CLAIMS

1. A bispecific antibody fusion protein which binds human OX40 and human serum albumin comprising:

a heavy chain comprising, in sequence from the N-terminal, a first heavy chain variable domain (V_H1), a CH1 domain and a second heavy chain variable domain (V_H2),

a light chain comprising, in sequence from the N-terminal, a first light chain variable domain (V_L1), a CL domain and a second light chain variable domain (V_L2),

wherein said heavy and light chains are aligned such that VH1 and VL1 form a first antigen binding site and VH2 and VL2 form a second antigen binding site,

wherein the antigen bound by the first antigen binding site is human OX40 and the antigen bound by the second antigen binding site is human serum albumin,

wherein the first variable domain of the heavy chain (V_H1) comprises the sequence given in SEQ ID NO:1 for CDR-H1, the sequence given in SEQ ID NO:2 for CDR-H2 and the sequence given in SEQ ID NO:3 for CDR-H3 and the first variable domain of the light chain (V_L1) comprises the sequence given in SEQ ID NO:4 for CDR-L1, the sequence given in SEQ ID NO:5 for CDR-L2 and the sequence given in SEQ ID NO:6 for CDR-L3,

wherein the second heavy chain variable domain (V_H2) has the sequence given in SEQ ID NO:11 and the second light chain variable domain (V_L2) has the sequence given in SEQ ID NO: 12 and

the second heavy chain variable domain (V_H2) and second light chain variable domain (V_L2) are linked by a disulphide bond.

2. A bispecific antibody fusion protein according to claim 1 which antagonises the binding of OX40 to OX40L.

3. A bispecific antibody fusion protein according to claim 1 or claim 2 in which there is a peptide linker between the CH1 domain and the second heavy chain variable domain (V_H2).

4. A bispecific antibody fusion protein according to any one of claims 1 to 3 in which there is a peptide linker between the CL domain and the second light chain variable domain (V_L1).

5. An antibody fusion protein according to any one of claims 1 to 4 wherein the first heavy chain variable domain (V_H1) comprises the sequence given in SEQ ID NO:8.

6. An antibody fusion protein according to any one of claims 1 to 5 wherein the first light chain variable domain (V_L1) comprises the sequence given in SEQ ID NO:7.

7. An antibody fusion protein according to any one of claims 1 to 6, wherein the heavy chain comprises or consists of the sequence given in SEQ ID NO:15.

8. An antibody fusion protein according to any one of claims 1 to 7, wherein the light chain comprises or consists of the sequence given in SEQ ID NO:16.

9. A bispecific antibody fusion protein which binds human OX40 and human serum albumin, having a heavy chain comprising the sequence given in SEQ ID NO:15 and a light chain comprising the sequence given in SEQ ID NO:16.

10. An isolated DNA sequence encoding the heavy and/or light chain(s) of an antibody fusion protein according to any one of claims 1 to 9.

11. A cloning or expression vector comprising one or more DNA sequences according to claim 10.
12. A vector according to claim 11, wherein the vector comprises the sequences given in SEQ ID NO:22 and SEQ ID NO:24.
13. A host cell comprising one or more cloning or expression vectors according to claim 11 or claim 12.
14. A process for the production of the antibody fusion protein of any one of claims 1 to 9, comprising culturing the host cell of claim 13 and isolating the antibody fusion protein.
15. A pharmaceutical composition comprising a bispecific antibody fusion protein according to any one of claims 1 to 9, in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.
16. A pharmaceutical composition according to claim 15, additionally comprising other active ingredients.
17. A bispecific antibody fusion protein according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 15 or claim 16, for use in therapy.
18. A bispecific antibody fusion protein according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 15 or claim 16, for use in the treatment or prophylaxis of a pathological disorder that is mediated by OX40 or that is associated with an increased level of OX40.
19. The use of a bispecific antibody fusion protein according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment or prophylaxis of a pathological disorder that is mediated by OX40 or that is associated with an increased level of OX40.
20. The use according to claim 18 or claim 19 wherein the pathological disorder is a disease selected from the group consisting of allergy, COPD, autoimmune disease, rheumatoid arthritis, asthma, graft versus host disease, Crohn's disease, ulcerative colitis, type- 1 diabetes, multiple sclerosis, Systemic lupus erythematosis, lupus nephritis, Myasthenia Gravis, Grave's disease, transplant rejection, Wegener's granulomatosis, Henoch-Schonlein purpura, systemic sclerosis and viral-induced lung inflammation.

CLAIMS

1. A bispecific antibody fusion protein that binds human OX40 and human serum albumin comprising:

a heavy chain comprising, in sequence from the N-terminal, a first heavy chain variable domain (V_H1), a CH1 domain and a second heavy chain variable domain (V_H2),

a light chain comprising, in sequence from the N-terminal, a first light chain variable domain (V_L1), a CL domain and a second light chain variable domain (V_L2),

wherein said heavy and light chains are aligned such that VH1 and VL1 form a first antigen binding site and VH2 and VL2 form a second antigen binding site,

wherein the antigen bound by the first antigen binding site is human OX40 and the antigen bound by the second antigen binding site is human serum albumin,

wherein the first variable domain of the heavy chain (V_H1) comprises the sequence given in SEQ ID NO:1 for CDR-H1, the sequence given in SEQ ID NO:2 for CDR-H2 and the sequence given in SEQ ID NO: 3 for CDR-H3 and the first variable domain of the light chain (V_L1) comprises the sequence given in SEQ ID NO:4 for CDR-L1, the sequence given in SEQ ID NO:5 for CDR-L2 and the sequence given in SEQ ID NO:6 for CDR-L3,

wherein the second heavy chain variable domain (V_H2) has the sequence given in SEQ ID NO: 11 and the second light chain variable domain (V_L2) has the sequence given in SEQ ID NO: 12 and

the second heavy chain variable domain (V_H2) and second light chain variable domain (V_L2) are linked by a disulphide bond.

