CLAIMS

1. An antigen binding protein which specifically binds to OSM and which inhibits the binding of OSM to the gp130 receptor but does not directly interact with site II residues.

2. An antigen binding protein according to claim 1 wherein the antigen binding protein does not directly bind to any one of residues Q20, G120, Q16, N124.

3. An antigen binding protein according to claim 1 which interacts with one or more of residues 82, 83, 84, 90, 94, 112,115, 122, 123, 152 of human OSM.

4. An antigen binding protein according to any one of claims 1-3 wherein the antigen binding protein comprises CDRH3 of SEQ ID NO. 3 or a variant of SEQ ID NO. 3 wherein the variant of SEQ ID NO. 3 comprises one or more of the following :
Position 95 is substituted for Ala, Glu, Gly, His, Leu, Met, Pro, Gln, Ser, Thr, or Val;
Position 96 is substituted for Ala, Cys, Phe, Gly, His, Lys, Leu, Ser, Thr, Trp or Tyr;
Position 97 is substituted for Ala, Cys, Phe, Met or Ser
Position 98 is substituted for Ala, Asp, Phe, Gly, Leu, Pro, Gln or Trp
Position 99 is substituted for Ala, Cys, Pro, Ser, Val or Tyr
Position 100B is substituted for Glu
Position 100C is substituted for Ala, Glu, Phe, Gly, Val or Trp
Position 100D is substituted for Ala, Cys, Asp, Glu, Gly, Leu, Ser, Thr, Val, Trp or Tyr
Position 101 is substituted for Glu, Gly, Ser, Thr or Val
Position 102 is substituted for Ala, Phe, Gly, Leu, Pro, Gln, Arg, Ser Tyr, His, Ile, Asp or Trp

5. An antigen binding protein according to any one of claims 1-3 wherein the antigen binding protein comprises:
i) CDRH3 as set out in SEQ ID NO. 3 or a variant of SEQ ID NO. 3 wherein Val 102 is substituted for Tyr, His, Ile, Ser, Asp or Gly
ii) CDRH2 as set out in SEQ ID NO. 2 or a variant of SEQ ID NO. 2 wherein Thr50 is substituted for Gly, Tyr, Phe, Ile, Glu or Val and/or Ile51 is substituted for Leu, Val, Thr, Ser or Asn and/or Ser52 is substituted for Phe, Trp or His and/or Gly53 is substituted for Asp, Ser or Asn and/orGly54 is substituted for Ser and/or Phe56 is substituted for Ser, Tyr, Thr, Asn, Asp or Arg and/or Tyr58 is substituted for Gly, His, Phe, Asp or Asn.
iii) CDRL1 as set out in SEQ ID NO. 4 or a variant of SEQ ID NO. 4 wherein Ser27A is substituted for Asn, Asp, Thr or Glu and/or Ser 27C is substituted for Asp, Leu, Tyr, Val, Ile, Asn, Phe, His, Gly or Thr and/or Asn 31 is substituted for Ser, Thr, Lys or Gly and/or Phe32 is substituted for Tyr, Asn, Ala, His, Ser or Arg and/or Met 33 is substituted for Leu, Val, Ile or Phe.
iv) CDRL3 as set out in SEQ ID NO. 6 or a variant of SEQ ID NO. 6 wherein Leu89 is substituted for Gln, Ser, Gly or Phe and/or His90 is substituted for Gln or Asn, Ser 91 is substituted for Asn, Phe, Gly, Arg, Asp, His, Thr, Tyr or Val and/or Arg92 is substituted for Asn, Tyr, Trp, Thr, Ser,

Gln, His, ala or Asp and/or Glu93 is substituted for Asn, Gly, His, Thr, Ser, Ar or Ala and/or Phe96 is substituted for Pro, Leu, Tyr, Arg, Ile,or Trp.

