

CLAIMS

1. A method of identifying a risk of severe disease in a subject infected with SARS-CoV-2, the method comprising:
 - 5 determining a level of one or more immune mediators in the subject's sample; and
 - identifying a risk of severe disease based on the level of the one or more immune mediators,
 - wherein the risk of severe disease is positively associated with the level of the
 - 10 one or more immune mediators and wherein the one or more immune mediators comprises at least one of cytokines, chemokines, growth factors or combinations thereof.
2. The method according to claim 1, wherein the one or more immune mediators
 - 15 comprises at least one of interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), interferon gamma-induced protein 10 (IP-10), interleukin-18 (IL-18), interleukin-1 receptor antagonist (IL-1RA), platelet-derived growth factor-BB (PDGF-BB), hepatocyte growth factor (HGF), macrophage inflammatory protein-1 alpha (MIP-1 α), interleukin-12p70 (IL-12p70), vascular endothelial growth
 - 20 factor A (VEGF-A) or combinations thereof.
3. The method according to claim 1 or claim 2, wherein the sample comprises a sample collected from the subject during a virus-shedding phase.
4. The method according to claim 1 or claim 2, wherein the one or more immune
 - 25 mediators comprises at least one of HGF, VEGF-A, MCP-1, IL-6 or combinations thereof.
5. The method according to claim 4, wherein the one or more immune mediators
 - 30 comprises at least one of HGF, VEGF-A or combinations thereof.
6. The method according to claim 4 or claim 5, wherein the sample comprises a sample collected from the subject during a convalescent phase.

7. The method according to any one of claims 1-6, wherein the sample comprises blood or a fraction thereof.
8. The method according to any one of claims 1-7, wherein determining a level of one or more immune mediators in a sample comprises contacting the sample with beads that are configured to bind to the one or more immune mediators.
9. A method of treating SARS-CoV-2 infection, the method comprising:
administering to a subject in need thereof, an agent that is capable of reducing a level of one or more immune mediators in the subject, wherein the one or more immune mediators comprises at least one of cytokines, chemokines, growth factors or combinations thereof.
10. The method according to claim 9, wherein the one or more immune mediators comprises at least one of IL-6, MCP-1, IP-10, IL-18, IL-1RA, PDGF-BB, HGF, MIP-1 α , IL-12p70, VEGF-A or combinations thereof.
11. The method according to claim 9 or claim 10, wherein the agent comprises an IL-6 inhibitor.
12. The method according to claim 11, wherein the IL-6 inhibitor comprises an antigen-binding protein comprising the following CDR sequences:
- heavy-chain CDR1: GYSITSDHA (SEQ ID NO: 1);
heavy-chain CDR2: ISYSGIT (SEQ ID NO: 2);
heavy-chain CDR3: ARSLARTTAMDY (SEQ ID NO: 3);
light-chain CDR1: QDISSY (SEQ ID NO: 4);
light-chain CDR2: YTS (SEQ ID NO: 5);
light-chain CDR3: QQGNTLPYT (SEQ ID NO: 6);
- heavy-chain CDR1: RFTFDDYA (SEQ ID NO: 9);
heavy-chain CDR2: ISWNSGRI (SEQ ID NO: 10);
heavy-chain CDR3: AKGRDSFDI (SEQ ID NO: 11);
light-chain CDR1: QGISSW (SEQ ID NO: 12);
light-chain CDR2: GAS (SEQ ID NO: 13);
light-chain CDR3: QQANSFPYT (SEQ ID NO: 14); or

conservative sequence variants thereof.

5 13. The method according to claim 12, wherein the antigen-binding protein comprises at least one of tocilizumab, sarilumab, antigen-binding fragments thereof or combinations thereof.

10 14. A method of evaluating the efficacy of a treatment regimen in a subject infected with SARS-CoV-2, the method comprising:
determining a level of one or more immune mediators in a sample collected from the subject at a first time point;
determining a level of the one or more immune mediators in a sample collected from the subject at a second time point following the administration of the treatment regimen;
15 comparing the level of the one or more immune mediators at the second time point to the first time point; and
identifying the treatment regimen as being effective when there is a reduction in the level of the one or more immune mediators at the second time point as compared to the first time point,
20 wherein the one or more immune mediators comprises at least one of cytokines, chemokines, growth factors or combinations thereof.

25 15. The method according to claim 14, wherein the one or more immune mediators comprises at least one of IL-6, MCP-1, IP-10, IL-18, IL-1RA, PDGF-BB, HGF, MIP-1 α , IL-12p70, VEGF-A or combinations thereof,
optionally wherein the one or more immune mediators comprises at least one of HGF, VEGF-A, MCP-1, IL-6 or combinations thereof,
further optionally wherein the one or more immune mediators comprises at least one of HGF, VEGF-A or combinations thereof.

30 16. The method according to claim 14 or claim 15, wherein where the treatment regimen is not identified as being effective, the method further comprises changing the treatment regimen administered to the subject.

17. The method according to any one of claims 14-16, wherein changing the treatment regimen comprises administering to the subject an agent that is capable of reducing a level of one or more immune mediators in the subject, optionally wherein the agent comprises an IL-6 inhibitor, further optionally wherein the IL-6 inhibitor comprises an antigen-binding protein comprising the following CDR sequences:

heavy-chain CDR1: GYSITSDHA;
heavy-chain CDR2: ISYSGIT;
heavy-chain CDR3: ARSLARTTAMDY;
light-chain CDR1: QDISSY;
light-chain CDR2: YTS;
light-chain CDR3: QQGNTLPYT;

heavy-chain CDR1: RFTFDDYA;
heavy-chain CDR2: ISWNSGRI;
heavy-chain CDR3: AKGRDSFDI;
light-chain CDR1: QGISSW;
light-chain CDR2: GAS;
light-chain CDR3: QQANSFPYT; or

conservative sequence variants thereof,

further optionally wherein the antigen-binding protein comprises at least one of tocilizumab, sarilumab, antigen-binding fragments thereof or combinations thereof.

18. The method according to any one of claims 14-17, wherein the sample comprises blood or a fraction thereof.

19. The method according to any one of claims 14-18, wherein determining a level of one or more immune mediators in a sample comprises contacting the sample with beads that are configured to bind to the one or more immune mediators.

20. A multiplex array for identifying a risk of severe disease in a subject infected with SARS-CoV-2 or for evaluating the efficacy of a treatment regimen in a subject infected with SARS-CoV-2, the array comprising:

5 beads that are configured to bind to one or more immune mediators selected from the group consisting of: IL-6, MCP-1, IP-10, IL-18, IL-1RA, PDGF-BB, HGF, MIP-1 α , IL-12p70, VEGF-A and combinations thereof.

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