

CLAIMS

What Is Claimed Is:

1. An isolated antibody or an antigen-binding fragment thereof that specifically binds to Respiratory Syncytial Virus (RSV) F protein (F), wherein the antibody or antigen-binding fragment thereof comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences of an antibody designated as Antibody Number 183 as disclosed in Table 6; and wherein said antibody or antigen-binding fragment thereof also has one or more of the following characteristics:
 - a) the antibody or the antigen-binding fragment thereof cross-competes with Antibody Number 183 or an antigen-binding fragment thereof for binding to RSV-F;
 - b) the antibody or the antigen-binding fragment thereof displays better binding affinity for the prefusion conformation (PreF) form of RSV-F relative to the postfusion conformation (PostF) form;
 - c) the antibody or the antigen-binding fragment thereof displays a clean or low polyreactivity profile;
 - d) the antibody or the antigen-binding fragment thereof displays neutralization activity towards RSV subtype A and RSV subtype B in vitro;
 - e) the antibody or the antigen-binding fragment thereof displays antigenic site specificity for RSV-F Site Ø;
 - f) the antibody or the antigen-binding fragment thereof displays antigenic site specificity for RSV-F Site Ø relative to RSV-F Site I, Site II, or Site IV;
 - g) at least a portion of the epitope with which the antibody or the antigen-binding fragment thereof interacts comprises the $\alpha 3$ helix and $\beta 3/\beta 4$ hairpin of PreF;
 - h) the antibody or the antigen-binding fragment thereof displays an in vitro neutralization potency (IC_{50}) of between 0.5 microgram/milliliter (ug/ml) to 5 ug/ml; between 0.05 ug/ml to 0.5 ug/ml; or less than 0.05 mg/ml;
 - i) the binding affinity and/or epitopic specificity of the antibody or the antigen-binding fragment thereof for any one of the RSV-F variants designated as 1, 2, 3, 4, 5, 6, 7, 8, 9, and DG in Figure 7A is reduced or eliminated relative to the binding affinity and/or epitopic specificity of said antibody or antigen-binding fragment thereof for the RSV-F or RSV-F DS-Cav1;
 - j) the antibody or the antigen-binding fragment thereof displays a cross-neutralization potency (IC_{50}) against human metapneumovirus (HMPV);

k) the antibody or the antigen-binding fragment thereof does not compete with MPE8, palivizumab, motavizumab, or AM-14; or

l) the antibody or the antigen-binding fragment thereof displays at least about 2-fold; at least about 3-fold; at least about 4-fold; at least about 5-fold; at least about 6-fold; at least about 7-fold; at least about 8-fold; at least about 9-fold; at least about 10-fold; at least about 15-fold; at least about 20-fold; at least about 25-fold; at least about 30-fold; at least about 35-fold; at least about 40-fold; at least about 50-fold; at least about 55-fold; at least about 60-fold; at least about 70-fold; at least about 80-fold; at least about 90-fold; at least about 100-fold; greater than about 100-fold; and folds in between any of the foregoing; greater neutralization potency (IC₅₀) than D25 and/or palivizumab.

2. The isolated antibody or the antigen-binding fragment thereof of claim 1, wherein the antibody or the antigen-binding fragment thereof comprises: at least two; at least three; at least 4; at least 5; at least 6; at least 7; at least 8; at least 9; at least 10; at least 11; or at least 12; of characteristics a) through l).

3. The isolated antibody or the antigen-binding fragment thereof of claim 1 or 2, wherein the antibody or the antigen-binding fragment thereof comprises:

a) a heavy chain (HC) amino acid sequence of the antibody designated as Antibody Number 183 as disclosed in Table 6; and

b) a light chain (LC) amino acid sequence of the antibody designated as Antibody Number 183 as disclosed in Table 6.

4. The isolated antibody or the antigen-binding fragment thereof of any one of claims 1 through 3, wherein the antibody is the antibody designated as Antibody Number 183.

5. An isolated nucleic acid sequence encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1 through 4.

6. An expression vector comprising the isolated nucleic acid sequence according to claim 5.

7. A host cell transfected, transformed, or transduced with the nucleic acid sequence according to claim 5 or the expression vector according to claim 6.

8. A pharmaceutical composition comprising:
the isolated antibody or the antigen-binding fragment thereof according to any one of claims 1 through 4; and
a pharmaceutically acceptable carrier and/or excipient.

9. A pharmaceutical composition comprising:
the nucleic acid sequence according to claim 5 or the expression vector according to claim 6;
and
a pharmaceutically acceptable carrier and/or excipient.

10. A non-human transgenic organism comprising the nucleic acid sequence according to claim 5; or the expression vector according to claim 6.

11. The antibody or the antigen-binding fragment thereof according to any of claims 1 through 4, the nucleic acid sequence according to claim 5, the expression vector according to claim 6, the host cell according to claim 7, or the pharmaceutical composition according to claim 8 or 9 for use in treating or preventing a Respiratory Syncytial Virus (RSV) infection, or at least one symptom associated with RSV infection, in a patient in need thereof or suspected of being in need thereof, such that the RSV infection is treated or prevented, or the at least one symptom associated with RSV infection is treated, alleviated, or reduced in severity.

12. The antibody or the antigen-binding fragment thereof according to any of claims 1 through 4, the nucleic acid sequence according to claim 5, the expression vector according to claim 6, the host cell according to claim 7, or the pharmaceutical composition according to claim 8 or 9 for use in treating or preventing either a Respiratory Syncytial Virus (RSV) infection or a human metapneumovirus (HMPV) infection, or at least one symptom associated with said RSV infection or said HMPV infection, in a patient in need thereof or suspected of being in need thereof, such that the

RSV infection is treated or prevented, or the at least one symptom associated with RSV infection is treated, alleviated, or reduced in severity.

13. The antibody or the antigen-binding fragment thereof, the nucleic acid sequence, the expression vector, the host cell, or the pharmaceutical composition for the use according to claims 11 or 12, wherein the use further comprises a second therapeutic agent that is to be administered to the patient.

14. The antibody or the antigen-binding fragment thereof, the nucleic acid sequence, the expression vector, the host cell, or the pharmaceutical composition for the use according to claim 13, wherein the second therapeutic agent is selected from the group consisting of: an antiviral agent; a vaccine specific for RSV, a vaccine specific for influenza virus, or a vaccine specific for metapneumovirus (MPV); an siRNA specific for an RSV antigen or a metapneumovirus (MPV) antigen; a second antibody specific for an RSV antigen or a metapneumovirus (MPV) antigen; an anti-IL4R antibody, an antibody specific for an influenza virus antigen, an anti-RSV-G antibody and a NSAID.

15. The pharmaceutical composition according to claim 8 for use in preventing a respiratory syncytial virus (RSV) infection in a patient in need thereof or suspected of being in need thereof, or for treating a patient suffering from an RSV infection, or for ameliorating at least one symptom or complication associated with the infection, wherein the infection is either prevented, or at least one symptom or complication associated with the infection is prevented, ameliorated, or lessened in severity and/or duration as a result of such use.

16. The pharmaceutical composition according to claim 8 for use in treating or preventing either a Respiratory Syncytial Virus (RSV) infection or a human metapneumovirus (HMPV) infection, or at least one symptom associated with said RSV infection or said HMPV infection, in a patient in need thereof or suspected of being in need thereof, wherein the infection is either prevented, or at least one symptom or complication associated with the infection is prevented, ameliorated, or lessened in severity and/or duration as a result of such use.