CLAIMS

We claim:

1. An isolated binding polypeptide comprising a CH1 domain, wherein the CH1 domain comprises an asparagine residue at amino acid position 114, according to Kabat numbering.

2. The binding polypeptide of claim 1, wherein the CH1 domain further comprises: any amino acid residue except proline at position 115, according to Kabat numbering; and a serine or threonine residue at position 116, according to Kabat numbering.

3. The binding polypeptide of claim 1 or 2, wherein the CH1 domain is an IgG1 CH1 domain, or variant thereof.

4. The binding polypeptide of claim 3, wherein the CH1 domain is a human IgG1 CH1 domain, or variant thereof.

5. The binding polypeptide of any one of the preceding claims, wherein the side chain of the asparagine residue is linked to a glycan though a β-glycosylamide linkage.

6. The binding polypeptide of claim 5, wherein the glycan is a biantennary glycan.

7. The binding polypeptide of claim 5 or 6, wherein the glycan is a naturally occurring mammalian glycoform.

8. The binding polypeptide of any one of claims 5-7, wherein the glycan comprises a reactive aldehyde group.

9. The binding polypeptide of any one of claims 5-8, wherein the glycan comprises an oxidized saccharide residue comprising a reactive aldehyde group.

10. The binding polypeptide of claim 9, wherein the oxidized saccharide residue is a terminal sialic acid or galactose.

11. The binding polypeptide of any one of claims 5-10, wherein the glycan is linked to an effector moiety.

12. The binding polypeptide of claim 11, wherein the effector moiety is a cytotoxin.

13. The binding polypeptide of claim 12, wherein the cytotoxin is selected from the group consisting of the cytotoxins listed in Table 1.

14. The binding polypeptide of claim 11, wherein the effector moiety is a detection agent.

15. The binding polypeptide of claim 11, wherein the effector moiety is a targeting moiety.

16. The binding polypeptide of claim 15, wherein the targeting moiety is a carbohydrate or glycopeptide.

17. The binding polypeptide of claim 15, wherein the targeting moiety is a glycan.

18. The binding polypeptide of claim of any one of claims 11-17, wherein the effector moiety is linked through an oxime or hydrazone linkage to saccharide residue of the glycan.

19. The binding polypeptide of claim 15, wherein the saccharide is a terminal sialic acid or galactose residue of the glycan.

20. The binding polypeptide of any one of claims 11-19, wherein the effector moiety comprises a pH-sensitive linker, disulfide linker, enzyme-senstive linker or other cleavable linker moiety.

21. The binding polypeptide of any one of claims 11-19, wherein the effector moiety comprises a linker moiety selected from the group of linker moieties depicted in Table 2 or 14.

22. An isolated binding polypeptide comprising a CH1 domain, wherein the CH1 domain comprises a free asparagine residue at amino acid position 114, according to Kabat numbering.

23. An isolated binding polypeptide comprising a CH1 domain, wherein the CH1 domain comprises a modified asparagine residue at amino acid position 114, according to Kabat numbering, wherein said asparagine residue is linked to an effector moiety.

24. The binding polypeptide of claim 23, wherein the effector moiety is linked through a side chain of the modified asparagine residue to a saccharide residue of a glycan.

25. The binding polypeptide of claim 24, wherein the saccharide is a terminal sialic acid or

galactose residue of the glycan.

26. The binding polypeptide of claim 24, wherein the effector moiety is linked through an oxime or hydrazone linkage to saccharide residue of the glycan.

27. The binding polypeptide of claim 24, wherein the saccharide is a terminal sialic acid or galactose residue of the glycan.

28. The binding polypeptide of any one of the preceding claims which is an antibody, or fragment or derivative thereof.

29. The binding polypeptide of any one of the preceding claims wherein the antibody, antibody fragment or derivative is linked to a drug effector moiety to form an antibody drug conjugate (ADC).

30. A composition comprising a binding polypeptide of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.

31. A method of treating a patient in thereof comprising administering an effective amount of the composition of claim 30.

