CLAIMS

1. A chimeric fusion polypeptide comprising an extracellular domain of a canine TNF receptor polypeptide, or a TNF binding fragment of the extracellular domain, conjoined to a polypeptide comprising an Fc region of a canine IgG immunoglobulin heavy chain, or a fragment thereof wherein the fragment comprises at least the CH2 and CH3 constant domains.

2. The chimeric fusion polypeptide as claimed in claim 1, wherein the canine TNF receptor polypeptide comprises canine TNF receptor polypeptide p80 or a TNF binding fragment thereof.

3. The chimeric fusion polypeptide as claimed in claim 2, wherein the canine TNF receptor polypeptide comprises SEQ ID NO:14 or a sequence having at least 95% sequence identity thereto.

4. The chimeric fusion polypeptide as claimed in claim 1, wherein the canine TNF receptor polypeptide comprises canine TNF receptor polypeptide p60 or a TNF binding fragment thereof.

5. The chimeric fusion polypeptide as claimed in claim 4, wherein the canine TNF receptor polypeptide comprises SEQ ID NO:1 or a sequence having at least 95% sequence identity thereto.

6. The chimeric fusion polypeptide as claimed in any one of claims 1 to 5 wherein the Fc region comprises a hinge region, a CH2 constant domain and a CH3 constant domain.

7. The chimeric fusion polypeptide as claimed in any one of claims 1 to 6 wherein the Fc region comprises an IgG subtype selected from the group consisting of subtype A, subtype B, subtype C and subtype D.

8. The chimeric fusion polypeptide as claimed in claim 7 wherein the Fc region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:5.

9. The chimeric fusion polypeptide as claimed in any preceding claim wherein the chimeric fusion polypeptide comprises a linker peptide functionally interposed between the canine TNF receptor polypeptide and the polypeptide comprising the Fc region.

10. The chimeric fusion polypeptide as claimed in claim 5 wherein the chimeric fusion polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and a sequence having at least 90% sequence homology to any of the foregoing.

11. The chimeric fusion polypeptide as claimed in claim 5 wherein the chimeric fusion polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and a sequence having at least 90% sequence homology to any of the foregoing.

12. The chimeric fusion polypeptide as claimed in claim 3 wherein the chimeric fusion polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18 and a sequence having at least 90% sequence homology to any of the foregoing.

13. The chimeric fusion polypeptide as claimed in claim 3 wherein the chimeric fusion polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing.

14. The chimeric fusion polypeptide as claimed in any preceding claim wherein the chimeric fusion polypeptide binds to canine TNF-alpha with a binding affinity having an equilibrium-dissociation constant (K_D) of $1x10^{-8}$ or less.

15. An isolated polypeptide comprising SEQ ID NO:14 or a sequence having at least 95% sequence homology thereto.

16. An isolated polynucleotide which encodes a polypeptide as claimed in claim 15.

17. A polynucleotide which encodes a chimeric fusion polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing.

18. A recombinant vector comprising a polynucleotide as claimed in claim 17.

19. The recombinant vector as claimed in claim 18, wherein said vector is positioned adjacent to and under the control of, or is operably linked to, an expression promoter.

20. A pharmaceutical composition comprising a chimeric fusion polypeptide as claimed in any one of claims 1 to 14 or a polynucleotide according to claim 17 and a pharmaceutically acceptable carrier or excipient.

21. A pharmaceutical composition comprising a chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, and a pharmaceutically acceptable carrier or excipient.

22. The pharmaceutical composition as claimed in claim 20 or 21 further comprising at least one further TNF antagonist compound and/or an anti-inflammatory compound.

23. The pharmaceutical composition as claimed in claim 22 wherein the TNF antagonist compound is methotrexate.

24. A chimeric fusion polypeptide according to any of claims 1 to 14, a polynucleotide according to claim 17, a vector according to claim 18 or 19 or a pharmaceutical composition according to any one of claims 20 to 23 for use as a medicament.

25. A chimeric fusion polypeptide according to any of claims 1 to 14, a polynucleotide according to claim 17, a vector according to claim 18 or 19 or a pharmaceutical composition according to any one of claims 20 to 23 for use in the treatment or prevention of a condition in a canine mediated by TNF expression.

26. The chimeric fusion polypeptide as claimed in claim 25 for the use as claimed in claim 25 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

27. Use of a chimeric fusion polypeptide according to any of claims 1 to 14, a polynucleotide according to claim 17, a vector according to claim 18 or 19 or a pharmaceutical composition according to any one of claims 20 to 23 in the preparation of a medicament for the treatment or prevention of a condition in a canine mediated by TNF expression.

