**[00136]** Together, these data suggest that inhibition of MK2 may provide therapeutic benefits to patients with fibrotic disorders or conditions, for example, idiopathic pulmonary fibrosis (IPF), acute lung injury (ALI), and transplant rejection. In this respect, the described invention offers an approach to intervene in the process of inflammation and fibrosis using cell-penetrating, peptide base inhibitors of MK2.

## SUMMARY OF THE INVENTION

**[00137]** According to one aspect, the disclosure provides use of a composition comprising (a) an antibody component containing a therapeutic amount of an anti-CD44 antibody; and (b) an MK2 inhibitor (MK2i) component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) selected from a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3), a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4), a polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5), a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6), and a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier; in the manufacture of a medicament, for attenuating lung allograft dysfunction after lung transplant, wherein the composition is effective to reduce at least one pathobiology of the lung allograft dysfunctionwithout other concurrent immunosuppressive medications. In an embodiment, the disclosure relates to a method to attenuate lung allograft dysfunction after lung transplant comprising administering a composition comprising an antibody component containing a therapeutic amount of an anti-CD44 antibody; and an MK2 inhibitor (MK2i) component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to the therapeutic domain thereof selected from a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8), a polypeptide of amino acid sequence KALARQLGVA (SEQ ID NO: 9) and a polypeptide of amino acid sequence KALARQLGVAA (SEQ ID NO: 1), or a functional equivalent thereof, and a pharmaceutically acceptable carrier; wherein the composition is effective to synergistically reduce at least one

pathobiology of the lung allograft dysfunction. According to one embodiment, the lung allograft dysfunction is characterized by an aberrant activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue compared to the activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue of a normal healthy control subject. According to another embodiment, the lung allograft dysfunction is a primary graft dysfunction. According to another embodiment, the lung allograft dysfunction is a chronic lung allograft dysfunction. According to another embodiment, the administering of the anti-CD44 antibody component of the composition is systemically. According to another embodiment, the administering of the MK2i component is systemically or by inhalation. According to another embodiment, the allograft dysfunction is characterized by inflammation. According to another embodiment, the composition is effective (i) to modulate at least one of TGFβ, CCL2, hyaluronic acid, and MMP9; (ii) to decrease plasma level of TNFα, IL6 or a combination thereof; (iii) to attenuate expression of α-smooth muscle actin; (iiv) to prevent TGFβ-induced myofibroblast activation, (v) to inhibit fibroblast invasion, or a combination thereof when compared to a control. According to another embodiment, the functional equivalent of the polypeptide

YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3). According to another embodiment, the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4). According to another embodiment, the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5). According to another embodiment, the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6). According to another embodiment, the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7). According to another embodiment, the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier. According to another embodiment, the MK2i component of the pharmaceutical composition is in a form of a dry powder. According to another embodiment, the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns. According to another embodiment, the administering of the therapeutic amount of the MK2i component of the pharmaceutical composition is via an inhalation device. According to another embodiment, the inhalation device is a nebulizer. According to another embodiment, the inhalation device is a metered-dose inhaler (MDI). According to another embodiment, the inhalation device is a dry powder inhaler (DPI). According to another embodiment, the inhalation device is a dry powder nebulizer.

**[00138]** According to another aspect, the disclosure provides a pharmaceutical composition for use in the treatment of lung allograft dysfunction after lung transplant comprising: (a) an antibody component containing a therapeutic amount of an anti-CD44 antibody; and (b) an MK2 inhibitor (MK2i) component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) selected from a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3), a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4), a

polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5), a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6), and a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier; wherein the composition is effective to reduce at least one pathobiology of the lung allograft dysfunction without other concurrent immunosuppressive medications. In an embodiment, the disclosure relates to a method for treating a severe pulmonary fibrosis characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject comprising: administering to the subject a pharmaceutical composition comprising an antibody component containing a therapeutic amount of an anti-CD44 antibody; an MK2 inhibitor component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to the therapeutic domain thereof selected from a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8), a polypeptide of amino acid sequence KALARQLGVA

## CLAIMS

What is claimed is:

1. Use of a composition comprising

(a) an antibody component containing a therapeutic amount of an anti-CD44 antibody; and

(b) an MK2 inhibitor (MK2i) component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) selected from a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3), a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4) , a polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5), a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6), and a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier;

in the manufacture of a medicament for attenuating lung allograft dysfunction after lung transplant, wherein the composition is effective to reduce at least one pathobiology of the lung allograft dysfunction without other concurrent immunosuppressive medications.

2. The use according to claim 1, wherein the lung allograft dysfunction is characterized by an aberrant activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue as compared to the activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue of a normal healthy control subject.

16. The use according to claim 12, wherein the inhalation device is a dry powder nebulizer.

17. A pharmaceutical composition for use in the treatment of lung allograft dysfunction after lung transplant comprising:

(a) an antibody component containing a therapeutic amount of an anti-CD44 antibody; and

(b) an MK2 inhibitor (MK2i) component containing a therapeutic amount of an MK2 inhibitor (MK2i) polypeptide of amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or at least one peptide functionally equivalent to YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) selected from a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3), a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4) , a polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5), a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6), and a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier;

wherein the composition is effective to reduce at least one pathobiology of the lung allograft dysfunction without other concurrent immunosuppressive medications.