

CLAIMS

What is claimed is:

1. A method of preventing or treating a virus-induced organ injury or failure in an individual, comprising administering to the individual an effective amount of an IL-22 dimer.
2. The method of claim 1, wherein the virus-induced organ injury or failure is virus-induced lung injury or failure.
3. The method of claim 2, wherein the virus-induced lung injury or failure is pulmonary fibrosis, pneumonia, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), Severe Acute Respiratory Syndrome coronavirus (SARS), Middle East Respiratory Syndrome coronavirus (MERS), Coronavirus disease 2019 (COVID-19), Influenza A virus subtype H1N1 (H1N1) swine flu, or Influenza A virus subtype H5N1 (H5N1) bird flu.
4. The method of claim 1, wherein the virus-induced organ injury or failure is virus-induced sepsis, septic shock, or multiple organ dysfunction syndrome (MODS).
5. The method of any one of claims 1-4, wherein the virus-induced organ injury or failure is caused by a virus of any one of the *Orthomyxoviridae*, *Filoviridae*, *Flaviviridae*, *Coronaviridae*, and *Poxviridae* families.
6. The method of claim 5, wherein the virus is an *Orthomyxoviridae* virus selected from the group consisting of Influenza A virus, Influenza B virus, Influenza C virus, and any subtype or reassortant thereof.
7. The method of claim 6, wherein the virus is an Influenza A virus or any subtype or reassortant thereof.
8. The method of claim 7, wherein the virus is Influenza A virus subtype H1N1 (H1N1) or Influenza A virus subtype H5N1 (H5N1).
9. The method of claim 5, wherein the virus is a *Coronaviridae* virus selected from the group consisting of alpha coronaviruses 229E (HCoV-229E), New Haven coronavirus NL63 (HCoV-NL63), beta coronaviruses OC43 (HCoV-OC43), coronavirus HKU1 (HCoV-HKU1), Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).
10. The method of claim 5, wherein the virus is a *Filoviridae* virus selected from Ebola virus

(EBOV) and Marburg virus (MARV).

11. The method of claim 5, wherein the virus is a *Flaviviridae* virus selected from the group consisting of Zika virus (ZIKV), West Nile virus (WNV), Dengue virus (DENV), and Yellow Fever virus (YFV).

12. The method of any one of claims 1-11, further comprising administering to the individual an effective amount of another therapeutic agent.

13. The method of claim 12, wherein the other therapeutic agent is selected from the group consisting of a corticosteroid, an anti-inflammatory signal transduction modulator, a β 2-adrenoreceptor agonist bronchodilator, an anticholinergic, a mucolytic agent, an antiviral agent, an anti-fibrotic agent, hypertonic saline, an antibody, a vaccine, or mixtures thereof.

14. The method of claim 13, wherein the antiviral agent is selected from the group consisting of remdesivir, lopinavir/ritonavir, IFN- α , lopinavir, ritonavir, penciclovir, galidesivir, disulfiram, darunavir, cobicistat, ASC09F, disulfiram, nafamostat, griffithsin, alisporivir, chloroquine, nitazoxanide, baloxavir marboxil, oseltamivir, zanamivir, peramivir, amantadine, rimantadine, favipiravir, laninamivir, ribavirin, umifenovir, and any combinations thereof.

15. The method of claim 14, wherein the other therapeutic agent is remdesivir, or lopinavir/ritonavir and IFN α , and the virus-induced organ injury or failure is induced by SARS-CoV-2.

16. The method of claim 14, wherein the other therapeutic agent is selected from the group consisting of oseltamivir, zanamivir, peramivir, lopinavir/ritonavir, IFN α , and any combinations thereof, and the virus-induced organ injury or failure is induced by H1N1 or H5N1.

17. The method of claim 13, wherein the anti-fibrotic agent is selected from the group consisting of nintedanib, pirfenidone, and *N*-Acetylcysteine (NAC).

18. The method of any one of claims 12-17, wherein the IL-22 dimer is administered simultaneously or sequentially with the other therapeutic agent.

19. A method of protecting an organ from virus-induced organ injury or failure in an individual, comprising administering to the individual an effective amount of an IL-22 dimer.

