the antibody or antigen binding fragment thereof is capable of avoiding off-target interactions.

[0186] Embodiment 30. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 29, where the antibody or antigen binding fragment is a human antibody, is a humanized antibody is a chimeric antibody, or is a bispecific or multi-specific antibody.

[0187] Embodiment 31. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 30, wherein the antibody or antigen binding fragment is a human antibody.

[0188] Embodiment 32. The anti-RSV F antibody or antigen binding fragment thereof according to any one of embodiments 1 to 31, wherein the antibody or antigen binding fragment is conjugated to polyethylene glycol (PEG) or to a therapeutic agent or to a diagnostic agent.

[0189] Embodiment 33. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding the anti-RSV F antibody or antigen-binding fragment thereof according to any one of embodiments 1 to 32.

[0190] Embodiment 34. An expression vector comprising the isolated nucleic acid sequence according to embodiment 33.

[0191] Embodiment 35. A host cell transfected, transformed, or transduced with the nucleic acid sequence according to embodiment 33 or the expression vector according to embodiment 34.

[0192] Embodiment 36. A method of preparing the anti-RSV F antibody or antigen-binding fragment thereof according to any one of embodiments 1 to 32, comprising culturing the host cell of embodiment 35 under conditions to produce the anti-RSV F antibody or antigen-binding fragment thereof, and recovering the anti-RSV F antibody or antigen-binding fragment thereof from the cell or cell culture.

[0193] Embodiment 37. A pharmaceutical composition comprising: one or more of the anti-RSV F antibodies or antigen-binding fragments thereof according to any one of embodiments 1 to 32; and a pharmaceutically acceptable carrier and/or excipient.

[0194] Embodiment 38. A pharmaceutical composition comprising: one or more nucleic acid sequences according to embodiment 33; or one or more the expression vectors according to embodiment 34; and a pharmaceutically acceptable carrier and/or excipient.

[0195] Embodiment 39. A transgenic organism comprising the nucleic acid sequence according to embodiment 33; or the expression vector according to embodiment 34.

[0196] Embodiment 40. A method of inhibiting at least one biological activity of RSV-F, comprising administering to a subject in need thereof or suspected of being in need thereof: (a) one or more antibodies or antigen-binding fragments thereof according to any of embodiments 1 to 32; (b) the nucleic acid molecule according to embodiment 33; (c) the expression vector according to embodiment 34; (d) the host cell according to embodiment 35; or (e) a pharmaceutical composition according embodiment 37 or embodiment 38.

- [0197] Embodiment 41. The method of any one of embodiment 40, wherein the subject is in need of treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection.
- [0198] Embodiment 42. The method of any one of embodiment 40 or embodiment 41, wherein the method reduces lung viral titers in the subject.
- [0199] Embodiment 43. The method of embodiment 42, wherein the method reduces lung viral titers by about 2 fold, about 3 fold, about 4 fold, about 5 fold, about 6 fold, about 7 fold, about 8 fold, about 9 fold, about 10 fold, about 20 fold, about 30 fold, about 40 fold, about 50 fold, about 60 fold, about 70 fold, about 80 fold, or about 88 fold as compared to a vehicle control.
- [0200] Embodiment 44. The method of any one of embodiments 40 to 43, wherein the method activates FcγRIIa and/or FcγRIIIa.
- [0201] Embodiment 45. The method of any one of embodiments 40 to 44, wherein any one of a)-e) of embodiment 40 are administered in a therapeutically effective amount.

SEQUENCE LISTING

SEQ ID NO	Description	Sequence
1	RSV Antibody 1 HCDR1	FPFEDHGLS
2	RSV Antibody 1 HCDR2	GLDWDGGHTGYADSVKG
3	RSV Antibody 1 HCDR3	AGTTSWYVHYLDH
4	RSV Antibody 1 LCDR1	RASHDIANYLA
5	RSV Antibody 1 LCDR2	AASTLES
6	RSV Antibody 1 LCDR3	QKYDSVPFA
7	RSV Antibody 1 Variable Heavy Chain (CDRs underlined)	EVQLVESGGRVVRPGGSLRLSCVTSGFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSYLEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTTLVTSS
8	RSV Antibody 1 Variable Light Chain (CDRs underlined)	DIVLTQSPSSLSASVGDRVTTITCRASHDIANYLAWYQQRPGKVPVLLI YA <u>ASTLES</u> GVPSRFSGSGSGADFTLIISLQPEDVATYYCQKYDSVPF AFGPGTKVDIK

9	RSV Antibody 1 non YTE Heavy Chain	EVQLVESGGRRVVRPGGSLRLSCVTSGFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPDSIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK
10	RSV Antibody 1 non YTE Light Chain	DIVLTQSPSSLSASVGRVTITCRASHDIANYLAWYQQRPVKPVLLI YAASTLESGVPSRFSGSGSGADFTLIISLQPEDVATYYCQKYDSVPF AFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSLTITLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
11	RSV Antibody 1 Heavy Chain - LALA	EVQLVESGGRRVVRPGGSLRLSCVTSGFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPDSIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK
12	Fab Heavy Chain	EVQLVESGGRRVVRPGGSLRLSCVTSGFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC
13	Fab Light Chain	DIVLTQSPSSLSASVGRVTITCRASHDIANYLAWYQQRPVKPVLLI YAASTLESGVPSRFSGSGSGADFTLIISLQPEDVATYYCQKYDSVPF AFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSLTITLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
14	hIgG1 heavy chain constant region	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK
15	RSV Antibody 1 Heavy Chain-YTE	EVQLVESGGRRVVRPGGSLRLSCVTSGFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPDSIAV

		EWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCV MHEALHNHYTQKSLSLSPGK
16	RSV Epitope	KNYIDKQLLPVIVNKQSCSIPNIETVIEF
17	LC Germlining 1	DIQLTQSPSSLSASVGDRVITITCRASHDIANYLAWYQQKPGKVPKLLI YAASTLESGVPSRFSGSGSGTDFTLTISLQPEDVATYYCQKYDSVPF AFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
18	LC Germlining 2	DIQLTQSPSSLSASVGDRVITITCRASHDIANYLAWYQQRPGKVPVLLI YAASTLESGVPSRFSGSGSGTDFTLTISLQPEDVATYYCQKYDSVPF AFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
19	ADI-59828 HCDR1	VIFRDSYMS
20	ADI-59828 HCDR2	DISPSSSYTNYADSVKG
21	ADI-59828 HCDR3	VRQRQRYDLGSYTNVFDY
22	ADI-59828 LCDR1	TGSSSNIGAGYDVH
23	ADI-59828 LCDR2	VNNNRPS
24	ADI-59828 LCDR3	QSYDRSLSGSV
25	ADI-59828 VH	EVQLLESGLGKLVKPGGSLRLSCAASRVIFRDSYMSWIRQAPGRGLEWI SDISPSSSYTNYADSVKGRFISIRDNAQNSLFLQMNGLRVDDTAVYYC VRQRQRYDLGSYTNVFDYWGQGTLLTVSS
26	ADI-59828 VL	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQLPGTAPKL LIFVNNNRPSGVPDRFSGSKSGTSASLAITGLQADDEADYYCQSYDRS LSGVSFVGGGTKLTVL
27	ADI-59818 HCDR1	YTFSHYGV
28	ADI-59818 HCDR2	WISAYNGNTNYVQKFQG
29	ADI-59818 HCDR3	ARDQPGSGVPPLDY
30	ADI-59818 LCDR1	RSSQSLEHSDTNTYLS
31	ADI-59818 LCDR2	KVSNRDS
32	ADI-59818 LCDR3	MQGTHWPLT
33	ADI-59818 VH	QVQLVQSGAEVKKPGASVKVSCKGSGYTFSHYGVSWVRQAPGQGLEWV GWISAYNGNTNYVQKFQGRVSMITDTSTSTAYMELRSLRSDDTAVYYC ARDQPGSGVPPLDYWGQGTLLTVSS
34	ADI-59818 VL	DIVMTQSPSLSLPATLGQFASISCRSSQSLEHSDTNTYLSWVQRRPGQS PRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQG THWPLTFGQGTKVDIK
35	ADI-59814 HCDR1	YTFSHYGIS
36	ADI-59814 HCDR2	FISAYTGNLEYAQKVQG
37	ADI-59814 HCDR3	ARDAVSADAGRLEFDN
38	ADI-59814 LCDR1	RSSQSLVYSDGNTYLS
39	ADI-59814 LCDR2	KVSHRDS
40	ADI-59814 LCDR3	MQGAHW
41	ADI-59814 VH	QVQLVQSGAEVRKPGASVKVSKATGYTFSHYGISWVRQAPGHGLEYL GFISAYTGNLEYAQKVQGRVTMTDTSTSTAYLEVRRLTSDDTAVYYC ARDAVSADAGRLEFDNWGQGTLLTVSS
42	ADI-59814 VL	DIVLTQSPSLSLPVTLGQFASISCRSSQSLVYSDGNTYLSWVHQRPGQS PRRLIYKVSNRDSGVPDRFSGSGSGTDFTLRISRVESDGLIYYCMQG AHWPRQGTKVEIK
43	ADI-59811 HCDR1	FPFEDHGLS

