CLAIMS

WHAT IS CLAIMED IS:

1. An isolated, synthetic or recombinant antibody or an antigen binding fragment thereof that specifically binds to complement control protein domain 18 (CCP18) of factor H (FH) comprising:

- a light chain CDR1 sequence comprising the sequence SSVTY (SEQ ID NO: 1) or the sequence TSVTY (SEQ ID NO: 13),
- a light chain CDR2 sequence comprising the sequence ATS (SEQ ID NO: 2) or the sequence ASS (SEQ ID NO: 14),
- a light chain CDR3 sequence comprising the sequence QHRSSSNPLT (SEQ ID NO: 3),
- a heavy chain CDR1 sequence comprising the sequence GFSLTNYG (SEQ ID NO: 5),
- a heavy chain CDR2 sequence comprising the sequence VWSGGTT (SEQ ID NO: 6) or the sequence of IWSGGTT (SEQ ID NO: 10), and
- a heavy chain CDR3 sequence comprising the sequence ARNFGNYAMDY (SEQ ID NO: 7) or the sequence ARNFGNYAMDF (SEQ ID NO: 11).

2. The antibody or fragment according to claim 1, comprising:

- a light chain CDR1 sequence comprising the sequence SSVTY (SEQ ID NO: 1),
- a light chain CDR2 sequence comprising the sequence ATS (SEQ ID NO: 2),
- a light chain CDR3 sequence comprising the sequence QHRSSSNPLT (SEQ ID NO: 3),
- a heavy chain CDR1 sequence comprising the sequence GFSLTNYG (SEQ ID NO: 5),
- a heavy chain CDR2 sequence comprising the sequence IWSGGTT (SEQ ID NO: 10), and
- a heavy chain CDR3 sequence comprising the sequence ARNFGNYAMDF (SEQ ID NO: 11).

3. The antibody or fragment according to claim 1, comprising:

- a light chain CDR1 sequence comprising the sequence SSVTY (SEQ ID NO: 1),
- a light chain CDR2 sequence comprising the sequence ATS (SEQ ID NO: 2),
- a light chain CDR3 sequence comprising the sequence QHRSSSNPLT (SEQ ID NO: 3),

- a heavy chain CDR1 sequence comprising the sequence GFSLTNYG (SEQ ID NO: 5),
- a heavy chain CDR2 sequence comprising the sequence VWSGGTT (SEQ ID NO: 6), and
- a heavy chain CDR3 sequence comprising the sequence ARNFGNYAMDY (SEQ ID NO: 7).

4. The antibody or fragment according to claim 1, comprising:
- a light chain CDR1 sequence comprising the sequence TSVTY (SEQ ID NO: 13),
- a light chain CDR2 sequence comprising the sequence ASS (SEQ ID NO: 14),
- a light chain CDR3 sequence comprising the sequence QHRSSSNPLT (SEQ ID NO: 3),
- a heavy chain CDR1 sequence comprising the sequence GFSLTNYG (SEQ ID NO: 5),
- a heavy chain CDR2 sequence comprising the sequence VWSGGTT (SEQ ID NO: 6), and
- a heavy chain CDR3 sequence having the sequence ARNFGNYAMDY (SEQ ID NO: 7).

5. The antibody or fragment according to claim 1, comprising:
- a light chain CDR1 sequence comprising the sequence TSVTY (SEQ ID NO: 13),
- a light chain CDR2 sequence comprising the sequence ASS (SEQ ID NO: 14),
- a light chain CDR3 sequence comprising the sequence QHRSSSNPLT (SEQ ID NO: 3),
- a heavy chain CDR1 sequence comprising the sequence GFSLTNYG (SEQ ID NO: 5),
- a heavy chain CDR2 sequence comprising the sequence IWSGGTT (SEQ ID NO: 10), and
- a heavy chain CDR3 sequence comprising the sequence ARNFGNYAMDF (SEQ ID NO: 11).

6. The antibody or fragment according to any one of claims 1-5, wherein the antibody or fragment has a binding affinity for FH with a K_D of 2.5 x 10^{-8} M or less and/or a binding affinity for a FH fragment comprised of CCP18-20 with a K_D of 0.1 x 10^{-9} M or less, or wherein the antibody or fragment has a binding affinity for FH with a K_D of 1.25 x 10^{-8} M or less and/or a binding affinity for a FH fragment comprised of CCP18-20 with a K_D of 0.04 x

10^{-9} M or less.

7. The antibody or fragment according to any one of claims 1-5, wherein the antibody or fragment has a binding affinity for FH with a K_D of 2.5 x 10^{-8} M or less and/or a binding affinity for a FH fragment comprised of CCP18-20 with a K_D of 0.1 x 10^{-9} M or less, or wherein the antibody or fragment has a binding affinity for FH with a K_D of 0.6 x 10^{-8} M or less and/or a binding affinity for a FH fragment comprised of CCP18-20 with a K_D of 0.6 x 10^{-11} M or less.

