SUMMARY

[0009] In one example, provided herein is a method of treating inflammation in lungs of a patient in need thereof, the method comprising: administering to the patient a composition comprising an agent that inhibits inflammasome signaling, whereby the inflammation in the lungs of the patient is treated. In some cases, the inflammation in the lungs is caused by a condition selected from a central nervous system (CNS) injury, a neurodegenerative disease, an autoimmune disease, asthma, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and acute respiratory distress syndrome. In some cases, the CNS injury is selected from the group consisting of traumatic brain injury (TBI), stroke and spinal cord injury (SCI). In some cases, the neurodegenerative disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS) and Parkinson's disease (PD). In some cases, the administration of the composition results in inhibition of inflammasome activation in lung cells of the patient. In some cases, the administration of the composition results in a reduction of caspase-1, nucleotide-binding leucine-rich repeat pyrin domain containing protein 1 (NLRP1), nucleotide-binding leucine-rich repeat pyrin domain containing protein 2 (NLRP2), nucleotide-binding leucine-rich repeat pyrin domain containing protein 3 (NLRP3), NLR family CARD domain-containing protein 4 (NLRC4), caspase-11, X-linked inhibitor of apoptosis protein (XIAP), pannexin-1, Apoptosis-associated Spec-like protein containing a Caspase Activating Recruitment Domain (ASC), interleukin-18 (IL-18), high mobility group box 1 (HMGB1) or absent in melanoma 2 (AIM2) levels in lung cells of the patient as compared to a control, wherein the control is an untreated patient. In some cases, the lung cells are Type II alveolar cells. In some cases, the administration of the composition results in a reduction in acute lung injury (ALI) as compared to a control, wherein the control is an untreated patient. In some cases, the reduction in ALI is evidenced by a reduction in neutrophil infiltration into alveolar and/or interstitial space, reduced or absent alveolar septal thickening or a combination thereof. In some cases, the agent is an extracellular vesicle (EV) uptake inhibitor, an antibody that binds to an inflammasome component or a combination thereof. In some cases, the EV uptake inhibitor is a compound or an antibody, wherein the antibody is selected from Table 1. In some cases, the agent is an EV uptake inhibitor in combination with an antibody that binds to an inflammasome component. In some cases, the EV uptake inhibitor is a

heparin. In some cases, the heparin is Enoxaparin. In some cases, the antibody that binds to an inflammasome component is an antibody that specifically binds to a component of a mammalian AIM2, NLRP1, NLRP2, NLRP3 or NLRC4 inflammasome. In some cases, the inflammasome component is caspase-1, ASC or AIM2. In some cases, the inflammasome component is ASC. In some cases, the antibody binds to an N-terminal PYRIN-PAAD-DAPIN domain (PYD), C-terminal caspase-recruitment domain (CARD) domain or an epitope derived from the PYD or CARD domain of the ASC protein. In some cases, the antibody binds to a protein having at least 85% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2. In some cases, the antibody inhibits ASC activity in the lungs of the patient. In some cases, the composition is formulated with a pharmaceutically acceptable carrier or diluent. In some cases, the composition is administered intracerebroventricularly, intraperitoneally, intravenously or by inhalation.

[0009a] In one aspect, the present disclosure refers to use of a composition comprising an agent that inhibits inflammasome signaling in the manufacture of a medicament for treating inflammation in lungs of a patient in need thereof, wherein the composition is to be administered to the patient, whereby the inflammation in the lungs of the patient is treated.

[0010] In another example, provided herein is a method of treating inflammation in lungs of a patient that has been subjected to a central nervous system (CNS) injury, the method comprising: administering to the patient a composition comprising an agent that inhibits inflammasome signaling, whereby the inflammation in the lungs of the patient is treated. In some cases, the CNS injury is selected from the group consisting of traumatic brain injury (TBI), stroke and spinal cord injury (SCI). In some cases, the administration of the composition results in inhibition of inflammasome activation in lung cells of the patient. In some cases, the administration of the composition results in a reduction of caspase-1, NLRP1, NLRP2, NLRP3, NLRC4, caspase-11, XIAP, pannexin-1, Apoptosis-associated Spec-like protein containing a Caspase Activating Recruitment Domain (ASC), interleukin-18 (IL-18), high mobility group box 1 (HMGB1) or absent in melanoma 2 (AIM2) levels in lung cells of the patient as compared to a control, wherein the control is an untreated patient. In some cases, the lung cells are Type II alveolar cells. In some cases, the administration of the composition results in a reduction in acute lung injury (ALI) as compared to a control, wherein the control is an untreated patient. In some cases, the reduction in ALI is evidenced by a reduction in neutrophil infiltration into alveolar and/or interstitial space, reduced or absent alveolar septal thickening or a combination thereof. In some cases, the agent is an extracellular vesicle (EV) uptake inhibitor, an antibody that binds to an inflammasome