2. A bispecific antibody fusion protein according to claim 1, which antagonises the binding of OX40 to OX40L.

3. A bispecific antibody fusion protein according to claim 1 or claim 2, in which there is a peptide linker between the CH1 domain and the second heavy chain variable domain (V_H2).

4. A bispecific antibody fusion protein according to any one of claims 1 to 3 in which there is a peptide linker between the CL domain and the second light chain variable domain (V_L2).

5. An antibody fusion protein according to any one of claims 1 to 4, wherein the first heavy chain variable domain (V_H1) comprises the sequence given in SEQ ID NO:8.

6. An antibody fusion protein according to any one of claims 1 to 5, wherein the first light chain variable domain (V_L1) comprises the sequence given in SEQ ID NO:7.

7. An antibody fusion protein according to any one of claims 1 to 6, wherein the heavy chain comprises or consists of the sequence given in SEQ ID NO:15.

8. An antibody fusion protein according to any one of claims 1 to 7, wherein the light chain comprises or consists of the sequence given in SEQ ID NO:16.

9. A bispecific antibody fusion protein which binds human OX40 and human serum albumin, having a heavy chain comprising the sequence given in SEQ ID NO:15 and a light chain comprising the sequence given in SEQ ID NO:16.

10. An antibody fusion protein according to claim 9, wherein the heavy chain consists of the sequence given in SEQ ID NO:15 and the light chain consists of the sequence given in SEQ ID NO:16.

11. An isolated DNA sequence encoding the heavy and/or light chain(s) of an antibody fusion protein according to any one of claims 1 to 10.

12. A cloning or expression vector comprising one or more DNA sequences according to claim 11.

13. A vector according to claim 12, wherein the vector comprises the sequences given in SEQ ID NO:22 and SEQ ID NO:24.

14. A host cell comprising one or more cloning or expression vectors according to claim 12 or claim 13.

15. A process for the production of an antibody fusion protein, comprising culturing the host cell of claim 13 and isolating the antibody fusion protein.

16. A pharmaceutical composition comprising a bispecific antibody fusion protein according to any one of claims 1 to 10, in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

17. A pharmaceutical composition according to claim 16, additionally comprising one or more other active ingredients.

18. A bispecific antibody fusion protein according to any one of claims 1 to 10 or a pharmaceutical composition according to claim 16 or claim 17, for use in therapy.

19. A bispecific antibody fusion protein according to any one of claims 1 to 10 or a pharmaceutical composition according to claim 16 or claim 17, for use in the treatment or prophylaxis of a pathological disorder that is mediated by OX40 or that is associated with an increased level of OX40, wherein the pathological disorder is selected from the group consisting of allergy, COPD, autoimmune disease, rheumatoid arthritis, asthma, graft versus host disease, Crohn's disease, ulcerative colitis, type- 1 diabetes, multiple sclerosis, Systemic lupus erythematosus, lupus nephritis, Myasthenia Gravis, Grave's disease, transplant rejection, Wegener's granulomatosis, Henoch-Schonlein purpura, systemic sclerosis and viral-induced lung inflammation.

20. The use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment or prophylaxis of a pathological disorder that is mediated by OX40 or that is associated with an increased level of OX40, wherein the pathological disorder is a disease selected from the group consisting of allergy, COPD, autoimmune disease, rheumatoid arthritis, asthma, graft versus host disease, Crohn's disease, ulcerative colitis, type- 1 diabetes, multiple sclerosis, Systemic lupus erythematosus, lupus nephritis, Myasthenia Gravis, Grave's disease, transplant rejection, Wegener's granulomatosis, Henoch-Schonlein purpura, systemic sclerosis and viral-induced lung inflammation.

21. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating allergy.

22. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating COPD.

23. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating autoimmune disease.

24. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating rheumatoid arthritis.

25. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating asthma.

26. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating graft versus host disease.

27. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Crohn's disease.

28. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating ulcerative colitis.

29. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating type-1 diabetes.

30. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating multiple sclerosis.

31. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Systemic lupus erythematosus.

32. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating lupus nephritis.

33. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Myasthenia Gravis.

34. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Grave's disease.

35. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating transplant rejection.

36. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Wegener's granulomatosis.

37. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating Henoch-Schonlein purpura.

38. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating systemic sclerosis.

39. A bispecific antibody fusion protein according to any one of claims 1 to 10 for use in treating viral-induced lung inflammation.

40. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating allergy.

41. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating COPD.

42. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating autoimmune disease.

43. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating rheumatoid arthritis.

44. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating asthma.

45. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating graft versus host disease.

46. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Crohn's disease.

47. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating ulcerative colitis.

48. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating type-1 diabetes.

49. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating multiple sclerosis.

50. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Systemic lupus erythematosus.

51. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating lupus nephritis.

52. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Myasthenia Gravis.

53. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Grave's disease.

54. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating transplant rejection.

55. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Wegener's granulomatosis.

56. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating Henoch-Schonlein purpura.

57. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating systemic sclerosis.

58. Use of a bispecific antibody fusion protein according to any one of claims 1 to 10 in the manufacture of a medicament for treating viral-induced lung inflammation.