6. An antigen binding protein according to claim 5 wherein the antigen binding protein further comprises:

i) CDRH1 as set out in SEQ ID NO. 1 or a variant of SEQ ID NO. 1 wherein Tyr 32 is substituted for Ile, His, Phe, Thr, Asn, Cys, Glu or Asp and/or Ala 33 is substituted for Tyr, Trp, Gly, Thr, Leu or Val and/or Met 34 is substituted for Ile, Val or Trp and/or Ser 35 is substituted for His, Glu, Asn, Gln, Tyr or Thr.

ii) CDRL2 as set out in SEQ ID NO. 5

7. An antigen binding protein according to any preceding claim wherein the antigen binding protein comprises CDR H3 of SEQ. ID. NO: 3: CDRH2: SEQ. ID. NO: 2: CDRL1: SEQ. ID. NO: 4 and CDRL3: SEQ. ID. NO: 6

8. An antigen binding protein according to claim 7 wherein the antigen binding protein further comprises CDR H1 of SEQ. ID. NO: 1 and CDRL2: SEQ. ID. NO: 5

9. An antigen binding protein according to claim 8 wherein the antigen binding protein comprises:

i) CDRH3 as set out in SEQ ID NO. 3
ii) CDRH1 as set out in SEQ ID NO. 1
iii) CDRH2 as set out in SEQ ID NO. 2
iv) CDRL1 as set out in SEQ ID NO. 4
v) CDRL2 as set out in SEQ ID NO. 5
vi) CDRL3 as set out in SEQ ID NO. 6; and
vii) the heavy chain framework comprises the following residues:

Position 2 Val, Ile or Gly,
Position 4 Leu or Val
Position 20 Leu, Ile, Met or Val
Position 22 Cys
Position 24 Thr, Ala, Val, Gly or Ser
Position 26 Gly
Position 29 Ile, Phe, Leu or Ser
Position 36 Trp
Position 47 Trp
Position 48 Ile, met, Val or Leu
Position 69 Ile, Leu, Phe, Met or Val
Position 71 Arg
Position 78 Ala, Leu, Val, Tyr or Phe
Position 80 Leu, Met,

Position 90 Tyr or Phe

Position 92 Cys

Position 94 Arg, Lys, Gly, Ser, His or Asn

10. An. The antigen binding protein according to any preceding claim wherein the antigen binding protein does not interact directly via CDR H1 or CDR L2 with OSM.

11. An. The antigen binding protein according to any one of claims 1 to 3 and further comprising a heavy chain variable region encoded by SEQ. ID. NO:73 and a light chain variable region encoded by SEQ. ID. NO:71.

12. An. The antigen binding protein according to any one of claims 1 to 3 and further comprising a heavy chain variable region of SEQ. ID. NO:74 and a light chain variable region of SEQ. ID. NO:72.

13. An antigen binding protein according to any preceding claim wherein the antigen binding protein is a humanised antibody.

14. An antigen binding protein according to claim 13 wherein the antibody is IgG1.

15. An antigen binding protein according to any one of claims 13-15 wherein when bound to OSM the co crystal comprises a unit cell having dimensions of about a=168.525 A, b=81.614A, c=55.540 A and beta=106.60 degrees

16. An antigen binding protein comprising the CDR's of any one of claims 1 to 10 wherein the antigen binding protein is a fragment which is a Fab, Fab', $F(ab')_2$, Fv, diabody, triabody, tetrabody, miniantibody, minibody, isolated VH or isolated VL.

17. An antigen binding protein according to any preceding claim wherein the antigen binding protein additionally binds non-human primate OSM

18. An antigen binding protein according to any one of the preceding claims and wherein the antigen binding protein binds OSM with an affinity of less than 40pm.

19. An antigen binding protein according to any preceding claim wherein the antigen binding protein does not compete with an antibody which has a heavy chain of SEQ ID NO.79 and a light chain of SEQ ID NO. 80 in a competition ELISA assay.

20. An antigen binding protein which competes with the antigen binding protein of any preceding claim.

21. An antigen binding protein which binds to both Marmoset and human OSM with an affinity stronger than 1nM when measured by Biacore or kinexa.