component or a combination thereof. In some cases, the EV uptake inhibitor is a compound or an antibody, wherein the antibody is selected from Table 1. In some cases, the agent is an EV uptake inhibitor in combination with an antibody that binds to an inflammasome component. In some cases, the EV uptake inhibitor is a heparin. In some cases, the heparin is Enoxaparin. In some cases, the antibody that binds to an inflammasome component is an antibody that specifically binds to a component of a mammalian AIM2, NLRP1, NLRP2, NLRP3 or NLRC4 inflammasome. In some cases, the inflammasome component is caspase-1, ASC or AIM2. In some cases, the inflammasome component is ASC. In some cases, the antibody binds to the PYD, CARD domain or an epitope derived from the PYD or CARD domain of the ASC protein. In some cases, the antibody binds to a protein having at least 85% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2. In some cases, the antibody inhibits ASC activity in the lungs of the patient. In some cases, the composition is formulated with a pharmaceutically acceptable carrier or diluent. In some cases, the composition is administered intracerebroventricularly, intraperitoneally, intravenously or by inhalation.

[0010a] In another aspect, the present disclosure refers to use of a composition comprising an agent that inhibits inflammasome signaling in the manufacture of a medicament for treating inflammation in lungs of a patient that has been subjected to a central nervous system (CNS) injury, wherein the composition is to be administered to the patient, whereby the inflammation in the lungs of the patient is treated.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] **FIG. 1A-1N** illustrateinflammasome activation in C57/BL6 mouse cortical and lung tissue post-TBI. **FIG. 1A** shows a representative immunoblot of active caspase-1, ASC, IL-18, IL-β, HMGB1, and AIM2 after TBI. Active caspase-1 (**FIG. 1B**), ASC (**FIG. 1C**), IL-18 (**FIG. 1D**), HMGB1 (**FIG. 1E**), AIM 2 (**FIG. 1F**), and IL-β, (**FIG. 1G**), are significantly elevated in cortical tissue at 4 and 24h post-TBI. Data presented as mean+/- SEM; ****$p<0.001$, ***$p<0.01$, $p<0.05$ compared to sham. N=4-5 per group. **FIG. 1H** shows a representative immunoblot of active caspase-1, ASC, IL-18, IL-β, HMGB1, and AIM2 in lung tissue. I, J, K, L, M, N) Active caspase-1 (**FIG. 1I**), ASC (**FIG. 1J**), IL-18 (**FIG. 1K**), HMGB1 (**FIG. 1L**), AIM 2 (**FIG. 1M**), and IL-β, (**FIG. 1N**) are significantly elevated in lung tissue 4 and 24h after TBI. Data presented as mean+/-SEM. N= 4-5 per group, **$p<0.01$., *$p<0.05$ compared to sham.

[0012] **FIG. 2A-2C** illustrates Expression of inflammasome proteins in Type II alveolar epithelial cells. **FIG. 2A** shows AIM2, **FIG. 2B** shows active Caspase-1 and **FIG. 2C** shows ASC immunoreactivity increases in lung tissue after CCI (4, 24 h) when compared to mice. Confocal

What is claimed is:

1. Use of a composition comprising an agent that inhibits inflammasome signaling in the manufacture of a medicament for treating inflammation in lungs of a patient in need thereof, wherein the composition is to be administered to the patient, whereby the inflammation in the lungs of the patient is treated.
2. The use of claim 1, wherein the inflammation in the lungs is caused by a condition selected from a central nervous system (CNS) injury, a neurodegenerative disease, an autoimmune disease, asthma, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and acute respiratory distress syndrome.
3. The use of claim 2, wherein the CNS injury is selected from the group consisting of traumatic brain injury (TBI), stroke and spinal cord injury (SCI).
4. The use of claim 2, wherein the neurodegenerative disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS) and Parkinson's disease (PD).
5. The use of any one of the above claims, wherein the administration of the composition results in inhibition of inflammasome activation in lung cells of the patient.
6. The use of any one of claims 1-4, wherein the administration of the composition results in a reduction of caspase-1, nucleotide-binding leucine-rich repeat pyrin domain containing protein 1 (NLRP1), nucleotide-binding leucine-rich repeat pyrin domain containing protein 2 (NLRP2), nucleotide-binding leucine-rich repeat pyrin domain containing protein 3 (NLRP3), NLR family CARD domain-containing protein 4 (NLRC4), caspase-11, X-linked inhibitor of apoptosis protein (XIAP), pannexin-1, Apoptosis-associated Spec-like protein containing a Caspase Activating Recruitment Domain (ASC), interleukin-18 (IL-18), high mobility group box 1 (HMGB1) or absent in melanoma 2 (AIM2) levels in lung cells of the patient as compared to a control, wherein the control is an untreated patient.
7. The use of claim 5 or 6, wherein the lung cells are Type II alveolar cells.

