domain (amino acids 29-157 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-C containing domain (amino acids 158-250 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-V and Ig-C domains (amino acids 29-250 of SEQ ID NO:73); or binds to an epitope within all or a portion of SEQ ID NO: 74 (mature human B7-H4) or binds to an epitope within all or a portion of SEQ ID NO: 73 (precursor human B7-H4). In some embodiments, the antibody binds to B7-H4 with an affinity of $\leq$ 50 nM. In some embodiments, the antibody is a monoclonal antibody. In some embodiments, the antibody is a human, humanized, or chimeric antibody. In some embodiments, the antibody is an IgG1, IgG2a or IgG2b antibody. In some embodiments, the antibody is an antibody fragment that binds B7-H4. In some embodiments, B7-H4 is human B7-H4 has the sequence of SEQ ID NO: 73.

[007a] In another aspect, there is provided an isolated monoclonal antibody that binds to B7-H4, wherein the antibody ~~has at least one of the following characteristics~~comprises: (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 58, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 59, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 60, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 61, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 62, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63~~(a) binds to an epitope within all or a portion of the B7-H4 Ig-V containing domain (amino acids 29-157 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-C containing domain (amino acids 158-250 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-V and Ig-C domains (amino acids 29-250 of SEQ ID NO:73); or binds to an epitope within all or a portion of SEQ ID NO: 74 (mature human B7-H4); or binds to an epitope within all or a portion of SEQ ID NO: 73 (precursor human B7-H4), and (b) binds to B7-H4 with an affinity of $\leq$ 50 nM~~.

[008] In some embodiments, the antibody comprises (a) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 7, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 10, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 6; or (b) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 15, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 14; or (c) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 23, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 26, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22; or (d) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 31, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 34, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 30; or (e) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 44, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40; or (f) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 60, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 59.

[009] In some embodiments, the antibody comprises (a) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 5, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 6, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 7; or (b) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 13, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 14, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 15; or (c) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 23; or (d) (i) HVR-H1

SEQ ID NO: 4, 28, a VH sequence of SEQ ID NO: 36, a VH sequence of SEQ ID NO: 37, a VH sequence of SEQ ID NO: 38, or a VH sequence of SEQ ID NO: 56.

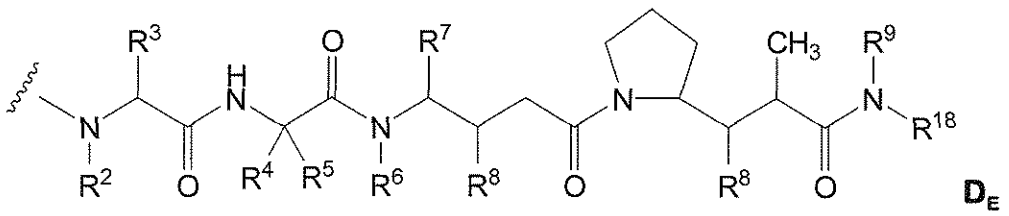
[016] In some embodiments, the antibody comprises a VL sequence of SEQ ID NO: 3, a VL sequence of SEQ ID NO: 11, a VL sequence of SEQ ID NO: 19, a VL sequence of SEQ ID NO: 27, a VL sequence of SEQ ID NO: 35, a VL sequence of SEQ ID NO: 55, or a VL sequence of SEQ ID NO: 57.

[017] In ~~another aspect, there is provided~~some embodiments, an isolated antibody comprisinges (a) a VH sequence of SEQ ID NO: 4 and a VL sequence of SEQ ID NO: 3; or (b) a VH sequence of SEQ ID NO: 20 and a VL sequence of SEQ ID NO: 19; or (c) a VH sequence of SEQ ID NO: 28 and a VL sequence of SEQ ID NO: 27; or (d) a VH sequence of SEQ ID NO: 36 and a VL sequence of SEQ ID NO: 35; or (e) a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 35; or (f) a VH sequence of SEQ ID NO: 38 and a VL sequence of SEQ ID NO: 35; or (g) a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 55; or (h) a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 57.

[017a] In another aspect, there is provided an isolated monoclonal antibody that binds to B7-H4 comprising a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 55.

[018] In another aspect, there is provided an isolated nucleic acid encoding the antibody described herein. In another aspect, there is provided a host cell comprising the nucleic acid described herein. Disclosed is a method of producing an antibody described herein. In another aspect, there is provided a method of producing an antibody comprising culturing the host cell described herein so that the antibody is produced.In some embodiments, the method comprises culturing the host cell comprising the nucleic acid that encodes an antibody.

[019] Disclosed are immunoconjugates. In another aspect, there is provided an immunoconjugate comprising the antibody described herein and a cytotoxic agent. In some embodiments, an immunoconjugate comprises an anti-B7-H4 antibody and a cytotoxic agent. In some embodiments, an immunoconjugate has the formula Ab-(L-D)p, wherein: (a) Ab is the an antibody described herein; (b) L is a linker; (c) D is a drug selected from a maytansinoid, an auristatin, a calicheamicin, a pyrrolobenzodiazepine, and a nemorubicin derivative; and (d) p ranges from 1-8. In some embodiments, D is an auristatin. In some such embodiments, D has formula D_E



D_E

wherein R^2 and R^6 are each methyl, R^3 and R^4 are each isopropyl, R^5 is H, R^7 is sec-butyl, each R^8 is independently selected from CH_3, O-CH_3, OH, and H; R^9 is H; and R^{18} is $-C(R^8)_2-C(R^8)_2$-aryl. In some embodiments, D is MMAE having the structure:

SEQ ID NO: 60; (l) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 61, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 62, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63.

[027a] In another aspect, there is provided a pharmaceutical formulation comprising the immunoconjugate described herein and a pharmaceutically acceptable carrier.

[028] In some embodiments, pharmaceutical formulations are provided. In some such embodiments, a pharmaceutical formulation comprises an immunoconjugate comprising an antibody that binds B7-H4, e.g., as described herein. In some embodiments, a pharmaceutical formulation further comprises an additional therapeutic agent. In some embodiments, the additional therapeutic agent is Avastin® (bevacizumab).

[28a] In another aspect, there is provided use of the immunoconjugate of any one of the embodiments described herein ~~in~~ for the ~~manufacture~~ preparation of a medicament for the treatment of a B7-H4-positive cancer in an individual~~treating an individual having a B7-H4-positive cancer~~. In yet another aspect, there is provided use of any one of the pharmaceutical formulations described herein for the preparation of a medicament for the treatment of a B7-H4 positive cancer.

