In one aspect, the present disclosure refers to use of an amount of a MASP-2 inhibitory monoclonal antibody or binding fragment thereof that specifically binds to a portion of SEQ ID NO:6 and inhibits lectin pathway complement activation without inhibiting C1q-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from COVID-19 induced acute respiratory distress syndrome (ARDS) or pneumonia, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:69.

In another example, the disclosure provides a method for treating, preventing or reducing the severity or coagulation or thrombosis in a human subject infected with SARS-CoV-2 comprising administering to the subject an amount of a MASP-2 inhibitory agent effective to treat, prevent or reduce the severity of coagulation or thrombosis in said subject. In one example, the subject has a D-Dimer level higher than the standard range prior to treatment and the MASP-2 inhibitory agent is administered in an amount and for a time sufficient to reduce the level of D-Dimer in said subject into the normal range of a healthy subject. In one example, the MASP-2 inhibitory agent provides anticoagulation and/or antithrombosis effects without affecting hemostatis. In one example, the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6. In one example, the MASP-2 inhibitory agent is a small molecule MASP-2 inhibitory compound.

In another example, the disclosure provides a method for treating, ameliorating, preventing or reducing the risk of developing one or more COVID-19-related long-term sequelae in a human subject that is currently infected with SARS-CoV-2 or has been infected with SARS-CoV-2, comprising administering to the subject an amount of a MASP-2 inhibitory agent effective to inhibit MASP-2-dependent complement activation. In one example, the subject is suffering from COVID-19-induced pneumonia or ARDS and the MASP-2 inhibitory agent is administered in an amount effective to improve respiratory function. In one example, the subject has recovered from COVID-19 induced pneumonia or ARDS and the MASP-2 inhibitory agent is administered in an amount to treat or ameliorate one or more long-term sequelae. In one example, the subject is suffering from COVID-19-induced coagulation or thrombosis and the MASP-2 inhibitory agent is administered to the subject in an amount effective to treat, prevent or reduce the severity of coagulation or thrombosis in said subject. In one example, the subject has recovered from COVID-19 induced coagulation or thrombosis and the MASP-2 inhibitory agent is administered in an amount to treat or ameliorate one or more long-term sequelae. In one example, the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6. In one example, the MASP-2 inhibitory agent is a small molecule MASP-2 inhibitory compound.

In another example, the disclosure provides a method for treating, inhibiting, alleviating or preventing acute respiratory distress syndrome, pneumonia or some other pulmonary or other manifestation of influenza virus infection, in a mammalian subject infected with influenza virus, comprising administering to the subject an amount of a MASP-2 inhibitory agent effective to inhibit MASP-2-dependent complement activation. In one example, the influenza virus is influenza virus A, influenza virus B or influenza virus C. In one example, the influenza virus A is selected from the group consisting of H1N1, H2N2, H3N2, H5N1, H7N7, H1N2, H9N2, H7N2, H7N3, H10N7, H7N9 and H6N1. In one example, the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6. In one example, the MASP-2 inhibitory agent is a small molecule MASP-2 inhibitory compound.

Description of the Drawings

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 is a diagram illustrating the genomic structure of human MASP-2;

FIGURE 2A is a schematic diagram illustrating the domain structure of human MASP-2 protein;

FIGURE 2B is a schematic diagram illustrating the domain structure of human MAp19 protein;

FIGURE 3 is a diagram illustrating the murine MASP-2 knockout strategy;

FIGURE 4 is a diagram illustrating the human MASP-2 minigene construct;

FIGURE 5A presents results demonstrating that MASP-2-deficiency leads to the loss of lectin-pathway-mediated C4 activation as measured by lack of C4b deposition on mannan, as described in Example 2;

FIGURE 5B presents results demonstrating that MASP-2-deficiency leads to the loss of lectin-pathway-mediated C4 activation as measured by lack of C4b deposition on zymosan, as described in Example 2;

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. Use of an amount of a MASP-2 inhibitory monoclonal antibody or binding fragment thereof that specifically binds to a portion of SEQ ID NO:6 and inhibits lectin pathway complement activation without inhibiting C1q-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from COVID-19 induced acute respiratory distress syndrome (ARDS) or pneumonia, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:69.

2. The use of claim 1, wherein:

(i) the subject is on a mechanical ventilator prior to treatment and the MASP-2 inhibitory antibody or binding fragment thereof is to be administered at a dosage and for a time period sufficient to discontinue the need for mechanical ventilation; and/or

(ii) the subject requires supplemental oxygen prior to treatment and the MASP-2 inhibitory antibody or binding fragment thereof is to be administered at a dosage and for a time period sufficient to discontinue the use of supplemental oxygen.

3. The use of claim 1, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody and a human antibody.

4. The use of claim 1, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 10% human serum with an IC_{50} of 30 nM or less.