Claims

1. C5 binding polypeptide, comprising a C5 binding motif, *BM*, which motif consists of an amino acid sequence selected from

i) $EX_2X_3X_4A\ X_6X_7EID\ X_{11}LPNL\ X_{16}X_{17}X_{18}QW\ X_{21}AFIX_{25}\ X_{26}LX_{28}D$,

wherein, independently of each other,
X_2 is selected from H, Q, S, T and V;
X_3 is selected from I, L, M and V;
X_4 is selected from A, D, E, H, K, L, N, Q, R, S, T and Y;
X_6 is selected from N and W;
X_7 is selected from A, D, E, H, N, Q, R, S and T;
X_{11} is selected from A, E, G, H, K, L, Q, R, S, T and Y;
X_{16} is selected from N and T;
X_{17} is selected from I, L and V;
X_{18} is selected from A, D, E, H, K, N, Q, R, S and T;
X_{21} is selected from I, L and V;
X_{25} is selected from D, E, G, H, N, S and T;
X_{26} is selected from K and S;
X_{28} is selected from A, D, E, H, N, Q, S, T and Y;

and

ii) an amino acid sequence which has at least 86 % identity to the sequence defined in i), wherein the polypeptide binds to C5.

2. C5 binding polypeptide according to claim 1, wherein X_2 is selected from H, T and V.

3. C5 binding polypeptide according to claim 2, wherein X_2 is selected from T and V.

4. C5 binding polypeptide according to claim 3, wherein X_2 is V.

5. C5 binding polypeptide according to any preceding claim, wherein X_3 is selected from I, L and V.

6. C5 binding polypeptide according to claim 5, wherein X_3 is selected from I and L.

7. C5 binding polypeptide according to claim 6, wherein X_3 is I.

8. C5 binding polypeptide according to claim 6, wherein X_3 is L.

9. C5 binding polypeptide according to any preceding claim, wherein X_4 is selected from A, D, E, K, L, Q and R.

10. C5 binding polypeptide according to claim 9, wherein X_4 is selected from A, D, E, K and R.

11. C5 binding polypeptide according to claim 10, wherein X_4 is selected from D and E.

12. C5 binding polypeptide according to any preceding claim, wherein X_6 is W.

13. C5 binding polypeptide according to any preceding claim, wherein X_7 is selected from A, D, N and T.

14. C5 binding polypeptide according to claim 13, wherein X_7 is selected from D and N.

15. C5 binding polypeptide according to claim 14, wherein X_7 is D.

16. C5 binding polypeptide according to claim 14, wherein X_7 is N.

17. C5 binding polypeptide according to any preceding claim, wherein X_{11} is selected from A, H, K, Q, R and S.

18. C5 binding polypeptide according to claim 17, wherein X_{11} is selected from A, H, K and R.

19. C5 binding polypeptide according to claim 18, wherein X_{11} is selected from A, K and R.

20. C5 binding polypeptide according to claim 19, wherein X_{11} is selected from K and R

21. C5 binding polypeptide according to any preceding claim, wherein X_{16} is T.

22. C5 binding polypeptide according to any preceding claim, wherein X_{17} is selected from I and L.

23. C5 binding polypeptide according to claim 22, wherein X_{17} is I.

24. C5 binding polypeptide according to claim 22, wherein X_{17} is L.

25. C5 binding polypeptide according to any preceding claim, wherein X_{18} is selected from A, D, E, N, Q, S and T.

26. C5 binding polypeptide according to claim 25, wherein X_{18} is selected from A, D, E, Q and S.

27. C5 binding polypeptide according to claim 26, wherein X_{18} is selected from D, E and Q.

28. C5 binding polypeptide according to claim 27, wherein X_{18} is selected from D and E.

29. C5 binding polypeptide according to claim 28, wherein X_{18} is D.

30. C5 binding polypeptide according to claim 28, wherein X_{18} is E.

31. C5 binding polypeptide according to any preceding claim, wherein X_{21} is selected from I and L.

32. C5 binding polypeptide according to claim 31, wherein X_{21} is I.

33. C5 binding polypeptide according to claim 31, wherein X_{21} is L.

34. C5 binding polypeptide according to any preceding claim, wherein X_{25} is selected from E, H, N and T.

