

CLAIMS

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

- ~~1. An isolated monoclonal antibody or antigen binding fragment thereof that specifically binds to the serine protease domain of human MASP-3 (amino acid residues 450 to 728 of SEQ ID NO:2) with high affinity (having a K_D of less than 500 pM), wherein the antibody or antigen binding fragment thereof inhibits alternative pathway complement activation.~~
- ~~2. The isolated antibody or antigen binding fragment thereof of claim 1, wherein the antibody or antigen binding fragment is characterized by at least one or more of the following properties:~~
 - ~~(a) inhibits pro-Factor D maturation;~~
 - ~~(b) does not bind to human MASP-1 (SEQ ID NO:8);~~
 - ~~(c) inhibits the alternative pathway at a molar ratio of from about 1:1 to about 2.5:1 (MASP-3 target to mAb) in a mammalian subject;~~
 - ~~(d) does not inhibit the classical pathway.~~
 - ~~(e) inhibition of hemolysis and/or opsonization;~~
 - ~~(f) inhibition of MASP-3 serine protease substrate specific cleavage;~~
 - ~~(g) a reduction of hemolysis or the reduction of C3 cleavage and C3b surface deposition;~~
 - ~~(h) a reduction of Factor B and Bb deposition on an activating surface;~~
 - ~~(i) a reduction of resting levels (in circulation, and without the experimental addition of an activating surface) of active Factor D relative to pro-Factor D;~~
 - ~~(j) a reduction of levels of active Factor D relative to pro-Factor D in response to an activating surface;~~
 - ~~(k) a reduction of the production of resting and surface-induced levels of fluid phase Ba, Bb, C3b, or C3a; and/or~~
 - ~~(l) a reduction in factor P deposition.~~
- ~~3. The isolated antibody or antigen binding fragment thereof of claims 1 or 2, wherein said antibody or antigen binding fragment thereof specifically binds to an epitope located~~

~~within the serine protease domain of human MASP 3, wherein said epitope is located within at least one or more of: VLRSQRRD¹TTV (SEQ ID NO:15), TAAHVLRSQRRD¹TV (SEQ ID NO:10), VLRSQRRD¹TTVI (SEQ ID NO:9), DFNIQNYNH¹DIALVQ (SEQ ID NO:11), PHAECKT¹SYESRS (SEQ ID NO:12), GNYSVTEN¹MFC (SEQ ID NO:13), VS¹NYVDWVWE (SEQ ID NO:14) and/or~~

~~4. The antibody or antigen binding fragment thereof of claim 3, wherein said antibody or antigen binding fragment binds to an epitope within SEQ ID NO:15.~~

~~5. The antibody or antigen binding fragment of claim 3, wherein said antibody or antigen binding fragment binds to an epitope within SEQ ID NO:10.~~

~~6. The antibody or antigen binding fragment of claim 3, wherein said antibody or antigen binding fragment binds to an epitope within SEQ ID NO:9.~~

~~7. The antibody or antigen binding fragment of claim 5, wherein said antibody or antigen binding fragment also binds to an epitope within SEQ ID NO:12.~~

~~8. The antibody or antigen binding fragment of claim 6, wherein said antibody or antigen binding fragment also binds to an epitope within at least one of SEQ ID NO:11, SEQ ID NO:13 and/or SEQ ID NO:14.~~

~~9. The antibody or antigen binding fragment of claim 1 or 2, wherein said antibody binds to an epitope within at least one of: ECGQPSRSLPSLV (SEQ ID NO:16); RNAEPGLFPWQ (SEQ ID NO:17); KWFGSGALLSASWIL (SEQ ID NO:18); EHVTVYLGLH (SEQ ID NO:19); PVPLGPHVMP (SEQ ID NO:20); APHMLGL (SEQ ID NO:21); SDVLQYVKLP (SEQ ID NO:22); and/or AFVIFDDLSQRW (SEQ ID NO:23).~~

~~10. An isolated antibody, or antigen-binding fragment thereof, that binds to human MASP-3 comprising:~~

~~(a) 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 (SE¹DV); and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:142 (KSSQSL¹LN¹SRTRK¹NYLA), SEQ ID NO:257 (KSSQSL¹LQSRTRK¹NYLA);~~

