has the amino acid sequence set forth in SEQ ID NO:2 or 1627. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_H CDR2, which has the amino acid sequence set forth in SEQ ID NO:3. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_H CDR3, which has the amino acid sequence set forth in SEQ ID NO:4. In some examples, an isolated antibody or antigen-binding fragment thereof provided herein contains a V_H CDR1, which has the amino acid sequence set forth in SEQ ID NO:2 or 1627; a V_H CDR2, which has the amino acid sequence set forth in SEQ ID NO:3; and a V_H CDR3, which has the amino acid sequence set forth in SEQ ID NO:4.

In some examples, an isolated antibody or antigen-binding fragment thereof provided herein contains a V_L CDR1, which has the amino acid sequence set forth in SEQ ID NO:6. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_L CDR2, which has the amino acid sequence of the V_L CDR2 is set forth in SEQ ID NO:7. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_L CDR3, which has the amino acid sequence set forth in SEQ ID NO:8. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_L CDR1, which has the amino acid sequence set forth in SEQ ID NO:6; a V_L CDR2, which has the amino acid sequence set forth in SEQ ID NO:7; and a V_L CDR3, which has the amino acid sequence set forth in SEQ ID NO:8.

In a first aspect, there is provided an antibody or antigen-binding fragment thereof comprising:

a V_H CDR1, comprising the sequence of amino acid residues set forth in SEQ ID NO:2;

a V_H CDR2, comprising the sequence of amino acid residues set forth in SEQ ID NO:3;

a V_H CDR3, comprising the sequence of amino acid residues set forth in SEQ ID NO:4;

a V_L CDR1, comprising the sequence of amino acid residues set forth in SEQ ID NO:6;

a V_L CDR2, comprising the sequence of amino acid residues set forth in SEQ ID NO:7; and

a V_L CDR3, comprising the sequence of amino acid residues set forth in SEQ ID NO:8,

wherein the antibody or antigen-binding fragment immunospecifically binds to Respiratory Syncytial Virus (RSV) fusion (F) protein and neutralizes RSV.

In some examples, an isolated antibody or antigen-binding fragment provided herein contains a heavy chain, which has the amino acid sequence set forth in SEQ ID NO:9. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_H domain, which has the amino acid sequence set forth in amino acids 1-125 of SEQ ID NO:9. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a light chain, which has the amino acid sequence set forth in SEQ ID NO:13. In some examples, an isolated antibody or antigen-binding fragment provided herein contains a V_L domain, which has the amino acid sequence set forth in 1-107 of SEQ ID NO:13. In a particular example, the isolated antibody or antigen-binding fragment is sc5.

portion form a multivalent antibody.

In a second aspect, there is provided a multivalent antibody, comprising:

a first antigen-binding portion comprising an antibody or antigen-binding fragment thereof as defined above wherein the first antigen-binding portion comprising an antibody or antigen-binding fragment thereof is conjugated to a multimerization domain; and

a second antigen-binding portion comprising an antigen-binding fragment of an antiviral antibody conjugated to a second multimerization domain, wherein:

the first multimerization domain and the second multimerization domain are complementary or the same, whereby the first antigen-binding portion and second antigen-binding portion form a multivalent antibody; and

the first and second antigen binding portions are the same or different.

In some examples, the multivalent antibodies provided herein contain 1, 2, 3, 4, or 5 additional antigen-binding portions. Exemplary multivalent antibodies include a bivalent, trivalent, tetravalent, pentavalent, hexavalent, or heptavalent antibodies. The multivalent antibodies provided herein include heterobivalent or homobivalent antibodies. The multivalent antibodies provided herein include multispecific antibodies. In some examples, the multispecific antibody is a bispecific, trispecific or tetraspecific antibody. In some examples, the multivalent antibodies provided herein contain an antigen-binding fragment that is a single-chain Fv (scFv), Fab, Fab', $F(ab')_2$, Fv, dsFv, diabody, Fd, or Fd' fragment. The first antigen-binding portion and/or second antigen-binding portion of the multivalent antibodies provided herein can be conjugated to a multimerization domain by covalent or non-covalent linkage. In some examples, the antigen-binding portion is conjugated to the multimerization domain via a linker, such as a chemical linker or a polypeptide linker. In some examples, the multimerization domain of the multivalent antibody provided herein is selected from among an immunoglobulin constant region (Fc), a leucine zipper, complementary hydrophobic regions, complementary hydrophilic regions, or compatible protein-protein interaction domains. In some examples, the Fc domain is an IgG, IgM or an IgE Fc domain.

