CLAIMS

1. A non-murine antigen binding protein which specifically binds to SAP and competes for binding to SAP with a reference antibody which comprises a heavy chain variable region sequence of SEQ ID NO:7, and a light chain variable region sequence of SEQ ID NO:9.

2. A non-murine antigen binding protein which binds to SAP and comprises CDRH3 set forth in SEQ ID NO: 3 or a functional variant of CDRH3.

3. An antigen binding protein according to claim 2, which further comprises one or more or all CDRs selected from: CDRH1 (SEQ ID NO:1), CDRH2 (SEQ ID NO:12, CDRL1 (SEQ ID NO:4), CDRL2 (SEQ ID NO:5), and CDRL3 (SEQ ID NO:6); or a functional variant of CDRH1, CDRH2, CDRL1, CDRL2 or CDRL3.

4. An antigen binding protein according to claim 2 or 3, wherein the CDRH3 functional variant is a variant of SEQ ID NO:3 wherein Ser 102 is substituted for Tyr, His, Val, Ile, Asp or Gly.

5. An antigen binding protein according to claim 3 or 4, wherein:

(a) the CDRH1 functional variant is a variant of SEQ ID NO:1 wherein Tyr 32 is substituted for Ile, His, Phe, Thr, Asn, Cys, Glu or Asp; Asn 33 is substituted for Tyr, Ala, Trp, Gly, Thr, Leu or Val; Met 34 is substituted for Ile, Val or Trp; and/or His 35 is substituted for Glu, Asn, Gln, Ser, Tyr or Thr;

(b) the CDRH2 functional variant is a variant of SEQ ID NO:2 wherein Tyr 50 is substituted for Arg, Glu, Trp, Gly, Gln, Val, Leu, Asn, Lys or Ala; Ile51 is substituted for Leu, Val, Thr, Ser or Asn; Tyr 52 is substituted for Asp, Leu, Asn or Ser, Gly 53 is substituted for Ala, Tyr, Ser, Lys, Thr or Asn, Asp 54 is substituted for Asn, Ser, Thr, Lys or Gly; Asn 56 is substituted for Tyr, Arg, Glu, Asp, Gly, Val, Ser or Ala; and/or Asn 58 is substituted for Lys, Thr, Ser, Asp, Arg, Gly, Phe or Tyr;

(c) the CDRL1 functional variant is a variant of SEQ ID NO:4 wherein Asn 28 is substituted for Ser, Asp, Thr or Glu; Ile 29 is substituted for Val; Tyr 30 is substituted for Asp, Leu, Val, Ile, Ser, Asn, Phe, His, Gly or Thr; Ser 31 is substituted for Asn, Thr, Lys or Gly; Tyr

32 is substituted for Phe, Asn, Ala, His, Ser or Arg; Leu 33 is substituted for Met, Val, Ile or Phe; and/or Ala 34 is substituted for Gly, Asn, Ser, His, Val or Phe;

(d) the CDRL2 functional variant is a variant of SEQ ID NO:5 wherein Ala 51 is substituted for Thr, Gly or Val; and/or

(e) the CDRL3 functional variant is a variant of SEQ ID NO:6 wherein Gln 89 is substituted for Ser, Gly, Phe or Leu; His 90 is substituted for Gln or Asn; His 91 is substituted for Asn, Phe, Gly, Ser, Arg, Asp, Thr, Tyr or Val; Tyr 92 is substituted for Asn, Trp, Thr, Ser, Arg, Gln, His, Ala or Asp; Gly 93 is substituted for Glu, Asn, His, Thr, Ser, Arg or Ala; Ala 94 is substituted for Asp, Tyr, Thr, Val, Leu, His, Asn, Ile, Trp, Pro or Ser; and/or Leu 96 is substituted for Pro, Tyr, Arg, Ile, Trp or Phe.

6. An antigen binding protein which specifically binds to SAP, wherein the antigen binding protein is a chimeric or a humanised antibody comprising the corresponding CDRH3 of the variable domain sequence of SEQ ID NO:7, or a functional variant of CDRH3.

7. An antigen binding protein according to claim 6, which further comprises one or more or all of corresponding CDRs selected from CDRH1 or CDRH2 of the variable domain sequence of SEQ ID NO:7; or CDRL1, CDRL2, CDRL3 of the variable domain sequence of SEQ ID NO:9; or a functional variant of CDRH1, CDRH2, CDRL1, CDRL2 or CDRL3.

8. An antigen binding protein which specifically binds to SAP, and comprises a binding unit H3 comprising Kabat residues 95-101 of SEQ ID NO:7, or a functional variant of binding unit H3.