[029] Disclosed are methods of treating individuals having B7-H4 positive cancers. In some such embodiments, a method comprises administering a pharmaceutical formulation comprising an immunoconjugate comprising an antibody that binds B7-H4, e.g., as described herein. In some such embodiments, the method comprises administering a pharmaceutical formulation comprising an immunoconjugate comprising an antibody that bind to the extracellular domain of B7-H4. In some embodiments, the B7-H4-positive cancer is selected from breast cancer, ovarian cancer, and endometrial cancer. In some embodiments, a method comprises administering an additional therapeutic agent to the individual. In some such embodiments, the additional therapeutic agent is Avastin® (bevacizumab).

[030] Disclosed are methods of inhibiting proliferation of a B7-H4-positive cell. In another aspect, there is provided an *in vitro* method of inhibiting proliferation of an B7-H4-positive cell, the method comprising exposing the cell to the immunoconjugate described herein under conditions permissive for binding of the immunoconjugate to B7-H4 on the surface of the cell, thereby inhibiting proliferation of the cell. In some embodiments, the method comprising exposing the cell to an immunoconjugate comprising an antibody that binds B7-H4 under conditions permissive for binding of the immunoconjugate to B7-H4 on the surface of the cell. In some embodiments, an antibody that binds B7-H4 is an antibody described herein. In some embodiments, proliferation of the cell is thereby inhibited. In some embodiments, the cell is a breast, ovarian, or endometrial cancer cell.

[031] In some embodiments, an antibody that binds B7-H4 is conjugated to a label. In some embodiments, an antibody that binds B-H4 is an antibody described herein. In some embodiments, the label is a positron emitter. In some embodiments, the positron emitter is ^{89}Zr.

[032] Disclosed is a method of detecting human B7-H4 in a biological sample. In one aspect, there is provided an *in vitro* method of detecting human B7-H4 in a biological sample comprising contacting the biological sample with the anti-B7-H4 antibody described herein under conditions permissive for binding of the anti-B7-H4 antibody to a naturally occurring human B7-H4, and detecting whether a complex is formed between the anti-B7-H4 antibody and a naturally occurring human B7-H4 in the biological sample.In some embodiments, a method comprises contacting the biological sample with an anti-B7-H4 antibody under conditions permissive for binding of the anti-B7-H4 antibody to a naturally occurring human B7-H4, and detecting whether a complex is formed between the anti-B7-H4 antibody and a naturally occurring human B7-H4 in the biological sample. In some embodiments, an anti-B7-H4 antibody is an antibody described

WHAT IS CLAIMED IS:

1. An isolated monoclonal antibody that binds to B7-H4, wherein the antibody comprises:

(i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 58, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 59, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 60, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 61, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 62, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63.

2. The antibody of claim 1, wherein the antibody is a humanized or chimeric antibody.

3. The antibody of claim 1 or claim 2, wherein the antibody is an antibody fragment that binds B7-H4.

4. The antibody of any one of claims 1 to 3, further comprising a heavy chain framework FR3 sequence of SEQ ID NO: 71; and/or a light chain framework FR2 sequence of SEQ ID NO: 65; and/or a light chain framework FR3 sequence of SEQ ID NO: 67.

5. The antibody of any one of claims 1 to 4, wherein the antibody comprises

(a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 56; and/or

(b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 55.

6. An isolated monoclonal antibody that binds to B7-H4 comprising a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 55.

7. The antibody of any one of claims 1 to 6, which is an IgG1, IgG2a or IgG2b antibody.

8. Isolated nucleic acid encoding the antibody of any one of claims 1 to 7.

9. A host cell comprising the nucleic acid of claim 8.

10. A method of producing an antibody comprising culturing the host cell of claim 9 so that the antibody is produced.

11. An immunoconjugate comprising the antibody of any one of claims 1 to 7 and a cytotoxic agent.

12. The immunoconjugate of claim 11 having the formula Ab-(L-D)p, wherein:

(a) Ab is the antibody;

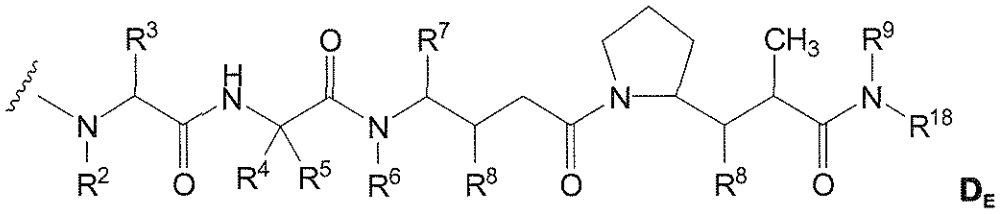
(b) L is a linker;

(c) D is a drug selected from a maytansinoid, an auristatin, a calicheamicin, a pyrrolobenzodiazepine, and a nemorubicin derivative; and

(d) p ranges from 1-8.

13. The immunoconjugate of claim 11, wherein the cytotoxic agent is an auristatin.

14. The immunoconjugate of claim 12, wherein D has formula D_E

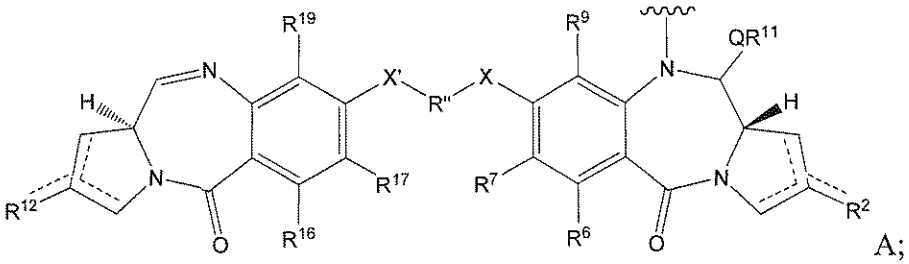


D_E

and wherein R^2 and R^6 are each methyl, R^3 and R^4 are each isopropyl, R^5 is H, R^7 is sec-butyl, each R^8 is independently selected from CH_3, O-CH_3, OH, and H; R^9 is H; and R^{18} is $-C(R^8)_2-C(R^8)_2-$aryl.

