Claims

1. An isolated immunoglobulin variable domain that binds TNF-alpha comprising four framework regions (FR1 to FR4) and three complementarity determining regions (CDR1 to CDR3), wherein:
a) CDR1 comprises: amino acid sequence TADMG (SEQ ID NO: 193);
b) CDR2 comprises: amino acid sequence RISGIDGTTYYDEPVKG (SEQ ID NO: 261); and
c) CDR3 comprises: amino acid sequence PRYADQWSAYDY (SEQ ID NO: 329).

2. The isolated immunoglobulin variable domain according to claim 1, wherein CDR1 consists of the amino acid sequence TADMG (SEQ ID NO: 193); CDR2 consists of the amino acid sequence RISGIDGTTYYDEPVKG (SEQ ID NO: 261); and CDR3 consists of the amino acid sequence PRYADQWSAYDY (SEQ ID NO: 329).

3. The isolated immunoglobulin variable domain according to claim 1, wherein the immunoglobulin variable domain is a humanized immunoglobulin variable domain.

4. The isolated immunoglobulin variable domain according to claim 1, wherein the immunoglobulin variable domain is NC55TNF_NC7 (SEQ ID NO: 125).

5. An isolated immunoglobulin variable domain that binds TNF-alpha, wherein the immunoglobulin variable domain is a humanized variant of immunoglobulin variable domain NC55TNF_NC7 (SEQ ID NO: 125).

6. An isolated polypeptide comprising at least one immunoglobulin variable domain according to claim 1.

7. The isolated polypeptide according to claim 6, further comprising at least one immunoglobulin variable domain that binds human serum albumin.

8. The isolated polypeptide according to claim 7, wherein the at least one immunoglobulin variable domain that binds human serum albumin has the CDR sequences present in ALB 8 (SEQ ID NO: 102).

9. The isolated polypeptide according to claim 7, wherein the immunoglobulin variable domain that binds TNF-alpha is linked to the immunoglobulin variable domain that binds human serum albumin via a linker.

10. The isolated polypeptide according to claim 9, wherein the linker that links the immunoglobulin variable domain that binds TNF-alpha to the immunoglobulin variable domain that binds human serum albumin is an amino acid sequence.

11. The isolated polypeptide according to claim 10, wherein the linker that links the immunoglobulin variable domain that binds TNF-alpha to the immunoglobulin variable domain that binds human serum albumin is an amino acid sequence that comprises 3 to 40 amino acids.

12. The isolated polypeptide according to claim 7, wherein the at least one immunoglobulin variable domain that binds human serum albumin is a humanized immunoglobulin variable domain.

13. The isolated polypeptide according to claim 7, wherein the at least one immunoglobulin variable domain that binds human serum albumin is selected from ALB3 (SEQ ID NO: 87), ALB 4 (SEQ ID NO: 88), ALB 5 (SEQ ID NO: 89), ALB 6 (SEQ ID NO: 100), ALB 7 (SEQ ID NO: 101), ALB 8 (SEQ ID NO: 102), ALB 9 (SEQ ID NO: 103), and ALB 10 (SEQ ID NO: 104).

14. The isolated polypeptide according to claim 6, wherein the polypeptide is pegylated.

15. An isolated nucleic acid comprising a nucleotide sequence that encodes an immunoglobulin variable domain according to claim 1.

16. An isolated host cell comprising a nucleic acid according to claim 15.

17. A method for preparing an immunoglobulin variable domain, comprising cultivating or maintaining a host cell according to claim 16 under conditions such that said host cell produces the immunoglobulin variable domain, optionally further comprising isolating the immunoglobulin variable domain.

18. A pharmaceutical composition, comprising at least one immunoglobulin variable domain according to claim 1, and optionally at least one pharmaceutically acceptable carrier.