~~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); or~~

~~(b) a heavy chain variable region comprising a HC-CDR1 set forth as SEQ ID NO:213 (SYGXX, wherein X at position 4 is M or I and wherein X at position 5 is S or T); a HC-CDR2 set forth as SEQ ID NO:74 (WINTYSGVPTYADDFKG); and a HC-CDR3 set forth as SEQ ID NO:214 (GGXAXDY, wherein X at position 3 is E or D and wherein X at position 5 is M or L); and a light chain variable region comprising a LC-CDR1 set forth as SEQ ID NO:215 (KSSQSLLDSXXXKTYLX, wherein X at position 10 is D, E or A; wherein X at position 11 is G or A; and wherein X at position 16 is N or S); a LC-CDR2 set forth as SEQ ID NO:155 (LVSKLDS); and a LC-CDR3 set forth as SEQ ID NO:216 (WQGTHFPXT), wherein X at position 8 is W or Y;~~

~~(c) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:209 (XXDIN, wherein X at position 1 is S or T and wherein X at position 2 is N or D); a HC CDR2 set forth as SEQ ID NO:210 (WIYPRDXXXKYNXXFXD, wherein X at position 7 is G or D; X at position 8 is S, T or R; X at position 9 is I or T; X at position 13 is E or D; X at position 14 is K or E; and X at position 16 is T or K); and a HC CDR3 set forth as SEQ ID NO:211 (XEDXY, wherein X at position 1 is L or V, and wherein X at position 4 is T or S); and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:212 (KSSQSLLXXRTRKNYLX, wherein X at position 8 is N, I, Q or A; wherein X at position 9 is S or T; and wherein X at position 17 is A or S); a LC CDR2 set forth as SEQ ID NO:144 (WASTRES) and a LC CDR3 set forth as SEQ ID NO:146 (KQSYNLYT).~~

~~11. The isolated antibody or antigen-binding fragment thereof of claim 10(a), wherein the LC CDR1 comprises SEQ ID NO:258.~~

~~12. The isolated antibody or antigen-binding fragment of claim 10(a), wherein the antibody or antigen-binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:30, SEQ ID NO:254 or SEQ ID NO:255 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:45, SEQ ID NO:256 or SEQ ID NO:280.~~

~~132.~~ The isolated antibody₁ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein ~~the HC-CDR1 of the heavy chain variable region according to (a)~~ comprises SEQ ID NO:72 (SYGMS).

~~143.~~ The isolated antibody₁ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein ~~the HC-CDR1 of the heavy chain variable region according to (a)~~ comprises SEQ ID NO:79 (SYGIT).

~~154.~~ The isolated antibody₁ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein ~~the HC-CDR3 of the heavy chain variable region according to (a)~~ comprises SEQ ID NO:76 (GGEAMDY).

~~165.~~ The isolated antibody₁ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein ~~the HC-CDR3 of the heavy chain variable region according to (a)~~ comprises SEQ ID NO:82 (GGDALDY).

~~176.~~ The isolated antibody₁ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the LC-CDR1 ~~of the light chain variable region according to (b)~~ comprises SEQ ID NO:153 (KSSQSLLDSDGKTYLN)₁.

7. The isolated antibody, or antigen-binding fragment thereof of Claim 1, wherein the LC-CDR1 comprises SEQ ID NO:261 (KSSQSLLDSEGKTYLN)₁.

8. The isolated antibody, or antigen-binding fragment thereof of Claim 1, wherein the LC-CDR1 comprises SEQ ID NO:262 (KSSQSLLDSAGKTYLN)₁.

9. The isolated antibody, or antigen-binding fragment thereof of Claim 1, wherein the LC-CDR1 comprises ~~or~~ SEQ ID NO:263 (KSSQSLLDSDAKTYLN).

~~18. The isolated antibody or antigen binding fragment thereof of claim 10(b), wherein the LC-CDR1 of the light chain variable region comprises SEQ ID NO:152.~~

~~19~~10. The isolated antibody₂ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the LC-~~CDR3-CDR1 of the light chain variable region according to (b)~~ comprises SEQ ID NO:159 (KSSQSLDSDGKTYLS).

11. The isolated antibody or antigen-binding fragment thereof of Claim 1, wherein the LC-CDR3 comprises SEQ ID NO:157 (WQGTHFPWT).

~~20~~12. The isolated antibody₂ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the LC-CDR3 ~~of the light chain variable region according to (b)~~ comprises SEQ ID NO:160 (WQGTHFPYT).

~~24~~13. The isolated antibody₂ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the HC-CDR1 comprises SEQ ID NO:72, the HC-CDR2 comprises SEQ ID NO:74, the HC-CDR3 comprises SEQ ID NO:76, the LC-CDR1 comprises SEQ ID NO:153, ~~SEQ ID NO:261, SEQ ID NO:262 or SEQ ID NO:263~~; the LC-CDR2 comprises SEQ ID NO:155 and the LC-CDR3 comprises SEQ ID NO:157.