15. The immunoconjugate of claim 11, wherein the cytotoxic agent is MMAE.

16. The immunoconjugate of claim 12, wherein D is a pyrrolobenzodiazepine of Formula A:



A;

wherein the dotted lines indicate the optional presence of a double bond between C1 and C2 or C2 and C3;

R^2 is independently selected from H, OH, =O, $=CH_2$, CN, R, OR, $=CH-R^D$, $=C(R^D)_2$, O-SO_2-R, CO_2R and COR, and optionally further selected from halo or dihalo, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

R^7 is independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

Q is independently selected from O, S and NH;

R^{11} is either H, or R or, where Q is O, SO_3M, where M is a metal cation;

R and R' are each independently selected from optionally substituted C_{1-8} alkyl, C_{3-8} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R

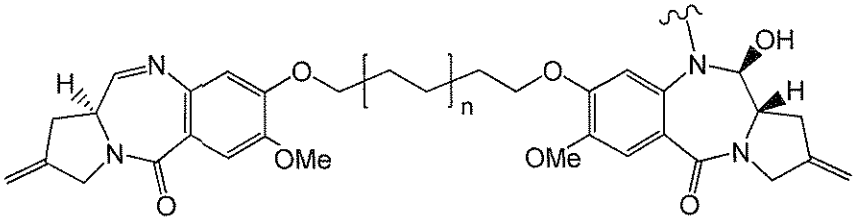
and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring;

R^{12}, R^{16}, R^{19} and R^{17} are as defined for R^2, R^6, R^9 and R^7 respectively;

R'' is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms and/or aromatic rings that are optionally substituted; and

X and X' are independently selected from O, S and N(H).

17. The immunoconjugate of claim 16, wherein D has the structure:

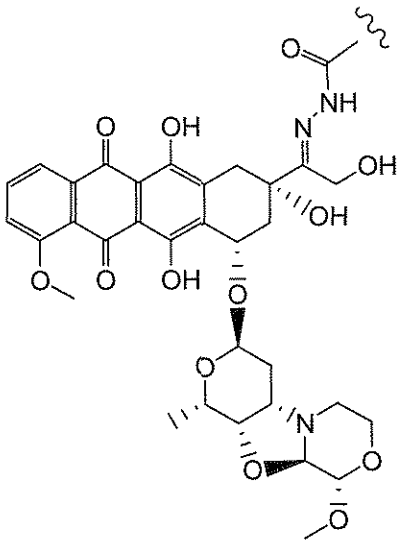


;

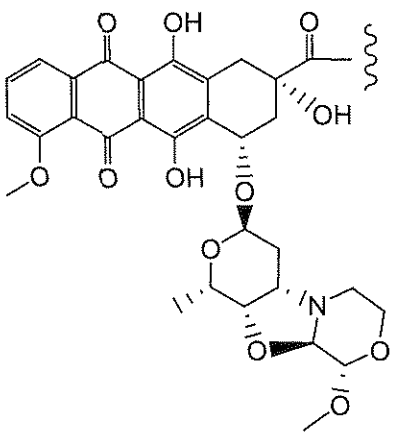
wherein n is 0 or 1.

18. The immunoconjugate of claim 11, wherein the cytotoxic agent is a nemorubicin derivative.

19. The immunoconjugate of claim 12, wherein D has a structure selected from:



; and



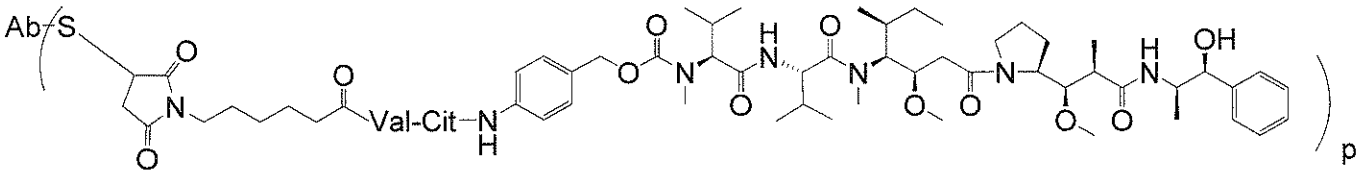
20. The immunoconjugate of any one of claims 12 to 19, wherein the linker is cleavable by a protease.

21. The immunoconjugate of claim 20, wherein the linker comprises a valine-citrulline dipeptide, an N-methyl-valine-citrulline dipeptide, an alanine-phenylalanine dipeptide, a phenylalanine-lysine dipeptide, or a phenylalanine-homolysine dipeptide.

22. The immunoconjugate of any one of claims 12 to 19, wherein the linker is acid-labile.

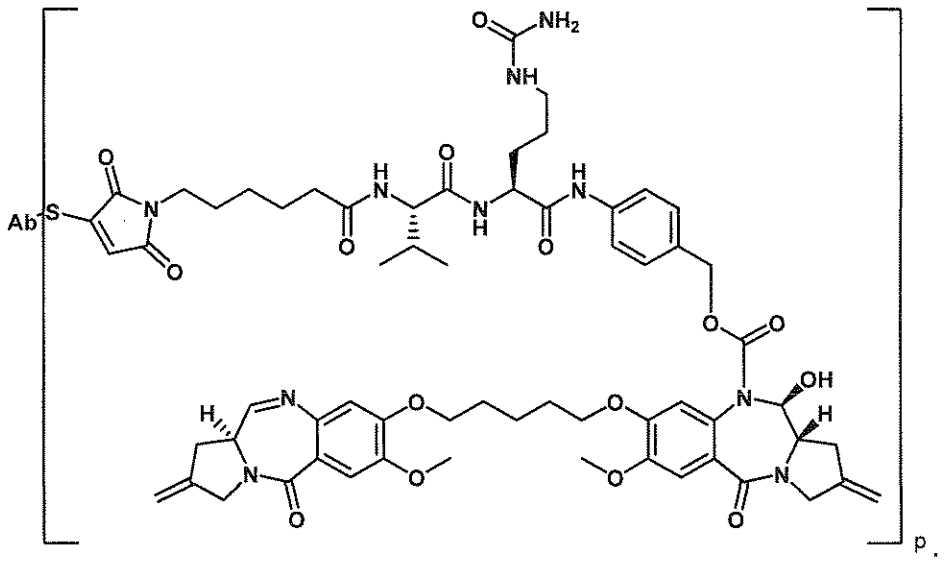
23. The immunoconjugate of claim 22, wherein the linker comprises hydrazone.