32. An isolated polynucleotide encoding the binding polypeptide of any one of claims 1-29.

33. A vector comprising the polynucleotide of claims 32.

34. A host cell comprising the polynucleotide of claim 32 or vector of claim 33.

35. A method of making a binding polypeptide comprising expressing the polynucleotide of polynucleotide of claim 32 or vector of claim 33 in a cell.

CLAIMS

We claim:

1. An isolated antibody or antigen-binding fragment thereof comprising a CH1 domain, wherein the CH1 domain comprises an asparagine residue at amino acid position 114, according to Kabat numbering; any amino acid residue except proline at position 115, according to Kabat numbering; and a serine or threonine residue at position 116, according to Kabat numbering, wherein the side chain of said asparagine residue is linked to a glycan.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the CH1 domain is an IgG1 CH1 domain, or variant thereof, optionally wherein the IgG1 CH1 domain is a human IgG1 CH1 domain.

3. The antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the side chain of the asparagine residue is linked to a glycan though a β-glycosylamide linkage.

4. The antibody or antigen-binding fragment thereof of claim 3, wherein one or more of the following conditions are met:

a) the glycan is a biantennary glycan;

b) the glycan is a naturally occurring mammalian glycoform;

c) the glycan comprises a reactive aldehyde group;

d) the glycan comprises an oxidized saccharide residue comprising a reactive aldehyde group; and

e) the glycan is linked to an effector moiety.

5. The antibody or antigen-binding fragment thereof of claim 4, wherein one or more of the following conditions are met:

a) the oxidized saccharide residue is a terminal sialic acid or galactose;

b) the effector moiety is a cytotoxin;

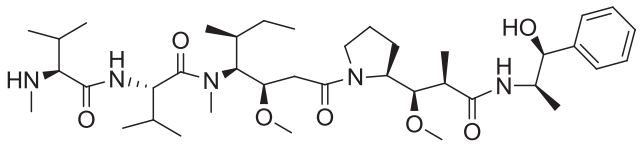
c) the effector moiety is a detection agent;

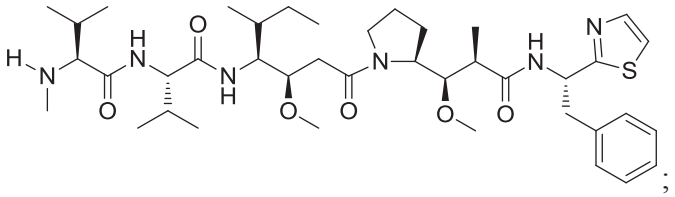
d) the effector moiety is a targeting moiety; and

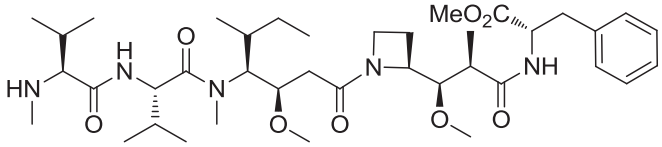
e) the effector moiety is linked through an oxime or hydrazone linkage to saccharide residue of the glycan.

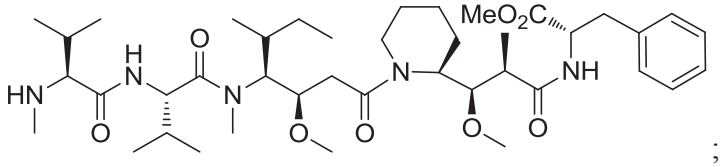
6. The antibody or antigen-binding fragment thereof of claim 5, wherein one or more of the following conditions are met:

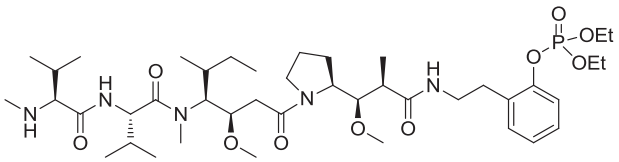
a) the cytotoxin is selected from the group consisting of:

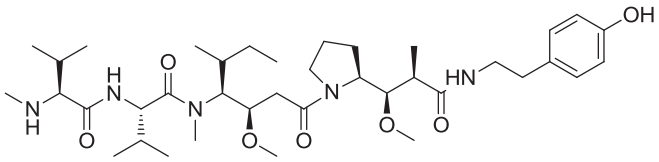

;

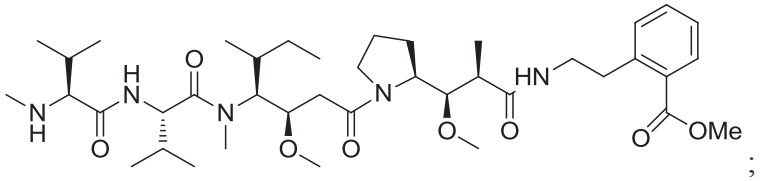

;

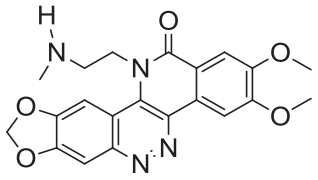

;

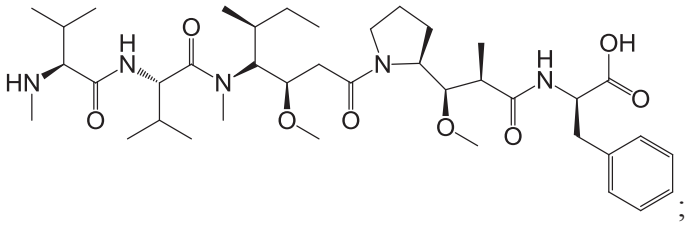

;

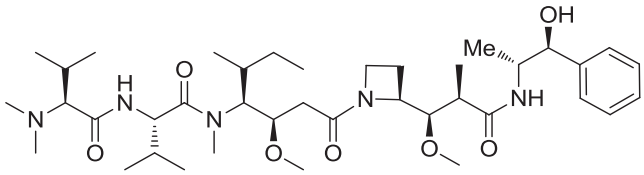

;

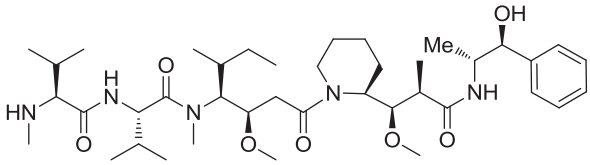

;

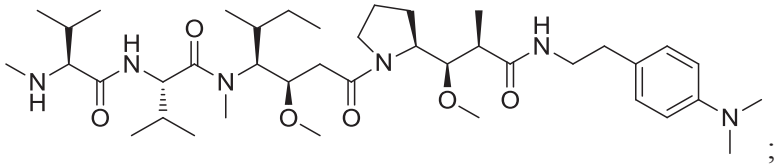

;

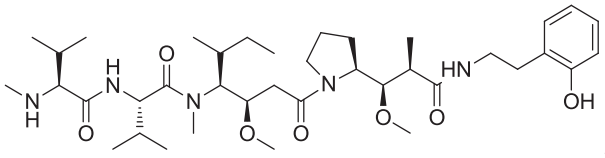

;

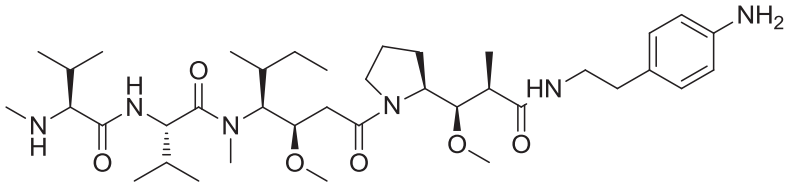

;

