Claims

1. A specific binding member that binds the Extra Domain-A (ED-A) isoform of fibronectin for use in a method of treatment of inflammatory bowel disease (IBD), such as Crohn's disease (CD) or ulcerative colitis (UC).

2. Use of a specific binding member that binds the ED-A isoform of fibronectin for the manufacture of a medicament for treating IBD, such as CD or UC.

3. A method of treating IBD in a patient, the method comprising administering to a patient a therapeutically effective amount of a medicament comprising a specific binding member which binds the ED-A isoform of fibronectin.

4. The specific binding member for use according to claim 1, the use of claim 2, or the method of claim 3, wherein the specific binding member binds the ED-A of fibronectin.

5. The specific binding member for use according to claim 1 or 4, the use of claim 2 or 4, or the method of claim 3 or 4, wherein the specific binding member is conjugated to an immunosuppressive or anti-inflammatory molecule, such as IL-10.

6. The specific binding member for use according to, the use or method of claim 5, wherein the specific binding member is conjugated to the bioactive molecule by a cleavable linker.

7. A specific binding member that binds the ED-A isoform of fibronectin for use in a method of diagnosis of IBD.

8. The specific binding member for use according to claim 7, wherein the specific binding member binds the ED-A of fibronectin.

9. The specific binding member for use according to claim 7 or 8, wherein the specific binding member is conjugated to a detectable label or a radioisotope.

10. A specific binding member that binds the ED-A isoform of fibronectin for use in the delivery to the neovasculature of IBD tissue of a molecule conjugated to the specific binding member.

11. The specific binding member for use according to claim 10, wherein the specific binding member binds the ED-A of fibronectin.

12. The specific binding member for use according to claim 10 or 11, wherein the molecule is an immunosuppressive or anti-inflammatory molecule, such as IL-10.

13. The specific binding member for use according to any one of claims 1 and 4-12, the use of claim 2, or the method of claim 3, wherein the specific binding member comprises a VH domain comprising a framework and a set of complementarity determining regions HCDR1, HCDR2 and HCDR3, wherein

HCDR1 has amino acid sequence SEQ ID NO: 1,
HCDR2 has amino acid sequence SEQ ID NO: 2,
HCDR3 has amino acid sequence SEQ ID NO: 3;

or wherein the VH domain comprises a set of complementarity determining regions having ten or fewer amino acid substitutions within the complementarity determining regions HCDR1, HCDR2 and HCDR3.

14. The specific binding member for use according to, the use or the method of claim 13, wherein the VH domain framework is a human germline framework.

15. The specific binding member for use according to, the use or the method of claim 14, wherein the VH domain has amino acid sequence SEQ ID NO: 7.

16. The specific binding member for use according to, the use or the method of any of one of claims 13-15, wherein the specific binding member further comprises a VL domain comprising a set of complementarity determining regions LCDR1, LCDR2 and LCDR3 and a framework.

17. The specific binding member for use according to, the use or the method of claim 16, wherein

LCDR1 has amino acid sequence SEQ ID NO: 4,

LCDR2 has amino acid sequence SEQ ID NO: 5, and

LCDR3 has amino acid sequence SEQ ID NO: 6;

or wherein the VL domain comprises a set of complementarity determining regions having ten or fewer amino acid substitutions within the complementarity determining regions LCDR1, LCDR2 and LCDR3.

18. The specific binding member for use according to, the use or the method of claim 16 or 17, wherein the VL domain framework is a human germline framework.

19. The specific binding member for use according to, the use or the method of claim 18, wherein the VL domain has amino acid sequence SEQ ID NO: 8.

20. The specific binding member for use according to, the use or the method of any one of claims 17-19, wherein the specific binding member comprises a single chain Fv.

21. The specific binding member for use according to, the use or the method of claim 20, wherein the binding member is a small immunoprotein (SIP).

22. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is not ulcerative colitis (UC).

23. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is collagenous colitis.

24. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is lymphocytic colitis.

25. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is ischaemic colitis.

26. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is diversion colitis.

27. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is Behçet's disease.

28. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is indeterminate colitis.

29. The specific binding member for use according to, the use or the method of any one of the preceding claims, wherein the IBD is Crohn's disease (CD).

30. A conjugate comprising a binding member which binds the ED-A isoform of fibronectin conjugated to IL-10, wherein the conjugate has the sequence shown in SEQ ID NO: 13.

Claims

1. Use of an antibody conjugate for the preparation of a medicament for the treatment of inflammatory bowel disease (IBD), wherein the antibody conjugate comprises an antibody, or an antigen-binding fragment thereof, that binds the Extra Domain-A (ED-A) of fibronectin and is conjugated to an immunosuppressive or anti-inflammatory molecule, said antibody comprising a V_H domain and a V_L domain, wherein

the V_H domain comprises the heavy chain CDR1, CDR2 and CDR3 amino acid sequences in SEQ ID NO: 7; and

the V_L domain comprises the light chain CDR1, CDR2 and CDR3 amino acid sequences in SEQ ID NO: 8.

