

What is claimed is:

1. Use of an anti-IL-18 antibody in the manufacture of a medicament for ~~A method of treating a condition associated with elevated IL-18, comprising administering to a subject in need thereof an effective amount of an anti-IL-18 antibody~~ wherein the anti-IL-18 antibody comprises:
 - (a) a HCDR1 having an amino acid sequence of SEQ ID NO: 122;
 - (b) a HCDR2 having an amino acid sequence of SEQ ID NO: 123;
 - (c) a HCDR3 having an amino acid sequence of SEQ ID NO: 124;
 - (d) a LCDR1 having an amino acid sequence of SEQ ID NO: 126;
 - (e) a LCDR2 having an amino acid sequence of SEQ ID NO: 127; and
 - (f) a LCDR3 having an amino acid sequence of SEQ ID NO: 128and, optionally wherein the condition associated with elevated IL-18 comprises any one or more of:
 - (a) inflammation, optionally wherein the inflammation is hyperinflammation;
 - (b) immune dysregulation that leads to multisystem organ failure;
 - (c) acute lung injury (ALI), optionally wherein the ALI is associated with a bacterial or viral infection, including coronavirus infection;
 - (d) acute respiratory distress syndrome (ARDS), optionally wherein the ARDS is associated with a bacterial or viral infection, including coronavirus infection;
 - (e) hemophagocytic lymphohistiocytosis (HLH), optionally where the HLH is associated with a bacterial or viral infection, including coronavirus infection;
 - (f) macrophage activation syndrome (MAS), optionally where the MAS is associated with a bacterial or viral infection, including coronavirus infection;
 - (g) cytokine storm that drives tissue injury and vascular permeability;
 - (h) post-infection pulmonary fibrosis;
 - (i) syndromes caused by NLRP3 overactivation/dysregulation due to viral infection; and
 - (j) pneumonia, optionally wherein the pneumonia is associated with a bacterial or viral infection, including coronavirus infection,thereby treating the condition.

2. The ~~method-use~~ of claim 1, wherein the ~~method-use~~ further comprises the following steps prior to ~~administering~~ administration of the anti-IL-18 antibody:
 - (a) contacting a biological sample isolated from the subject with an anti-IL-18 antibody;
 - (b) incubating the biological sample to allow an anti-IL-18 antibody to bind to IL-18; and
 - (c) detecting the presence of complexes formed between an anti-IL-18 antibody and IL-18 in the biological sample.
3. The ~~method-use~~ of claim 2, wherein the detection of IL-18 indicates that treatment of the condition associated with elevated IL-18 with an anti-IL-18 antibody will be effective.
4. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating COVID-19 infection ~~comprising administering an anti-IL-18 antibody to~~ in a subject in need thereof.
5. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating severe COVID-19 pneumonia ~~comprising administering an anti-IL-18 antibody to~~ in a subject in need thereof.
6. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating acute inflammatory disease in a subject in need thereof, optionally wherein the acute inflammatory disease is associated with COVID-19, ~~comprising administering an anti-IL-18 antibody to a subject in need thereof~~.
7. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating respiratory failure associated with COVID-19 ~~comprising administering an anti-IL-18 antibody to~~ in a subject in need thereof.
8. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating cytokine storm comprising ~~administering an anti-IL-18 antibody to~~ in a subject in need thereof.
9. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating Acute Respiratory Distress Syndrome (ARDS) in a subject in need thereof, optionally wherein the Acute Respiratory Distress Syndrome (ARDS) is associated with COVID-19, ~~comprising administering an anti-IL-18 antibody to a subject in need thereof~~.
10. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method of treating hemophagocytic lymphohistiocytosis (HLH) in a subject in need

thereof, optionally wherein the hemophagocytic lymphohistiocytosis (HLH) is
associated with COVID-19, ~~comprising administering an anti-IL-18 antibody to a~~
~~subject in need thereof.~~

11. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method
~~of~~ treating macrophage activation syndrome (MAS) in a subject in need thereof,
optionally wherein the macrophage activation syndrome (MAS) is associated with
COVID-19, ~~comprising administering an anti-IL-18 antibody to a subject in need~~
~~thereof.~~

12. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method
~~of~~ preventing progression to ARDS in a subject, wherein comprising
~~administering an anti-IL-18 antibody to the subject~~ is not yet having ARDS and is
having a condition associated with elevated IL-18.

13. Use of an anti-IL-18 antibody in the manufacture of a medicament for A method
~~of~~ preventing the need for ventilation/intubation of a subject, wherein comprising
~~administering an anti-IL-18 antibody to the subject~~ is not yet intubated/ventilated
and is having a condition associated with elevated IL-18.

