

CLAIMS

1. A polypeptide comprising an immunoglobulin chain variable domain which binds to TNF-alpha, wherein the immunoglobulin chain variable domain comprises three complementarity determining regions (CDR1-CDR3) and four framework regions (FR1-FR4), wherein CDR1 comprises a sequence sharing 60% or greater sequence identity with SEQ ID NO: 1, CDR2 comprises a sequence sharing 80% or greater sequence identity with SEQ ID NO: 2 CDR3 comprises a sequence sharing 80% or greater sequence identity with SEQ ID NO: 3.
2. The polypeptide according to claim 1, wherein the residue of CDR3 corresponding to residue number 3 of SEQ ID NO: 3 is H.
3. The polypeptide according to either claim 1 or 2, wherein the sequence of CDR3 is SEQ ID NO: 3, SEQ ID NO: 70, SEQ ID NO: 71 or SEQ ID NO: 72.
4. The polypeptide according to any one of claims 1 to 3, wherein CDR1 comprises a sequence sharing 80% or greater sequence identity with SEQ ID NO: 1.
5. The polypeptide according to any one of claims 1 to 4, wherein the sequence of CDR1 is SEQ ID NO: 1, SEQ ID NO: 59 or SEQ ID NO: 60.
6. The polypeptide according to any one of claims 1 to 5, wherein the residue of CDR2 corresponding to residue number 10 of SEQ ID NO: 2 is H.
7. The polypeptide according to any one of claims 1 to 6 wherein the sequence of CDR2 is SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 2, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69.
8. The polypeptide according to any one of claims 1 to 7 which comprises SEQ ID NO: 8.
9. The polypeptide according to any one of claims 1 to 8, wherein the polypeptide is an antibody fragment.
10. The polypeptide according to any one of claims 1 to 9, which is selected from the list consisting of: a VHH, a VH, a VL, a V-NAR, a Fab fragment and a F(ab')₂ fragment.
11. The polypeptide according to any one of claims 1 to 10, which neutralizes human TNF-alpha cytotoxicity in the normal L929 assay with an EC₅₀ of 1 nM or less.
12. The polypeptide according to any one of claims 1 to 11, which is substantially resistant to one or more proteases.

13. The polypeptide according to claim 12, wherein the one or more proteases are present in a small intestine.
- 5 14. The polypeptide according to claim 12, wherein the one or more proteases are selected from the group consisting of enteropeptidase, trypsin, chymotrypsin and inflammatory bowel disease inflammatory proteases.
- 10 15. The polypeptide according to claim 14, wherein the inflammatory bowel disease inflammatory proteases are one or more proteases selected from the group consisting of MMP3, MMP12 and cathepsin.
16. A pharmaceutical composition comprising the polypeptide according to any one of claims 1 to 15 and one or more pharmaceutically acceptable diluents or carriers.
- 15 17. The pharmaceutical composition according to claim 16 wherein the composition is presented in enterically coated form.
- 20 18. Use of a polypeptide or pharmaceutical composition according to any one of claims 1 to 17 for the manufacture of a medicament for the treatment of autoimmune and/or inflammatory disease.
- 25 19. The use according to claim 18 wherein the autoimmune and/or inflammatory disease is selected from the list consisting of Crohn's disease, ulcerative colitis, irritable bowel syndrome, diabetes type II, glomerulonephritis, autoimmune hepatitis, Sjogren's syndrome, celiac disease, drug- or radiation-induced mucositis, pemphigus, psoriasis, eczema and scleroderma.
20. The use according to either claim 18 or 19 wherein the polypeptide is to be administered to a subject orally.