1989, J. Virol. 63:2941-50; Garcia-Barreno *et al.*, 1989, J. Virol. 63:925-32; Taylor *et al.*, 1984, Immunology 52: 137-142; Walsh *et al.*, 1984, Infection and Immunity 43:756-758; and U.S. Pat. Nos. 5,842,307 and 6,818,216. Neutralizing epitopes on the F glycoprotein were originally mapped by identifying amino acids that were altered in antibody escape variants and by assessing antibody binding to RSV F-derived peptides. These studies demonstrated neutralizing antibodies are often targeted to two distinct linear epitopes. See Graham *et al.*, 2015, Curr Opin Immunol 35:30-38 for a review of the antigenic sites for the pre-fusion and post-fusion F forms. Antigenic site II (also called site A) includes residues 255 to 275 and is the target of palivizumab (SYNAGIS®, AstraZeneca). This epitope was predicted to be conformationally dependent, and the structure of a more potent derivative of palivizumab in complex with this epitope revealed that the linear epitope adopts a helix-loop-helix conformation. Antigenic site IV (also called site C) includes residues 422 to 438 and is the target of antibodies MAb19 and 101F. This epitope is C-terminal to the cysteine-rich region and is part of domain II, which in homologous paramyxovirus F glycoproteins remains structurally unchanged between pre- and post-fusion conformations. 5C4, AM22 and D25 delineate an epitope designated as site 0 which is only present on the pre-fusion F protein and were 50 times as potent as palivizumab. See McLellan *et al.*, 2013, Science 340:1113–1117; International Patent Application No. WO 2008/147196 and U.S. Pat. No. 8,568,726. Other hRSV antibodies are described in International Patent Application Nos. WO94/06448 and WO92/04381 and U.S. Pat. No. 8,221,759.

An RSV vaccine for active immunization, if available, could not be utilized for the treatment of newborn babies with immature immune systems or patients who are immunosuppressed. In patients where prophylactic passive immunotherapy is required, as a result of a more chronic form of disease, current therapy is mediated via periodic intravenous inoculation of human IgG prepared from pooled plasma. This type of therapy, due to the low titers of neutralizing anti-RSV antibodies, involves a large quantity of globulin (*e.g.*, 0.75 gm per kg) and consequently requires administration intravenously, in a clinic or hospital, over a lengthy period (2 to 4 hours), on a monthly basis during the high risk months (fall, winter and early spring).

SUMMARY

The disclosure provides anti-RSV F-protein antibodies and antigen binding fragments thereof comprising the structural and functional features specified below.

In one aspect, there is provided an isolated antibody or antigen binding fragment comprising a heavy chain variable region having the amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8.

In another aspect, there is provided a composition comprising the antibody or antigen binding fragment as defined herein and a pharmaceutically acceptable carrier or diluent.

In another aspect, there is provided an immunogenic composition comprising the antibody or antigen binding fragment as defined herein and an antigen selected from RSV F protein and RSV G protein and fragments thereof.

In another aspect, there is provided an isolated antibody or antigen binding fragment thereof comprising a light chain immunoglobulin consisting of the amino acid sequence set forth in SEQ ID NO: 25 and a heavy chain immunoglobulin consisting of the amino acid sequence set forth in SEQ ID NO: 2.

CLAIMS

1. An isolated antibody or antigen binding fragment comprising a heavy chain variable region having the amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8.

2. The antibody or antigen binding fragment of claim 1, wherein the antibody or antigen binding fragment thereof binds to human RSV prefusion F protein with a KD value of about 1 x 10^{-9} M to about 1 x 10^{-12} M as determined by surface plasmon resonance.

3. The isolated antibody or antigen binding fragment of claim 1, which is a full-length antibody having two light chains and two heavy chains, wherein each light chain comprises: a variable region comprising SEQ ID NO: 8 and a human kappa light chain (SEQ ID NO: 14); and each heavy chain comprises: a variable region comprising SEQ ID NO: 7 and a human IgG1 constant region (SEQ ID NO: 13).

4. The isolated antibody of claim 3, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 and a light chain comprising the amino acid sequence of SEQ ID NO: 25.

5. The isolated antibody of claim 3, wherein the amino acid sequence of the heavy chain consists of the amino acid sequence of SEQ ID NO: 23 and the amino acid sequence of the light chain consists of the amino acid sequence of SEQ ID NO: 25.

6. The isolated antibody or antigenic binding fragment of claim 1 which is an IgG antibody.

7. The isolated antibody or antigen binding fragment of claim 1, which is an antibody, wherein the antibody is produced in a CHO cell.

8. A composition comprising the antibody or antigen binding fragment of claim 1 and a pharmaceutically acceptable carrier or diluent.

9. The composition of claim 8, further comprising an antibody or an antigen binding fragment thereof against a respiratory pathogen selected from influenza, human cytomegalovirus (hCMV), human metapneumovirus (hMPV), human parainfluenza (hPIV), human rhinovirus (hRV), mycoplasma pneumonia, streptococcus pneumoniae, adenovirus, bocavirus, enterovirus, norovirus or BK virus.

10. The composition of claim 9, wherein the respiratory pathogen is influenza, hCMV, hMPV, hPIV, norovirus, or BK virus.

11. An immunogenic composition comprising the antibody or antigen binding fragment of claim 1 and an antigen selected from RSV F protein and RSV G protein and fragments thereof.

12. An isolated antibody or antigen binding fragment thereof comprising a light chain immunoglobulin consisting of the amino acid sequence set forth in SEQ ID NO: 25 and a heavy chain immunoglobulin consisting of the amino acid sequence set forth in SEQ ID NO: 23.