14. The ~~method-use~~ of any one of claims 4-13, wherein the anti-IL-18 antibody
comprises:

- (a) a HCDR1 having an amino acid sequence of SEQ ID NO: 122;
- (b) a HCDR2 having an amino acid sequence of SEQ ID NO: 123;
- (c) a HCDR3 having an amino acid sequence of SEQ ID NO: 124;
- (d) a LCDR1 having an amino acid sequence of SEQ ID NO: 126;
- (e) a LCDR2 having an amino acid sequence of SEQ ID NO: 127; and
- (f) a LCDR3 having an amino acid sequence of SEQ ID NO: 128.

15. The ~~use method~~ of any one of the preceding claims, wherein the anti-IL-18
antibody comprises a VH domain having an amino acid sequence that is at least
90% identical to the full sequence of SEQ ID NO: 121.

16. The ~~use method~~ of any one of the preceding claims, wherein the anti-IL-18
antibody comprises a VH domain having an amino acid sequence that is identical
to the full sequence of SEQ ID NO: 121.

17. The ~~use method~~ of any one of the preceding claims, wherein the anti-IL-18
antibody comprises a VL domain having an amino acid sequence that is at least
90% identical to the full sequence of SEQ ID NO: 125.

18. The ~~use method~~ of any one of the preceding claims, wherein the anti-IL-18 antibody comprises a VL domain having an amino acid sequence that is identical to the full sequence of SEQ ID NO: 125.
19. The ~~use method~~ of any one of the preceding claims, wherein the anti-IL-18 antibody comprises an antibody VH domain and an antibody VL domain, wherein the amino acid sequence of the antibody VH domain and the antibody VL domain are at least 90% identical to the full sequence of SEQ ID NOS: 121 and 125.
20. The ~~use method~~ of any one of claims 1-3 or 15-19, wherein the condition associated with elevated IL-18 is secondary hemophagocytic lymphohistiocytosis (sHLH).
21. The ~~use method~~ of any one of claims 1-3, wherein the condition associated with elevated IL-18 is a COVID-19 infection.
22. The ~~use method~~ of claim 20, wherein the hemophagocytic lymphohistiocytosis (HLH) is secondary hemophagocytic lymphohistiocytosis (sHLH).
23. The ~~use method~~ of any of the preceding claims, wherein the anti-IL-18 antibody ~~administered to the subject~~ suppresses T cell activation ~~in the subject~~.
24. The ~~use method~~ of any of the preceding claims, wherein the anti-IL-18 antibody ~~administered to the subject~~ suppresses increased expression of cytokines ~~in the subject~~.
25. The ~~method use~~ of claim 24, wherein the anti-IL-18 antibody ~~administered to the subject~~ suppresses increased expression of IFN- γ ~~in the subject~~.
26. The ~~method use~~ of any of the preceding claims, wherein the anti-IL-18 antibody ~~administered to the subject~~ reduces the subject's risk of mortality or morbidity.
27. The ~~method use~~ of any one of the preceding claims, wherein the subject is human.
28. The ~~method use~~ of any one of claims 1-3 or 15-19, wherein the subject has a respiratory disease, optionally caused by a coronavirus infection.
29. The ~~method use~~ of any one of claims 1-3 or 15-19, wherein the subject has pneumonia.
30. The ~~method use~~ of any one of claims 1-3 or 15-19, wherein the subject has acute lung injury (ALI).
31. The ~~method use~~ of any one of claims 1-3 or 15-19, wherein the subject has acute respiratory distress syndrome (ARDS).

32. The method-use of any one of claims 1-3 or 15-19, wherein the subject has a mild coronavirus infection.

33. The method-use of any one of claims 1-3 or 15-19, wherein the subject has a moderate coronavirus infection.

5 34. The method-use of any one of claims 1-3 or 15-19, wherein the subject has a severe coronavirus infection.

35. The method-use of any one of claims 1-3 or 15-19, wherein the subject is at the Early Infection (Stage I) of a coronavirus infection.

10 36. The method-use of any one of claims 1-3 or 15-19, wherein the subject is at the Pulmonary Phase (Stage II) of a coronavirus infection.

37. The method-use of any one of claims 1-3 or 15-19, wherein the subject is at the Hyperinflammation Phase (Stage III) of a coronavirus infection.

38. The method-use of any one of the preceding claims, wherein the subject is a pediatric subject.

15 39. The method-use of any one of the preceding claims, wherein the subject is an adult.

40. A kit for use according to in a method of any one of the preceding claims, wherein the kit comprising comprises an anti-IL-18 antibody as defined in any one of the preceding claims and reagents for carrying out the methodsaid use.

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