35. C5 binding polypeptide according to claim 34, wherein X_{25} is selected from E and N.

36. C5 binding polypeptide according to claim 35, wherein X_{25} is N.

37. C5 binding polypeptide according to any preceding claim, wherein X_{26} is K.

38. C5 binding polypeptide according to any preceding claim, wherein X_{28} is selected from A, D, E, H, N, Q and S.

39. C5 binding polypeptide according to claim 38, wherein X_{28} is selected from A, D, E and S.

40. C5 binding polypeptide according to claim 39, wherein X_{28} is selected from A, D and E.

41. C5 binding polypeptide according to claim 40, wherein X_{28} is selected from D and E.

42. C5 binding polypeptide according to claim 41, wherein X_{28} is D.

43. C5 binding polypeptide according to any one of claims 8-11, wherein X_3X_4 is selected from LE and LD.

44. C5 binding polypeptide according to any one of claims 22-30, wherein $X_{17}X_{18}$ is selected from IE and LD.

45. C5 binding polypeptide according to any one of the preceding claims, wherein the amino acid i) fulfills at least four of the following eight conditions I-VIII:

I. X_2 is V;
II. X_3 is selected from I and L;
III. X_6 is W;
IV. X_7 is selected from D and N;
V. X_{17} is selected from I and L;
VI. X_{21} is L;
VII. X_{25} is N;
VIII. X_{28} is D.

46. C5 binding polypeptide according to claim 45, wherein the amino acid sequence i) fulfills at least five of the eight conditions I-VIII.

47. C5 binding polypeptide according to claim 46, wherein the amino acid sequence i) fulfills at least six of the eight conditions I-VIII.

48. C5 binding polypeptide according to claim 47, wherein the amino acid sequence i) fulfills at least seven of the eight conditions I-VIII.

49. C5 binding polypeptide according to claim 48, wherein the amino acid sequence i) fulfills all of the eight conditions I-VIII.

50. C5 binding polypeptide according to any preceding claim, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-248.

51. C5 binding polypeptide according to claim 50, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-12, SEQ ID NO:20, SEQ ID NO:23-24, SEQ ID NO:26-28, SEQ ID NO:32-35, SEQ ID NO:38-39, SEQ ID NO:41, SEQ ID NO:46, SEQ ID NO:49, SEQ ID NO:56-57, SEQ ID NO:59, SEQ ID NO:66, SEQ ID NO:78-79, SEQ ID NO:87, SEQ ID NO:92, SEQ ID NO:106, SEQ ID NO:110, SEQ ID NO:119, SEQ ID NO:125, SEQ ID NO:141, SEQ ID NO:151, SEQ ID NO:161, SEQ ID NO:166, SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:203, SEQ ID NO:205, SEQ ID NO:215 and SEQ ID NO:243.

52. C5 binding polypeptide according to claim 51, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-12.

53. C5 binding polypeptide according to claim 52, wherein the amino acid sequence is selected from any one of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:5.

54. C5 binding polypeptide according to claim 53, wherein the amino acid sequence is selected from SEQ ID NO:1 and SEQ ID NO:4.

55. C5 binding polypeptide according to any preceding claim, in which said C5 binding motif forms part of a three-helix bundle protein domain.

56. C5 binding polypeptide according to claim 55, in which said C5 binding motif essentially forms part of two alpha helices with an interconnecting loop, within said three-helix bundle protein domain.

57. C5 binding polypeptide according to claim 55 or 56, in which said three-helix bundle protein domain is selected from domains of Protein A from *Staphylococcus aureus* and derivatives thereof.

58. C5 binding polypeptide according to any preceding claim, which comprises an amino acid sequence selected from:

i) K-[*BM*]-DPSQS X_aX_bLLX_c EAKKL NDX_dQ;

wherein

[*BM*] is a C5 binding motif as defined in any one of claims 1-54;

X_a is selected from A and S;

X_b is selected from N and E;

X_c is selected from A, S and C;

X_d is selected from A and S;

and

ii) an amino acid sequence which has at least 79% identity to any one of the sequences defined above.