24. The immunoconjugate of claim 12 having the formula:

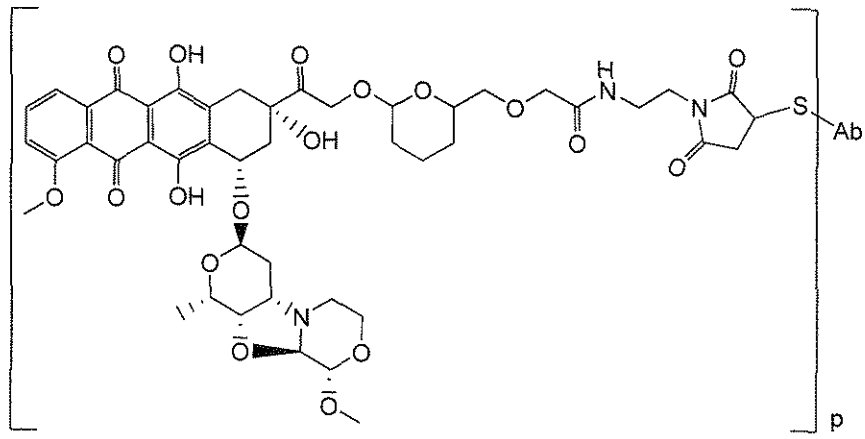


wherein S is a sulfur atom.

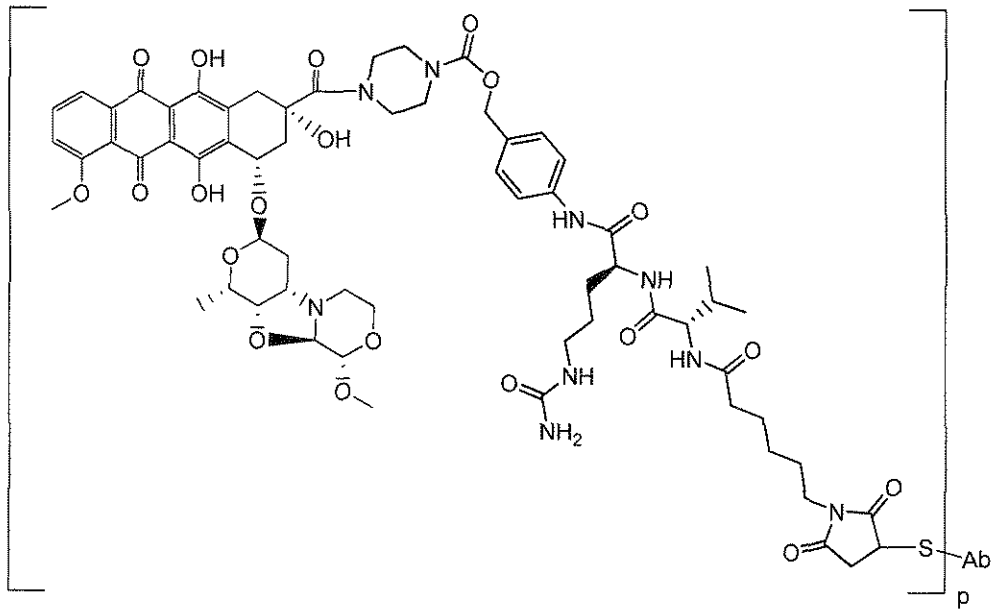
25. The immunoconjugate of claim 17 having the formula:



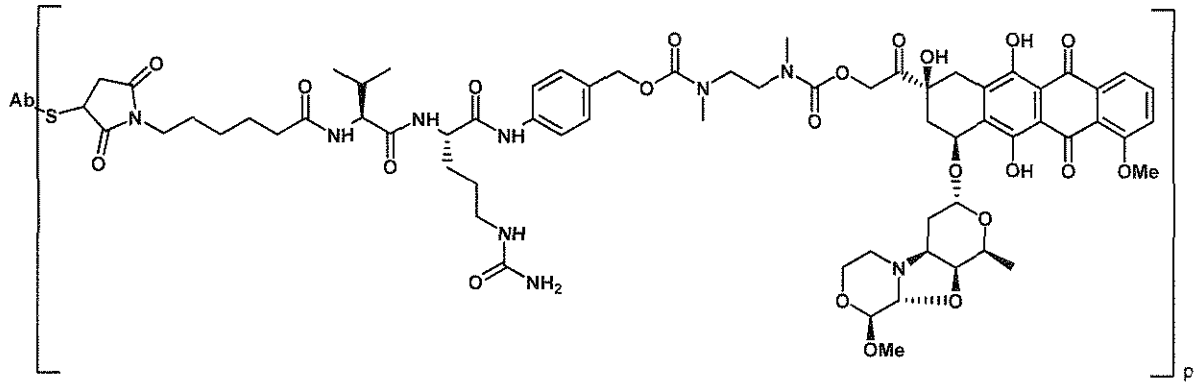
26. The immunoconjugate of claim 19 having a formula selected from:



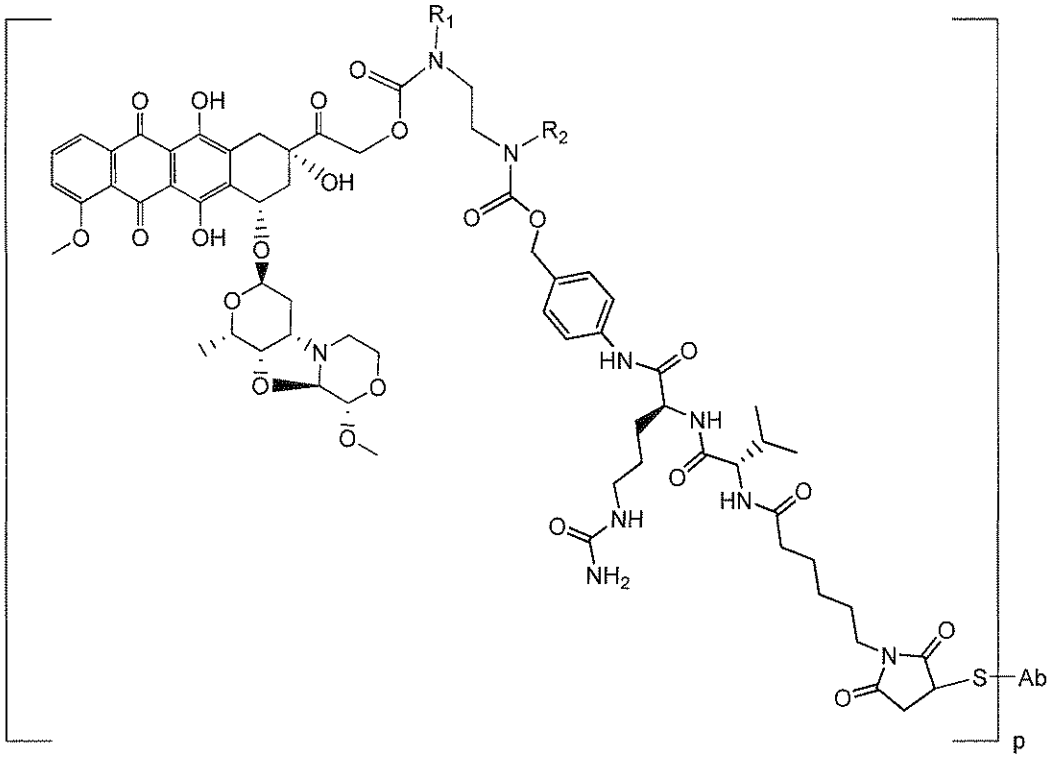
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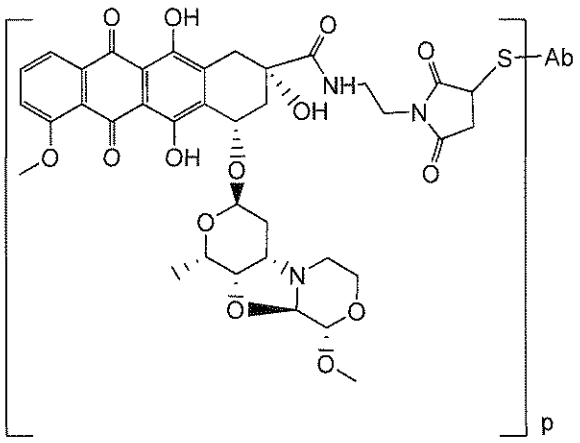
;