44	ADI-59811 HCDR2	GLDWDGGHTGYADSVKG
45	ADI-59811 HCDR3	VRAGTTSWYVHYLDH
46	ADI-59811 LCDR1	RASHDIANYLA
47	ADI-59811 LCDR2	AASTLES
48	ADI-59811 LCDR3	QKYDSVPFA
49	ADI-59811 VH	EVQLVESGGGRVVRPGGSLRLSCVTSGFPPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLYLEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTLLTVSS
50	ADI-59811 VL	DIVLTQSPSSLSASVGDRVITITCRASHDIANYLAWYQQRPGKVPVLLI YAASTLESQVPSRFGSGSGADFTLIISLQPEDVATYYCQKYDSVPF AFGPGTKVDIK
51	ADI-59110 HCDR1	FSIGGYSMN
52	ADI-59110 HCDR2	SITGGSNYIDYRDSVKG
53	ADI-59110 HCDR3	ATRGTEGGAFNI
54	ADI-59110 LCDR1	SGSSSNIGAGYDVH
55	ADI-59110 LCDR2	GDANRPS
56	ADI-59110 LCDR3	QSYDRSLSGYL
57	ADI-59110 VH	EVQLLESGGGPVKPGGSLRLSCAASGFSIGGYSMNWVRQAPGKGLEWV SSITGGSNYIDYRDSVKGRFTISRDNARNSLYLQMNSLRVEDTAVYYC ATRGTEGGAFNIWGQGTMTVTVSS
58	ADI-59110 VL	QSVVTQEPSVSGAPGQRVTISCSGSSSNIGAGYDVHWYQQLPGTAPKL LIYGDANRPSGVDPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRS LSGYLFGTGKTLTVL
59	ADI-59148 HCDR1	GNFGNYAIS
60	ADI-59148 HCDR2	QTIPALETATYAQKFRD
61	ADI-59148 HCDR3	ARGGGDCRSGKCSDF
62	ADI-59148 LCDR1	RASQSCSSNLA
63	ADI-59148 LCDR2	DASTRAT
64	ADI-59148 LCDR3	QQYNNWPWT
65	ADI-59148 VH	QVQLVQSGAEVKKPGSSVKVCKASGGNFGNYAISWLRQAPGQGLEWM GQTIPALETATYAQKFRDRATITAETKWTSTVYLELSSLKTDAAVYYC ARGGGDCRSGKCSDFWGQGTLLTVSS
66	ADI-59148 VL	DIVMTQSPATVSVSPGERATLSCRASQSCSSNLAWYQQKPGQAPRLLI YDASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYHCQQYNNWPW TFGQGTKVDIK
67	ADI-59149 HCDR1	YTFTNYGLS
68	ADI-59149 HCDR2	WISAYNGNTKYAQKLQG
69	ADI-59149 HCDR3	ARESGAEAAGTLDY
70	ADI-59149 LCDR1	RSSQSLVYSDGNTYLS
71	ADI-59149 LCDR2	KVSKRDS
72	ADI-59149 LCDR3	MQAIHWPRT
73	ADI-59149 VH	QVQLVQSGAEVKKPGASVRVCKSGSYTFTNYGLSWVRQAPGQGLEWM GWISAYNGNTKYAQKLQGRVTMTTDTSTSTAYMELRRLRSDDTAVYYC ARESGAEAAGTLDYWGQAGALVTVSS
74	ADI-59149 VL	DIRVTQSPPLSLPVTLGQPASISCRSSQSLVYSDGNTYLSWVQQRPGQS PRRLIYKVKRDSGVDPDRFSGSGSGTDFLTISRVEAEDVGVYYCMQA IHWPRTFGQGTKVEIK
75	ADI-59090 HCDR1	SDLSGYGMI
76	ADI-59090 HCDR2	SISASSNYIYYADSVKG
77	ADI-59090 HCDR3	ATDLTFYGGRTIYGEVLTS

78	ADI-59090 LCDR1	SGTSSNIGAGFDVH
79	ADI-59090 LCDR2	ANNNRPS
80	ADI-59090 LCDR3	QSYDRGLSGVI
81	ADI-59090 VH	GVQLVESGGGLVKPGGSLRLSCVASGSDLSGYGMWVRQAPRKGLEWV SSISASSNYIYYADSVKGRFTVSRDNAENSLFLQMNSLRVEDTAVYYC ATDLTFYGGRTIYGEVLTWSWGRGALVTVSS
82	ADI-59090 VL	QSVLTQPPSVSGAPGQRVITISCSGTSSNIGAGFDVHWYQQPLPGTAPKL LIYANNNRPSGVPDRFSGSQSGTSASLAITGLQAEDEADYYCQSYDRG LSGVIFGGGTKLTVL
83	ADI-59062 HCDR1	FAFSSYGMN
84	ADI-59062 HCDR2	SISAGSSYSDYADSVKG
85	ADI-59062 HCDR3	AREMLPPGTGGPWFD
86	ADI-59062 LCDR1	TGSSSNIGAGYDVH
87	ADI-59062 LCDR2	GNNNRPS
88	ADI-59062 LCDR3	QSYDRSLSGV
89	ADI-59062 VH	QVQLVQSGGGLVKPGGSLRLSCEASGFASFSSYGMNWVRQVPGKGLEWV SSISAGSSYSDYADSVKGRFTISRDNAKRSLYLQMNSLGGEDTAVYFC AREMLPPGTGGPWFDWPGQGTLVTVSS
90	ADI-59062 VL	QPVLTQPPSVSGAPGQRVITISCTGSSSNIGAGYDVHWYQQPLPGTAPKL LIYGNNNRPSGVPDRFSGAKSGTSASLAIIGLQAEDEADYYCQSYDRS LSGVFGGGTKVTVL
91	ADI-59828 HC	EVQLLESGGGLVKPGGSLRLSCAASRVIFRDSYMSWIRQAPGRGLEWI SDISPSSSYTNYADSVKGRFSISRDNQNSLFLQMNGLRVDDTAVYYC VRQRQRYDLGSYTNVFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
92	ADI-59818 HC	QVQLVQSGAEVKKPGASVKVSCKGSGYTFSHYGVSWVRQAPGQGLEWV GWISAYNGNTNYVQKFQGRVSMTTDTSTSTAYMELRLSRDDTAVYYC ARDQPGSGVPPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS HEALHNHYTQKSLSLSPGK
93	ADI-59814 HC	QVQLVQSGAEVRKPGASVKVSCKATGYTFSHYGISWVRQAPGHGLEYL GFISAYTGNLEYAQKVQGRVTMTTDTSTSTAYLEVRRLTSDDTAVYYC ARDAVSADAGRLFDNWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPGK

94	ADI-59811 HC	EVQLVESGGRVVRPGGSLRLSCVTSGFPPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYLEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSV MHEALHNHYTQKSLSLSPGK
95	ADI-59110 HC	EVQLLESGGGPVKPGGSLRLSCAASGFSIGGYSMNWVRQAPGKGLEWV SSITGGSNYIDYRDSVKGRFTISRDNARNSLYLQMNLSRVEDTAVYYC ATRGTEGGAFNIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP SVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHE ALHNHYTQKSLSLSPGK
96	ADI-59148 HC	QVQLVQSGAEVKKPGSSSVKVSCKASGGNFGNYAISWLRQAPGGGLEWM GQTIPALETATYAQKFRDRATITAEKWTSTVYLELSSSLKTDDAAVYYC ARGGGDCRSKGKCSDFWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSV MHEALHNHYTQKSLSLSPGK
97	ADI-59149 HC	QVQLVQSGAEVKKPGASVRVSCKSGSYTFTNYGLSWVRQAPGGGLEWM GWISEAYNGNTKYAQKLQGRVTMTTDTSTSTAYMELRRRLRSDDTAVYYC ARESGAEAAGTLDYWGQGALVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVM HEALHNHYTQKSLSLSPGK
98	ADI-59090 HC	GVQLVESGGGLVKPGGSLRLSCVASGSDLSGYGMIWVRQAPRKGLEWV SSISASSNYIYYADSVKGRFTVSRDNAENSLFLQMNLSRVEDTAVYYC ATDLTFYGGRTIYGEVLT SWGRGALVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FCSCVMHEALHNHYTQKSLSLSPGK

99	ADI-59062 HC	QVQLVQSGGGLVKPGGSLRLSCEASGFAFSSYGMNWVRQVPGKGLEWV SSISAGSSSYSDYADSVKGRFTISRDNAKRSLYLQMNSLGGEDTAVYFC AREMLPPGTGGPWFDPPWGQGTILVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
100	ADI-59828 LC	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQLPGTAPKL LIFVNNNRPSGVPDRFSGSKSGTSASLAITGLQADDEADYYCQSYDRS LSGSVFGGGTKLTVLRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC
101	ADI-59818 LC	DIVMTQSPSLSPATLGQFPASISCRSSQSLHSDTNTYLSWFGQRPQGS PRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQG THWPLTFGGQTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY YPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
102	ADI-59814 LC	DIVLTQSPSLSPVTLGQFPASISCRSSQSLVSDGNTYLSWFGHQRPGQS PRRLIYKVSNRDSGVPDRFSGSGSGTDFTLRISRVESED LGIYYCMQG AHWPRQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC
103	ADI-59811 LC	DIVLTQSPSSLSASVGRVTITCRASHDIANYLAWYQQRPGKVPVLLI YAASTLESQVPSRFSGSGSGADFTLIISLQPEDVATYYCQKYDSVPF AFGGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
104	ADI-59110 LC	QSVVTQEPSPVSGAPGQRVTISCSGSSSNIGAGYDVHWYQQLPGTAPKL LIYGDANRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDRS LSGYLFGGTGKLTVLRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC
105	ADI-59148 LC	DIVMTQSPATVSVSPGERATLSCRASQSCSSNLAWYQQKPGQAPRLLI YDASTRATGIPAREFSGSGSGTEFTLTISLQSEDFAVYHCQQYNNWPW TFGQGTGKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
106	ADI-59149 LC	DIRVTQSPSLSPVTLGQFPASISCRSSQSLVSDGNTYLSWFGQRPQGS PRRLIYKVSNRDSGVPDRFSGSGSGTDFTLTISRVEAEDVGVYYCMQA IHWPRTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY YPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
107	ADI-59090 LC	QSVLTQPPSVSGAPGQRVTISCSGTSSNIGAGFDVHWYQQLPGTAPKL LIYANNNRPSGVPDRFSGSQSGTSASLAITGLQAEDEADYYCQSYDRG LSGVIFGGGTGKLTVLRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC

108	ADI-59062 LC	QPVLTPPPSVSGAPGQRTISCTGSSSNIGAGYDVHWYQQLPGTAPKL LIYGNNNRPSGVPDRFSGAKSGTSASLAIIGLQAEDEADYYCQSYDRS LSGVFGGGTKVTVLRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP REAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC
109	ADI-59828 HC LALA	EVQLLESGGGVLKPGGSLRLSCAASRVIFRDSYMSWIRQAPGRGLEWI SDISPPSSSYTNYADSVKGRFSISRDNANSLFLQMNGLRVDDTAVYYC VRQRQRYDLGSYTNVFDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTST GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCTPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
110	ADI-59818 HC LALA	QVQLVQSGAEVKKPGASVKVSCKGSGYTFSHYGVSWVRQAPGGGLEWV GWISAYNGNTNYVQKQGRVSMTTDTSTSTAYMELRSLRSDDTAVYYC ARDQPGSGVPLDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCTPPCPAPEAAG GPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS HEALHNHYTQKSLSLSPGK
111	ADI-59814 HC LALA	QVQLVQSGAEVRKPGASVKVSCKATGYTFSHYGISWVRQAPGHGLEYL GFISAYTGNLEYAQKVGQGRVTMTTDTSTSTAYLEVRRLTSDDTAVYYC ARDAVSADAGRLFDNWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCTPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPGK
112	ADI-59811 HC LALA	EVQLVESGGRVVRPGGSLRLSCVTSGFPPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCTPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPGK
113	ADI-59110 HC LALA	EVQLLESGGGPVKPGGSLRLSCAASGFSIGGYSMNWVRQAPGKGLEWV SSITGGSNYIDYRDSVKGRFTISRDNARNSLYLQMNSLRVEDTAVYYC ATRGTEGGAFNIWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCTPPCPAPEAAGP SVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN

		AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
114	ADI-59148 HC LALA	QVQLVQSGAEVKKPGSSVKVCKASGGNFGNYAISWLRQAPGGLEWM GQTIPALETATYAQKFRDRATITA EKWTSTVYLELSSLTDDAAVYYC ARGGGDCRS GKCSDFWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
115	ADI-59149 HC LALA	QVQLVQSGAEVKKPGASVRVCKGSGYTFTNYGLSWVRQAPGGLEWM GWISAYNGNTKYAQKLQGRVTMTTDTSTSTAYMELRRLRSDDTAVYYC ARESGAEAAGTLDYWGQALVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVM HEALHNHYTQKSLSLSPGK
116	ADI-59090 HC LALA	GVQLVESGGGLVKPGGSLRLSCVASGSDLSGYGMIWVRQAPRGLEWV SSISASSNYIYYADSVKGRFTVSRDNAENSLFLQMNSLRVEDTAVYYC ATDLTFYGGRTIYGEVLT SWGRGALVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
117	ADI-59062 HC LALA	QVQLVQSGGGLVKPGGSLRLSCEASGFASFSSYGMNWVRQVPGGLEWV SSISAGSSYSDYADSVKGRFTISRDNAKRSLYLQMNSLGGEDTAVYFC AREMLPPGTGGPWFD PWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA AGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
118	ADI-59828 HC YTE	EVQLLESGGGLVKPGGSLRLS CAASRVIFRDSYMSWIRQAPGRGLEWI SDISPSSSYTNYADSVKGRFISRDN AQNSLFLQMNGLRVDDTAVYYC VRQRQR YDLGSYTNVFDYWGQGLTVTVSSASTKGPSVFPLAPSSKST SGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL

		PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
119	ADI-59818 HC YTE	QVQLVQSGAEVKKPGASVKVSCKGSGYTFSHYGVSWVRQAPGGLEWV GWISAYNGNTINYVKFQGRVSMTTDTSTSTAYMELRSLRSDDTAVYYC ARDQPGSGVPPLDYWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS HEALHNHYTQKSLSLSPGK
120	ADI-59814 HC YTE	QVQLVQSGAEVRKPGASVKVSKATGYTFSHYGISWVRQAPGHGLEYL GFISAYTGNLEYAQKVQGRVTMTTDTSTSTAYLEVRRLTSDDTAVYYC ARDAVSADAGRLFDNWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPGK
121	ADI-59811 HC YTE	EVQLVESGGRRVVRPGGSLRLSCVTSQFPFEDHGLSWVRQAPGKGLEWV AGLDWDGGHTGYADSVKGRFTVSRDRAKKSLEYLEMTSLGVDDTALYYC VRAGTTSWYVHYLDHWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPGK
122	ADI-59110 HC YTE	EVQLLESGGGPKVPGGSLRLSCAASGFSIGGYSMNWVRQAPGKGLEWV SSITGGSNYIDYRDSVKGRFTISRDNARNSLYLQMNSLRVEDTAVYYC ATRGTEGGAFNIWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP SVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS ALHNHYTQKSLSLSPGK
123	ADI-59148 HC YTE	QVQLVQSGAEVKKPGSSVKVSCKASGGNFGNYAISWLRQAPGGLEWM GQTIPALETATYAKFRDRATITA EKWTSTVYLELSSSLKTDDAAVYYC ARGGGDCRSKCSDFWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV

		EWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
124	ADI-59149 HC YTE	QVQLVQSGAEVKKPGASVRVSCCKGSGYTFTNYGLSWVRQAPGGGLEWM GWISAYNGNTKYAQKLQGRVTMTTDTSTSTAYMELRRLRSDDTAVYYC ARESGAEAAGTLDYWGQALVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
125	ADI-59090 HC YTE	GVQLVESGGGLVCKPGGSLRLSCVASGSDLSGYGMIWVRQAPRKGLEWV SSISASSNYIYYADSVKGRFTVSRDNAENSLFLQMNSLRVEDTAVYYC ATDLTFYGGRTIYGEVLTWSGRGALVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF SCSVMHEALHNHYTQKSLSLSPGK
126	ADI-59062 HC YTE	QVQLVQSGGGLVCKPGGSLRLSCEASGFSSYGMNWVRQVPGKGLEWV SSISAGSSYSYADSVKGRFTISRDNAKRSLYLQMNSLGGEDTAVYFC AREMLPPGTGGPWFDWPGQGLVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDG EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
170	IgG1_G1m(17) allotype constant region	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
171	YTE constant region	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
172	LALA constant region	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR E

		MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
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EXAMPLES

[0202] **Example 1: Preparation of an Anti-RSV F Antibody**

[0203] Anti-RSV F antibodies were prepared as generally described in US 20200223906, the disclosure of which is herein incorporated by reference in its entirety. Briefly, peripheral blood mononuclear cells were obtained from an adult donor approximately between 20-35 years of age, and monoclonal antibodies from RSV prefusion F-reactive memory B cells were isolated therefrom. Detailed methods are described below.

[0204] PMBC Donor Samples: Heparinized blood samples (50-100 cc) were drawn from 4 donors identified as IML #3512, 3483, 2992, and 3529. The samples were processed to obtain plasma and to isolate peripheral blood-derived B cells. Isolated cells and plasma were stored frozen in aliquots at –80° C.

[0205] Antigens and Antibodies: Production of recombinant hMPV preF (A+B) and RSV preF (A) were generated as described in Rappazzo et al., Immunity 55(9):1710-24 (2022).

[0206] Single B-cell Sorting of Memory B cells: B cells were purified using a MACS B cell isolation kit (Miltenyi Biotec; cat #130-091-151; Miltenyi Biotec; Bergisch Gladbach, Germany) and stained using anti-human CD19 (PE-Cy7), CD3 (PerCP-Cy5.5), CD8 (PerCP-Cy5.5), CD14 (PerCP-Cy5.5), CD16 (PerCP-Cy5.5), IgM (BV711), IgD (APC-Cy7), IgA (AF488), IgG (BV605), and a mixture of labeled (APC or PE) hMPV preF (A+B) and RSV preF (A) protein tetramers (25 nM). B cells that showed reactivity to the hMPV and/or RSV preF protein tetramers were single cell sorted. Single cells were sorted using a BD FACS Aria II (BD Biosciences; Franklin Lakes, NJ) into 96-well PCR plates containing 20 uL/well of lysis buffer [5 μL of 5× first strand cDNA buffer (Invitrogen), 0.625 μL of NP-40 (New England Biolabs; Ipswich, MA), 0.25 μL RNaseOUT (Invitrogen; Waltham, MA), 1.25 μL dithiothreitol (Invitrogen), and 12.6 μL dH2O]. Plates were immediately stored at –80° C until cloning.

[0207] Amplification and Cloning of Antibody Variable Genes: Antibody variable genes (IgH, IgK, and IgL) were amplified by reverse transcription PCR and nested PCRs using cocktails of IgG- and IgM-specific primers, as described previously (Tiller et al, J Immunol 2008). The primers used in the second round of PCR contained 40 base pairs of 5' and 3' homology to the digested expression vectors to allow for cloning by homologous recombination

into *S. cerevisiae*. The lithium acetate chemical transformation method was used to clone the PCR products into *S. cerevisiae* (Gietz and Schiestl, Nat Protoc 2007). Unpurified heavy chain and light chain PCR product and restriction-digested expression vectors were combined in each transformation reaction. Following transformation, individual yeast colonies were picked for sequencing and characterization.

[0208] Expression and Purification of IgGs and Fab Fragments: IgGs were expressed in *S. cerevisiae* cultures grown in 24-well plates, as described previously (Bornholdt et al, Science 2016, PMID:26912366). After 6 days, the cultures were harvested by centrifugation and IgGs were purified by protein A-affinity chromatography. Fab fragments were generated by digesting the IgGs with papain and the Fab and Fc mixtures were passed over Protein A agarose to remove Fc fragments and undigested IgG. The flowthrough of the Protein A resin was then passed over CaptureSelect™ IgG-CH1 affinity resin (ThermoFischer Scientific), to purify the Fab away from undesired species. All IgG and Fab samples were prepared in PBS buffer.