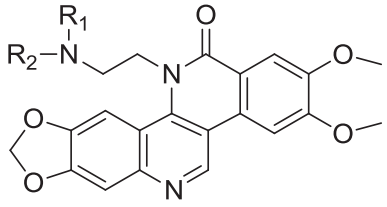

;

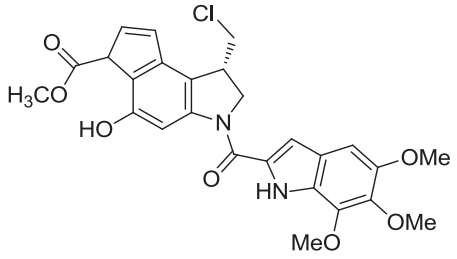

;

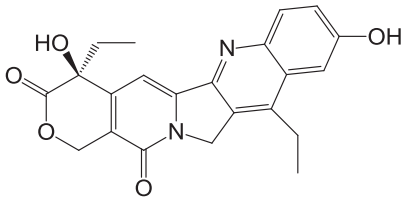

;

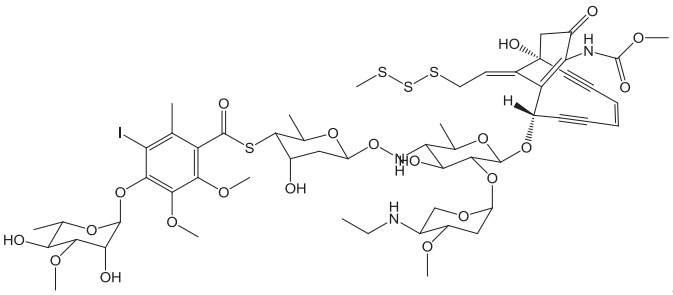

;

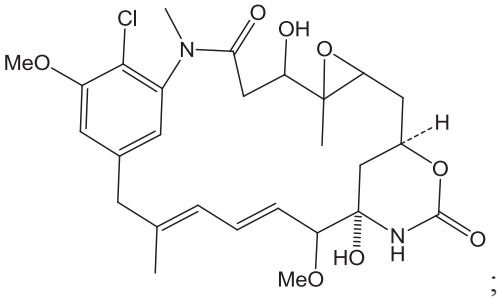

;

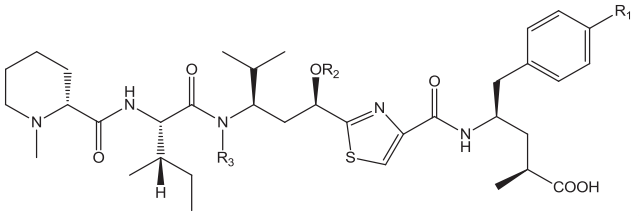

;


;


;


;


; and



;

wherein R_1 may be any alkyl, aryl, alkoxy, or aryloxy moiety and R_2 and R_3 may be any alkyl or aryl moiety;

b) the targeting moiety is a carbohydrate or glycopeptide;

c) the targeting moiety is a glycan;

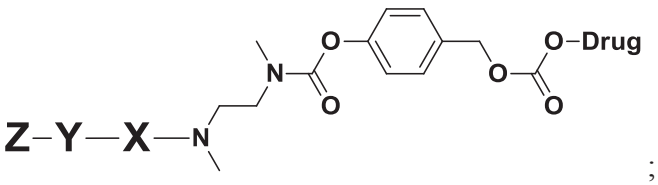
d) the saccharide is a terminal sialic acid or galactose residue of the glycan;

e) the effector moiety comprises a pH-sensitive linker, disulfide linker, enzyme-sensitive linker or other cleavable linker moiety; and

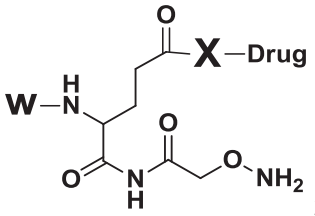
f) the effector moiety comprises a linker moiety selected from the group consisting of:



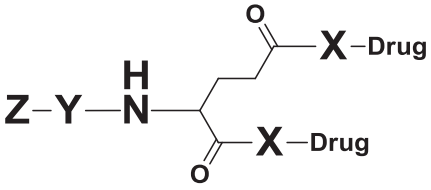
;



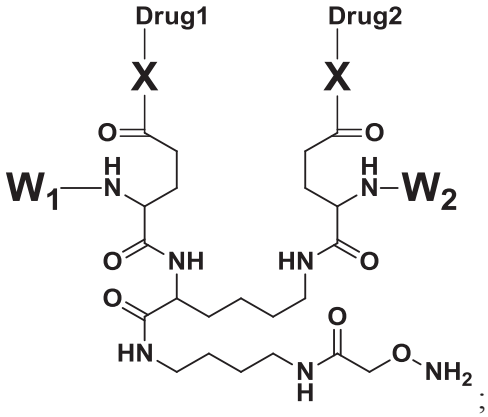
;



;

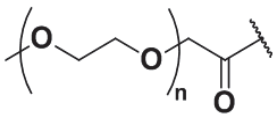


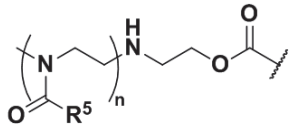
; and

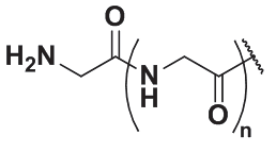


;

wherein W, W_1, and W_2 are each independently selected from the group consisting of:

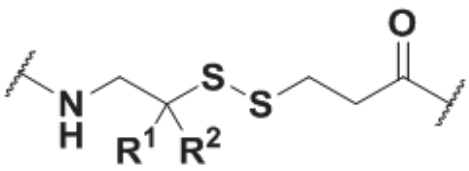


;


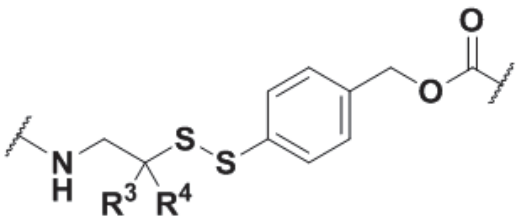
; or


;

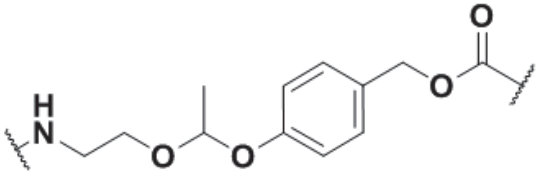
wherein each X is selected independently from:



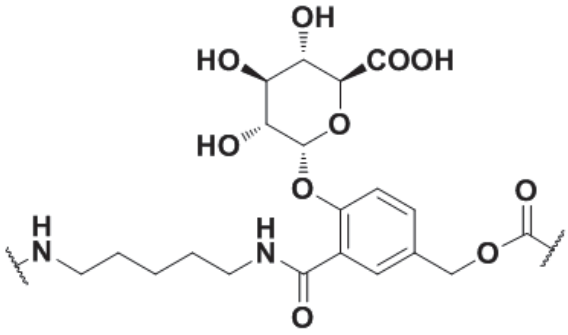
;



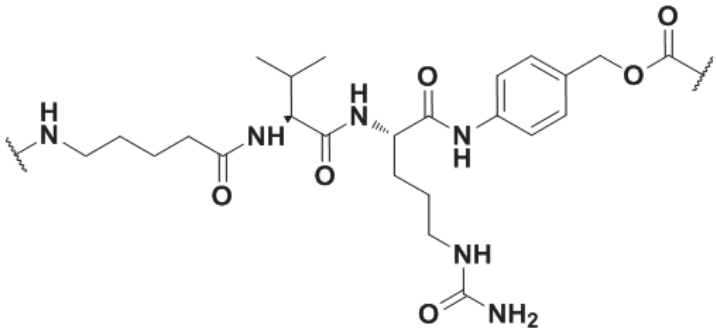
;