;



wherein R_1 and R_2 are independently selected from H and C_1-C_6 alkyl; and



27. The immunoconjugate of any one of claims 12 to 26, wherein p ranges from 2-5.

28. The immunoconjugate of any one of claims 12 to 27, comprising the antibody of claim 6.

29. A pharmaceutical formulation comprising the immunoconjugate of any one of claims 12 to 28 and a pharmaceutically acceptable carrier.

30. The pharmaceutical formulation of claim 29, further comprising an additional therapeutic agent.

31. The pharmaceutical formulation of claim 30, wherein the additional therapeutic agent is Avastin® (bevacizumab).

32. Use of the immunoconjugate of any one of claims 12 to 28 for the preparation of a medicament for the treatment of a B7-H4-positive cancer in an individual.

33. The use of claim 32, wherein the B7-H4-positive cancer is selected from breast cancer, ovarian cancer, and endometrial cancer.

34. The use of claim 32, wherein the medicament further comprises an additional therapeutic agent.

35. The use of claim 34, wherein the additional therapeutic agent is Avastin® (bevacizumab).

36. An *in vitro* method of inhibiting proliferation of a B7-H4-positive cell, the method comprising exposing the cell to the immunoconjugate of any one of claims 12 to 28 under conditions permissive for binding of the immunoconjugate to B7-H4 on the surface of the cell, thereby inhibiting proliferation of the cell.

37. The method of claim 36, wherein the cell is a breast, ovarian, or endometrial cancer cell.

38. The antibody of any one of claims 1 to 7 conjugated to a label.

39. The antibody of claim 38, wherein the label is a positron emitter.

40. The antibody of claim 39, wherein the positron emitter is ^{89}Zr.

41. An *in vitro* method of detecting human B7-H4 in a biological sample comprising contacting the biological sample with the anti-B7-H4 antibody of any one of claims 1 to 7 under conditions permissive for binding of the anti-B7-H4 antibody to a naturally occurring human B7-H4, and detecting whether a complex is formed between the anti-B7-H4 antibody and a naturally occurring human B7-H4 in the biological sample.

42. The method of claim 41, wherein the anti-B7-H4 antibody is the antibody as in claim 6.

43. The method of claim 41 or claim 42, wherein the biological sample is a breast cancer sample, ovarian cancer sample, or endometrial cancer sample.

44. A method for detecting a B7-H4-positive cancer comprising (i) administering a labeled anti-B7-H4 antibody to a subject having or suspected of having a B7-H4-positive cancer, wherein the labeled anti-B7-H4 antibody comprises the anti-B7-H4 antibody of any one of claims 1 to 7, and (ii) detecting the labeled anti-B7-H4 antibody in the subject, wherein detection of the labeled anti-B7-H4 antibody indicates a B7-H4-positive cancer in the subject.

45. The method of claim 44, wherein the labeled anti-B7-H4 antibody is the antibody in claim 4 that is labeled.

46. The method of claim 44 or claim 45, wherein the labeled anti-B7-H4 antibody comprises an anti-B7-H4 antibody conjugated to a positron emitter.

47. The method of claim 46, wherein the positron emitter is ^{89}Zr.

48. Use of the pharmaceutical formulations of any one of claims 29 to 31 for the preparation of a medicament for the treatment of a B7-H4 positive cancer.

WHAT IS CLAIMED IS:

1. An isolated antibody that binds to B7-H4, wherein the antibody has at least one of the following characteristics:

(a) binds to an epitope within all or a portion of the B7-H4 Ig-V containing domain (amino acids 29-157 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-C containing domain (amino acids 158-250 of SEQ ID NO: 73); or binds to an epitope within all or a portion of the B7-H4 Ig-V and Ig-C domains (amino acids 29-250 of SEQ ID NO:73); or binds to an epitope within all or a portion of SEQ ID NO: 74 (mature human B7-H4); or binds to an epitope within all or a portion of SEQ ID NO: 73 (precursor human B7-H4), and

(b) binds to B7-H4 with an affinity of $\leq$ 50 nM.

2. The antibody of claim 1, which is a monoclonal antibody.

3. The antibody of claim 1, which is a human, humanized, or chimeric antibody.

4. The antibody of claim 1, which is an antibody fragment that binds B7-H4.

5. The antibody of claim 1, wherein B7-H4 is human B7-H4 of SEQ ID NO: 73.

6. The antibody of claim 1, wherein the antibody comprises:

(a) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 7, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 10, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 6; or

(b) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 15, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 14; or

(c) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 23, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 26, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22; or

(d) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 31, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 34, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 30; or

(e) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 44, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40; or

(f) (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 60, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 59.

7. The antibody of claim 1, wherein the antibody comprises:

(a) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 5, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 6, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 7; or

(b) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 13, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 14, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 15; or

(c) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 23; or

(d) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 29, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 30, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 31; or

(e) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41; or

(f) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 58, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 59, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 60.