20. The method of any one of claims 1-19, wherein the virus-induced organ injury or failure comprises endothelial cell injury, dysfunction, or death.

21. A method of promoting regeneration of injured tissue or organ due to virus infection in an individual, comprising administering to the individual an effective amount of an IL-22 dimer.

22. The method of claim 21, wherein the injured tissue or organ comprises injured or dysfunctional endothelial cells.
23. The method of claim 20 or 22, wherein endothelial dysfunction comprises endothelial glycocalyx degradation.
24. A method of treating or preventing endothelial dysfunction in an injured tissue or organ due to virus infection in an individual, comprising administering to the individual an effective amount of an IL-22 dimer.
25. The method of any one of claims 20-24, wherein the method comprises preventing and/or reducing endothelial glycocalyx degradation, down-regulating Toll-like Receptor 4 (TLR4) signaling, and/or regenerating endothelial glycocalyx.
26. The method of any one of claims 20 and 22-25, wherein the endothelial cell is a pulmonary endothelial cell.
27. A method of reducing inflammation due to virus infection in an individual, comprising administering to the individual an effective amount of an IL-22 dimer.
28. The method of any one of claims 1-27, wherein the IL-22 dimer comprises two monomeric subunits, and wherein each monomeric subunit comprises an IL-22 monomer and a dimerization domain.
29. The method of claim 28, wherein the IL-22 monomer is connected to the dimerization domain via an optional linker.
30. The method of claim 29, wherein the linker comprises the sequence of any one of SEQ ID NOs: 1-20 and 32.
31. The method of claim 29 or 30, wherein the linker is about 6 to about 30 amino acids in length.
32. The method of any one of claims 29-31, wherein the linker comprises the sequence of SEQ ID NO: 1 or 10.
33. The method of any one of claims 28-32, wherein the dimerization domain comprises at least two cysteines capable of forming intermolecular disulfide bonds.
34. The method of any one of claims 28-33, wherein the dimerization domain comprises at least a portion of an Fc fragment.
35. The method of claim 34, wherein the Fc fragment comprises CH2 and CH3 domains.
36. The method of claim 34 or 35, wherein the Fc fragment comprises the sequence of SEQ

ID NO: 22 or 23.

37. The method of any one of claims 28-36, wherein the IL-22 monomer comprises the sequence of SEQ ID NO: 21.

38. The method of any one of claims 28-37, wherein the IL-22 monomer is N-terminal to the dimerization domain.

39. The method of any one of claims 28-37, wherein the IL-22 monomer is C-terminal to the dimerization domain.

40. The method of any one of claims 28-39, wherein each monomeric subunit comprises the sequence of any of SEQ ID NOs: 24-27.

41. The method of any one of claims 28-38 and 40, wherein each monomeric subunit comprises the sequence of SEQ ID NO: 24.

42. The method of any one of claims 1-41, wherein the effective amount of the IL-22 dimer is about 2 $\mu\text{g/kg}$ to about 200 $\mu\text{g/kg}$.

43. The method of any one of claims 1-42, wherein the effective amount of the IL-22 dimer is about 5 $\mu\text{g/kg}$ to about 80 $\mu\text{g/kg}$.

44. The method of any one of claims 1-43, wherein the effective amount of the IL-22 dimer is about 10 $\mu\text{g/kg}$ to about 45 $\mu\text{g/kg}$.

45. The method of any one of claims 1-44, wherein the effective amount of the IL-22 dimer is about 30 $\mu\text{g/kg}$ to about 45 $\mu\text{g/kg}$.

46. The method of any one of claims 1-45, wherein the IL-22 dimer is administered intravenously, intrapulmonarily, or via inhalation or insufflation.

47. The method of any one of claims 1-46, wherein the IL-22 dimer is administered at least once a week.

48. The method of any one of claims 1-47, wherein the IL-22 dimer is administered on day 1 and day 6 of a 10-day treatment cycle, or day 1 and day 8 of a 14-day treatment cycle.

49. The method of any one of claims 1-48, wherein the individual is at least about 55 years old.

50. The method of any one of claims 1-49, further comprising selecting the individual based on that the individual is at least about 55 years old.