In some examples, the multivalent antibodies provided herein contain two or more anti-RSV antibodies or antigen-binding fragments thereof. In a particular example, the multivalent antibodies provided herein contain two or more anti-RSV antibodies or antigen-binding fragments thereof.

Provided herein are multivalent antibodies, containing a first antigen-binding portion containing an anti-RSV antibody or antigen-binding fragment thereof provided herein conjugated to a multimerization domain; and a second antigen-binding portion containing an anti-RSV antibody or antigen-binding fragment thereof, selected from among palivizumab, motavizumab, AFFF, P12f2, P12f4, P11d4, A1e9, A12a6, A13c4, A17d4, A4B4, A8c7, 1X-493L1, FR H3-3F4, M3H9, Y10H6, DG, AFFF(1), 6H8, L1-7E5, L2-15B10, A13a11, A1h5, A4B4(1), A4B4L1FR-S28R, A4B4-F52S, rsv6, rsv11, rsv13, rsv19, rsv21, rsv22, rsv23, RF-1, RF-2 or an antigen-binding fragment thereof, conjugated to a second multimerization domain.

Provided herein are multivalent antibodies, containing a first antigen-binding portion containing an anti-RSV antibody or antigen-binding fragment thereof provided herein conjugated to a multimerization domain; and a second antigen-binding portion containing an antiviral antibody that immunospecifically binds an antigen of parainfluenza virus (PIV) or human metapneumovirus (hMPV), conjugated to a second multimerization domain.

Provided herein are combinations, which contain an isolated polypeptide, antibody or antigen-binding fragment thereof provided herein or a multivalent antibody provided herein, and an antiviral agent.

In a third aspect, there is provided a combination, comprising:

an isolated antibody or antigen-binding fragment as defined above or a multivalent antibody as defined above; and

one or both of an antiviral agent and one more additional antiviral antibodies that differ from the first antibody.

In some examples, the antiviral agent is ribavirin. Provided herein are combinations, which contain an isolated polypeptide, antibody or antigen-binding fragment thereof provided herein and an antiviral agent formulated as a single composition or as separate compositions.

Provided herein are combinations, which contain an isolated polypeptide, antibody or antigen-binding fragment thereof provided herein or a multivalent antibody provided herein, and one or more additional antiviral antibodies. In some examples, the combination contains two or more different anti-RSV antibodies or antigen-binding fragments thereof. In some examples, the combination contains two or more different anti-RSV antibodies or antigen-binding fragments selected from among an antibody or antigen-binding fragment provided herein. In some examples, the combination contains an antibody or antigen-binding fragment thereof provided herein and an antibody selected from among palivizumab, motavizumab, AFFF, P12f2, P12f4, P11d4, A1e9, A12a6, A13c4, A17d4, A4B4, A8c7, 1X-493L1, FR H3-3F4, M3H9, Y10H6, DG, AFFF(1), 6H8, L1-7E5, L2-15B10, A13a11, A1h5, A4B4(1), A4B4L1FR-S28R, A4B4-F52S, rsv6, rsv11, rsv13, rsv19, rsv21, rsv22, rsv23, RF-1, RF-2 or antigen-binding fragments thereof. In some examples, the

combination contains an antibody or antigen-binding fragment thereof provided herein and an antibody selected from among an antibody or antigen-binding fragment thereof that immunospecifically binds an antigen of parainfluenza virus (PIV) or human metapneumovirus (hMPV). In some examples, the PIV antigen is an antigen of human PIV type 1, human PIV type 2, human PIV type 3, and/or human PIV type 4. In some examples, the PIV antigen is selected from among a PIV nucleocapsid

examples, the PIV antigen is an antigen of human PIV type 1, human PIV type 2, human PIV type 3, and/or human PIV type 4. In some examples, the PIV antigen is selected from among a PIV nucleocapsid phosphoprotein, a PIV fusion (F) protein, a PIV phosphoprotein, a PIV large (L) protein, a PIV matrix (M) protein, a PIV hemagglutinin-neuraminidase (HN) glycoprotein, a PIV RNA-dependent RNA polymerase, a PIV Y1 protein, a PIV D protein, a PIV C protein, and allelic variants thereof. In some examples, the hMPV antigen is an antigen of hMPV type A or hMPV type B. In some examples, the hMPV antigen is an antigen of hMPV subtype A1, hMPV subtype A2, hMPV subtype B1, or hMPV subtype B2. In some examples, the hMPV antigen is selected from among a hMPV nucleoprotein, a hMPV phosphoprotein, a hMPV matrix protein, a hMPV small hydrophobic protein, a hMPV RNA-dependent RNA polymerase, a hMPV F protein, a hMPV G protein, and allelic variants thereof.