8. The antibody of claim 7, further comprising a heavy chain framework FR3 sequence of SEQ ID NO: 51, 52 or 53.

9. The antibody of claim 7 or claim 8, further comprising:

(a) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 9, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 10; or

(b) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 16, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 17, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18; or

(c) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 24, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 25, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 26; or

(d) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 32, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 33, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 34; or

(e) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 42, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 43, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 44; or

(f) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 61, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 62, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63.

10. The antibody of claim 1, wherein the antibody comprises:

(a) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 9, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 10; or

(b) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 16, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 17, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18; or

(c) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 24, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 25, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 26; or

(d) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 32, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 33, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 34; or

(e) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 42, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 43, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 44; or

(f) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 61, (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 62, and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 63.

11. The antibody of claim 9 or claim 10, further comprising a light chain framework FR2 sequence of SEQ ID NO: 65 or 66 or a light chain framework FR3 sequence of SEQ ID NO: 47.

12. The antibody of claim 1, wherein the antibody comprises

(a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 4;

(b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 3; or

(c) a VH sequence as in (a) and a VL sequence as in (b); or

(d) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 12; or

(e) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 11; or

(f) a VH sequence as in (d) and a VL sequence as in (e); or

(g) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 20; or

(h) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; or

(i) a VH sequence as in (g) and a VL sequence as in (h); or

(j) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 28; or

(k) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 27; or

(l) a VH sequence as in (j) and a VL sequence as in (k); or

(m) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or

(n) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; or

(o) a VH sequence as in (m) and a VL sequence as in (n); or

(p) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 37; or

(q) a VH sequence as in (p) and a VL sequence as in (n); or

(r) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 38; or

(s) a VH sequence as in (r) and a VL sequence as in (n); or

(t) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 56; or

(u) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 55; or

(v) a VH sequence as in (t) and a VL sequence as in (v); or

(w) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 57; or

(x) a VH sequence as in (t) and a VL sequence as in (w).

13. The antibody of claim 12, comprising a VH sequence of SEQ ID NO: 4, a VH sequence of SEQ ID NO: 12, a VH sequence of SEQ ID NO: 20, a VH sequence of SEQ ID NO: 4, 28, a VH sequence of SEQ ID NO: 36, a VH sequence of SEQ ID NO: 37, a VH sequence of SEQ ID NO: 38, or a VH sequence of SEQ ID NO: 56.

14. The antibody of claim 12, comprising a VL sequence of SEQ ID NO: 3, a VL sequence of SEQ ID NO: 11, a VL sequence of SEQ ID NO: 19, a VL sequence of SEQ ID NO: 27, a VL sequence of SEQ ID NO: 35, a VL sequence of SEQ ID NO: 55, or a VL sequence of SEQ ID NO: 57.

15. An isolated antibody comprising (a) a VH sequence of SEQ ID NO: 4 and a VL sequence of SEQ ID NO: 3; or (b) a VH sequence of SEQ ID NO: 20 and a VL sequence of SEQ ID NO: 19; or (c) a VH sequence of SEQ ID NO: 28 and a VL sequence of SEQ ID NO: 27; or (d) a VH sequence of SEQ ID NO: 36 and a VL sequence of SEQ ID NO: 35; or (e) a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 35; or (f) a VH sequence of SEQ ID NO: 38 and a VL sequence of SEQ ID NO: 35; or (g) a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 55; or (h) a VH sequence of SEQ ID NO: 56 and a VL sequence of SEQ ID NO: 57.

16. The antibody of any one of claims 1 to 15, which is an IgG1, IgG2a or IgG2b antibody.

17. Isolated nucleic acid encoding the antibody of any one of claims 1 to 16.

18. A host cell comprising the nucleic acid of claim 17.

19. A method of producing an antibody comprising culturing the host cell of claim 18 so that the antibody is produced.

20. An immunoconjugate comprising the antibody of any one of claims 1 to 16 and a cytotoxic agent.

21. The immunoconjugate of claim 20 having the formula Ab-(L-D)p, wherein:

(a) Ab is the antibody of any one of claim 1 to 15;

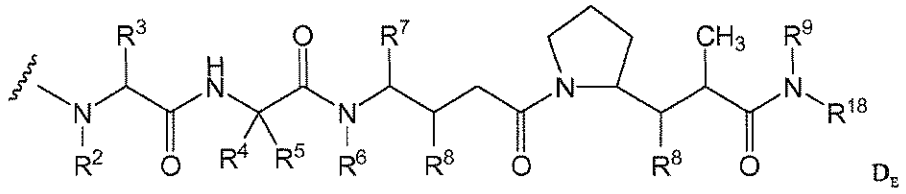
(b) L is a linker;

(c) D is a drug selected from a maytansinoid, an auristatin, a calicheamicin, a pyrrolobenzodiazepine, and a nemorubicin derivative; and

(d) p ranges from 1-8.

22. The immunoconjugate of claim 21, wherein D is an auristatin.

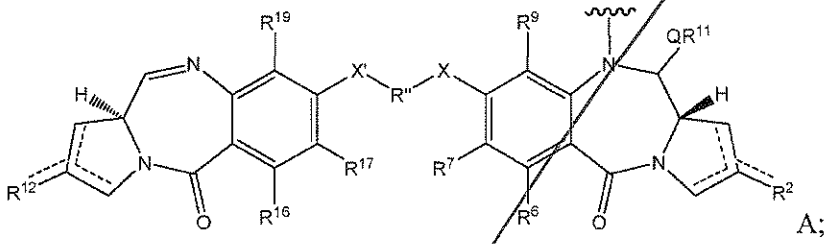
23. The immunoconjugate of claim 22, wherein D has formula D_E



and wherein R^2 and R^6 are each methyl, R^3 and R^4 are each isopropyl, R^5 is H, R^7 is sec-butyl, each R^8 is independently selected from CH_3, O-CH_3, OH, and H; R^9 is H; and R^{18} is $-C(R^8)_2-C(R^8)_2-$aryl.