14. The isolated antibody or antigen-binding fragment thereof of Claim 1, wherein the HC-CDR1 comprises SEQ ID NO:72, the HC-CDR2 comprises SEQ ID NO:74, the HC-CDR3 comprises SEQ ID NO:76, the LC-CDR1 comprises SEQ ID NO:263, the LC-CDR2 comprises SEQ ID NO:155 and the LC-CDR3 comprises SEQ ID NO:157.

~~22~~15. The isolated antibody₂ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the HC-CDR1 comprises SEQ ID NO:79, the HC-CDR2 comprises SEQ ID NO:74, the HC-CDR3 comprises SEQ ID NO:82, the LC-CDR1 comprises SEQ ID NO:159, the LC-CDR2 comprises SEQ ID NO:155 and the LC-CDR3 comprises SEQ ID NO:160.

~~23~~16. The isolated antibody₂ or antigen-binding fragment thereof of ~~claim 10(b)~~Claim 1, wherein the ~~antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprises an amino acid sequence selected from the group consisting of~~comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:251 or ~~and~~ SEQ ID NO:252 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:43, SEQ ID NO:253 or ~~SEQ ID NO:279~~.

17. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:253 and SEQ ID NO:279.

~~24. The isolated antibody or antigen binding fragment thereof of claim 10(b), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:29 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:44.~~

~~25. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR1 of the heavy chain variable region according to (a) comprises SEQ ID NO:56 (TDDIN).~~

~~26. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR1 of the heavy chain variable region according to (a) comprises SEQ ID NO:62 (SNDIN).~~

~~27. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR2 of the heavy chain variable region according to (a) comprises SEQ ID NO:58 (WIYPRDDRTKYNDKFKD).~~

~~28. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR2 of the heavy chain variable region according to (a) comprises SEQ ID NO:63 (WIYPRDGSIKYNEKFTD).~~

~~29. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR2 of the heavy chain variable region according to (a) comprises SEQ ID NO:67 (WIYPRDGTTKYNEEFTD).~~

~~30. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR2 of the heavy chain variable region according to (a) comprises SEQ ID NO:69 (WIYPRDGTTKYNEKFTD).~~

~~31. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR3 of the heavy chain variable region according to (a) comprises SEQ ID NO:60 (LEDTY).~~

~~32. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR3 of the heavy chain variable region according to (a) comprises SEQ ID NO:65 (VEDSY).~~

~~33. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the LC CDR1 of the light chain variable region according to (b) comprises SEQ ID NO:142 (KSSQSLLNSRTRKNYLA); SEQ ID NO:257 (KSSQSLLQSRTRKNYLA), SEQ ID NO:258 (KSSQSLLASRTRKNYLA); or SEQ ID NO:259 (KSSQSLLNTRTRKNYLA).~~

~~34. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the LC CDR1 of the light chain variable region according to (b) comprises SEQ ID NO:149 (KSSQSLLISRTRKNYLS).~~

~~35. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR1 comprises SEQ ID NO:56, the HC CDR2 comprises SEQ ID NO:58, the HC CDR3 comprises SEQ ID NO:60 and wherein the LC CDR1 comprises SEQ ID NO:142, SEQ ID NO:257, SEQ ID NO:258 or SEQ ID NO:259; wherein the LC CDR2 comprises SEQ ID NO:144 and wherein the LC CDR3 comprises SEQ ID NO:146.~~

~~36. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the HC CDR1 comprises SEQ ID NO:62, the HC CDR2 comprises SEQ ID NO:63, SEQ ID NO:67 or SEQ ID NO:69, the HC CDR3 comprises SEQ ID NO:65 and wherein the LC CDR1 comprises SEQ ID NO:149, the LC CDR2 comprises SEQ ID NO:144 and the LC CDR3 comprises SEQ ID NO:146.~~

~~37. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:24, SEQ ID NO:248 or SEQ ID NO:249 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:40, SEQ ID NO:250 or SEQ ID NO:278.~~

~~38. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:25 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:41.~~

~~39. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:26 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:42.~~

~~40. The isolated antibody or antigen binding fragment thereof of claim 10(c), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:27 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:42.~~

~~41. An isolated antibody, or antigen binding fragment thereof, that binds to MASP-3 comprising:~~

~~(a) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:91 (GYWIE); a HC CDR2 set forth as SEQ ID NO:93 (EMLPGSGSTHYNEKFKG), and a HC CDR3 set forth as SEQ ID NO:95 (SIDY); and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:163 (RSSQSLVQSNGNTYLH), a LC CDR2 set forth as SEQ ID NO:165 (KVSNRFS) and a LC CDR3 set forth as SEQ ID NO:167 (SQSTHVPPT); or~~