[0209] Polyreactivity Assay: Polyspecificity reagent (PSR) binding was assessed as previously described (Xu et al. 2013 Protein Eng Des 26:663-70). Briefly, soluble membrane protein (SMP) and soluble cytosolic protein (SCP) fractions were prepared from CHO cells and biotinylated with NHS-LC-Biotin reagent (Pierce, ThermoFisher Cat#21336). 2 million IgG-presenting yeast were transferred to a 96-well assay plate, pelleted to remove supernatant, then the pellets were resuspended in 50 µL of 1:10 diluted stock of biotinylated SCPs and SMPs and incubated on ice for 20 min. Cells were washed twice with ice-cold PBSF, and the samples were incubated in 50 µL of secondary labeling mix (Extravidin-R-PE, goat F(ab')₂-anti human kappa-FITC, and propidium iodide) on ice for 20 min. The samples were analyzed for polyspecificity reagent binding using a FACSCanto II (BD Biosciences) with HTS sample injector. Flow cytometry data were analyzed for mean fluorescence intensity (MFI) in the R-PE channel and normalized to three control antibodies exhibiting low, medium, and high MFI values.

[0210] Example 2: Characterization of Anti-RSV F Antibodies

[0211] Anti-RSV F antibodies were analyzed first in a 3-day virus neutralization assay using HeLa cells and RSV lab strain, rgRSV224 (RSV A A2-eGFP). For this purpose, 10 µL of antibody was added to a black 384-well clear-bottom microtiter plate in a 4-fold serial dilution. Subsequently, 20 µL of HeLa cells (ATCC, CCL-2tm) at a density of 1.5×10^5 cells/mL were

added (i.e., 3000 cells/well) followed by the addition of 10 μ L rgRSV224 virus at a multiplicity of infection (MOI) of 1. Cell controls (no virus added) and virus controls (cells infected with virus but no antibody added) were taken along on each plate. After three days of incubation at 37°C and 5% CO₂, viral replication was quantified by measuring eGFP expression using an Acumen Cellista instrument. IC₅₀ values, calculated from the dose-response curves, are listed in Table 2.

[0212] The anti-RSV F antibodies were subsequently tested for neutralization of RSV B clinical isolate 05-036549 mCherry. In this assay, 10 μ L of each antibody was added to a black 384-well clear-bottom microtiter plate in a 4-fold serial dilution. Subsequently, 20 μ L of HeLa cells (ATCC, CCL-2tm) at a density of 1.5x10⁵ cells/mL were added (i.e., 3000 cells/well) followed by the addition of 10 μ L RSV B 05-036549 mCherry virus at a multiplicity of infection (MOI) of 1.5. Cell controls (no virus added) and virus controls (cells infected with virus but no antibody added) were taken along on each plate. After three days of incubation at 37°C and 5% CO₂, viral replication was quantified by measuring RFP signal using an Envision instrument. IC₅₀ values, calculated from the dose-response curves, are listed in Table 2.

[0213] A subset of anti-RSV F antibodies was tested for their ability to inhibit the related paramyxovirus hMPV in a 3-day virus neutralization assay using LLC-MK2 cells and hMPV virus strain, CAN97-83 (hMPV-eGFP). In brief, 10 μ L of antibody was added to a black 384-well clear-bottom microtiter plate in a 4-fold serial dilution. Subsequently, 20 μ L of LLC-MK2 cells at a density of 3.0x10⁵ cells/mL were added (i.e., 6000 cells/well) followed by the addition of 10 μ L CAN97-83 virus at a multiplicity of infection (MOI) of 0.1. Cell controls (no virus added) and virus controls (cells infected with virus but no antibody added) were taken along on each plate. After three days of incubation at 37°C and 5% CO₂, viral replication was quantified by measuring eGFP expression using an Acumen Cellista instrument. IC₅₀ values, calculated from the dose-response curves, are listed in Table 2.

Table 2: Average IC₅₀ values (in μ M) for neutralization of RSV A A2-eGFP, RSV B 05-036549 mCherry and hMPV CAN97-83 eGFP by anti-RSV F antibodies (empty cells mean not tested).

	RSV A A2 eGFP (N=2)	RSV B 05-036549 mCherry (N=1 or 2)	hMPV CAN97-83 eGFP (N=1)
ADI-59811	2.6E-05	1.5E-04	
ADI-59814	7.3E-05	6.3E-04	
ADI-59818	7.7E-05	4.6E-04	

ADI-59149	8.1E-05	6.4E-04	
ADI-59148	9.2E-05	6.4E-04	
ADI-59828	1.3E-04	6.1E-04	9.2E-05
ADI-59090	2.1E-04	6.8E-04	3.3E-04
ADI-59062	3.2E-04	7.4E-04	9.7E-05
ADI-59110	3.9E-04	1.0E-03	4.7E-04

[0214] **Example 3: Further Development of anti-RSV F Antibody ADI-59811**

[0215] Anti-RSV F antibody ADI-59811 of Example 2 was further developed and analyzed for its use in methods of treating, preventing, and/or inhibiting RSV infection. In particular, variants of the anti-RSV F antibody comprising the heavy chain CDRs of SEQ ID NOs: 1-3, and the light chain CDRs of SEQ ID NOs: 4-6 were further developed and analyzed for their use in methods of treating, preventing, and/or inhibiting RSV infection.

[0216] In particular, an anti-RSV F antibody designated RSV antibody 1 non-YTE was developed as a human IgG1 monoclonal antibody. The anti-RSV antibody 1 non-YTE was constructed using a heavy chain constant region based on the IgG1-G1m(17) allotype (SEQ ID NO:170). The anti-RSV antibody 1 non-YTE comprised the variable heavy chain of SEQ ID NO: 7 and the variable light chain of SEQ ID NO: 8, and the heavy chain of SEQ ID NO: 9 and the light chain of SEQ ID NO: 10.

[0217] An anti-RSV F antibody designated RSV antibody 1 was developed as a human IgG1 monoclonal antibody, comprising the variable heavy chain of SEQ ID NO: 7 and the variable light chain of SEQ ID NO: 8. The RSV antibody 1 was constructed by swapping the heavy chain constant region of SEQ ID NO:9 for a YTE heavy chain constant region (SEQ ID NO:171), such that RSV antibody 1 comprised a heavy chain of SEQ ID NO:15 and a light chain of SEQ ID NO: 10. The YTE heavy chain constant region comprised the substitutions M252Y, S254T, and T256E, according to EU numbering, in the fragment crystallizable (Fc) domain (SEQ ID NO:171).

[0218] An anti-RSV F antibody designated RSV antibody 1 non-YTE LALA was developed as a human IgG1 monoclonal antibody, comprising the variable heavy chain of SEQ ID NO: 7 and the variable light chain of SEQ ID NO: 8, and further comprising the heavy chain and light chain sequences of SEQ ID NO: 9 and the light chain of SEQ ID NO: 10, respectively, wherein the sequence of SEQ ID NO: 9 was modified to incorporate the substitutions L234A and L235A, according to EU numbering, in the fragment crystallizable (Fc) domain.

[0219] **Example 4: Binding of anti-RSV F Antibody to Recombinant RSV A and B F proteins**

[0220] The binding affinity of the RSV antibody 1 non-YTE to recombinant RSV F proteins stabilized in the prefusion conformation (sometimes referred to as prefusion form) was assessed with surface plasmon resonance (SPR) (Table 3) using standard protocols. No binding could be detected to post fusion F protein.

[0221] Antibody Binding Kinetics by Octet: Antibody kinetics measurements to hMPV preF and RSV preF antigens were performed by Octet BLI assay. Affinity measurements were performed on an Octet HTX generally as previously described (see, e.g., Estep et al, High throughput solution-based measurement of antibody-antigen affinity and epitope binning. Mabs 5(2), 270-278 (2013)). Briefly, Octet measurements were performed by loading IgG samples on AHC sensors were equilibrated off-line in assay buffer for 30 min and then monitored on-line for 60 seconds for baseline establishment. Sensors with loaded IgG were exposed to 100 nM antigen in solution for 3 minutes, and afterwards were transferred to assay buffer for 3 min for off-rate measurement. All kinetics were analyzed using the 1:1 binding model.

Table 3: Kinetic parameters of RSV antibody 1 binding to stabilized RSV A and B preF

Antigen	k _a (1/Ms)	k _d (1/s)	K _D (M)
RSV A prefusion F	2.49×10 ⁶	3.08×10 ⁻⁴	1.24×10 ⁻¹⁰
RSV B prefusion F	8.42×10 ⁶	1.29×10 ⁻³	1.59×10 ⁻¹⁰

[0222] **Example 5: Anti-RSV F Antibody Binding Site**

[0223] The structure of a fragment antigen-binding (Fab) fragment of RSV antibody 1 bound to preF of RSV A2 was determined by cryogenic electron microscopy (cryo-EM) to a resolution of 3.2 Å (data not shown). Both the heavy and light chains of **RSV antibody 1** were observed to interact with antigenic site Ø.

[0224] The sequence conservation of the RSV antibody 1 binding site was assessed by examination of 5,719 F protein sequences derived from clinical and laboratory RSV isolates obtained from GenBank, Global Initiative on Sharing Avian Influenza Data (GISAID), and internal databases (collection period: 1956-2022). The percent conservation of each amino acid within the binding site was calculated for the different subtypes (i.e., 2,911 RSV A sequences and 2,808 RSV B sequences). Sequence analysis revealed that the RSV antibody 1 binding site is

highly conserved (>99%) at all 13 positions in RSV A and at 11 of the 13 positions in RSV B (Table 4). The 2 remaining positions (i.e., 206 and 209) were found to be less conserved due to mutations I206M and Q209R, which emerged in RSV B between 2016 and 2018. Recent RSV B strains containing M206 and R209 were included in the strain panel used in the virus neutralization assays.