59. C5 binding polypeptide according to claim 58, wherein X_a is A.

60. C5 binding polypeptide according to claim 58, wherein X_a is S.

61. C5 binding polypeptide according to any one of claims 58-60, wherein X_b is N.

62. C5 binding polypeptide according to any one of claims 58-60, wherein X_b is E.

63. C5 binding polypeptide according to any one of claims 58-62, wherein X_c is A.

64. C5 binding polypeptide according to any one of claims 58-62, wherein X_c is S.

65. C5 binding polypeptide according to any one of claims 58-62, wherein X_c is C.

66. C5 binding polypeptide according to any one of claims 58-65, wherein X_d is A.

67. C5 binding polypeptide according to any one of claims 58-65, wherein X_d is S.

68. C5 binding polypeptide according to claim 58, wherein X_a is A; X_b is N; X_c is A and X_d is A.

69. C5 binding polypeptide according to claim 58, wherein X_a is A; X_b is N; X_c is C and X_d is A.

70. C5 binding polypeptide according to claim 58, wherein X_a is S; X_b is E; X_c is S and X_d is S.

71. C5 binding polypeptide according to claim 58, wherein X_a is S; X_b is E; X_c is C and X_d is S.

72. C5 binding polypeptide according to any one of claims 58-71, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-496.

73. C5 binding polypeptide according to claim 72, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-260, SEQ ID NO:268, SEQ ID NO:271-272, SEQ ID NO:274-276, SEQ ID NO:280-283, SEQ ID NO:286-287, SEQ ID NO:289, SEQ ID NO:294, SEQ ID NO:297, SEQ ID NO:304-305, SEQ ID NO:307, SEQ ID NO:314, SEQ ID NO:326-327, SEQ ID NO:335, SEQ ID NO:340, SEQ ID NO:354, SEQ ID NO:358, SEQ ID NO:367, SEQ ID NO:373, SEQ ID NO:389, SEQ ID NO:399, SEQ ID NO:409, SEQ ID NO:414, SEQ ID NO:435, SEQ ID NO:445, SEQ ID NO:451, SEQ ID NO:453, SEQ ID NO:463 and SEQ ID NO:491.

74. C5 binding polypeptide according to claim 73, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-260.

75. C5 binding polypeptide according to claim 74, wherein the amino acid sequence is selected from any one of SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252 and SEQ ID NO:253.

76. C5 binding polypeptide according to claim 75, wherein the amino acid sequence is selected from any one of SEQ ID NO:249 and SEQ ID NO:252.

77. C5 binding polypeptide according to any one of claims 1-57, which comprises an amino acid sequence selected from:

i) YAK-[*BM*]-DPSQS SELLX_c EAKKL NDSQA P;

wherein [*BM*] is a C5 binding motif as defined in any one of claims 1-54 and X_c is selected from S and C; and

ii) an amino acid sequence which has at least 81% identity to any one of the sequences defined above.

78. C5 binding polypeptide according to any one of claims 1-57, which comprises an amino acid sequence selected from:

i) FNK-[*BM*]-DPSQS ANLLX$_c$ EAKKL NDAQA P;

wherein [*BM*] is a C5 binding motif as defined in any one of claims 1-54 and X$_c$ is selected from A and C; and

ii) an amino acid sequence which has at least 81 % identity to any one of the sequences defined above.

79. C5 binding polypeptide according to any one of claims 1-57, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-757.

80. C5 binding polypeptide according to claim 79, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-508, SEQ ID NO:516, SEQ ID NO:519-520, SEQ ID NO:522-524, SEQ ID NO:528-531, SEQ ID NO:534-535, SEQ ID NO:537, SEQ ID NO:542, SEQ ID NO:545, SEQ ID NO:552-553, SEQ ID NO:555, SEQ ID NO:562, SEQ ID NO:574-575, SEQ ID NO:583, SEQ ID NO:588, SEQ ID NO:602, SEQ ID NO:606, SEQ ID NO:615, SEQ ID NO:621, SEQ ID NO:637, SEQ ID NO:647, SEQ ID NO:657, SEQ ID NO:662, SEQ ID NO:683, SEQ ID NO:693, SEQ ID NO:699, SEQ ID NO:701, SEQ ID NO:711, SEQ ID NO:739 and SEQ ID NO:746-757.