22. A recombinant transformed, transfected or transduced host cell comprising at least one expression cassette, whereby said expression cassette comprises a polynucleotide encoding a heavy chain of an antigen binding protein according to claim 12 and further comprises a polynucleotide encoding a light chain of an antigen binding protein or according to claim 12

23. The host cell according to claim 22 wherein the cell is mammalian

24. The host cell according to claim 23 wherein the cell is CHO or NSO.

25. A pharmaceutical composition comprising an antigen binding protein according to any preceding claim and a pharmaceutically acceptable carrier.

26. A method of treating a human patient afflicted with an inflammatory disorder or disease which method comprises the step of administering the composition of claim 25

27. Use of the composition of claim 25 in treating a human patient afflicted with an inflammatory arthropathy, rheumatoid arthritis, osteoarthritis, idiopathic pulmonary fibrosis (IPF), Systemic sclerosis, Sjogrens syndrome, Scleroderma and/or psoriasis.

28. A method for humanising a non-human antibody or antibody fragment thereof which method comprises the steps of:

a) incorporating one or more non-human CDR's onto a human acceptor framework to produce a chimeric or humanised antibody

b) binding the chimeric or humanised antibody to its antigen

c) determining the epitope/paratope structure of the bound antibody to antigen.

d) determining the residues of the antibody involved directly in binding to the antigen

e) mutating one or more of the residues not involved in step (d) to human germline sequence;

f) recovering said antibody.

29. An antibody obtainable by the method of claim 28.

CLAIMS

1. An antigen binding protein which specifically binds to OSM and which inhibits the binding of OSM to the gp130 receptor but does not directly interact with site II residues and wherein the antigen binding protein comprises:

i) CDRH3 as set out in SEQ ID NO. 3 or a variant of SEQ ID NO. 3 wherein Val 102 is substituted for Tyr, His, Ile, Ser, Asp or Gly

ii) CDRH2 as set out in SEQ ID NO. 2 or a variant of SEQ ID NO. 2 wherein Thr50 is substituted for Gly, Tyr, Phe, Ile, Glu or Val and/or Ile51 is substituted for Leu, Val, Thr, Ser or Asn and/or Ser52 is substituted for Phe, Trp or His and/or Gly53 is substituted for Asp, Ser or Asn and/orGly54 is substituted for Ser and/or Phe56 is substituted for Ser, Tyr, Thr, Asn, Asp or Arg and/or Tyr58 is substituted for Gly, His, Phe, Asp or Asn.

iii) CDRL1 as set out in SEQ ID NO. 4 or a variant of SEQ ID NO. 4 wherein Ser27A is substituted for Asn, Asp, Thr or Glu and/or Ser 27C is substituted for Asp, Leu, Tyr, Val, Ile, Asn, Phe, His, Gly or Thr and/or Asn 31 is substituted for Ser, Thr, Lys or Gly and/or Phe32 is substituted for Tyr, Asn, Ala, His, Ser or Arg and/or Met 33 is substituted for Leu, Val, Ile or Phe.

iv) CDRL3 as set out in SEQ ID NO. 6 or a variant of SEQ ID NO. 6 wherein Leu89 is substituted for Gln, Ser, Gly or Phe and/or His90 is substituted for Gln or Asn, Ser 91 is substituted for Asn, Phe, Gly, Arg, Asp, His, Thr, Tyr or Val and/or Arg92 is substituted for Asn, Tyr, Trp, Thr, Ser, Gln, His, ala or Asp and/or Glu93 is substituted for Asn, Gly, His, Thr, Ser, Ar or Ala and/or Phe96 is substituted for Pro, Leu, Tyr, Arg, Ile,or Trp.

