

CLAIMS

1. An isolated antibody or an antigen-binding fragment thereof, comprising an immunoglobulin heavy chain variable region that comprises an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 35; and an immunoglobulin light chain variable region that comprises an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 5, wherein the antibody or antigen-binding fragment thereof is capable of binding specifically:

to a biantennary Le^B/Le^B antigen comprising Fuc₄(Galβ1→3GlcNAc)₂ **[I]** or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc]₂ **[III]**,

to a biantennary Le^Y/Le^Y antigen comprising Fuc₄(Galβ1→4GlcNAc)₂ **[III]** or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc]₂ **[IV]**,

to a biantennary Le^B/Le^Y antigen comprising Fuc₂(Galβ1→3GlcNAc)[Fuc₂(Galβ1→4GlcNAc)] **[V]**, or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc][Fucα1-2Galβ1-4(Fucα1-3)GlcNAc] **[VI]**,

and to a biantennary Le^Y/Le^B antigen comprising Fuc₂(Galβ1-4GlcNAc)[Fuc₂(Galβ1-3GlcNAc)] **[VII]** or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc][Fucα1-2Galβ1-3(Fucα1-4)GlcNAc] **[VIII]**,

and wherein the antibody or antigen-binding fragment thereof does not bind specifically to a monoantennary Le^x antigen that comprises Galβ1→4(Fucα1→3)GlcNAc **[IX]**, or to a biantennary Le^x antigen that comprises [Galβ1→4(Fucα1→3)GlcNAc]₂ **[X]**, or to a monoantennary Le^A antigen that comprises Galβ1-3(Fucα1-4)GlcNAc **[XI]**, or to a monoantennary H antigen type 2 that comprises Fucα1-2Galβ1-4GlcNAc **[XII]**, or to a biantennary H antigen type 2 that comprises (Fucα1-2Galβ1-4GlcNAc)₂ **[XIII]** or to a monoantennary H antigen type 1 that comprises Fucα1-2Galβ1-3GlcNAc **[XIV]**.

2. The isolated antibody or an antigen-binding fragment thereof of claim 1, comprising:

(a) an immunoglobulin heavy chain variable region that comprises a heavy chain complementarity determining region 1 (VH CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 2 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO:2; a heavy chain complementarity determining region 2 (VH CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 3 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO:3; and a heavy chain complementarity determining region 3 (VH CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 4 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO:4; and

(b) an immunoglobulin light chain variable region that comprises a light chain complementarity determining region 1 (VL CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 6 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO:6; a light chain complementarity determining region 2 (VL CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 7 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 7; and a light chain complementarity determining region 3 (VL CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 8 or an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 8.

3. The isolated antibody or an antigen-binding fragment thereof of claim 1, comprising (i), (ii), (iii), (iv), (v), or (vi), as follows, or a combination thereof:

(i) a VH CDR1 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 2, wherein the variant consists of a Y→A substitution at position 33 of SEQ ID NO: 35; and/or

(ii) a VH CDR3 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 4, wherein the variant consists of a Y→A substitution at position 104 of SEQ ID NO: 35;

(iii) a VH CDR3 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 4, wherein the variant consists of a A→H substitution at position 106 of SEQ ID NO: 35;

(iv) a VL CDR1 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 6, wherein the variant consists of a Y→A substitution at position 30 of SEQ ID NO: 5;

(v) a VL CDR2 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 7, wherein the variant consists of a G→A substitution at position 50 of SEQ ID NO: 5; or

(vi) a VL CDR3 comprising a variant of the amino acid sequence set forth in SEQ ID NO: 8, wherein the variant consists of a T→S substitution at position 93 of SEQ ID NO: 5.

4. An isolated antibody or antigen-binding fragment thereof, comprising: (a) an immunoglobulin heavy chain variable region that comprises a heavy chain complementarity determining region 1 (VH CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 2; a heavy chain complementarity determining region 2 (VH CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 3; and a heavy chain complementarity determining region 3 (VH CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 4; and (b) an immunoglobulin light chain variable region that comprises a light chain complementarity determining region 1 (VL CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 6; a light chain complementarity determining region 2 (VL CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 7; and a light chain complementarity determining region 3 (VL CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 8; wherein the antibody or antigen-binding fragment thereof is capable of binding specifically:

to a biantennary Le^B/Le^B antigen comprising Fuc₄(Galβ1→3GlcNAc)₂ [I] or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc]₂ [II],

to a biantennary Le^Y/Le^Y antigen comprising Fuc₄(Galβ1→4GlcNAc)₂ [III] or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc]₂ [IV],

to a biantennary Le^B/Le^Y antigen comprising Fuc₂(Galβ1→3GlcNAc)[Fuc₂(Galβ1→4GlcNAc)] [V], or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc][Fucα1-2Galβ1-4(Fucα1-3)GlcNAc] [VI],