81. C5 binding polypeptide according to claim 80, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-508 and SEQ ID NO:746-757.

82. C5 binding polypeptide according to claim 81, wherein the amino acid sequence is selected from any one of SEQ ID NO:497, SEQ ID NO:498, SEQ ID NO:499, SEQ ID NO:500, SEQ ID NO:501, SEQ ID NO:746, SEQ ID NO:747 SEQ ID NO:748, SEQ ID NO:750 and SEQ ID NO:753.

83. C5 binding polypeptide according to claim 82, wherein the amino acid sequence is selected from any one of SEQ ID NO:497 and SEQ ID NO:500, SEQ ID NO:748 and SEQ ID NO:753.

84. C5 binding polypeptide according to any preceding claim, which inhibits cleavage of C5.

85. C5 binding polypeptide according to any preceding claim, wherein the C5 binding polypeptide binds to C5 such that the K_D value of the interaction is at most 1 x 10^{-6} M, such as at most 1 x 10^{-7} M, such as at most 1 x 10^{-8} M, such as at most 1 x 10^{-9} M.

86. C5 binding polypeptide according to any preceding claim, comprising further C terminal and/or N terminal amino acids that improves production, purification, stabilization *in vivo* or *in vitro*, coupling, or detection of the polypeptide.

87. C5 binding polypeptide according to any preceding claim in multimeric form, comprising at least two C5 binding polypeptide monomer units, the amino acid sequences of which may be the same or different.

88. C5 binding polypeptide according to claim 87, in which the C5 binding polypeptide monomer units are expressed as a fusion protein.

89. C5 binding polypeptide according to claim 87 or 88, in dimeric form.

90. C5 binding compound, comprising at least one C5 binding polypeptide according to any preceding claim; at least one albumin binding domain of streptococcal protein G, or a derivative thereof, and at least one linking moiety for linking said at least one domain or derivative thereof to the C or N terminal of said at least one C5 binding polypeptide.

91. C5 binding compound according to claim 90, having a structure selected from
[*CBP1*]-[*L1*]-[*ALBD*];
[*CBP1*]-[*CBP2*]-[*L1*]-[*ALBD*];
[*CBP1*]-[*L1*]-[*ALBD*]-[*L2*]-[*CBP2*];
[*ALBD*]-[*L1*]-[*CBP1*];
[*ALBD*]-[*L1*]- [*CBP1*]-[*CBP2*];
[*CBP1*]-[*L1*]- [*CBP2*]-[*L2*]-[*ALBD*]; and
[*ALBD*]-[*L1*]- [*CBP1*]- [*L2*]- [*CBP2*]
wherein, independently of each other,
[*CBP1*] and [*CBP2*] are C5 binding polypeptides which may be the same or different;
[*L1*] and [*L2*] are linking moieties which may be the same or different; and
[*ALBD*] is an albumin binding domain of streptococcal protein G, or derivative thereof.

92. C5 binding compound according to claim 91, having a structure selected from

[*CBP1*]-[*L1*]-[*ALBD*];
[*CBP1*]-[*CBP2*]-[*L1*]-[*ALBD*]; and
[*CBP1*]-[*L1*]-[*ALBD*]-[*L2*]-[*CBP2*].

93. C5 binding compound according to claim 91, wherein the linking moiety is selected from G, GS; $[G_2S]_n$; $[G_3S]_n$; $[G_4S]_n$; $GS[G_4S]_n$, wherein n is 0-7; $[S_2G]_m$; $[S_3G]_m$;$[S_4G]_m$; wherein m is 0-7, and VDGS.

94. C5 binding compound according to claim 93, wherein the linking moiety is selected from GS and $GS[G_4S]_2$.

95. C5 binding compound according to any one of claims 90-94, wherein said albumin-binding domain is as set out in SEQ ID NO:759.