28. Use as claimed in claim 27 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic

arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

29. A method for treating or preventing a condition mediated by TNF expression in a canine in need thereof comprising the step of administering a chimeric fusion polypeptide according to any of claims 1 to 14, a polynucleotide according to claim 17, a vector according to claim 18 or 19 or a pharmaceutical composition according to any one of claims 20 to 23 to the canine.

30. The method as claimed in claim 29 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

31. The method as claimed in claim 29 or claim 30 further comprising the step of administering at least one additional pharmaceutical composition.

32. The method as claimed in claim 31 wherein the additional pharmaceutical composition comprises a drug selected from the group consisting of a TNF antagonist, an anti-inflammatory compound, methotrexate, a chimeric or caninised antibody to canine TNF, an anti-canine TNF antibody fragment, at least one analgesic, a compound which is a cytokine suppressing anti-inflammatory drug, an NSAID, an opioid, a corticosteroid, a steroid and an antagonist of nerve growth factor.

33. A chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, or a polynucleotide encoding said amino acid sequence, for use as a medicament.

34. A chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, or a polynucleotide encoding said amino acid sequence, for use in the treatment or prevention of a canine condition mediated by TNF expression.

35. The chimeric fusion polypeptide as claimed in claim 34 for the use as claimed in claim 34 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

36. Use of a chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, or a polynucleotide encoding said amino acid sequence, in the preparation of a medicament for the treatment and/or prevention of a canine condition mediated by TNF expression.

37. Use of the chimeric fusion polypeptide as claimed in claim 36 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

38. A method for treating or preventing a condition mediated by TNF expression in a canine in need thereof comprising the step of:

- administering a chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, or a vector comprising a polynucleotide encoding said amino acid sequence, to the canine in a therapeutically effective amount.

39. The method as claimed in claim 38 wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.

40. The method as claimed in claim 38 or claim 39 further comprising the step of administering at least one additional pharmaceutical composition.

41. The method as claimed in claim 40 wherein the additional pharmaceutical composition comprises a drug selected from the group consisting of a TNF antagonist, an anti-inflammatory compound, methotrexate, a chimeric or caninised antibody to canine TNF, an anti-canine TNF antibody fragment, at least one analgesic, a compound which is a cytokine suppressing anti-inflammatory drug, an NSAID, an opioid, a corticosteroid, a steroid and an antagonist of nerve growth factor.

42. A method for reducing tumour necrosis factor levels in a canine in need thereof, said method comprising the steps of:

- administering a chimeric fusion polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO: 15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO: 19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and a sequence having at least 90% sequence homology to any of the foregoing, or a vector comprising a polynucleotide encoding said amino acid sequence, to the canine in a therapeutically effective amount.

43. The method as claimed in claim 42 further comprising the step of administering at least one additional pharmaceutical composition.

44. The method as claimed in claim 43 wherein the additional pharmaceutical composition comprises a drug selected from the group consisting of a TNF antagonist, an anti-inflammatory compound, methotrexate, a chimeric or caninised antibody to canine TNF, an anti-canine TNF antibody fragment, at least one analgesic, a compound which is a cytokine suppressing anti-inflammatory drug, an NSAID, an opioid, a corticosteroid, a steroid and an antagonist of nerve growth factor.

45. A method for producing a chimeric fusion polypeptide as claimed in any one of claims 1 to 14, the method comprising:

(i) providing a recombinant host cell comprising a vector which can express a polynucleotide encoding a chimeric fusion polypeptide as claimed in any one of claims 1 to 14;

(ii) culturing the recombinant host cell under conditions suitable for expression of the chimeric fusion polypeptide, and

(iii) recovering the chimeric fusion polypeptide.

46. A method of purifying a dimer form of a chimeric fusion polypeptide comprising an extracellular domain of a canine TNF receptor polypeptide, or a TNF binding fragment of the extracellular domain, conjoined to a polypeptide comprising an Fc region of a canine IgG immunoglobulin type B heavy chain, or a fragment thereof comprising at least the CH2 and CH3 constant domains, the method comprising a step of eluting the dimer form of the chimeric fusion polypeptide from Protein A at a pH of 4.7 to 5.3.