2. Use of an antibody conjugate for the preparation of a medicament for the delivery of an immunosuppressive or anti-inflammatory molecule to sites of inflammatory bowel disease (IBD) in a patient, wherein the antibody conjugate comprises an antibody, or an antigen-binding fragment thereof, that binds the Extra Domain-A (ED-A) of fibronectin and is conjugated to the immunosuppressive or anti-inflammatory molecule, said antibody comprising a V_H domain and a V_L domain, wherein

the V_H domain comprises the heavy chain CDR1, CDR2 and CDR3 amino acid sequences in SEQ ID NO: 7; and

the V_L domain comprises the light chain CDR1, CDR2 and CDR3 amino acid sequences in SEQ ID NO: 8.

3. The use according to claim 1 or 2, wherein the V_H domain and/or the V_L domain comprises a human germline framework.

4. The use according to claim 3, wherein the human germline framework in the V_H domain is from a human DP47 gene and/or the human germline framework in the V_L domain is from a human DPK22 gene.

5. The use according to claim 1 or 2, wherein the V_H domain comprises the amino acid sequence of SEQ ID NO: 7; and the V_L domain comprising the amino acid sequence of SEQ ID

NO: 8.

6. The use according to any one of claims 1-5, wherein said antibody or antigen-binding fragment is conjugated to a detectable label.

7. The use according to claim 6, wherein the detectable label is a radioisotope.

8. The use according to any one of claims 1-7, wherein said anti-inflammatory molecule is a cytokine.

9. The use according to claim 8, wherein said cytokine is human interkeukin-10 (IL-10).

10. The use according to any one of claims 1-9, wherein said antibody or antigen-binding fragment is conjugated to said immunosuppressive or anti-inflammatory molecule by a cleavable linker.

11. The use according to any one of claims 1-9, wherein said antibody or antigen-binding fragment is conjugated to said immunosuppressive or anti-inflammatory molecule via a peptide linker.

12. The use according to claim 11, wherein said peptide linker comprises 15 amino acids.

13. The use according to claim 12, wherein said peptide linker consists of the amino acid residues $(SSSSG)_3$ (SEQ ID NO: 10).

14. The use according to any one of claims 1-13, wherein the antibody conjugate comprises an antigen-binding fragment of said antibody.

15. The use according to claim 14, wherein said antigen-binding fragment comprises a small immunoprotein (SIP).

16. The use according to claim 14 or 15, wherein said antigen-binding fragment comprises a single chain Fv (scFv).

17. The use according to claim 16, wherein the V_H domain and the V_L domain in the scFv are conjugated to each other via an amino acid linker.

18. The use according to claim 17, wherein said amino acid linker comprises 5 to 25 amino acids.

19. The use according to claim 14 or 15, wherein said antigen-binding fragment is a diabody that comprises a polypeptide comprising the V_H and V_L domains, wherein the V_H and V_L domains in the polypeptide are conjugated to each other via an amino acid linker comprising 1-5 amino acids.

20. The use according to claim 19, wherein said amino acid linker consists of the amino acid residues GGSGG (SEQ ID NO: 9).

21. The use according to claim 20, wherein said antibody conjugate comprises (i) the diabody and (ii) human interleukin-10 (IL-10) conjugated to the V_L domain of the diabody via a peptide linker comprising the amino acid residues $(SSSSG)_3$ (SEQ ID NO: 10).

22. The use according to claim 20, wherein said antibody conjugate consists of (i) the diabody and (ii) human interleukin-10 (IL-10) conjugated to the V_L domain of the diabody via a peptide linker consisting of the amino acid residues $(SSSSG)_3$ (SEQ ID NO: 10).

23. Use of an antibody conjugate for the preparation of a medicament for the treatment of inflammatory bowel disease (IBD), wherein said antibody conjugate comprises the amino acid sequence of SEQ ID NO: 13.

24. Use of an antibody conjugate for the preparation of a medicament for the treatment of inflammatory bowel disease (IBD), wherein said antibody conjugate consists of the amino acid sequence of SEQ ID NO: 13.

25. Use of an antibody conjugate for the preparation of a medicament for the delivery of human IL-10 to sites of inflammatory bowel disease (IBD) in a patient, wherein said antibody conjugate comprises the amino acid sequence of SEQ ID NO: 13.

26. Use of an antibody conjugate for the preparation of a medicament for the delivery of human IL-10 to sites of inflammatory bowel disease (IBD) in a patient, wherein said antibody conjugate consists of the amino acid sequence of SEQ ID NO: 13.

27. The use according to any one of the preceding claims, wherein said IBD is selected from any of the following: ulcerative colitis (UC), collagenous colitis, lymphocytic colitis, ischaemic colitis, diversion colitis, Behcet's disease, indeterminate colitis, and Crohn's disease (CD).