9. An antigen binding protein according to claim 8, which further comprises one or more or all binding units selected from: H1 comprising Kabat residues 31-32 of SEQ ID NO:7, H2 comprising Kabat residues 52-56 of SEQ ID NO:7, L1 comprising Kabat residues 30-34 of SEQ ID NO:9, L2 comprising Kabat residues 50-55 of SEQ ID NO:9; and L3 comprising Kabat residues 89-96 of SEQ ID NO:9; or a functional variant of binding unit H1, H2, L1, L2 or L3.

10. An antigen binding protein according to any one of claims 1-9, wherein the antigen binding protein comprises a heavy chain and/or a light chain wherein:

(a) the heavy chain framework comprises the following residues: Val, Ile or Gly at position 2; Leu or Val at position 4; Leu, Ile, Met or Val at position 20; Cys at position 22; Thr, Ala, Val, Gly or Ser at position 24; Gly at position 26; Ile, Phe, Leu or Ser at position 29; Trp at position 36; Trp or Tyr at position 47; Ile, Met, Val or Leu at position 48; Ile, Leu, Phe, Met or Val at position 69; Val, Ala or Leu at position 71; Ala, Leu, Val, Tyr or Phe at position 78; Leu or Met at position 80; Tyr or Phe at position 90; Cys at position 92; and/or Arg, Lys, Gly, Ser, His or Asn at position 94; and/or

(b) the light chain framework comprises the following residues: Ile, Leu or Val at position 2; Val, Gln, Leu or Glu at position 3; Met or Leu at position 4; Cys at position 23; Trp at position 35; Tyr, Leu or Phe at position 36; Leu, Arg or Val at position 46; Tyr, His, Phe or Lys at position 49; Tyr or Phe at position 71; Cys at position 88; and/or Phe at position 98.

11. An antigen binding protein according to any one of claims 1-10, wherein: the heavy chain framework comprises the following residues: Val at position 2, Leu at position 4, Val at position 20, Cys at position 22, Ala at position 24, Gly at position 26, Phe at position 29, Trp at position 36, Trp at position 47, Met at position 48, Ile at position 69, Ala at position 71, Ala at position 78, Met at position 80, Tyr at position 90, Cys at position 92, and Arg at position 94, and/or the light chain framework comprises the following residues: Ile at position 2, Gln at position 3, Met at position 4, Cys at position 23, Trp at position 35, Tyr at position 36, Leu at position 46, His at position 49, Phe at position 71, Cys at position 88, and Phe at position 98.

12. An antigen binding protein according to any one of claims 1-11, which further comprises a heavy chain variable domain antibody framework having 75% or greater sequence identity to the framework regions as shown in SEQ ID NO:25; and/or a light chain variable domain antibody framework having 75% or greater sequence identity to the framework regions as shown in SEQ ID NO:32.

13. An antigen binding protein which specifically binds to SAP and comprises a heavy chain variable region selected from SEQ ID NO:27-31; and/or a light chain variable region selected from SEQ ID NO:34-36; or a variant heavy chain variable region or light chain variable region with 75% or greater sequence identity.

14. An antigen binding protein which specifically binds to SAP and comprises a heavy chain of SEQ ID NO:62; and/or a light chain of SEQ ID NO:64; or a variant heavy chain or light chain with 75% or greater sequence identity.

15. An antigen binding protein as claimed in any one of claims 1-14, wherein the SAP is human SAP which is bound to amyloid fibrils *in vivo*.

16. An antigen binding protein as claimed in any one of claims 1-15, wherein the antigen binding protein binds to the A face of human SAP.

17. An antigen binding protein as claimed in any one of claims 1-16, wherein the antigen binding protein activates the human complement system.

18. An antigen binding protein according to any one of claims 1-5, 8, 9 or 15-17, which is chimeric, humanised, or human.

19. An antigen binding protein according to any one of the previous claims, wherein the antigen binding protein comprises a human IgG1 or IgG3 human constant domain.

20. A nucleic acid molecule which encodes an antigen binding protein as defined in any one of claims 1-19.

21. A nucleic acid molecule as claimed in claim 20, wherein the nucleic acid sequence comprises SEQ ID NO:54 and/or SEQ ID NO:59.

22. A nucleic acid molecule as claimed in claim 21, wherein the nucleic acid sequence comprises SEQ ID NO:61 and/or SEQ ID NO:63.

23. An expression vector comprising a nucleic acid molecule as defined in any one of claims 20-22.

24. A recombinant host cell comprising an expression vector as defined in claim 23.

25. A method for the production of an antigen binding protein as defined in any one of claims 1-19, which method comprises the step of culturing a host cell as defined in claim 24 and recovering the antigen binding protein.