Table 4: Sequence conservation of the RSV antibody 1 binding site in RSV A and B

Position		RSV A 2,911 sequences	RSV B 2,808 sequences
1	197	N (100%)	N (99.3%)
2	198	Y (100%)	Y (100%)
3	201	K (99.9%)	N (99.1%)
4	202	Q (100%)	Q (99.9%)
5	203	L (100%)	L (100%)
6	205	P (100%)	P (100%)
7	206	I (99.5%)	I (74.0%) M (26.0%)
8	209	K (99.7%)	Q (70.0%) R (25.8%) K (3.6%)
9	210	Q (100%)	Q (99.9%)
10	215	S (100%)	S (100%)
11	216	N (100%)	N (100%)
12	219	T (100%)	T (100%)
13	222	E (100%)	E (100%)

[0225] Example 6: In Vitro Neutralization of RSV A and B Strains by an anti-RSV F Antibody

[0226] The neutralization potency of RSV antibody 1 against RSV A and B was evaluated in a 3-day virus neutralization assay. The RSV F protein sequence for each virus tested is provided below in Table 5. For each virus tested, a 9-points 4-fold serial dilution of antibody was added to a separate black 96-well clear bottom tissue-culture treated microtiter plate (50 µL/well). Subsequently, 100 µL HeLa cell suspension (5000 cells/well) and 50 µL RSV virus at the appropriate dilution in RPMI-1640 culture medium supplemented with 10% (v/v) fetal calf serum (FCS), 25 mM HEPES, 2 mM L-alanyl-Glutamine, and 20 µg/mL gentamicin (200 µL final volume) was added. Virus dilutions were determined by titration of the virus and RT-qPCR readout. Cell controls (no virus added) and virus controls (cells infected with virus but no antibody added) were taken along in each plate. After 3 days of incubation at 37°C, 5% CO₂,

supernatant was removed from the wells. Plates were washed twice with ice-cold PBS (100 μ L/well), sealed and then stored overnight at -80°C . Next, 50 μ L of 1x lysis solution supplemented with DNase was added to the wells and incubated for 5 minutes at RT followed by the addition of 5 μ L stop solution (Ambion Cell-to-CT bulk lysis reagent buffer). Finally, quantitative reverse transcription polymerase chain reaction (qRT-PCR) for negative strand (genomic) RSV RNA was performed. In brief, cell lysate was added to 0.27 μ M (final concentration) RSV A or RSV B or β -actin forward primers. After a quick denaturation step (75°C for 5 min), 10x PCR buffer BI (containing 15 mM MgCl_2), MgCl_2 (3.5 mM), dNTP (1 mM), RNase inhibitor (1 U/ μ L), and Expand Reverse Transcriptase (0.33 U/ μ L; Roche) were added for cDNA synthesis based on antigenomic RNA (replicative intermediate). Reverse transcription was performed at 42°C for 30 minutes, followed by denaturation at 99°C for 5 minutes. The PCR reaction mixture was prepared by adding 2x Roche LightCycler 480 Probes Master, RSV A or RSV B forward and reverse primers at 0.3 μ M each, RSV A or RSV B probes at 0.1 μ M, β -actin forward and reverse primers at 0.3 μ M each, and β -actin probe at 0.1 μ M to the cDNA product. The PCR reaction consisted of a denaturation step (95°C for 600 sec), followed by 45 cycles of denaturation (95°C for 15 sec), annealing/elongation (60°C for 60 sec), and a final cooling step (40°C for 10 sec). Delta Cp values, normalized for β -actin, were used to determine the concentration of antibody necessary to reduce the viral RNA by 50% compared to untreated control (IC_{50}). Data analysis was performed using Graphpad Prism and Excel.

[0227] Referring to FIG. 1, RSV antibody 1 was able to neutralize all 28 RSV viruses with IC_{50} values ranging from 2 to 139 pM and a median IC_{50} value of 7 pM or 1.0 ng/mL. RSV antibody 1 neutralized RSV A with a median IC_{50} of 6.2 pM (range 2.4 - 21.6) and RSV B with a median IC_{50} of 12.5 pM (range 3.1 - 138.9). RSV B strain 18537 (also known as B Washington) was neutralized by RSV antibody 1 with an IC_{50} value of 139 pM, which is approximately 20-fold higher compared to the median value calculated for all strains. This reduction in potency can be explained by the presence of an RSV B 18537 specific mutation in the RSV antibody 1 binding site on RSV preF. These data show that RSV antibody 1 non-YTE has overall broad and potent neutralizing activity against both RSV A and B subtypes.

[0228] In FIG. 1, each symbol represents the mean of 3 to 12 replicates measured in at least 2 independent experiments. RSV antibody 1 or RSV antibody 1 non-YTE was used in each of

the virus neutralization assays. It is noted that RSV B strains 17-058221, MEP-OUT-13-D1, MEP-OUT-01-D1 and 18-002094 contained F mutations I206M and Q209R.

Table 5: RSV Virus F protein sequence

Strain name (SEQ ID NO:)	F protein sequence
Long (SEQ ID NO:127)	MELPILKANAIITTLAAVTFCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTSAANNRRARRELPRFMNYTLNNTKKTNTVTL KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLPVIVNKQSCRSINIEVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSIKEEVLAYVVQPLPGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLYVKGEPIINFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
A2 (SEQ ID NO:128)	MELLILKANAIITTLTAVTFCFASGQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK KNKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTQATNNRRARRELPRFMNYTLNNAKKTNTVTL KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLPVIVNKQSCRSINIEVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSIKEEVLAYVVQPLPGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLYVKGEPIINFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
Memphis 37 (SEQ ID NO:129)	MELPILKTNAIITTLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTPAANNRRARRELPRFMNYTLNNTKNNVTLS KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKNALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLPVIVNKQSCRSINIEVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSIKEEVLAYVVQPLPGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLYVKGEPIINFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLLLIAVGLFLYCKARSTPVTLSKDQLSGINNIAFSN
1.01 (SEQ ID NO:130)	MELPILKTNAIITTLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTPAANNRRARRELPRFMNYTLNNTKNNVTLS KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKNALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLPVIVNKQSCRSINIEVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSIKEEVLAYVVQPLPGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLYVKGEPIINFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLLLIAVGLFLYCKARSTPVTLSKDQLSGINNIAFSN
1.09 (SEQ ID NO:131)	MELPILKTNAIITTLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTPAANNRRARRELPRFMNYTLNNTKNNVTLS KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLPVIVNKQSCRSINIEVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSIKEEVLAYVVQPLPGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLYVKGEPIINFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLLLIAVGLFLYCKARSTPVTLSKDQLSGINNIAFSN
1.11 (SEQ ID NO:132)	MELPILKTNAIITTLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNNGTDAKVKLIKQELDKYKNAVTELOLLMQSTPAANNRRARRELPRFMNYTLNNTKTNTVTL KKRKRRLGFLGSGAISGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL

	KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSS
2.25 (SEQ ID NO:133)	MDLPILKTNAITAILAAVLLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANNRARELPRFMNYTLNNTKNNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLFLYCKARSTPVTLSKDQLSGINNIAFSN
2.03 (SEQ ID NO:134)	MELPILKANAITITLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANNRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSS
2.24 (SEQ ID NO:135)	MELPILKTNAITITLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANNRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IREEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAV STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSS
2.35 (SEQ ID NO:136)	MELPILKTNAITITLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANNRARELPRSMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSS
07-041911 (SEQ ID NO:137)	MELPILKTNAITITLAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSNGCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPI INFYDPLVFPSEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK STTNIMITTIIIVIIIVILLSLIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
09-000457 (SEQ ID NO:138)	MELPILKTNAITITLAAVTLCFTSSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSNNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKIHTSPLCTTN

	TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
11-014288 (SEQ ID NO:139)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
11-050878 (SEQ ID NO:140)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANNRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
BR NCH 815 (SEQ ID NO:141)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TNEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
NCH 755 (SEQ ID NO:142)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNAKYTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYDPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
NCH 763 (SEQ ID NO:143)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPI INFYNPLVFPSEDFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITITIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
12-049454 (SEQ ID NO:144)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNCGTDAKVKLKQELDKYKNAVTELQLLMQSTPAANSRARELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVSAGIASGIAVSKVLHLEGEVNIKSALLSTNKAVVSLSNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRTRDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGI IKTFSSNGCDYVSNKGVDIVSVGNT

	LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
12-049766 (SEQ ID NO:145)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
NCH 796 (SEQ ID NO:146)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
13-010381 (SEQ ID NO:147)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
13-000323 (SEQ ID NO:148)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYINKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
NCH 1036 (SEQ ID NO:149)	MELPILKTNAITTILAAVTLCFAYSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN
18-001989 (SEQ ID NO:150)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRELPRSMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSASIAAGIAVSKVLHLEGEVNIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLP IVNKQSCSISNIETVIEFQKNNRLEITREFSVNAGVTTTPVSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQAECKVQSNRVFCDTMNSLTLPSEVNLNCNIDIFNPK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKTFSGNCDYVSNKGVDIVSVGNT LYYVKNQEGKSLYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVILLALIAVGLLLYCKARSAPVTLSKDQLSGINNIAFSN

18-004500 (SEQ ID NO:151)	MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSNIK ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPAANSRARRRELPRFMNYTLNNTKNTNVTLS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKSALLSTNKAVVSLNNGVSVLTSKVLDL KNYIDKQLLPVIVNQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTTPVSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN TKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDVSSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKQEGKSLEYVKGEPIINFYDPLVFPSPDEFDASISQVNEKINQSLAFIRKSDDELLHNVNAGK STTNIMITTIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLTKDQLSGINNIAFSN
Wash/18537 (SEQ ID NO:152)	MELLIHRSSAIFLTLAVNALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNRLLPVIVNQQSCRISNIETVIEFQQMNSRLEITREFSVNAGVTTPLSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKLEGKNLYVKGEPIINYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITTIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLTKDQLSGINNIAFSK
9320 (SEQ ID NO:153)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLTQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KSYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPLSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKLEGKNLYVKGEPIINYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITTIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLTKDQLSGINNIAFSK
2.07 (SEQ ID NO:154)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSDIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPLSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKLEGKNLYVKGEPIINYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIVIIIVVLLSLIAIGLLLYCKAKNTPVTXSKDQLSGINNIAFSK
2.11 (SEQ ID NO:155)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPLSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKLEGKNLYVKGEPIINYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITVIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLTKDQLSGINNIAFSK
2.30 (SEQ ID NO:156)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTETKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVLGVSIAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPLSTYMLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGTKCTASNKNRGIKFTSNGCDYVSNKGVDIVSVGNT LYYVVKLEGKNLYVKGEPIINYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLTKDQLSGINNIAFSK
2.39 (SEQ ID NO:157)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS

	KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTXSKDQLSGINNIAFSK
2.41 (SEQ ID NO:158)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITVIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLSKQDQLSGINNIAFSK
03-034613 (SEQ ID NO:159)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTHMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLSKQDQLSGINNIAFSK
05-036549 (SEQ ID NO:160)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIQ ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNHTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQNCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKKTPVTXSKDQLSGINNIAFSK
11-014548 (SEQ ID NO:161)	MELLIHRSSSIFLTLAINAFYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSVIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTLSKQDQLSGINNIAFSK
NCH 766 (SEQ ID NO:162)	MELLIHRSSAIFLALAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSVIKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASKNRGIKTFSSNGCDVSNKGVDIVSVGNT LYYVKNLEGKNLYVKGEPIINYDPLVFPSPDEFDASISQVNEKINQSLSFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTXSKDQLSGINNIAFSK
NCH 770 (SEQ ID NO:163)	MELLIHRSSAIFLTLAINAFYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLKQELDKYKNAVTELQLLMQNTPAANNRAREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLGVSAGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLNNGVSVLTSKVLDL KNYINNQLLPVNNQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTYMLTNSSELLSL

	INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTXSKDQLSGINNIAFSK
14-006938 (SEQ ID NO:164)	MELLIHRSSAIFLTLAINTLYLTSSQNITEEFYQSTCSAVSRGYFSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALLSTNKAVVSLSNGVSVLTSSKVLDDL KNYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHDVNTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTL SKDQLSGINNIAFSK
17-058221 (SEQ ID NO:165)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAVNNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALQLTNKAVVSLSNGVSVLTSSRVLDL KNYINNQLLPMVNRQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTL SKDQLSGINNIAFSK
MEP-OUT- 13-D1 (SEQ ID NO:166)	MELLIHRPSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAVNNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALQLTNKAVVSLSNGVSVLTSSRVLDL KNYINNQLLPMVNRQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTL SKDQLSGINNIAFSK
MEP-OUT- 01-D1 (SEQ ID NO:167)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAVNNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALQLTNKAVVSLSNGVSVLTSSRVLDL KNYINNQLLPMVNRQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTL SKDQLSGINNIAFSK
18-002094 (SEQ ID NO:168)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAVNNRARRREAPQYMNNTINTTKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALQLTNKAVVSLSNGVSVLTSSRVLDL KNYINNQLLPMVNRQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN IKEGSNICLTRDRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNTDIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYVKNLEGKNLYVKGEPI INYYDPLVFPSPDEFDASISQVNEKINQSLAFIRRSDELLHNVTGK STTNIMITAIIIVIIIVVLLSLIAIGLLLYCKAKNTPVTL SKDQLSGINNIAFSK
18-006171 (SEQ ID NO:169)	MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIELSNIK ETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAVNNRARRREAPQYMNNTINTAKNLNVSIS KKRKRRLGFLFLGVGSAIASGIAVSKVLHLEGEVNIKIKNALQLTNKAVVSLSNGVSVLTSSKVLDDL KNYINNQLLPVIVNQQSCRISNIETVIEFQQKNSRLEITREFSVNAGVTTPYSTMYLTNSELLSL INDMPITNDQKKLMSSNVQIVRQQSYSIMSI IKEEVLAYVVQLPIYGVIDTPCWKLHTSPLCTTN

	IKEGSNICLTRTDGRGWYCDNAGSVSFFPQADTCKVQSNRVFCDTMNSLTLPSEVSLCNDTIFNSK YDCKIMTSKTDISSSVITSLGAIVSCYGKTKCTASNKNRGI IKTF SNGCDYVSNKGVDTVSVGNT LYYV NKLEGNLYVKGEPI INYYDPLVFP SDEFDASISQVNEKINQSLAFIRRSDELLHNVNTGK STTNIMITAI IIVIIVVLLSLIAIGLLLYCKAKNTPVTLSKDQLSGINNIAFSK
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[0229] Example 7: Prophylactic Efficacy of RSV antibody 1 non-YTE in Cotton Rat Models of RSV A and B Infection

[0230] The prophylactic efficacy of RSV antibody 1 without half-life extending mutations (i.e., RSV antibody 1 non-YTE) was evaluated in cotton rats infected with 10⁵ plaque-forming units (pfu) RSV A Long, RSV B 9320, or RSV B 18537. Briefly, 6-8 weeks old male Sigmodon hispidus cotton rats (Source: Sigmovir Biosystems, Inc., Rockville MD) (n=5 to 6 animals/group) were dosed via intramuscular injection with RSV antibody 1 non-YTE at 6 different doses. Another group of cotton rats (n=5/6) receiving buffer solution only served as a vehicle control group. Twenty-four hours post-administration the animals were challenged intranasally with 10⁵ pfu RSV-A Long, RSV B 9320, or RSV B 18537. Four days after viral challenge, prophylactic efficacy was evaluated by measuring the RSV viral titer in the lung tissue of these animals by plaque assay. For analysis of RSV A Long data, data from 2 independent studies were combined.

[0231] Referring now to FIG. 2A-FIG. 2C, prophylactic treatment with RSV antibody 1 non-YTE resulted in a dose-dependent reduction in lung viral titers in all 3 cotton rat models. The mean reductions versus vehicle control were statistically significant (alpha=0.05) in dose groups 2.5 to 0.03 mg/kg (RSV A Long), 3.0 to 0.1 mg/kg (RSV B 9320), and 3.0 to 0.3 mg/kg (RSV B 18537).

[0232] Example 8: Determination of In Vivo EC₉₀ in RSV A Long, RSV B 9320, and RSV B 18537 (Washington) Infected Cotton Rats

[0233] Serum concentrations of RSV antibody 1 non-YTE in each dose group (described in example 7) on Day 4 post infection were quantified using a Meso-Scale Discovery (MSD)-based assay. The assay method is briefly described as follows: MSD Gold Small-spot streptavidin plate (Cat: L45SA-1) was blocked for 30 minutes with 1x PBS + 1% BSA buffer and tapped dry. Next, 30 µL final working concentration of capture and detection reagent master mix (biotinylated and ruthenium-labeled anti-human Fc mAb; R10Z8E9) was added to each well combined with 20 µL of diluted standards, QCs, or samples (50 µL/well) and incubated for 60 minutes at RT with shaking. The MSD plate was washed and 1x MSD-T read buffer was added

to all wells. The plate was immediately read on the MSD Sector S600 imager (Meso Scale Discovery; Rockville, MD). MSD output files containing the raw ECL counts were swept into Cyberlab Content Manager (Agilent; Santa Clara, CA) and imported into Watson LIMS (Thermo Fisher Scientific; Waltham, MA) regression software for analysis. The Watson study regression was predefined during assay qualification and a 5-parameter logistic (Auto-estimate) fit with 1/Y2 weighting factor was used.

[0234] Effective concentrations yielding a 90% reduction (EC₉₀) in the log₁₀ lung viral titer relative to vehicle control were determined by plotting antibody serum concentrations vs log₁₀ lung viral titer reductions (% protection) (FIG. 3A-FIG. 3C). From these plots, the *in vivo* EC₉₀ values were calculated for RSV A Long, RSV B 9320, and RSV B 18537 using nonlinear regression analysis (Table 6). RSV antibody 1 exhibits similar EC₉₀ values of 2.0 and 2.5 µg/ml against, respectively, RSV A Long and RSV B 9320 and a 6 to 7.5-fold higher EC₉₀ value of 15 µg/ml against RSV B 18537. The lower activity against RSV B 18537 is in line with *in vitro* neutralization data and can be explained by the presence of a mutation in the RSV antibody 1 binding site that is unique to RSV B 18537.

[0235] In conclusion, RSV antibody 1 non-YTE is effective at reducing lung viral load in cotton rats with similar EC₉₀ values for the two prototype strains RSV A Long or RSV B 9320.

Table 6: EC₉₀ values of RSV antibody 1 against RSV A Long, RSV B 9320, and RSV B 18537

	RSV A Long	RSV B 9320	RSV B 18537
EC ₉₀ (95% CI) (µg/mL)	2.0 (1.8-2.4)	2.5 (2.0-3.2)	15.1 (10.2-22.4)

CI, confidence interval; EC₉₀, 90% effective concentration

[0236] Example 9: In Vitro and in Vivo Assessment of Fc-mediated Effector Functions of RSV antibody 1

[0237] It has been well established that Fc-mediated effector functions, such as viral clearance by ADCP and killing of infected cells by ADCC, can contribute to the *in vivo* efficacy of antiviral antibodies including RSV mAbs (Tanget al., *Nat Commun.*10(1):4153 (2019); DiLillo et al., *Nat Med.* 20(2):143-151 (2014); van Erp et al., *Front Immunol.* 10:548 (2019)). To investigate if Fc-mediated effector functions also have a role in the efficacy of RSV antibody 1, its activity was compared with 2 Fc variants in ADCC and ADCP reporter bioassays and in a

mouse model of RSV infection. The first variant, RSV antibody 1 non-YTE, contains a wild-type Fc domain without half-life-extending mutations, as described above, which based on findings with other mAbs (Borrok et al., *J Pharm Sci.*106(4):1008-1017 (2017) is expected to have higher affinity for both FcγRIIa and FcγRIIIa. The second variant, RSV antibody 1 non-YTE LALA, contains Fc-silencing mutations L234A/L235A in a wild-type Fc background, as described above. Both variants are indistinguishable from RSV antibody 1 in direct antiviral activity.

