

[0010] The disclosure provides vectors and host cells comprising said nucleic acid molecules, as well as methods of recombinantly producing the polypeptides encoded by the nucleic acid molecules.

[0011] Non-human transgenic animals or plants that express the heavy and/or light chain of said anti-MAdCAM antibody, or antigen-binding portion thereof, are also provided.

[0011a] In one aspect, the present disclosure provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a heavy chain, or an antigen-binding portion thereof, and a nucleotide sequence that encodes or a light chain, or an antigen-binding portion thereof, of a human monoclonal antibody that specifically binds to Mucosal Addressin Cell Adhesion Molecule (MAdCAM), wherein the nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof comprises SEQ ID NO: 149 and the nucleotide sequence that encodes the light chain or an antigen-binding portion thereof comprises SEQ ID NO: 35.

[0011b] In another aspect, the present disclosure provides a vector comprising the nucleic acid as described herein. In yet another aspect, the present disclosure provides a host cell comprising the vector as described herein. In yet another aspect, the present disclosure provides a host cell comprising a first nucleic acid sequence encoding a heavy chain, or an antigen-binding portion thereof, and a second nucleic acid sequence encoding the light chain, or an antigen-binding portion thereof, of a monoclonal antibody that binds to human MAdCAM, wherein said first nucleic acid has a sequence of SEQ ID NO: 149, and the second nucleic acid has a sequence of SEQ ID NO: 35.

[0011c] In a further aspect, the present disclosure provides a method for producing a human monoclonal antibody or antigen-binding portion thereof that specifically binds MAdCAM, comprising culturing the host cell as described herein under suitable conditions and recovering said antibody or antigen-binding portion. ~~In a further aspect, the present disclosure provides a 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 nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof comprises SEQ ID NO: 149 and the nucleotide sequence that encodes the light chain or an antigen-binding portion thereof comprises SEQ ID NO: 35.

[0012] In examples, a human monoclonal antibody or an antigen-binding portion thereof is provided that specifically binds to Mucosal Addressin Cell Adhesion Molecule (MAdCAM).

[0013] In examples, the human monoclonal antibody or antigen-binding portion possesses at least one of the following properties: (a) binds to human cells; (b) has a selectivity for MAdCAM over VCAM or fibronectin of at least 100 fold; (c) binds to human MAdCAM with a K_d of 3×10^{-10} M or less; or (d) inhibits the binding of $\alpha_4\beta_7$ expressing cells to human MAdCAM. (e) inhibits the recruitment of lymphocytes to gastrointestinal lymphoid tissue.

[0014] In examples, the human monoclonal antibody or antigen-binding portion binds human MAdCAM with a K_d of 3×10^{-10} M or less and inhibits $\alpha_4\beta_7$ binding to human MAdCAM.

[0015] In examples, the heavy chain comprises an amino acid sequence at least 80%, 85%, or 90% identical to SEQ ID NO: 148.

[0016] In examples, the heavy chain comprises an amino acid sequence identical to SEQ ID NO: 148.

[0017] In examples, heavy chain comprises between 1 and 25 amino acid substitutions as compared to SEQ ID NO: 148.

[0018] In examples, the heavy chain comprises between 1 and 10 amino acid substitutions as compared to SEQ ID NO: 148.

CLAIMS

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a heavy chain, or an antigen-binding portion thereof, ~~or~~ and a nucleotide sequence that encodes a light chain, or an antigen-binding portion thereof, of a human monoclonal antibody that specifically binds to Mucosal Addressin Cell Adhesion Molecule (MAdCAM), wherein the nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof comprises SEQ ID NO: 149 and the nucleotide sequence that encodes the light chain or an antigen-binding portion thereof comprises SEQ ID NO: 35.
2. The isolated nucleic acid molecule of claim 1, wherein nucleotide sequence defined by SEQ ID NO: 149 encodes amino acid sequence SEQ ID NO: 148 without the signal sequence.
3. The isolated nucleic acid molecule of claim 1, wherein the nucleotide sequence defined by SEQ ID NO: 35 encodes amino acid SEQ ID NO: 150 without the signal sequence.
4. A vector comprising the nucleic acid of claim 1.
5. The vector of claim 4 comprising an expression control sequence operably linked to the nucleic acid.
6. A host cell comprising the vector of claim 5.
7. A host cell comprising a first nucleic acid sequence encoding a heavy chain, or an antigen-binding portion thereof, and a second nucleic acid sequence encoding the light chain, or an antigen-binding portion thereof, of a monoclonal antibody that binds to human MAdCAM, wherein said first nucleic acid has a sequence of SEQ ID NO: 149, and the second nucleic acid has a sequence of SEQ ID NO: 35.
8. The host cell of claim 7, wherein the sequence of SEQ ID NO: 149 encodes amino acid sequence SEQ ID NO: 148 without the signal sequence.

9. The host cell of claim 7, wherein the sequence of SEQ ID NO: 35 encodes amino acid SEQ ID NO: 150 without the signal sequence.

10. A method for producing a human monoclonal antibody or antigen-binding portion thereof that specifically binds MAdCAM, comprising culturing the host cell according to claim 7 under suitable conditions and recovering said antibody or antigen-binding portion, wherein the nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof comprises SEQ ID NO: 149 and the nucleotide sequence that encodes the light chain or an antigen-binding portion thereof comprises SEQ ID NO: 35.

~~11. — A 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 nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof comprises SEQ ID NO: 149 and the nucleotide sequence that encodes the light chain or an antigen-binding portion thereof comprises SEQ ID NO: 35.~~

~~1211.~~ The method of claim ~~1110~~, wherein nucleotide sequence defined by SEQ ID NO: 149 encodes amino acid sequence SEQ ID NO: 148 without the signal sequence.

~~1312.~~ The method of claim ~~1110~~, wherein the nucleotide sequence defined by SEQ ID NO: 35 encodes amino acid SEQ ID NO: 150 without the signal sequence.