

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. An isolated antibody, or antigen-binding fragment thereof, that binds to MASP-3 comprising: a heavy chain variable region comprising a HC-CDR1 set forth as SEQ ID NO:84 (GKWIE); a HC-CDR2 set forth as SEQ ID NO:86 (EILPGTGSTNYNEKFKG) or SEQ ID NO:275 (EILPGTGSTNYAQKFQG); and a HC-CDR3 set forth as SEQ ID NO:88 (SEDV); and a light chain variable region comprising a LC-CDR1 set forth as SEQ ID NO:142 (KSSQSLLNSRTRKNYLA), SEQ ID NO:257 (KSSQSLLQSRTRKNYLA); SEQ ID NO:258 (KSSQSLLASRTRKNYLA); or SEQ ID NO:259 (KSSQSLLNTRTRKNYLA), a LC-CDR2 set forth as SEQ ID NO:144 (WASTRES); and a LC-CDR3 set forth as SEQ ID NO:161 (KQSYNIPT).

2. The antibody or antigen binding fragment thereof of Claim 1, wherein the antibody or antigen-binding fragment is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a murine antibody, and an antigen-binding fragment of any of the foregoing.

3. The antibody or antigen-binding fragment thereof of Claim 1, wherein said antibody or antigen binding fragment thereof is selected from the group consisting of a single chain antibody, an ScFv, a Fab fragment, an Fab' fragment, an F(ab')₂ fragment, a univalent antibody lacking a hinge region and a whole antibody.

4. The antibody or antigen-binding fragment thereof of Claim 1, further comprising an immunoglobulin constant region.

5. The antibody or antigen binding fragment thereof of Claim 1, wherein the antibody or antigen-binding fragment is humanized.

6. The antibody or antigen-binding fragment thereof of Claim 1, wherein said antibody binds to the serine protease domain of human MASP-3 with an affinity of less than 500 pM.

7. The antibody or antigen-binding fragment thereof of Claim 1, wherein said antibody inhibits alternative pathway activation in mammalian blood.
8. An isolated DNA sequence encoding the heavy and/or light chain variable regions of an antibody or antigen-binding fragment thereof from any one of claims 1-7.
9. A cloning or expression vector comprising one or more DNA sequences of Claim 8.
10. A host cell comprising one or more cloning or expression vectors of claim 9.
11. A process for producing the antibody or antigen-binding fragment of any of claims 1-7 comprising culturing the host cell of claim 10 and isolating the antibody or antigen-binding fragment thereof.
12. A composition comprising the antibody or antigen-binding fragment of any of Claims 1-7 and a pharmaceutically acceptable excipient.
13. Use of a composition according to claim 12 in the manufacture of a medicament for inhibiting alternative pathway complement activation in a mammal, wherein the composition comprising a high affinity MASP-3 inhibitory antibody or antigen-binding fragment thereof is in an amount sufficient to inhibit alternative pathway complement pathway activation in the mammalian subject.
14. The isolated antibody or antigen-binding fragment thereof of Claim 1, wherein the LC-CDR1 comprises SEQ ID NO:258.
15. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the HC-CDR2 comprises SEQ ID NO:86.
16. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the HC-CDR2 comprises SEQ ID NO:275.
17. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the LC-CDR1 comprises SEQ ID NO:142.

18. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the LC-CDR1 comprises SEQ ID NO:257.

19. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the LC-CDR1 comprises SEQ ID NO:259.

20. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the HC-CDR1 comprises SEQ ID NO:84, the HC-CDR2 comprises SEQ ID NO:86, the HC-CDR3 comprises SEQ ID NO:88, the LC-CDR1 comprises SEQ ID NO:258, the LC-CDR2 comprises SEQ ID NO:144 and the LC-CDR3 comprises SEQ ID NO:161.

21. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the HC-CDR1 comprises SEQ ID NO:84, the HC-CDR2 comprises SEQ ID NO:275, the HC-CDR3 comprises SEQ ID NO:88; the LC-CDR1 comprises SEQ ID NO:258, the LC-CDR2 comprises SEQ ID NO:144 and the LC-CDR3 comprises SEQ ID NO:161.

22. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO:30.

23. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO:45.

24. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO:30 and the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO:45.

25. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO:254 or SEQ ID NO:255.

26. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the light chain variable region comprises the amino acid sequence set forth as SEQ ID NO:256 or SEQ ID NO:280.

27. An isolated antibody or antigen-binding fragment thereof that binds to human MASP-3, comprising a heavy chain variable region comprising SEQ ID NO:254 or SEQ ID NO:255 and a light chain variable region comprising SEQ ID NO:256 or SEQ ID NO:280.
28. The isolated antibody or antigen-binding fragment thereof of claim 27, wherein the heavy chain variable region comprises SEQ ID NO:254 and the light chain variable region comprises SEQ ID NO:256.
29. The isolated antibody or antigen-binding fragment thereof of claim 27, wherein the heavy chain variable region comprises SEQ ID NO:255 and the light chain variable region comprises SEQ ID NO:256.
30. The isolated antibody or antigen-binding fragment thereof of claim 27, wherein the heavy chain variable region comprises SEQ ID NO:254 and the light chain variable region comprises SEQ ID NO: 280.
31. The isolated antibody or antigen-binding fragment thereof of claim 27, wherein the heavy chain variable region comprises SEQ ID NO:255 and the light chain variable region comprises SEQ ID NO: 280.
32. The isolated antibody of claim 27, wherein the antibody is selected from the group consisting of a single chain antibody, an ScFv, a Fab fragment, an Fab' fragment, an F(ab')₂ fragment, a univalent antibody lacking a hinge region and a whole antibody.
33. The isolated antibody of claim 27, further comprising an immunoglobulin constant region.