[0238] Evaluation of RSV antibody 1 Fc Variants in Human ADCC and ADCP Reporter Bioassays: The potential of RSV antibody 1, RSV antibody 1 non-YTE, and RSV antibody 1 non-YTE LALA to induce ADCP and ADCC was assessed *in vitro* using Jurkat/NFAT-luc effector cells expressing, respectively, FcγRIIa or FcγRIIIa and RSV A2-infected A549 target cells. In brief, the set up for the FcγRIIIa-V ADCC reporter bioassay was as follows; A549 cells were pre-seeded on day -1 at 2×10^4 cells in 96 well plates (Corning, 3903). On day 0 they were infected with RSV-GFP5 at a multiplicity of infection (MOI) of 1 and incubated overnight at 37°C, 5% CO₂. 24 hours after infection, cells were washed and the ADCC FcγRIIIa-V (V158), high affinity variant, reporter bioassay (Promega) was carried out as described by the manufacturer. Briefly; 25 µl of a 7-point, 4-fold antibody dilution series were prepared in assay buffer and transferred to RSV-infected A549 cells in 25 µl assay buffer. 25 µl of ADCC effector cells (630 µl in 3.6 ml of assay buffer) were subsequently added to the wells. Plates were incubated for 6 hours at 37°C, 5% CO₂, assay reagent was added to each well and luminescence was measured on a Viewlux microplate imager with 0.3 seconds exposure at 3x binning. For the FcγRIIa-H ADCP reporter bioassay A549 RSV-infected cells were set up as described for the ADCC reporter bioassay. The high-affinity variant (H131) ADCP reporter bioassay (Promega) was carried out essentially according to manufacturer instructions. Briefly; 25 µl of 2-fold antibody dilutions were prepared in assay buffer and transferred to RSV-infected A549 cells in 25 µl assay buffer. Antibodies were allowed to bind to cells for 15 minutes at 37°C. 25 µl of ADCP effector cells (700 µl in 3.4 ml of assay buffer) were subsequently added to the wells. Plates were incubated for 6 hours at 37°C, 5% CO₂, assay reagent was added to each well and luminescence was measured on a Viewlux microplate imager with 1 second exposure at 2x binning.

[0239] Increasing concentrations of RSV antibody 1, RSV antibody 1 non-YTE, RSV antibody 1 non-YTE LALA and a negative control mAb were tested in ADCP and ADCC

reporter bioassays for their ability to activate, respectively, FcγRIIa and FcγRIIIa expressed on Jurkat cells using RSVA2-infected A549 cells as a target. Referring to FIG. 4A-FIG. 4B, each datapoint is the mean of 3 independent replicates and error bars represent standard deviation (SD).

[0240] Further referring to FIG. 4A-FIG. 4B, the results indicated that RSV antibody 1 was able to engage and activate both human FcγRs, albeit to a different extent (FIG. 4A-FIG. 4B). RSV antibody 1 non-YTE was more effective in activating both FcγRIIa and FcγRIIIa than RSV antibody 1, while RSV antibody 1 non-YTE LALA showed virtually no activity in this assay.

[0241] Evaluation of RSV antibody 1 Fc Variants in a Mouse Model of RSV A Infection: The prophylactic efficacy of RSV antibody 1, RSV antibody 1 non-YTE, and RSV antibody 1 non-YTE LALA was compared in BALB/c mice (n=6/group) infected with 1.7×10⁶ pfu RSV A2. RSV antibody 1 and its Fc variants were administered IM at 4 different doses 1 day prior to intranasal RSV infection. Lung viral titers were determined by plaque assay on Day 4 after infection. Serum antibody concentrations on Day 4 post infection were quantified using an MSD-based assay and plotted versus the relative reductions in log lung viral titer (FIG. 5A-FIG. 5C). From these plots, *in vivo* EC₉₀ values were calculated using nonlinear regression analysis (Table 7). The data analyzed were from 2 independent studies. The dotted line in each graph of FIG. 5A-FIG. 5C indicates the EC₉₀ for viral reduction. In conclusion, all 3 RSV antibody 1 Fc variants exhibited similar EC₉₀ values against RSV A2 indicating that Fc-mediated effector functions did not contribute to the prophylactic efficacy of RSV antibody 1 in RSV-infected mice.

Table 7: EC₉₀ values of RSV antibody 1 Fc variants against RSV A2

	EC ₉₀ (95% CI) (μg/mL)
RSV antibody 1	1.5 (1.1-2.0)
RSV antibody 1 non-YTE	1.2 (0.9-1.6)
RSV antibody 1 non-YTE LALA	2.1 (1.6-2.8)

CI, confidence interval; EC₉₀, 90% effective concentration; Fc, fragment crystallizable; LALA, L234A/L235A; RSV, respiratory syncytial virus; RSV, respiratory syncytial virus; YTE, M252Y/S254T/T256E

[0242] Example 10: Binding Specificity in Human Plasma Membrane Protein Cell Array (Retrogenix Cell Microarray Technology)

[0243] The *in vitro* human plasma membrane protein array is a research-grade screening tool to evaluate potential off-target binding of antibody therapeutics. These screens are conducted at Charles River, Chinley, High Peak, Derbyshire, UK. Briefly, to create the microarray, expression vectors encoding for full-length human proteins, are spotted onto glass slides. Subsequently, human embryonic kidney (HEK) 293 cells are applied to the slides and the cells are reverse transfected to express the individual proteins. The cells are then fixed prior to application of the test material.

[0244] Potential for off-target binding of RSV antibody 1 was screened against a library of 6,018 human plasma membrane proteins (secreted and cell-surface-tethered secreted proteins) and 397 human heterodimers expressed in human HEK293 cells in a protein array assay as described above. RSV antibody 1 was selective to RSV preF as indicated by specific interaction with the soluble, recombinant target protein RSVF (RSV190373-preF) incorporated in the test system (Data not shown). No off-target interactions with the tested human proteins were observed.

[0245] Example 11: Pharmacokinetics in cynomolgus monkeys

[0246] The pharmacokinetics of RSV antibody 1 were characterized in a non-GLP PK study in 4 female cynomolgus monkeys following a single IV dose of 5 mg/kg. Additionally, a control molecule (i.e., nirsevimab; an anti-RSV mAb containing a YTE mutation) was included in 2 females in the study. Serum drug exposure analysis of RSV antibody 1 and nirsevimab was performed using a fit-for-purpose electrochemiluminescent immunoassay (ECLIA) method read on an MSD Sector Imager S600. Both assay methods applied anti-human Fc-specific (CH2 domain) mouse mAb as capture and detection reagents in a homogenous sandwich format. Serum RSV antibody 1 and nirsevimab concentration-time data from both groups were fit with a linear 2 compartment PK model for PK parameter estimation.

[0247] The mean observed concentration-time points of serum RSV antibody 1 and nirsevimab in cynomolgus monkeys along with the PK model fittings are shown FIG. 6. Referring to FIG. 6, lines represent model prediction; and symbols represent mean observed data from each animal at each sampling point over time. One animal in the RSV antibody 1 group had abnormally poor clearance. This animal showed no clinical symptoms that may impact PK and

was not ADA-positive throughout the study. This animal was considered an outlier and was removed from the analysis of the RSV antibody 1 group.

[0248] Example 12: Sequence Optimization

[0249] The sequence of RSV Antibody 1 was analyzed for potential immunogenicity using the T-regulatory (Treg) adjusted scores from the EpiVax Epimatrix *in silico* immunogenicity prediction program (De Groot, A. S. & Martin, W. Reducing risk, improving outcomes: bioengineering less immunogenic protein therapeutics. Clin Imm, 2009. 131:189-201). EpiVax scores of -27.98 and 45.78 were obtained for the heavy chain (SEQ ID 9) and light chain (SEQ ID 10) respectively. Two variants of RSV antibody 1 were created by reverting residues 3, 39, 46, and 74 (SEQ ID NO:17) or residues 3 and 74 (SEQ ID NO:18) to those found in germline IGK1-27, resulting in Treg adjusted Epivax scores of -2.79 and 8.24, respectively. The binding affinity of these variants to RSV F protein was determined by SPR as described in Example 4. The binding affinity of each variant was indistinguishable from that of RSV antibody 1, indicating maintenance of activity for the designed mutants.

[0250] It will be evident to one skilled in the art that the present disclosure is not limited to the foregoing illustrative examples, and that it can be embodied in other specific forms without departing from the essential attributes thereof. It is therefore desired that the examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing examples, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

[0251] It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

[0252] All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains.

[0253] The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms “comprising,” “consisting essentially of,” and “consisting of” may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any

equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described. Other embodiments are within the following claims.

CLAIMS

We claim:

1. An isolated or recombinant anti-Respiratory Syncytial Virus (RSV) F protein (F) antibody or antigen binding fragment thereof that specifically binds to a Respiratory Syncytial Virus (RSV) F protein (F), wherein the anti-RSV F antibody or antigen binding fragment thereof comprises a variable heavy chain region (V_H) comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, and a variable light chain region (V_L) comprising a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the amino acid sequences of:

- (1) SEQ ID NOs:1, 2, 3, 4, 5, and 6, respectively;
- (2) SEQ ID NOs:19, 20, 21, 22, 23, and 24, respectively;
- (3) SEQ ID NOs:27, 28, 29, 30, 31, and 32, respectively;
- (4) SEQ ID NOs:35, 36, 37, 38, 39, and 40, respectively;
- (5) SEQ ID NOs:43, 44, 45, 46, 47, and 48, respectively;
- (6) SEQ ID NOs:51, 52, 53, 54, 55, and 56, respectively;
- (7) SEQ ID NOs:59, 60, 61, 62, 63, and 64, respectively;
- (8) SEQ ID NOs:67, 68, 69, 70, 71, and 72, respectively;
- (9) SEQ ID NOs:75, 76, 77, 78, 79, and 80, respectively; or
- (10) SEQ ID NOs:83, 84, 85, 86, 87, and 88, respectively.