47. The method as claimed in claim 46 wherein the dimer form of the chimeric fusion polypeptide is eluted from Protein A at a pH of 4.8 to 5.2.

48. The method as claimed in claim 47 wherein the dimer form of the chimeric fusion polypeptide is eluted from Protein A at a pH of 4.9 to 5.1.

49. The method as claimed in claim 48 wherein the dimer form of the chimeric fusion polypeptide is eluted from Protein A at a pH of 5.0.

50. The method as claimed in any one of claims 46 to 49, wherein the canine TNF receptor polypeptide comprises canine TNF receptor polypeptide p80 or a TNF binding fragment thereof.

51. The method as as claimed in claim 50, wherein the canine TNF receptor polypeptide comprises SEQ ID NO:14 or a sequence having at least 95% sequence identity thereto.

52. The chimeric fusion polypeptide as claimed in any one of claims 46 to 49, wherein the canine TNF receptor polypeptide comprises canine TNF receptor polypeptide p60 or a TNF binding fragment thereof.

53. The chimeric fusion polypeptide as claimed in claim 52, wherein the canine TNF receptor polypeptide comprises SEQ ID NO:1 or a sequence having at least 95% sequence identity thereto.

54. The chimeric fusion polypeptide as claimed in any one of claims 46 to 53 wherein the Fc region comprises SEQ ID NO:3.

55. The chimeric fusion polypeptide as claimed in any one of claims 46 to 54 wherein the chimeric fusion polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:16, SEQ ID NO:20 and a polypeptide sequence having at least 90% sequence homology to any of the foregoing.

56. The chimeric fusion polypeptide as claimed in claim 55 wherein the chimeric fusion polypeptide comprises SEQ ID NO:7, or a polypeptide sequence having at least 90% sequence homology thereto.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An isolated polypeptide comprising the extracellular domain of canine tumour necrosis factor (TNF) receptor p80 polypeptide, or a TNF binding fragment thereof, wherein the extracellular domain comprises amino acid residues 23 to 260 of SEQ ID NO:14, or a sequence having at least 95% sequence identity thereto.

2. The polypeptide as claimed in claim 1, comprising amino acid residues 23 to 260 of SEQ ID NO:14.

3. The polypeptide as claimed in claim 1 or claim 2, consisting of amino acid residues 23 to 260 of SEQ ID NO:14.

4. A chimeric fusion polypeptide comprising the polypeptide as claimed in any one of claims 1 to 3, conjoined to a polypeptide comprising an Fc region of a canine IgG immunoglobulin heavy chain, or a fragment thereof, wherein the fragment comprises a CH2 constant domain and a CH3 constant domain.

5. The chimeric fusion polypeptide as claimed in claim 4, wherein the Fc region comprises a hinge region, a CH2 constant domain and a CH3 constant domain.

6. The chimeric fusion polypeptide as claimed in claim 4 or claim 5, wherein the chimeric fusion polypeptide comprises a linker peptide functionally interposed between the canine TNF receptor p80 polypeptide, or fragment thereof, and the polypeptide comprising the CH2 and CH3 domains.

7. The chimeric fusion polypeptide as claimed in any one of claims 4 to 6, wherein the Fc region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:5.

8. The chimeric fusion polypeptide as claimed in any one of claims 4 to 7, wherein the chimeric fusion polypeptide comprises an amino acid sequence

selected from the group consisting of SEQ ID NO:15 to 22 and a sequence having at least 90% sequence identity to any of the foregoing.

9. A pharmaceutical composition comprising the chimeric fusion polypeptide as claimed in any one of claims 4 to 8 and a pharmaceutically acceptable carrier or excipient.

10. Use of the polypeptide as claimed in any one of claims 1 to 3 or the chimeric fusion polypeptide as claimed in any one of claims 4 to 8 in the manufacture of a medicament for the treatment or prevention of a condition mediated by TNF expression in a canine in need thereof.

11. Use as claimed in claim 10, wherein the condition mediated by TNF expression is selected from the group consisting of an inflammatory mediated condition, a chronic inflammatory disease, arthritis, such as immune mediated polyarthritis, rheumatoid arthritis, osteoarthritis, polyarthritidies, juvenile idiopathic arthritis and psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriasis, systemic vasculitis, atopic dermatitis, congestive heart failure, refractory uveitis, bronchial asthma, allergic conditions, sepsis, shock, diabetes mellitus, and neuro-degenerative conditions, such as Alzheimer's disease, Parkinson's disease, stroke and amyotrophic lateral sclerosis.