In a fourth aspect, there is provided a~~Provided herein are~~ methods of detecting RSV infection, which involve (a)

assaying the level of RSV antigen in a fluid, cell, or tissue sample using an antibody or antigen-binding fragments thereof provided herein; (b) comparing the assayed level of RSV antigen with a control level whereby an increase in the assayed level of RSV antigen compared to the control level of the RSV antigen is indicative of a RSV infection. In some examples, the cell or tissue sample is obtained from a human subject. In some examples, the cell or tissue sample is a blood, urine, saliva, lung sputum, lavage, or lymph sample.

Provided herein are isolated nucleic acids that encode the polypeptide, antibody or antigen-binding fragments thereof provided herein.

In a fifth aspect, there is provided a nucleic acid molecule(s) that encodes the antibody or antigen-binding fragment as defined above.

Provided herein are

vectors that contain a nucleic acid encoding the polypeptide, antibody or antigen-binding fragments thereof provided herein.

Provided herein are isolated cells the contain an antibody or antigen-binding fragment thereof provided herein, a nucleic acid provided herein, or a vector provided herein.

In a sixth aspect, there is provided an isolated cell, comprising the antibody or antigen-binding fragment as defined above, or the nucleic acid molecule as defined above.

The cells provided herein can be, for example, prokaryotic or eukaryotic cells. Also provided herein are transgenic animals that contain a nucleic acid provided herein or a vector provided herein. Also provided herein are methods of expressing an isolated antibody or antigen-binding fragment thereof, which involve culturing the

isolated cells provided herein under conditions which express the encoded antibody or by isolation of the antibody or antigen-binding fragment from the transgenic animal provided herein. In some examples, the antibody or antigen-binding fragment is isolated from the serum or milk of the transgenic animal.

In a seventh aspect, there is provided a method of producing an antibody or antigen-binding fragment thereof, comprising culturing the cell as defined above under conditions in which the encoded antibody or antigen binding fragment is expressed.

Provided herein are kits containing a polypeptide, antibody or antigen-binding fragment of provided herein, a multivalent antibody provided herein, or a combination provided herein, in one or more containers, and instructions for use.

In an eighth aspect, there is provided an antibody or antigen-binding fragment as defined above or a multivalent antibody as defined above for use in the treatment or prevention of a viral infection.

Also provided herein are uses of an antibody or antigen-binding fragment thereof provided herein for the prevention and/or treatment of viral infection in a subject. Also provided herein are uses of an antibody or antigen-binding fragment thereof provided herein for treating or inhibiting one or more symptoms of a viral infection in a subject.

Also provided herein are uses of an antibody or antigen-binding fragment provided herein for the formulation of a medicament for the prevention and/or treatment of viral infection in a subject. Also provided herein are uses of an antibody or antigen-binding fragment provided herein for the formulation of a medicament for treating or inhibiting one or more symptoms of a viral infection in a subject.

DETAILED DESCRIPTION

Outline

A. DEFINITIONS
B. OVERVIEW
    1. Respiratory Syncytial Virus
C. ANTI-RSV ANTIBODIES
    1. General Antibody Structure and Functional Domains
        a. Structural and Functional Domains of Antibodies
        b. Antibody Fragments

2. Exemplary Anti-RSV Antibodies
    a. Derivative Antibodies
        i. Single Chain Antibodies
        ii. Anti-idiotypic Antibodies
        iii. Multi-specific Antibodies and Antibody Multimerization

D. ADDITIONAL MODIFICATIONS OF ANTI-RSV ANTIBODIES
1. Modifications to reduce immunogenicity
2. Fc Modifications
3. Pegylation
4. Conjugation of a Detectable Moiety