;

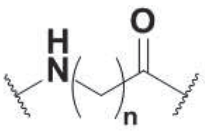


; and

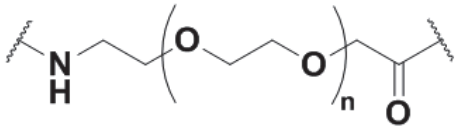


;

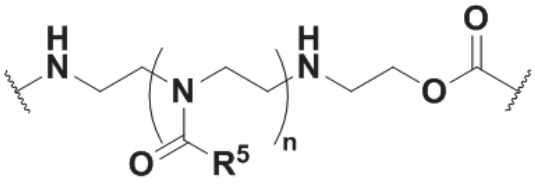
Y is selected from:



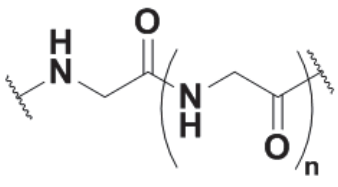
;



;

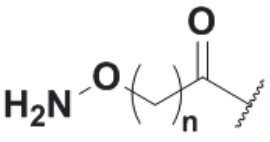
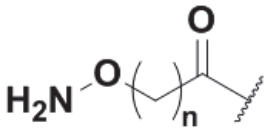


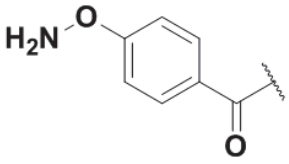
; and

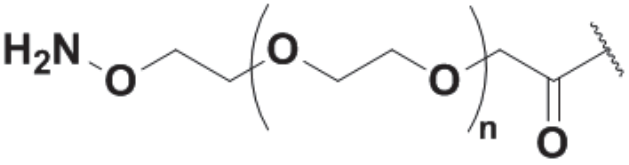


;

Z is selected from:



; ;


; and


;

and wherein R^1-R^5 are each independently selected from a group consisting of: H, an alkyl moiety, or an aryl moiety.

7. An isolated antibody or antigen-binding fragment thereof comprising a CH1 domain, wherein the CH1 domain comprises ~~a free~~ an unconjugated asparagine residue at amino acid position 114, according to Kabat numbering; any amino acid residue except proline at position 115, according to Kabat numbering; and a serine or threonine residue at position 116, according to Kabat numbering.

8. An isolated antibody or antigen-binding fragment thereof comprising a CH1 domain, wherein the CH1 domain comprises a modified asparagine residue at amino acid position 114, according to Kabat numbering; any amino acid residue except proline at position 115, according to Kabat numbering; and a serine or threonine residue at position 116, according to Kabat numbering, wherein said asparagine residue is linked to an effector moiety.

9. The antibody or antigen-binding fragment thereof of claim 8, wherein one or more of the following conditions are met:

a) the effector moiety is linked through a side chain of the modified asparagine residue to a saccharide residue of a glycan;

b) the saccharide is a terminal sialic acid or galactose residue of the glycan;

c) the effector moiety is linked through an oxime or hydrazone linkage to saccharide residue of the glycan; and

d) the saccharide is a terminal sialic acid or galactose residue of the glycan.

10. The antibody or antigen-binding fragment thereof of any one of the preceding claims, comprising an antibody, antibody fragment or derivative thereof, wherein the antibody or antigen-binding fragment thereof is optionally linked to a drug effector moiety to form an antibody drug conjugate (ADC).

11. A composition comprising an antibody or antigen-binding fragment thereof of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.

12. The composition of claim 11 for use in treatment of a disease or disorder.

13. An isolated polynucleotide encoding the antibody or antigen-binding fragment thereof of any one of claims 1-10, wherein the isolated polynucleotide is optionally comprised within a vector, and wherein the vector is optionally comprised within a host cell.

14. A method of making an antibody or antigen-binding fragment thereof comprising expressing the polynucleotide or vector of claim 13 in a cell.