96. C5 binding compound according to any one of claims 90-95, wherein each of said C5 binding polypeptides is independently selected from a polypeptide as defined in any one of claims 79-83.

97. C5 binding compound according to claim 96, wherein each of said C5 binding polypeptides is independently selected from a polypeptide as defined in claim 83.

98. Polynucleotide encoding a polypeptide according to any one of claims 1-89 or a compound according to any one of claims 90-97.

99. Expression vector comprising a polynucleotide according to claim 98.

100. Host cell comprising an expression vector according to claim 99.

101. Combination of a C5 binding polypeptide according to any one of claims 1-89 or a C5 binding compound according to any one of claims 90-97 with a therapeutic agent.

102. C5 binding polypeptide according to any one of claims 1-89, C5 binding compound according to any one of claims 90-97 or combination according to claim 101 for use in therapy.

103. C5 binding polypeptide according to any one of claims 1-89, C5 binding compound according to any one of claims 90-97 or combination according to claim 101 for treatment of a C5 related condition.

104. C5 binding polypeptide according to any one of claims 1-89, C5 binding compound according to any one of claims 90-97 or combination according to claim 101 for treatment of a C5 related condition selected from inflammatory disease; autoimmune disease; infectious disease; cardiovascular disease; neurodegenerative disorders; cancer; graft injury; wounds; eye disease; kidney disease; pulmonary diseases; hematological diseases; allergic diseases and dermatological diseases.

105. C5 binding polypeptide according to any one of claims 1-89, C5 binding compound according to any one of claims 90-97 or combination according to claim 101 for treatment of paroxysmal nocturnal hemoglobinuria (PNH).

106. Method of treatment of a C5 related condition, comprising administering a C5 binding polypeptide according to any one of claims 1-89, C5 binding compound according to any one of claims 90-97 or combination according to claim 101 to a mammalian subject in need thereof.

107. Method of treatment according to claim 106, in which binding of the C5 binding polypeptide, the C5 binding compound or the combination to C5 inhibits cleavage of C5.

108. Method of treatment according to claim 106 or 107, wherein said C5 related condition is selected from inflammatory disease; autoimmune disease; infectious disease; cardiovascular disease; neurodegenerative disorders; cancer; graft injury; wounds; eye disease; kidney disease; pulmonary diseases; hematological diseases; allergic diseases and dermatological diseases.

109. Method of treatment according to claim 108, wherein said C5 related condition is paroxysmal nocturnal hemoglobinuria (PNH).

110. Method of treatment according to any one of claims 106 to 109, wherein the said C5 binding polypeptide is administered intravenously, subcutaneously, by inhalation, nasally, orally, intravitreally, or topically.

Claims

1. C5 binding polypeptide, comprising a C5 binding motif, *BM*, which motif consists of an amino acid sequence selected from

i) $EX_2X_3X_4A\ X_6X_7EID\ X_{11}LPNL\ X_{16}X_{17}X_{18}QW\ X_{21}AFIX_{25}\ X_{26}LX_{28}D$,

wherein, independently of each other,
X_2 is selected from H, Q, S, T and V;
X_3 is selected from I, L, M and V;
X_4 is selected from A, D, E, H, K, L, N, Q, R, S, T and Y;
X_6 is selected from N and W;
X_7 is selected from A, D, E, H, N, Q, R, S and T;
X_{11} is selected from A, E, G, H, K, L, Q, R, S, T and Y;
X_{16} is selected from N and T;
X_{17} is selected from I, L and V;
X_{18} is selected from A, D, E, H, K, N, Q, R, S and T;
X_{21} is selected from I, L and V;
X_{25} is selected from D, E, G, H, N, S and T;
X_{26} is selected from K and S;
X_{28} is selected from A, D, E, H, N, Q, S, T and Y;

and

ii) an amino acid sequence which has at least 86 % identity to the sequence defined in i), wherein the polypeptide binds to C5.