24. The immunoconjugate of claim 21, wherein the drug is MMAE.

25. The immunoconjugate of claim 22, wherein D is a pyrrolobenzodiazepine of Formula A:



A;

wherein the dotted lines indicate the optional presence of a double bond between C1 and C2 or C2 and C3;

R^2 is independently selected from H, OH, =O, $=CH_2$, CN, R, OR, $=CH-R^D$, $=C(R^D)_2$, O-SO_2-R, CO_2R and COR, and optionally further selected from halo or dihalo, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

R^7 is independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

Q is independently selected from O, S and NH;

R^{11} is either H, or R or, where Q is O, SO_3M, where M is a metal cation;

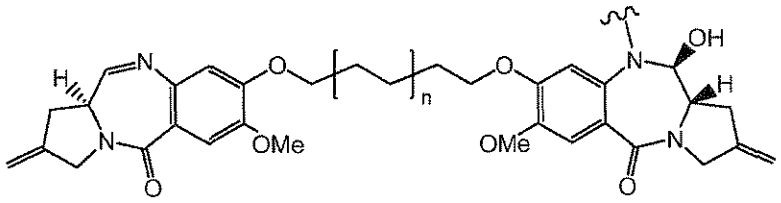
R and R' are each independently selected from optionally substituted C_{1-8} alkyl, C_{3-8} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring;

R^{12}, R^{16}, R^{19} and R^{17} are as defined for R^2, R^6, R^9 and R^7 respectively;

R'' is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms and/or aromatic rings that are optionally substituted; and

X and X' are independently selected from O, S and N(H).

26. The immunoconjugate of claim 25, wherein D has the structure:

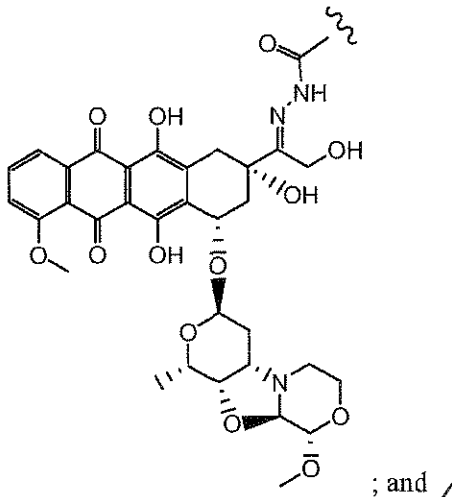


;

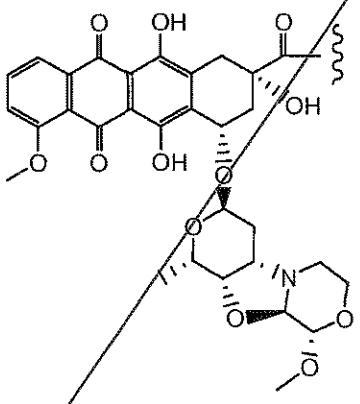
wherein n is 0 or 1.

27. The immunoconjugate of claim 21, wherein D is a nemorubicin derivative.

28. The immunoconjugate of claim 27, wherein D has a structure selected from:



; and



.

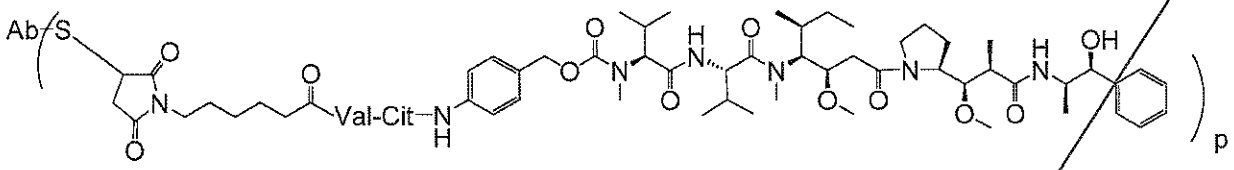
29. The immunoconjugate of any one of claims 21 to 28, wherein the linker is cleavable by a protease.

30. The immunoconjugate of claim 29, wherein the linker comprises a val-cit dipeptide or a Phe-homoLys dipeptide.

31. The immunoconjugate of any one of claims 21 to 28, wherein the linker is acid-labile.

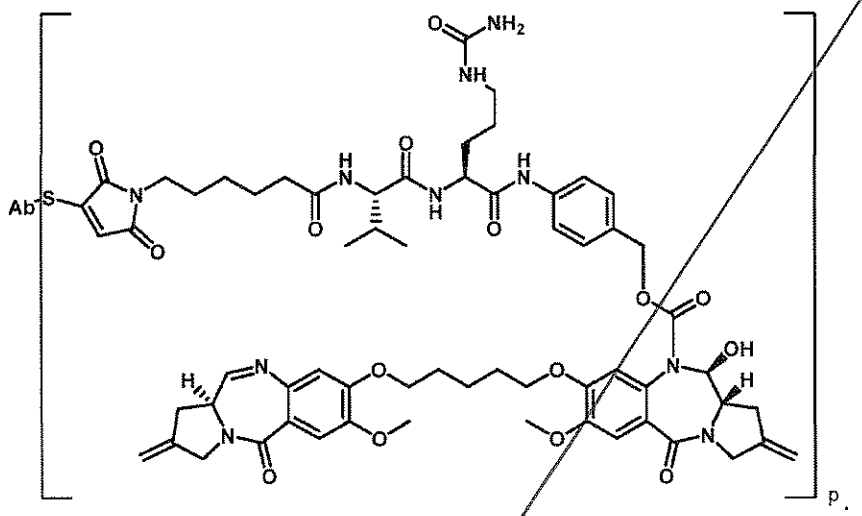
32. The immunoconjugate of claim 31, wherein the linker comprises hydrazone.

33. The immunoconjugate of claim 23 having the formula:

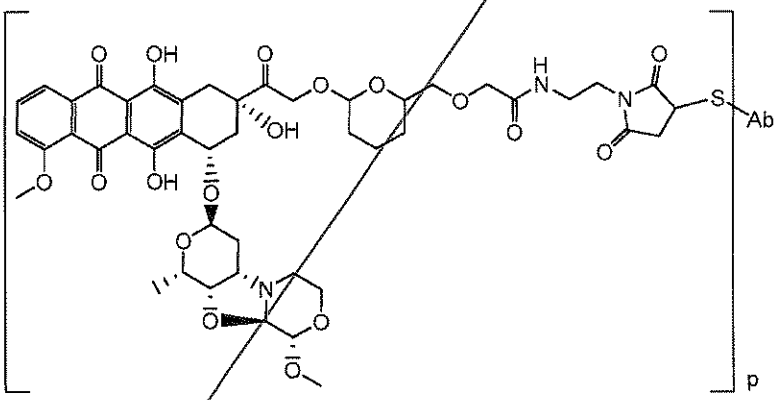


wherein S is a sulfur atom.