26. A pharmaceutical composition comprising an antigen binding protein as defined in any one of claims 1-19 and a pharmaceutically acceptable carrier.

27. A method of treating a subject afflicted with a disease associated with amyloid deposition, which method comprises the step of administering to said subject a therapeutically effective amount of an antigen binding protein as defined in any one of claims 1-19 or the composition of claim 26.

28. A method of preventing a disease associated with amyloid deposition in a subject, which method comprises the step of administering to said subject a prophylactically effective amount of an antigen binding protein as defined in any one of claims 1-19 or the composition of claim 26.

29. A method according to claim 27 or 28, wherein the antigen binding protein is to be administered with a SAP depleting compound.

30. An antigen binding protein as defined in any one of claims 1-19 for use in treating or preventing a disease associated with amyloid deposition, wherein said antigen binding protein is to be administered with a SAP depleting compound.

31. A SAP depleting compound for use in treating or preventing a disease associated with amyloid deposition, wherein said SAP depleting compound is to be administered with an antigen binding protein as defined in any one of claims 1-19.

32. A method according to claim 27, 28 or 29, an antigen binding protein according to claim 29, or a SAP depleting compound according to claim 31, wherein the administration of the antigen binding protein and SAP depleting compound is sequential.

33. A method, an antigen binding protein, or a SAP depleting compound according to claim 32, wherein the SAP depleting compound is to be administered first.

34. A method, an antigen binding protein, or a SAP depleting compound according to claim 33, wherein the antigen binding protein is to be administered when substantially all of the SAP circulating in the subject has been cleared.

35. A method according to claim 27, 28, 29, 31, 33, or 34, an antigen binding protein according to claim 30, 32, 33, or 34, or a SAP antagonist compound according to claim 31, 32, 33, or 34, wherein the disease is selected from the group consisting of: systemic amyloidosis, local amyloidosis, Alzheimer's disease, type 2 diabetes, dialysis-related amyloidosis, monoclonal immunoglobulin chain (AL) amyloidosis and cerebral amyloid angiopathy.

36. A method according to claim 27, 28, 29, 32, 33, 34, or 35, an antigen binding protein according to claim 30, 32, 33, 34, or 35, or a SAP depleting compound according to claim 31, 32, 33, 34, or 35, wherein the SAP depleting compound is a D-proline derivative or a glycerol cyclic pyruvate derivative.

37. A method, antigen binding protein or SAP depleting compound according to claim 36, wherein the D-proline derivative is CPHPC.

CLAIMS

1. An antibody which specifically binds to SAP, wherein the heavy chain variable region is SEQ ID NO: 28, the light chain variable region is SEQ ID NO: 35 and wherein the antibody comprises a human IgG1 or IgG3 human constant domain.

2. An antibody as defined in claim 1, which comprises a heavy chain of SEQ ID NO:62 and a light chain of SEQ ID NO:64..

3. A nucleic acid molecule which encodes an antibody as defined in any one of claims 1-2.

4. A nucleic acid molecule as defined in claim 3, comprising SEQ ID NO:54 and SEQ ID NO:59.

5. A nucleic acid molecule as defined in claim 3, comprising SEQ ID NO:61 and SEQ ID NO:63.

6. An expression vector comprising a nucleic acid molecule as defined in claim 3, 4 or 5.

7. A recombinant host cell comprising an expression vector as defined in claim 6.

8. A method for the production of an antibody as defined in any one of claims 1-2, which method comprises the step of culturing a host cell as defined in claim 7 and recovering the antibody.

9. A pharmaceutical composition comprising an antibody as defined in any one of claims 1-2 and a pharmaceutically acceptable carrier.

10. An antibody as defined in any one of claims 1-2 for use in treating or preventing a disease associated with amyloid deposition, wherein said antibody is to be administered with ((2*R*)-1-[6-[(2*R*)-2-Carboxypyrrolidin-1-yl]-6-oxohexanoyl]pyrrolidine-2-carboxylic acid;

(CPHPC) or a pharmaceutically acceptable salt or mono- or diester thereof, wherein the administration of the antibody and CPHPC is sequential and wherein the CPHPC is to be administered first.

11. An antibody for use according to claim 10, wherein the antibody is to be administered when substantially all of the SAP circulating in the subject has been cleared.

12. An antibodyfor use according to any one of claims 10 or 11 wherein the disease is selected from the group consisting of: systemic amyloidosis, local amyloidosis, Alzheimer's disease, type 2 diabetes, dialysis-related amyloidosis, monoclonal immunoglobulin chain (AL) amyloidosis and cerebral amyloid angiopathy.