2. C5 binding polypeptide according to any one of the preceding claims, wherein the amino acid i) fulfills at least four of the following eight conditions I-VIII:

I. X_2 is V;

II. X_3 is selected from I and L;

III. X_6 is W;

IV. X_7 is selected from D and N;

V. X_{17} is selected from I and L;

VI. X_{21} is L;

VII. X_{25} is N;

VIII. X_{28} is D.

3. C5 binding polypeptide according to any preceding claim, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-248.

4. C5 binding polypeptide according to claim 3, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-12, SEQ ID NO:20, SEQ ID NO:23-24, SEQ ID NO:26-28, SEQ ID NO:32-35, SEQ ID NO:38-39, SEQ ID NO:41, SEQ ID NO:46, SEQ ID NO:49, SEQ ID NO:56-57, SEQ ID NO:59, SEQ ID NO:66, SEQ ID NO:78-79, SEQ ID NO:87, SEQ ID NO:92, SEQ ID NO:106, SEQ ID NO:110, SEQ ID NO:119, SEQ ID NO:125, SEQ ID NO:141, SEQ ID NO:151, SEQ ID NO:161, SEQ ID NO:166, SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:203, SEQ ID NO:205, SEQ ID NO:215 and SEQ ID NO:243.

5. C5 binding polypeptide according to claim 4, wherein the amino acid sequence is selected from any one of SEQ ID NO:1-12.

6. C5 binding polypeptide according to any preceding claim, in which said C5 binding motif forms part of a three-helix bundle protein domain.

7. C5 binding polypeptide according to any preceding claim, which comprises an amino acid sequence selected from:

i) K-[*BM*]-DPSQS X_aX_bLLX_c EAKKL NDX$_d$Q;

wherein

[*BM*] is a C5 binding motif as defined in any one of claims 1-5;

X_a is selected from A and S;

X_b is selected from N and E;

X_c is selected from A, S and C;

X_d is selected from A and S;

and

ii) an amino acid sequence which has at least 79% identity to any one of the sequences defined above.

8. C5 binding polypeptide according to claim 7, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-496.

9. C5 binding polypeptide according to claim 8, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-260, SEQ ID NO:268, SEQ ID NO:271-272, SEQ ID NO:274-276, SEQ ID NO:280-283, SEQ ID NO:286-287, SEQ ID NO:289, SEQ ID NO:294, SEQ ID NO:297, SEQ ID NO:304-305, SEQ ID NO:307, SEQ ID NO:314, SEQ ID NO:326-327, SEQ ID NO:335, SEQ ID NO:340, SEQ ID NO:354, SEQ ID NO:358, SEQ ID NO:367, SEQ ID NO:373, SEQ ID NO:389, SEQ ID NO:399, SEQ ID NO:409, SEQ ID NO:414, SEQ ID NO:435, SEQ ID NO:445, SEQ ID NO:451, SEQ ID NO:453, SEQ ID NO:463 and SEQ ID NO:491.

10. C5 binding polypeptide according to claim 9, wherein the amino acid sequence is selected from any one of SEQ ID NO:249-260.

11. C5 binding polypeptide according to any one of claims 1-10, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-757.

12. C5 binding polypeptide according to claim 11, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-508, SEQ ID NO:516, SEQ ID NO:519-520, SEQ ID NO:522-524, SEQ ID NO:528-531, SEQ ID NO:534-535, SEQ ID NO:537, SEQ ID NO:542, SEQ ID NO:545, SEQ ID NO:552-553, SEQ ID NO:555, SEQ ID NO:562, SEQ ID NO:574-575, SEQ ID NO:583, SEQ ID NO:588, SEQ ID NO:602, SEQ ID NO:606, SEQ ID NO:615, SEQ ID NO:621, SEQ ID NO:637, SEQ ID NO:647, SEQ ID NO:657, SEQ ID NO:662, SEQ ID NO:683, SEQ ID NO:693,

SEQ ID NO:699, SEQ ID NO:701, SEQ ID NO:711, SEQ ID NO:739 and SEQ ID NO:746-757.

13. C5 binding polypeptide according to claim 12, wherein the amino acid sequence is selected from any one of SEQ ID NO:497-508 and SEQ ID NO:746-757.

