dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns. According to another embodiment, the therapeutic amount of the pharmaceutical composition is administered 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).

[00140a] According to an aspect, the present disclosure provides the use of a pharmaceutical composition in the manufacture of a medicament for delivery to lung tissue of a subject for therapeutic treatment of a lung disease or condition progressing to loss of lung function, the lung disease or condition comprising an interstitial lung disease or a pulmonary fibrosis comprising one or more of an aberrant deposition of collagen in a pulmonary interstitium, an aberrant promotion of fibroblast proliferation in the lung, an aberrant induction of myofibroblast differentiation in the lung, and/or an aberrant promotion of attachment of myofibroblasts to an extracellular matrix compared to a normal healthy control subject, wherein the lung tissue 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,

wherein the pharmaceutical composition is in a form for delivery by inhalation,

wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1), or a functional equivalent thereof, wherein the functional equivalent is, a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3); or a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4); or a polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5); or a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6); or a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier thereof, wherein 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 and

wherein the therapeutic amount is effective to reduce one or more of:

(i) development of fibrotic foci in the lung;

(ii) collagen accumulation in the lung; or

(iii) progression of collagen deposition in the lung compared to a control vehicle.

[00141] According to another embodiment, the present disclosure provides use of a pharmaceutical composition in the manufacture of a medicament for treating a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject, wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, and wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

[00142] According to another embodiment, the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). According to another embodiment, the disease or the condition is radiation-induced fibrosis. According to another embodiment, the disease or the condition is transplant rejection. According to another embodiment, the tissue is a lung tissue. According to another embodiment, the disease or the condition is an interstitial lung disease. According to another embodiment, the disease or the condition is pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis is idiopathic pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis is caused by administration of bleomycin. According to another embodiment, the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof. According to another embodiment, the disease or the condition is further characterized by an inflammation in the tissue. According to another embodiment, the inflammation is an acute or a chronic inflammation. According to another embodiment, the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β). According to another embodiment, the aberrant

CLAIMS

We claim:

1. Use of a pharmaceutical composition in the manufacture of a medicament for delivery to lung tissue of a subject for therapeutic treatment of a lung disease or condition progressing to loss of lung function, the lung disease or condition comprising an interstitial lung disease or a pulmonary fibrosis comprising one or more of an aberrant deposition of collagen in a pulmonary interstitium, an aberrant promotion of fibroblast proliferation in the lung, an aberrant induction of myofibroblast differentiation in the lung, and/or an aberrant promotion of attachment of myofibroblasts to an extracellular matrix compared to a normal healthy control subject, wherein the lung tissue 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,

wherein the pharmaceutical composition is in a form for delivery by inhalation,

wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1), or a functional equivalent thereof, wherein the functional equivalent is, a polypeptide of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3); or a polypeptide of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4); or a polypeptide of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5); or a polypeptide of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6); or a polypeptide of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7), and a pharmaceutically acceptable carrier thereof, wherein 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 and

wherein the therapeutic amount is effective to reduce one or more of:

(i) development of fibrotic foci in the lung;

(ii) collagen accumulation in the lung; or

(iii) progression of collagen deposition in the lung compared to a control vehicle.

2. The use of claim 1, wherein the therapeutic amount is effective to inhibit kinase activity of a kinase selected from the group of a Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) and a Mitogen-Activated Protein Kinase-Activated Protein Kinase 3 (MK3).

3. The use according to claim 1, wherein the pulmonary fibrosis is idiopathic pulmonary fibrosis.

4. The use according to claim 1, wherein the pulmonary fibrosis is caused by administration of bleomycin.

5. The use according to claim 1, wherein the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof.

6. The use according to any one of the preceding claims, wherein the disease or the condition is further characterized by an inflammation in the tissue.

7. The use according to claim 6, wherein the inflammation is an acute or a chronic inflammation.

8. The use according to claim 6, wherein the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β).

9. The use according to any one of the preceding claims, wherein the pharmaceutical composition further comprises at least one additional therapeutic agent.

10. The use according to claim 9, wherein the additional therapeutic agent is selected from the group consisting of a purified bovine Type V collagen, an IL-13 receptor antagonist, a protein tyrosine kinase inhibitor, an endothelial receptor antagonist, a dual endothelin receptor antagonist, a prostacyclin analog, an anti-CTGF monoclonal antibody, an endothelin receptor antagonist (A-selective), AB0024, a lysyl oxidase-like 2 (LOXL2) monoclonal antibody, a c-Jun N-terminal kinase (JNK) inhibitor, pirfenidone, IFN-γ1b, a pan-neutralizing IgG4 human antibody against all three TGF-β isoforms, a TGF-β activation inhibitor, a recombinant human Pentraxin-2 protein (rhPTX-2), a bispecific IL-4/IL-13 antibody, a humanized monoclonal antibody targeting integrin avβ6, N-acetylcysteine, sildenafil, a Tumor Necrosis Factor (TNF) antagonist (etanercept), and a combination thereof.

11. The use according to claim 9, wherein the additional therapeutic agent is a glucocorticoid selected from the group consisting of prednisone, budesonide, mometasone furoate, fluticasone propionate, fluticasone furoate, and a combination thereof.

12. The use according to claim 9, wherein the additional therapeutic agent is a bronchodilator selected from the group consisting of a leukotriene modifier, an anticholinergic bronchodilator, a short-acting β2-agonist, and long-acting β2-agonist, and a combination thereof.

13. The use according to claim 9, wherein the additional therapeutic agent is an analgesic agent.

14. The use according to claim 9, wherein the additional therapeutic agent is an anti-infective agent.

15. The use according to any one of the preceding claims, wherein the pharmaceutical composition is in a form of a dry powder.

16. The use according to claim 15, wherein the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns.

17. The use according to claim 15, wherein the therapeutic amount of the pharmaceutical composition is to be administered to a subject via an inhalation device.

18. The use according to claim 17, wherein the inhalation device is a nebulizer.

19. The use according to claim 17, wherein the inhalation device is a metered-dose inhaler (MDI).

20. The use according to claim 17, wherein the inhalation device is a dry powder inhaler (DPI).

21. The use according to claim 17, wherein the inhalation device is a dry powder nebulizer.

COMPOSITIONS AND METHODS FOR PREVENTING OR TREATING DISEASES, CONDITIONS, OR PROCESSES CHARACTERIZED BY ABERRANT FIBROBLAST PROLIFERATION AND EXTRACELLULAR MATRIX DEPOSITION

Abstract

The described invention provides compositions and methods for preventing or treating a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject. The method includes administering a therapeutic amount of a pharmaceutical composition comprising a polypeptide having the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or functional equivalent thereof, and a pharmaceutically acceptable carrier.

(FIGURE 1)