

Claims

1. A human monoclonal antibody or an antigen-binding portion thereof that specifically binds to Mucosal Addressin Cell Adhesion Molecule (MAdCAM), wherein the antibody comprises the amino acid sequences of SEQ ID NO: 148 and SEQ ID NO: 150.
2. The human monoclonal antibody of claim 1, wherein SEQ ID NO: 148 is encoded by the nucleotide sequence of SEQ ID NO: 149.
3. The human monoclonal antibody of claim 1, wherein SEQ ID NO: 150 is encoded by the nucleotide sequence of SEQ ID NO: 35.
4. The human monoclonal antibody or antigen-binding portion according to claim 1, wherein said antibody or portion possesses at least one of the following properties:
 - (a) has a selectivity for MAdCAM over VCAM or fibronectin of at least 100 fold;
 - (b) binds to human MAdCAM with a K_d of 3×10^{-10} M or less; or
 - (c) inhibits the binding of $\alpha 4\beta 7$ expressing cells to human MAdCAM.
5. A nucleic acid sequence encoding the amino acid sequences of claim 1 or 2.
6. The nucleic acid sequence of claim 5, wherein nucleotides defined by SEQ ID NO: 149 encodes amino acid sequence SEQ ID NO: 148.
7. The nucleic acid sequence of claim 5, wherein the nucleotides defined by SEQ ID NO: 35 without the signal sequence encodes amino acid SEQ ID NO: 150.
8. A cell comprising the nucleic acid sequence of claim any one of claims 5-7.
9. A hybridoma cell line that produces the human monoclonal antibody according to claim 1.

10. The human monoclonal antibody or antigen binding portion thereof produced by the hybridoma cell line according to claim 9.
11. A human monoclonal antibody or an antigen-binding portion thereof, wherein the heavy chain of said antibody or portion thereof comprises the heavy chain CDR1, CDR2 and CDR3 or wherein the light chain comprises the light chain CDR1, CDR2 and CDR3 of a monoclonal antibody encoded by the nucleic acid of any one of claims 5-7.
12. The human monoclonal antibody according to any one of the preceding claims is an immunoglobulin G (IgG), an IgM, an IgE, and IgA or an IgD molecule, a humanized antibody, a chimeric antibody or a bispecific antibody.
13. The antigen-binding portion according to any one of the preceding claims is an Fab fragment, an F(ab')₂ fragment, an FV fragment or a single chain antibody.
14. A pharmaceutical composition comprising an effective amount of the monoclonal antibody or antigen-binding portion thereof of any one of the preceding claims.
15. Use of the monoclonal antibody or antigen-binding portion thereof according to any one of claims 1 to 4 or 10 to 13 in the manufacture of a pharmaceutical composition for treating inflammatory disease in a subject in need thereof, wherein said antibody or antigen-binding portion inhibits binding of MAdCAM to $\alpha 4\beta 7$.
16. The use of claim 15, wherein the inflammatory disease is inflammatory disease of the gastrointestinal tract.
17. The use of claim 16, wherein the inflammatory disease of the gastrointestinal tract is selected from the group consisting of inflammatory bowel disease, Crohn's disease, ulcerative

colitis, diverticula disease, gastritis, liver disease, primary biliary sclerosis and sclerosing cholangitis.

18. The use of claim 17, wherein the inflammatory bowel disease is Crohn's disease, ulcerative colitis or both.

19. The use of claim 18, wherein the inflammatory diseases are insulin-dependent diabetes and graft versus host disease.

20. An isolated cell line that produces the monoclonal antibody or antigen-binding portion according to any one of the preceding claims or the heavy chain or light chain of said antibody or of said portion thereof.

21. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof or the light chain or an antigen-binding portion thereof of an antibody according to any one of the preceding claims, and wherein the nucleic acid sequence that encodes the heavy chain variable sequence is SEQ ID NO: 149, and wherein the nucleic acid sequence that encodes the light chain sequence is SEQ ID NO: 35.

22. A vector comprising the nucleic acid molecule according to claim 21, wherein the vector optionally comprises an expression control sequence operably linked to the nucleic acid molecule.

23. A host cell comprising the vector according to claim 22 or the nucleic acid molecule according to claim 20.

24. A host cell according to claim 23 comprising a nucleic acid molecule encoding the heavy chain variable sequence or an antigen-binding portion thereof and a nucleic acid molecule

encoding the light chain or an antigen-binding portion thereof of an antibody or antigen-binding portion according to any one of claims 1-7.

25. An *ex vivo* method for producing a human monoclonal antibody or antigen-binding portion thereof that specifically binds MAdCAM, comprising culturing the host cell according to claim 23 or 24 or the cell line according to claim 20 under suitable conditions and recovering said antibody or antigen-binding portion.

26. A non-human transgenic animal or transgenic plant comprising (a) nucleic acid molecule encoding the heavy chain variable sequence or an antigen-binding portion thereof; (b) a nucleic acid molecule encoding the light chain or an antigen-binding portion thereof; or (c) both (a) and (b) of an antibody according to any one of claims 1-3, wherein the non-human transgenic animal or transgenic plant expresses said heavy chain variable or light chain sequence or both.

27. A pharmaceutical composition comprising the antibody of any one of claims 1-3.

28. The pharmaceutical composition of claim 27 further comprising one or more additional anti-inflammatory or immunomodulatory agents.

29. The pharmaceutical composition according to claim 28, wherein the one or more additional anti-inflammatory or immunomodulatory agents are selected from the group consisting of: corticosteroids, aminosaliclates, azathioprine, methotrexate, cyclosporin, FK506, IL-10, GM-CSF, rapamycin, anti-TNF α agents and adhesion molecule antagonists.

30. A vaccine comprising an effective amount of the human antibody thereof according to any one of claims 1-7 or antigen-binding portion and a pharmaceutically acceptable carrier.

31. The vaccine according to claim 30, wherein the vaccine is mucosal.

32. An *ex vivo* method of manufacturing a human monoclonal antibody or an antigen-binding fragment portion thereof that specifically binds to Mucosal Addressin Cell Adhesion Molecule (MAdCAM), wherein the antibody comprises the amino acid sequences of SEQ ID NO: 148 and SEQ ID NO: 150.
33. The method of claim 32, wherein the human monoclonal antibody amino acid sequence identified by SEQ ID NO: 148 is encoded by the nucleotide sequence of SEQ ID NO: 149.
34. The method of claim 32 or 33, wherein the human monoclonal antibody amino acid sequence identified by SEQ ID NO: 150 is encoded by the nucleotide sequence of SEQ ID NO: 35 without the signal sequence.
35. A monoclonal antibody, or antigen-binding portion thereof, that binds MAdCAM comprising the variable region of the light chain of SEQ ID NO: 150 and the variable region of the heavy chain of SEQ ID NO: 148.
36. A monoclonal antibody, or antigen-binding fragment thereof, that binds MAdCAM comprising a heavy chain variable region encoded by nucleotide SEQ ID NO: 149, and a light chain variable region encoded by nucleotide SEQ ID NO: 35.
37. The monoclonal antibody or antigen-binding portion thereof according to any one of claims 1 to 4 or 10 to 13 for use in therapy.