14. C5 binding polypeptide according to claim 13, wherein the amino acid sequence is selected from any one of SEQ ID NO:497, SEQ ID NO:498, SEQ ID NO:499, SEQ ID NO:500, SEQ ID NO:501, SEQ ID NO:746, SEQ ID NO:747 SEQ ID NO:748, SEQ ID NO:750 and SEQ ID NO:753.

15. C5 binding polypeptide according to any preceding claim, which inhibits cleavage of C5.

16. C5 binding polypeptide according to any preceding claim, wherein the C5 binding polypeptide binds to C5 such that the K_D value of the interaction is at most 1×10^{-6} M, such as at most 1×10^{-7} M, such as at most 1×10^{-8} M, such as at most 1×10^{-9} M.

17. C5 binding polypeptide according to any preceding claim, comprising further C terminal and/or N terminal amino acids that improves production, purification, stabilization *in vivo* or *in vitro*, coupling, or detection of the polypeptide.

18. C5 binding polypeptide according to any preceding claim in multimeric form, comprising at least two C5 binding polypeptide monomer units, the amino acid sequences of which may be the same or different.

19. C5 binding compound, comprising at least one C5 binding polypeptide according to any preceding claim; at least one albumin binding domain of streptococcal protein G, or a derivative thereof, and at least one linking moiety for linking said at least one domain or derivative thereof to the C or N terminal of said at least one C5 binding polypeptide.

20. C5 binding compound according to claim 19, having a structure selected from

[*CBP1*]-[*L1*]-[*ALBD*];

[*CBP1*]-[*CBP2*]-[*L1*]-[*ALBD*];

[*CBP1*]-[*L1*]-[*ALBD*]-[*L2*]-[*CBP2*];

[*ALBD*]-[*L1*]-[*CBP1*];

[*ALBD*]-[*L1*]- [*CBP1*]-[*CBP2*];

[*CBP1*]-[*L1*]- [*CBP2*]-[*L2*]-[*ALBD*]; and

[*ALBD*]-[*L1*]- [*CBP1*]- [*L2*]- [*CBP2*]

wherein, independently of each other,

[*CBP1*] and [*CBP2*] are C5 binding polypeptides which may be the same or different;

[*L1*] and [*L2*] are linking moieties which may be the same or different; and

[*ALBD*] is an albumin binding domain of streptococcal protein G, or derivative thereof.

21. C5 binding compound according to claim 20, wherein the linking moiety is selected from G, GS; $[G_2S]_n$; $[G_3S]_n$; $[G_4S]_n$; $GS[G_4S]_n$, wherein n is 0-7; $[S_2G]_m$; $[S_3G]_m$;$[S_4G]_m$; wherein m is 0-7, and VDGS.

22. C5 binding compound according to any one of claims 19-21, wherein said albumin-binding domain is as set out in SEQ ID NO:759.

23. C5 binding compound according to any one of claims 19-22, wherein each of said C5 binding polypeptides is independently selected from a polypeptide as defined in any one of claims 11-14.

24. Polynucleotide encoding a polypeptide according to any one of claims 1-18 or a compound according to any one of claims 19-23.

25. Combination of a C5 binding polypeptide according to any one of claims 1-18 or a C5 binding compound according to any one of claims 19-23 with a therapeutic agent.

26. C5 binding polypeptide according to any one of claims 1-18, C5 binding compound according to any one of claims 19-23 or combination according to claim 25 for use in therapy.

27. C5 binding polypeptide according to any one of claims 1-18, C5 binding compound according to any one of claims 19-23 or combination according to claim 25 for use in the treatment of a C5 related condition.

28. C5 binding polypeptide according to any one of claims 1-18, C5 binding compound according to any one of claims 19-23 or combination according to claim 25 for use in the treatment of a C5 related condition selected from inflammatory disease; autoimmune disease; infectious disease; cardiovascular disease; neurodegenerative disorders; cancer; graft injury; wounds; eye disease; kidney disease; pulmonary diseases; hematological diseases; allergic diseases and dermatological diseases.

29. C5 binding polypeptide according to any one of claims 1-18, C5 binding compound according to any one of claims 19-23 or combination according to claim 25 for use in the treatment of paroxysmal nocturnal hemoglobinuria (PNH).