8. The antibody or fragment according to any one of claims 1-7, wherein the antibody or fragment:
- inhibits C3 deposition on lipopolysaccharide *in vitro* with an IC_{50} value of 38 nM or less, such as with an IC_{50} value of 30 nM or less, in the presence of 10% (v/v) serum; and/or
- inhibits hemolytic activity *in vitro* with an IC_{50} value of 150 nM or less, such as with an IC_{50} value of 130 nM or less, in the presence of 10% (v/v) serum; and/or
- decreases K_D (increases binding affinity) of FH for C3b *in vitro* to at most 2 μM and/or increases binding affinity of FH for C3b *in vitro* by at least 3-fold.

9. The antibody or fragment according to any one of claims 1-8, comprising:
- a variable light chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 4 or 16,
- a variable heavy chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 8 or 12.

10. The antibody or fragment according to any one of claims 1-9, comprising a variable light chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 4 and a variable heavy chain sequence comprising a sequence which has at least 80%, 85%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to 8.

11. The antibody or fragment according to any one of claims 1-9, comprising a variable light chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 4, and a variable heavy chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 12.

12. The antibody or fragment according to any one of claims 1-9, comprising a variable light chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 16, and a variable heavy chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 8.

13. The antibody or fragment according to any one of claims 1-9, comprising a variable light chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 16, and a variable heavy chain sequence comprising a sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 12.

14. The antibody or fragment according to any one of claims 1 to 13, wherein the antibody or fragment potentiates FH activity, optionally wherein the FH activity is inhibition of alternative complement activation, further optionally wherein inhibition of alternative complement activation comprises:
- an inhibition of hemolytic activity,
- an inhibition of complement component 3 (C3) deposition, and/or
- an increase of binding of FH to C3b, iC3b and/or C3d.

15. The antibody or fragment according to any one of claims 1 to 14, wherein the antibody or fragment comprises an immunoglobulin heavy chain variable region and an immunoglobulin light chain variable region, and further comprises an immunoglobulin heavy chain constant region and an immunoglobulin light chain constant region.

16. The antibody or fragment according to any one of claims 1 to 15, wherein the antibody or fragment comprises a Fab fragment.

17. The antibody or fragment according to any one of claims 1 to 16, wherein the antibody or fragment is monoclonal.

18. The antibody or fragment according to any one of claims 1 to 17, wherein the antibody or fragment comprises human light chain and heavy chain constant regions.

19. The antibody or fragment according to any one of claims 1-18, wherein the antibody or fragment is PEGylated.

20. The antibody or fragment according to claim 19, wherein the antibody or fragment is a PEGylated Fab fragment.

21. An isolated, synthetic or recombinant nucleic acid comprising a nucleic acid sequence encoding the antibody or fragment according to any one of claims 1 to 20.

22. A vector comprising a nucleic acid according to claim 21.

23. The vector of claim 22, wherein the vector is an AAV vector.

24. The vector of claim 23, wherein the AAV vector is selected from the group consisting of: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, and AAV12.

25. A recombinant cell comprising the nucleic acid according to claim 21 or the vector

according to any one of claims 22-24.

26. A pharmaceutical composition comprising the antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, or the recombinant cell according to claim 25, and a pharmaceutically acceptable carrier, diluent and/or excipient.

27. The antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26 for use in therapy.

28. The antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26 for use in inhibiting alternative complement activation.

29. The antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26 for use in the treatment, alleviation or prevention of a disorder associated with alternative pathway complement activation.

30. The antibody or fragment, nucleic acid, recombinant cell, or pharmaceutical composition for use according to claim 29, wherein the disorder is selected from the group consisting of atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), age-related macular degeneration (AMD), membranoproliferative glomerulonephritis (MPGN), and IgA Nephropathy.

31. Use of the antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26 for the preparation of a medicament for the treatment, alleviation or prevention of a disorder

associated with alternative pathway complement activation.

32. The use according to claim 31 wherein the disorder is selected from the group consisting of atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), age-related macular degeneration (AMD), membranoproliferative glomerulonephritis (MPGN) and IgA Nephropathy.

33. A method for treating, alleviating, or preventing a disorder associated with alternative pathway complement activation, the method comprising administering to a subject in need thereof a therapeutically effective amount of the antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26.

34. The method according to claim 33, wherein the disorder is selected from the group consisting of atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), age-related macular degeneration (AMD), membranoproliferative glomerulonephritis (MPGN), and IgA Nephropathy.

35. A method for inhibiting alternative complement activation comprising administering to a subject the antibody or fragment according to any one of claims 1 to 20, the nucleic acid according to claim 21, the vector according to any one of claims 22-24, the recombinant cell according to claim 25, or the pharmaceutical composition according to claim 26.

36. A method for producing an antibody or fragment, the method comprising providing a cell with the nucleic acid according to claim 21 or the vector according to any one of claims 22-24, and allowing the cell to translate the nucleic acid sequence comprised by the nucleic acid or vector, thereby producing the antibody or fragment according to any one of claims 1 to 20.

37. The method according to claim 36 further comprising harvesting, purifying and/or isolating the antibody or fragment.