CLAIMS

1. An anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain comprising an amino acid sequence that is at least 95, 96, 97, 98 or 99% identical (or is 100% identical) to the amino acid sequence of DOM1h-574-188, DOM1h-574-189, DOM1h-574-190, DOM1h-574-191, DOM1h-574-192, DOM1h-574-195, DOM1h-574-196, DOM1h-574-201, DOM1h-574-202, DOM1h-574-203, DOM1h-574-204, DOM1h-574-205, DOM1h-574-206, DOM1h-574-207, DOM1h-574-208, DOM1h-574-209, DOM1h-574-211, DOM1h-574-212, DOM1h-574-213 or DOM1h-574-214, wherein the single variable domain has an OD_{320} <1.0, <0.9, <0.8, <0.7, <0.6, <0.5, or <0.4 after incubation in PBS at 40°C for 40 hours.

2. A multispecific ligand comprising an immunoglobulin single variable domain of claim 1 and optionally at least one immunoglobulin single variable domain that specifically binds serum albumin (SA).

3. A multispecific ligand according to claim 2, wherein the ligand comprises (i) an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1, (ii) at least one anti-serum albumin (SA) immunoglobulin single variable domain that specifically binds SA, wherein the anti-SA single variable domain comprises an amino acid sequence that is at least 80, 85, 90, 95, 96, 97, 98 or 99 % identical (or 100% identical) to the sequence of DOM7h-11-3, and (iii) optionally wherein a linker is provided between the anti-TNFR1 single variable domain and the anti-SA single variable domain.

4. The ligand of claim 3, wherein the linker comprises the amino acid sequence AST, (optionally ASTSGPS), or wherein the linker is $AS(G_4S)_n$, where n is 1, 2, 3 , 4, 5, 6, 7 or 8, for example $AS(G_4S)_3$.

5. A TNFR1 antagonist comprising a single variable domain or multispecific ligand of any preceding claim.

6. A TNFα receptor type 1 (TNFR1; p55) antagonist according to claim 5, for oral delivery, delivery to the GI tract of a patient, pulmonary delivery, delivery to the lung of a patient or systemic delivery.

7. A TNFα receptor type 1 (TNFR1; p55) antagonist according to claim 5 or 6, for treating and/or prophylaxis of an inflammatory condition.

8. The use of the TNFR1 antagonist of claim 5 or 6 in the manufacture of a medicament for treating and/or prophylaxis of an inflammatory condition.

9. A method of treating and/or prophylaxis of an inflammatory condition in a patient, the method comprising administering the antagonist of claim 5 or 6 to the patient.

10. A multispecific ligand comprising or consisting of DMS5535, DMS5541, DMS5542 or DMS5544.

11. A nucleic acid comprising a nucleotide sequence that is at least 80, 85, 90, 95, 96, 97, 98 or 99 % identical (or 100% identical) identical to the nucleotide sequence of DMS5535, DMS5541, DMS5542 or DMS5544.

12. A nucleic acid comprising a nucleotide sequence that encodes an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1.

13. A nucleic acid comprising a nucleotide sequence that encodes an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to

claim 1, wherein the nucleotide sequence is at least 70, 75 80, 85, 90, 95, 96, 97, 98 or 99% identical (or is 100% identical) to the nucleotide sequence of DOM1h-574-188, DOM1h-574-189, DOM1h-574-190, DOM1h-574-191, DOM1h-574-192, DOM1h-574-193, DOM1h-574-194, DOM1h-574-195, DOM1h-574-196, DOM1h-574-201, DOM1h-574-202, DOM1h-574-203, DOM1h-574-204, DOM1h-574-205, DOM1h-574-206, DOM1h-574-207, DOM1h-574-208, DOM1h-574-209, DOM1h-574-211, DOM1h-574-212, DOM1h-574-213 or DOM1h-574-214.

14. A vector comprising a nucleic acid according to claim 11, 12 or 13.

15. A host cell (optionally a non-human embryonic cell) comprising a vector according to claim 14.

CLAIMS

1. An anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain comprising the amino acid sequence of SEQ ID NO: 59.

2. A multispecific ligand comprising an immunoglobulin single variable domain of claim 1.

3. A multispecific ligand comprising an immunoglobulin single variable domain of claim 1 and at least one immunoglobulin single variable domain that specifically binds serum albumin (SA).

4. A multispecific ligand according to claim 2 or 3, wherein the ligand comprises (i) an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1, (ii) at least one anti-serum albumin (SA) immunoglobulin single variable domain that specifically binds SA, wherein the anti-SA single variable domain comprises an amino acid sequence that is at least 80, 85, 90, 95, 96, 97, 98 or 99% identical (or 100% identical) to the sequence of SEQ ID NO: 76, and (iii) optionally wherein a linker is provided between the anti-TNFR1 single variable domain and the anti-SA single variable domain.

5. The ligand of claim 4, wherein the linker comprises the amino acid sequence AST, (optionally ASTSGPS), or wherein the linker is $AS(G_4S)_n$, where n is 1, 2, 3, 4, 5, 6, 7 or 8, for example $AS(G_4S)_3$.

6. A multispecific ligand comprising the amino acid sequence of SEQ ID NO: 66.

7. A multispecific ligand consisting of the amino acid sequence of SEQ ID NO: 66.

8. A TNFα receptor type 1 (TNFR1; p55) antagonist comprising a single variable domain or multispecific ligand as defined in any one of claims 1-7.

9. A TNFα receptor type 1 (TNFR1; p55) antagonist comprising a single variable domain or multispecific ligand as defined in any one of claims 1-8 for use in therapy.

10. The TNFR1 antagonist for use in therapy according to claim 9, wherein the antagonist is delivered orally, delivered to the GI tract of a patient, delivered pulmonary, delivered to the lung of a patient or delivered systemically.

11. The TNFR1 antagonist for use according to claim 9 or 10, in treating and/or prophylaxis of an inflammatory condition.

12. The TNFR1 antagonist for use according to claim 9 or 10 in the treatment of arthritis, rheumatoid arthritis or juvenile rheumatoid arthritis.

13. A nucleic acid comprising a nucleotide sequence that is at least 80, 85, 90, 95, 96, 97, 98 or 99% identical (or 100% identical) to the nucleotide sequence of SEQ ID NO: 32.

14. A nucleic acid comprising a nucleotide sequence that encodes an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1.

15. The nucleic acid according to claim 14 comprising a nucleotide sequence that encodes an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1, wherein the nucleotide sequence is at least 90, 95, 96, 97, 98 or 99% identical (or is 100% identical) to the nucleotide sequence of SEQ ID NO: 25.

16. The nucleic acid according to claim 14 or 15 comprising a nucleotide sequence that encodes an anti-TNFα receptor type 1 (TNFR1; p55) immunoglobulin single variable domain according to claim 1, wherein the nucleotide sequence is the nucleotide sequence of SEQ ID NO: 25.

17. A vector comprising a nucleic acid according to claim 13, 14, 15 or 16.

18. A host cell (optionally a non-human embryonic cell) comprising a vector according to claim 17.

19. A pharmaceutical composition comprising a) a TNFα receptor type 1 (TNFR1; p55) antagonist as defined in any one of claims 1 to 8, and b) one or more pharmaceutically acceptable excipients.