~~(b) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:109 (RVHFAIRDTNYWMQ), a HC CDR2 set forth as SEQ ID NO:110 (AIYPGNGDTSYNQKFKG), a HC CDR3 set forth as SEQ ID NO:112 (GSHYFDY); and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:182 (RASQSIGTSIH), a LC CDR2 set forth as SEQ ID NO:184 (YASESIS) and a LC CDR3 set forth as SEQ ID NO:186 (QQSNSWPYT); or~~

~~(c) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:125 (DYVMN), a HC CDR2 set forth as SEQ ID NO:127 (DVNPNNDGTTYNQKFKG), a HC CDR3 set forth as SEQ ID NO:129 (CPFYYLGKGTHFDY); and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:196 (RASQDISNFLN);~~

- ~~a LC CDR2 set forth as SEQ ID NO:198 (YTSRLHS) and a LC CDR3 set forth as SEQ ID NO:200 (QQGFTLPWT); or~~
- ~~(d) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:132, a HC CDR2 set forth as SEQ ID NO:133, a HC CDR3 set forth as SEQ ID NO:135; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:203, a LC CDR2 set forth as SEQ ID NO:165 and a LC CDR3 set forth as SEQ ID NO:204; or~~
- ~~(e) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:137 a HC CDR2 set forth as SEQ ID NO:138, a HC CDR3 set forth as SEQ ID NO:140; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:206, a LC CDR2 set forth as SEQ ID NO:207 and a LC CDR3 set forth as SEQ ID NO:208; or~~
- ~~(f) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:98, a HC CDR2 set forth as SEQ ID NO:99, a HC CDR3 set forth as SEQ ID NO:101; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:169, a LC CDR2 set forth as SEQ ID NO:171 and a LC CDR3 set forth as SEQ ID NO:173; or~~
- ~~(g) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:103, a HC CDR2 set forth as SEQ ID NO:105, a HC CDR3 set forth as SEQ ID NO:107; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:176, a LC CDR2 set forth as SEQ ID NO:178 and a LC CDR3 set forth as SEQ ID NO:193; or~~
- ~~(h) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:114, a HC CDR2 set forth as SEQ ID NO:116, a HC CDR3 set forth as SEQ ID NO:118; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:188, a LC CDR2 set forth as SEQ ID NO:178 and a LC CDR3 set forth as SEQ ID NO:190; or~~
- ~~(i) a heavy chain variable region comprising a HC CDR1 set forth as SEQ ID NO:114, a HC CDR2 set forth as SEQ ID NO:121, a HC CDR3 set forth as SEQ ID NO:123; and a light chain variable region comprising a LC CDR1 set forth as SEQ ID NO:191, a LC CDR2 set forth as SEQ ID NO:178 and a LC CDR3 set forth as SEQ ID NO:193.~~

~~42. The isolated antibody or antigen binding fragment thereof of Claim 41(a), wherein the antibody or antigen binding fragment thereof comprise a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:31 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:46.~~

~~43. The antibody or antigen binding fragment thereof of Claim 41(b), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:32 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:47.~~

~~44. The antibody or antigen binding fragment thereof of Claim 41(c), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:33 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:48.~~

~~45. The antibody or antigen binding fragment thereof of Claim 41(d), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:34 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:49.~~

~~46. The antibody or antigen binding fragment thereof of Claim 41(e), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:35 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:50.~~

~~47. The antibody or antigen binding fragment thereof of Claim 41(f), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:36 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:51.~~

~~48. The antibody or antigen binding fragment thereof of Claim 41(g), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:37 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:52.~~

~~49. The antibody or antigen binding fragment thereof of Claim 41(h), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:38 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:53.~~

~~50. The antibody or antigen binding fragment thereof of Claim 41(i), wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:39 and a light chain comprising at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to SEQ ID NO:54.~~

~~51~~18. The antibody or antigen binding fragment thereof of any of Claims ~~1, 10 or 41~~1-17, 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.

~~52~~19. The antibody or antigen-binding fragment thereof of any of Claims ~~1, 10 or 41~~1-17, 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.

~~53. The antibody or antigen binding fragment thereof of any of Claims 1, 10 or 41, further comprising an immunoglobulin constant region.~~

~~54. The antibody or antigen binding fragment thereof of any one of paragraphs 1-23, wherein the antibody or antigen binding fragment is humanized.~~

~~55. The antibody or antigen binding fragment thereof of any of Claims 1, 10 or 41, wherein said antibody binds to the serine protease domain of human MASP-3 with an affinity of less than 500 pM.~~

~~56~~20. The antibody or antigen-binding fragment thereof of any of Claims ~~1, 10 or 41~~1-17, wherein said antibody inhibits alternative pathway activation in mammalian blood.