2. The anti-RSV F antibody or antigen binding fragment thereof according to claim 1, wherein the antibody or antigen binding fragment thereof comprises a V_H having an amino acid sequence at least 90% identical to SEQ ID NO:7, 25, 33, 41, 49, 57, 65, 73, 81, or 89, or a V_L having an amino acid sequence at least 90% identical to SEQ ID NO:8, 26, 34, 42, 50, 58, 66, 74, 82, or 90.

3. The anti-RSV F antibody or antigen binding fragment thereof according to claim 2, comprising:

- (1) a V_H having the amino acid sequence of SEQ ID NO:7, and a V_L having the amino acid sequence of SEQ ID NO:8;
- (2) a V_H having the amino acid sequence of SEQ ID NO:25, and a V_L having the amino acid sequence of SEQ ID NO:26;

- (3) a V_H having the amino acid sequence of SEQ ID NO:33, and a V_L having the amino acid sequence of SEQ ID NO:34;
 - (4) a V_H having the amino acid sequence of SEQ ID NO:41, and a V_L having the amino acid sequence of SEQ ID NO:42;
 - (5) a V_H having the amino acid sequence of SEQ ID NO:49, and a V_L having the amino acid sequence of SEQ ID NO:50;
 - (6) a V_H having the amino acid sequence of SEQ ID NO:57, and a V_L having the amino acid sequence of SEQ ID NO:58;
 - (7) a V_H having the amino acid sequence of SEQ ID NO:65, and a V_L having the amino acid sequence of SEQ ID NO:66;
 - (8) a V_H having the amino acid sequence of SEQ ID NO:73, and a V_L having the amino acid sequence of SEQ ID NO:74;
 - (9) a V_H having the amino acid sequence of SEQ ID NO:81, and a V_L having the amino acid sequence of SEQ ID NO:82; or
 - (10) a V_H having the amino acid sequence of SEQ ID NO:89, and a V_L having the amino acid sequence of SEQ ID NO:90.
4. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 3, wherein the antibody or antigen binding fragment comprises an antigen binding fragment comprising a heavy chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99.
5. The anti-RSV F antibody or antigen binding fragment thereof according to claim 4, wherein the antibody or antigen binding fragment comprises the antigen binding fragment comprising the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12, 91, 92, 93, 94, 95, 96, 97, 98, or 99.
6. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 3, wherein the antibody or antigen binding fragment comprises an antigen binding fragment comprising a light chain polypeptide sequence having an amino acid sequence at least 90% identical to SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108.
7. The anti-RSV F antibody or antigen binding fragment thereof according to claim 6, wherein the antibody or antigen binding fragment comprises the antigen binding fragment

comprising the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13, 100, 101, 102, 103, 104, 105, 106, 107, or 108.

8. The anti-RSV F antibody or antigen binding fragment thereof according to claim 1, wherein the antibody or antigen binding fragment comprises the antigen binding fragment comprising:

(1) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 12 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO: 13;

(2) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:91 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:100;

(3) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:92 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:101;

(4) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:93 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:102;

(5) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:94 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:103;

(6) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:95 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:104;

(7) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:96 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:105;

(8) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:97 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:106;

(9) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:98 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:107; or

(10) the heavy chain polypeptide sequence having the amino acid sequence of SEQ ID NO:99 and the light chain polypeptide sequence having the amino acid sequence of SEQ ID NO:108.

9. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 8, wherein the antibody or antigen binding fragment comprises a heavy chain polypeptide comprising substitutions M252Y, S254T, and T256E.

10. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 9, wherein the antibody or antigen binding fragment comprises a heavy chain polypeptide comprising substitutions L234A and L235A.

11. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 10, wherein the antibody or antigen binding fragment comprises the heavy chain polypeptide having the amino acid sequence selected from:

- (1) SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:15;
- (2) SEQ ID NO:91, SEQ ID NO:109, or SEQ ID NO:118;
- (3) SEQ ID NO:92, SEQ ID NO:110, or SEQ ID NO:119;
- (4) SEQ ID NO:93, SEQ ID NO:111, or SEQ ID NO:120;
- (5) SEQ ID NO:94, SEQ ID NO:112, or SEQ ID NO:121;
- (6) SEQ ID NO:95, SEQ ID NO:113, or SEQ ID NO:122;
- (7) SEQ ID NO:96, SEQ ID NO:114, or SEQ ID NO:123;
- (8) SEQ ID NO:97, SEQ ID NO:115, or SEQ ID NO:124;
- (9) SEQ ID NO:98, SEQ ID NO:116, or SEQ ID NO:125; or
- (10) SEQ ID NO:99, SEQ ID NO:117, or SEQ ID NO:126.

12. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 11, wherein the antibody or antigen binding fragment thereof comprises the light chain polypeptide having the amino acid sequence of SEQ ID NO: 10, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, or SEQ ID NO:108.

13. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 12, wherein the antibody or antigen binding fragment thereof comprises the heavy chain polypeptide and the light chain polypeptide, respectively, selected from:

(1) SEQ ID NO:15 and SEQ ID NO: 10, SEQ ID NO: 9 and SEQ ID NO: 10, or SEQ ID NO: 11 and SEQ ID NO: 10;

(2) SEQ ID NO:91 and SEQ ID NO:100, SEQ ID NO:109 and SEQ ID NO:100, SEQ ID NO:118 and SEQ ID NO:100;

(3) SEQ ID NO:92 and SEQ ID NO:101, SEQ ID NO:110 and SEQ ID NO:101, or SEQ ID NO:119 and SEQ ID NO:101;

(4) SEQ ID NO:93 and SEQ ID NO:102, SEQ ID NO:111 and SEQ ID NO:102, or SEQ ID NO:120 and SEQ ID NO:102;

(5) SEQ ID NO:94 and SEQ ID NO:103, SEQ ID NO:112 and SEQ ID NO:103, or SEQ ID NO:121 and SEQ ID NO:103;

(6) SEQ ID NO:95 and SEQ ID NO:104, SEQ ID NO:113 and SEQ ID NO:104, or SEQ ID NO:122 and SEQ ID NO:104;

(7) SEQ ID NO:96 and SEQ ID NO:105, SEQ ID NO:114 and SEQ ID NO:105, or SEQ ID NO:123 and SEQ ID NO:105;

(8) SEQ ID NO:97 and SEQ ID NO:106, SEQ ID NO:115 and SEQ ID NO:106, or SEQ ID NO:124 and SEQ ID NO:106;

(9) SEQ ID NO:98 and SEQ ID NO:107, SEQ ID NO:116 and SEQ ID NO:107, or SEQ ID NO:125 and SEQ ID NO:107; or

(10) SEQ ID NO:99 and SEQ ID NO:108, SEQ ID NO:117 and SEQ ID NO:108, or SEQ ID NO:126 and SEQ ID NO:108.

14. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 13, wherein the antibody or antigen binding fragment thereof is capable of neutralizing or blocking RSV-F activity by inhibition of at least one biological activity of RSV-F.

15. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 14, wherein the antibody or antigen binding fragment thereof is capable of binding to the PreF conformation of RSV-F with a higher binding affinity relative to the PostF conformation of RSV-F.

16. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 15, where the antibody or antigen binding fragment is a human antibody, is a humanized antibody, is a chimeric antibody, or is a bispecific or multi-specific antibody.
17. The anti-RSV F antibody or antigen binding fragment thereof according to claim 16, wherein the antibody or antigen binding fragment is a human antibody.
18. The anti-RSV F antibody or antigen binding fragment thereof according to any one of claims 1 to 17, wherein the antibody or antigen binding fragment is conjugated to polyethylene glycol (PEG) or to a therapeutic agent or to a diagnostic agent.
19. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding the anti-RSV F antibody or antigen-binding fragment thereof according to any one of claims 1 to 18.
20. An expression vector comprising the isolated nucleic acid sequence according to claim 19.
21. A host cell comprising the expression vector according to claim 20.
22. A method of preparing the anti-RSV F antibody or antigen-binding fragment thereof according to any one of claims 1 to 17, comprising culturing the host cell of claim 21 under conditions to produce the anti-RSV F antibody or antigen-binding fragment thereof, and recovering the anti-RSV F antibody or antigen-binding fragment thereof from the cell or cell culture.
23. A pharmaceutical composition comprising: one or more of the anti-RSV F antibodies or antigen-binding fragments thereof according to any one of claims 1 to 18, and a pharmaceutically acceptable carrier and/or excipient.
24. A pharmaceutical composition comprising: one or more nucleic acid sequences according to claim 19; or one or more the expression vectors according to claim 20; and a pharmaceutically acceptable carrier and/or excipient.
25. A method of inhibiting at least one biological activity of RSV-F, comprising administering to a subject in need thereof or suspected of being in need thereof: a) one or more antibodies or antigen-binding fragments thereof according to any of claims 1 to 18; b) the nucleic acid molecule according to claim 19; c) the expression vector according to claim 20; d) the host cell according to claim 21; or e) a pharmaceutical composition according claim 23 or 24.

26. The method of claim 25, wherein the subject is in need of treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection.
27. The method of claim 25 or 26, wherein the method reduces lung viral titers in the subject.
28. The method of any one of claims 25 to 27, wherein any one of a)-e) are administered in a therapeutically effective amount.
29. Use of one or more of the anti-RSV F antibodies or antigen-binding fragments thereof according to any one of claims 1 to 18 in the manufacture of a medicament for inhibiting at least one biological activity of RSV-F in a subject.
30. Use of one or more of the anti-RSV F antibodies or antigen-binding fragments thereof according to any one of claims 1 to 18 in the manufacture of a medicament for treating, preventing, or ameliorating a Respiratory Syncytial Virus (RSV) infection, or treating, preventing, or ameliorating at least one symptom associated with RSV infection in a subject.