2. An antigen binding protein according to claim 1 wherein the antigen binding protein further comprises:

i) CDRH1 as set out in SEQ ID NO. 77 or a variant of SEQ ID NO. 77 wherein Tyr 32 is substituted for Ile, His, Phe, Thr, Asn, Cys, Glu or Asp and/or Ala 33 is substituted for Tyr, Trp, Gly, Thr, Leu or Val and/or Met 34 is substituted for Ile, Val or Trp and/or Ser 35 is substituted for His, Glu, Asn, Gln, Tyr or Thr.

ii) CDRL2 as set out in SEQ ID NO. 5

3. An antigen binding protein according to any preceding claim wherein the antigen binding protein comprises CDR H3 of SEQ. ID. NO: 3: CDRH2: SEQ. ID. NO: 2: CDRL1: SEQ. ID. NO: 4 and CDRL3: SEQ. ID. NO: 6

4. An antigen binding protein according to claim 3 wherein the antigen binding protein further comprises CDR H1 of SEQ. ID. NO: 77 and CDRL2: SEQ. ID. NO: 5

5. An antigen binding protein according to claim 4 wherein the antigen binding protein comprises:

i) CDRH3 as set out in SEQ ID NO. 3

ii) CDRH1 as set out in SEQ ID NO. 77

iii) CDRH2 as set out in SEQ ID NO. 2

iv) CDRL1 as set out in SEQ ID NO. 4

v) CDRL2 as set out in SEQ ID NO. 5

vi) CDRL3 as set out in SEQ ID NO. 6; and

vii) the heavy chain framework comprises the following residues:

Position 2 Val, Ile or Gly,

Position 4 Leu or Val

Position 20 Leu, Ile, Met or Val

Position 22 Cys

Position 24 Thr, Ala, Val, Gly or Ser

Position 26 Gly

Position 29 Ile, Phe, Leu or Ser

Position 36 Trp

Position 47 Trp

Position 48 Ile, met, Val or Leu

Position 69 Ile, Leu, Phe, Met or Val

Position 71 Arg

Position 78 Ala, Leu, Val, Tyr or Phe

Position 80 Leu, Met,

Position 90 Tyr or Phe

Position 92 Cys

Position 94 Arg, Lys, Gly, Ser, His or Asn

6. An antigen binding protein according to any preceding claim wherein the antigen binding protein does not interact directly via CDR H1 or CDR L2 with OSM.

7. An antigen binding protein according to any preceding claim wherein the antigen binding protein comprises a heavy chain variable region encoded by SEQ. ID. NO:73 and a light chain variable region encoded by SEQ. ID. NO:71.

8. An antigen binding protein according to any preceding claim wherein the antigen binding protein comprises a heavy chain variable region of SEQ. ID. NO:74 and a light chain variable region of SEQ. ID. NO:72.

9. An antigen binding protein according to any preceding claim wherein the antigen binding protein is a humanised antibody.

10. An antigen binding protein according to claim 9 wherein the antibody is IgG1.

11. An antigen binding protein according to any preceding claim wherein the antigen binding protein additionally binds non-human primate OSM.

12. An antigen binding protein according to any one of the preceding claims and wherein the antigen binding protein binds OSM with an affinity of less than 40pm.

13. An antigen binding protein according to any preceding claim wherein the antigen binding protein does not compete with an antibody which has a heavy chain of SEQ ID NO.79 and a light chain of SEQ ID NO. 80 in a competition ELISA assay.

14. An antigen binding protein according to claim 1 wherein the antigen binding protein binds to both Marmoset and human OSM with an affinity stronger than 1nM when measured by Biacore or kinexa.

15. A pharmaceutical composition comprising an antigen binding protein according to any preceding claim and a pharmaceutically acceptable carrier.

16. Use of the composition of claim 15 in the manufacture of a medicament for treating a human patient afflicted with an inflammatory disorder or disease.

17. Use of the composition of claim 15 in the manufacture of a medicament for treating a human patient afflicted with an inflammatory arthropathy, rheumatoid arthritis, osteoarthritis, idiopathic pulmonary fibrosis (IPF), Systemic sclerosis, Sjogrens syndrome, Scleroderma and/or psoriasis.