and to a biantennary Le^Y/Le^B antigen comprising Fuc₂(Galβ1-4GlcNAc)[Fuc₂(Galβ1-3GlcNAc)] [VII] or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc][Fucα1-2Galβ1-3(Fucα1-4)GlcNAc] [VIII],

and wherein the antibody or antigen-binding fragment thereof does not bind specifically to a monoantennary Le^x antigen that comprises Galβ1→4(Fucα1→3)GlcNAc [IX], or to a biantennary Le^x antigen that comprises [Galβ1→4(Fucα1→3)GlcNAc]₂ [X], or to a monoantennary Le^A antigen that comprises Galβ1-3(Fucα1-4)GlcNAc [XI], or to a monoantennary H antigen type 2 that comprises Fucα1-2Galβ1-4GlcNAc [XII], or to a biantennary H antigen type 2 that comprises (Fucα1-2Galβ1-4GlcNAc)₂ [XIII] or to a monoantennary H antigen type 1 that comprises Fucα1-2Galβ1-3GlcNAc [XIV].

5. An isolated antibody or antigen-binding fragment thereof, comprising: an immunoglobulin heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 35; and an immunoglobulin light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 5, wherein the antibody or antigen-binding fragment thereof is capable of binding specifically:

to a biantennary Le^B/Le^B antigen comprising Fuc₄(Galβ1→3GlcNAc)₂ [I] or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc]₂ [II],

to a biantennary Le^Y/Le^Y antigen comprising Fuc₄(Galβ1→4GlcNAc)₂ [III] or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc]₂ [IV],

to a biantennary Le^B/Le^Y antigen comprising Fuc₂(Galβ1→3GlcNAc)[Fuc₂(Galβ1→4GlcNAc)] [V], or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc][Fucα1-2Galβ1-4(Fucα1-3)GlcNAc] [VI],

and to a biantennary Le^Y/Le^B antigen comprising Fuc₂(Galβ1-4GlcNAc)[Fuc₂(Galβ1-3GlcNAc)] **[VII]** or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc][Fucα1-2Galβ1-3(Fucα1-4)GlcNAc] **[VIII]**,

and wherein the antibody or antigen-binding fragment thereof does not bind specifically to a monoantennary Le^x antigen that comprises Galβ1→4(Fucα1→3)GlcNAc **[IX]**, or to a biantennary Le^x antigen that comprises [Galβ1→4(Fucα1→3)GlcNAc]₂ **[X]**, or to a monoantennary Le^A antigen that comprises Galβ1-3(Fucα1-4)GlcNAc **[XI]**, or to a monoantennary H antigen type 2 that comprises Fucα1-2Galβ1-4GlcNAc **[XII]**, or to a biantennary H antigen type 2 that comprises (Fucα1-2Galβ1-4GlcNAc)₂ **[XIII]** or to a monoantennary H antigen type 1 that comprises Fucα1-2Galβ1-3GlcNAc **[XIV]**.

6. An isolated antibody comprising an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO: 10 and an immunoglobulin light chain having the amino acid sequence set forth in SEQ ID NO: 11.

7. The isolated antibody of claim 6, which is monoclonal.

8. The isolated antibody or antigen-binding fragment thereof of claim 4, wherein the antibody is monoclonal.

9. The isolated antibody or antigen-binding fragment thereof of claim 4, wherein the antibody is a humanized antibody.

10. The isolated antibody or antigen-binding fragment thereof of claim 4, wherein the antigen-binding fragment is selected from a Fab fragment, an F(ab')₂ fragment, an Fv fragment, a single chain Fv (ScFv) antibody, and a diabody.

11. A pharmaceutical composition comprising: the isolated antibody or an antigen-binding fragment thereof of claim 4; and a pharmaceutical carrier.

12. The antibody or antigen-binding fragment of claim 4, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90 percent identity to the amino acid sequence set forth in SEQ ID NO: 35, and the immunoglobulin light chain variable region comprises an amino acid sequence that has at least 90 percent identity to the amino acid sequence set forth in SEQ ID NO: 5.

13. The antibody or antigen-binding fragment of claim 4, wherein the heavy chain variable region comprises an amino acid sequence that has at least 95 percent identity to the amino acid sequence set forth in SEQ ID NO: 35, and the immunoglobulin light chain variable region comprises an amino acid sequence that has at least 95 percent identity to the amino acid sequence set forth in SEQ ID NO: 5.

14. The antibody or antigen-binding fragment of claim 4, wherein the heavy chain variable region comprises an amino acid sequence that has at least 97 percent identity to the amino acid sequence set forth in SEQ ID NO: 35, and the immunoglobulin light chain variable region comprises an amino acid sequence that has at least 97 percent identity to the amino acid sequence set forth in SEQ ID NO: 5.