21. An isolated antibody or antigen-binding fragment thereof that binds to human MASP-3, comprising a heavy chain variable region selected from the group consisting of SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:251 and SEQ ID NO:252 and a light chain variable region selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:253 and SEQ ID NO:279.

22. The isolated antibody or antigen-binding fragment thereof of claim 21, wherein the heavy chain variable region comprises SEQ ID NO:28 and the light chain variable region comprises SEQ ID NO:43.

23. The isolated antibody or antigen-binding fragment thereof of claim 21, wherein the heavy chain variable region comprises SEQ ID NO:28 and the light chain variable region comprises SEQ ID NO:43.

24. The isolated antibody or antigen-binding fragment thereof of claim 21, wherein the heavy chain variable region comprises SEQ ID NO:251 or SEQ ID NO:252 and the light chain variable region comprises SEQ ID NO:253.

25. The isolated antibody or antigen-binding fragment thereof of claim 21, wherein the heavy chain variable region comprises SEQ ID NO:251 or SEQ ID NO:252 and the light chain variable region comprises SEQ ID NO:279.

26. The isolated antibody of any of claims 21-25, 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.

27. The isolated antibody or antigen-binding fragment thereof of any of claims 21-25, wherein said antibody inhibits alternative pathway activation in mammalian blood.

28. A composition comprising the antibody or antigen-binding fragment of any of claims 1-17 or 21-25 and a pharmaceutically acceptable excipient.

~~57~~29. 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-~~56~~25.

~~58~~30. A cloning or expression vector comprising one or more DNA sequences of Claim ~~57~~29.

~~5931.~~ A host cell comprising one or more cloning or expression vectors of claim ~~5830~~.

~~6032.~~ A process for producing the antibody or antigen-binding fragment thereof of any of claims 1-~~56-25~~ comprising culturing the host cell of Claim ~~59-31~~ and isolating the antibody or antigen-binding fragment thereof.

~~61. A composition comprising the antibody or antigen-binding fragment of any of Claims 1-56 and a pharmaceutically acceptable excipient.~~

~~6233. Use of a composition according to claim 28 in the manufacture of a medicament for~~A method of inhibiting alternative pathway complement activation in a mammalian subject, 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 activation in the mammalian subject the method comprising administering to a mammal subject in need thereof an amount of a composition according to claim 61 comprising a high affinity MASP-3 inhibitory antibody or antigen-binding fragment thereof sufficient to inhibit alternative pathway complement pathway activation in the mammal.

~~63. The method of claim 62, wherein the antibody, or antigen-binding fragment thereof binds to MASP-3 with an affinity of less than 500 pM~~

~~64. The method of claim 62 or 63, wherein the antibody inhibits the alternative pathway at a molar ratio of from about 1:1 to about 2.5:1 (MASP-3 target to MASP-3 inhibitory mAb).~~

~~65. The method of claim 62, wherein the antibody or antigen-binding fragment thereof selectively inhibits the alternative pathway without affecting the classical pathway activation.~~

~~66. The method of claim 62, wherein the subject in need thereof is suffering from, or at risk for developing an alternative pathway disease or disorder selected from the group consisting of: paroxysmal nocturnal hemoglobinuria (PNH), age-related macular degeneration (AMD, including wet and dry AMD), ischemia reperfusion injury, arthritis,~~

~~disseminated intravascular coagulation, thrombotic microangiopathy (including hemolytic uremic syndrome (HUS), atypical hemolytic uremic syndrome (aHUS), thrombotic thrombocytopenic purpura (TTP) or transplant associated TMA), asthma, dense deposit disease, pauci-immune necrotizing crescentic glomerulonephritis, traumatic brain injury, aspiration pneumonia, endophthalmitis, neuromyelitis optica, Behcet's disease, multiple sclerosis, Guillain Barre Syndrome, Alzheimer's disease, Amyotrophic lateral sclerosis (ALS), lupus nephritis, systemic lupus erythematosus (SLE), Diabetic retinopathy, Uveitis, Chronic obstructive pulmonary disease (COPD), C3 glomerulopathy, transplant rejection, Graft-versus-host disease (GVHD), hemodialysis, sepsis, Systemic inflammatory response syndrome (SIRS), Acute Respiratory Distress Syndrome (ARDS), ANCA vasculitis, Anti-phospholipid syndrome, Atherosclerosis, IgA Nephropathy and Myasthenia Gravis.~~