8. The use of any one of claims 1-5, wherein the administration of the composition results in a reduction in acute lung injury (ALI) as compared to a control, wherein the control is an untreated patient.
9. The use of claim 8, wherein the reduction in ALI is evidenced by a reduction in neutrophil infiltration into alveolar and/or interstitial space, reduced or absent alveolar septal thickening or a combination thereof.
10. The use of any one of the above claims, wherein the agent is an extracellular vesicle (EV) uptake inhibitor, an antibody that binds to an inflammasome component or a combination thereof.
11. The use of claim 10, wherein the EV uptake inhibitor is a compound or an antibody, wherein the antibody is selected from Table 1.
12. The use of any of claims 10-11, wherein the agent is an EV uptake inhibitor in combination with an antibody that binds to an inflammasome component.
13. The use of claim 12, wherein the EV uptake inhibitor is a heparin.
14. The use of claim 13, wherein the heparin is Enoxaparin.
15. The use of any of claims 10-14, wherein the antibody that binds to an inflammasome component is an antibody that specifically binds to a component of a mammalian AIM2, NLRP1, NLRP2, NLRP3 or NLRC4 inflammasome.
16. The use of claim 10 or 15, wherein the inflammasome component is caspase-1, ASC or AIM2.
17. The use of claim 16, wherein the inflammasome component is ASC.
18. The use of claim 17, wherein the antibody binds to an N-terminal PYRIN-PAAD-DAPIN domain (PYD), C-terminal caspase-recruitment domain (CARD) domain or an epitope derived from the PYD or CARD domain of the ASC protein.
19. The use of claim 17, wherein the antibody binds to an amino acid having at least 85% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.
20. The use of any of claims 17-19, wherein the antibody inhibits ASC activity in the lungs of the patient.

21. The use of any one of the above claims, wherein the composition is formulated with a pharmaceutically acceptable carrier or diluent.
22. The use of any one of the above claims, wherein the composition is to be administered intracerebroventricularly, intraperitoneally, intravenously or by inhalation.
23. Use of a composition comprising an agent that inhibits inflammasome signaling in the manufacture of a medicament for treating inflammation in lungs of a patient that has been subjected to a central nervous system (CNS) injury, wherein the composition is to be administered to the patient, whereby the inflammation in the lungs of the patient is treated.
24. The use of claim 23, wherein the CNS injury is selected from the group consisting of traumatic brain injury (TBI), stroke and spinal cord injury (SCI).
25. The use of any one of claims 23-24, wherein the administration of the composition results in inhibition of inflammasome activation in lung cells of the patient.
26. The use of any one of claims 23-24, wherein the administration of the composition results in a reduction of caspase-1, NLRP1, NLRP2, NLRP3, NLRC4, caspase-11, XIAP, pannexin-1, Apoptosis-associated Spec-like protein containing a Caspase Activating Recruitment Domain (ASC), interleukin-18 (IL-18), high mobility group box 1 (HMGB1) or absent in melanoma 2 (AIM2) levels in lung cells of the patient as compared to a control, wherein the control is an untreated patient.
27. The use of claim 25 or 26, wherein the lung cells are Type II alveolar cells.
28. The use of any one of claims 23-27, wherein the administration of the composition results in a reduction in acute lung injury (ALI) as compared to a control, wherein the control is an untreated patient.
29. The use of claim 28, wherein the reduction in ALI is evidenced by a reduction in neutrophil infiltration into alveolar and/or interstitial space, reduced or absent alveolar septal thickening or a combination thereof.
30. The use of any one of claims 23-29, wherein the agent is an extracellular vesicle (EV) uptake inhibitor, an antibody that binds to an inflammasome component or a combination thereof.

31. The use of claim 30, wherein the EV uptake inhibitor is a compound or an antibody, wherein the antibody is selected from Table 1.
32. The use of any of claims 30-31, wherein the agent is an EV uptake inhibitor in combination with an antibody that binds to an inflammasome component.
33. The use of claim 32, wherein the EV uptake inhibitor is a heparin.
34. The use of claim 33, wherein the heparin is Enoxaparin.
35. The use of any of claims 30-34, wherein the antibody that binds to an inflammasome component is an antibody that specifically binds to a component of a mammalian AIM2, NLRP1, NLRP2, NLRP3 or NLRC4 inflammasome.
36. The use of claim 30 or 35, wherein the inflammasome component is caspase-1, ASC or AIM2.
37. The use of claim 36, wherein the inflammasome component is ASC.
38. The use of claim 37, wherein the antibody binds to the PYD, CARD domain or an epitope derived from the PYD or CARD domain of the ASC protein.
39. The use of claim 37, wherein the antibody binds to an amino acid having at least 85% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.
40. The use of any of claims 37-39, wherein the antibody inhibits ASC activity in the lungs of the patient.
41. The use of any one of claims 23-40, wherein the composition is formulated with a pharmaceutically acceptable carrier or diluent.
42. The use of any one of claims 23-41, wherein the composition is to be administered intracerebroventricularly, intraperitoneally, intravenously or by inhalation.