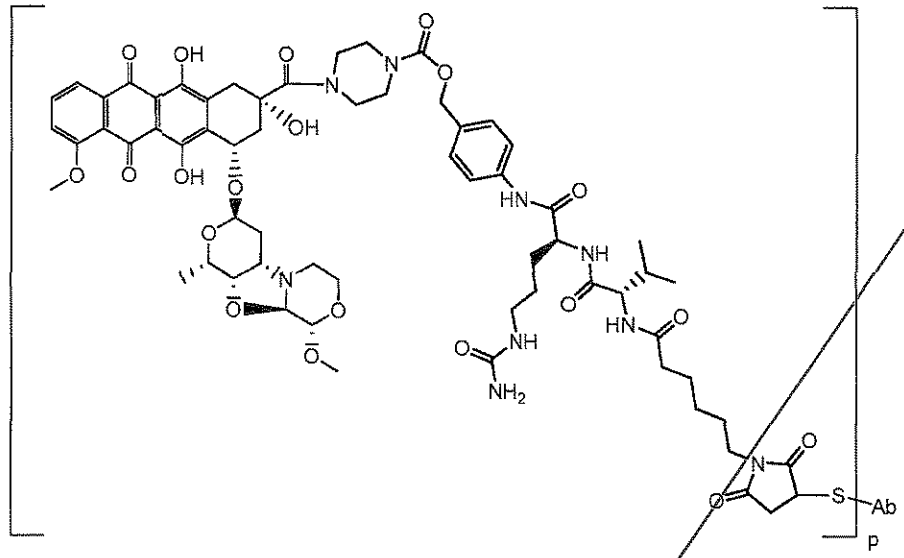
34. The immunoconjugate of claim 26 having the formula:

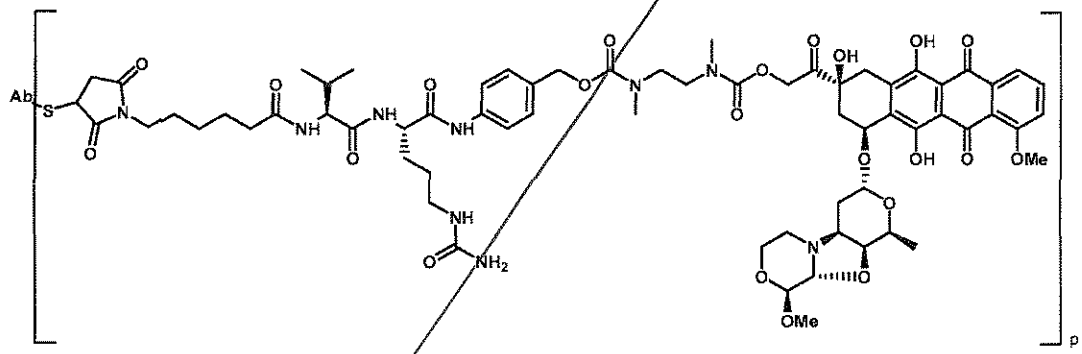


35. The immunoconjugate of claim 28 having a formula selected from:

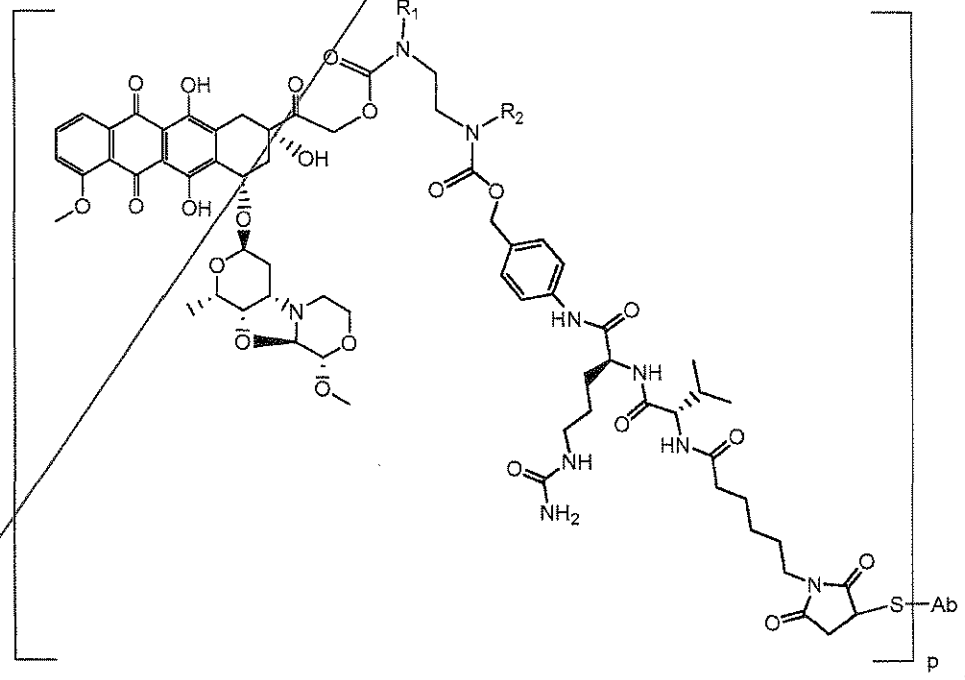


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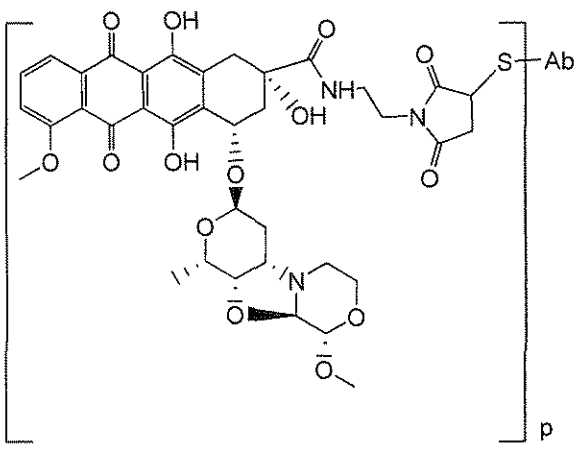




;



; and



36. The immunoconjugate of any one of claims 21 to 35, wherein p ranges from 2-5.

37. The immunoconjugate of any one of claims 21 to 36, comprising the antibody of claim 9.

38. The immunoconjugate of any one of claims 21 to 36, comprising the antibody of claim 15.

39. A pharmaceutical formulation comprising the immunoconjugate of any one of claims 21 to 38 and a pharmaceutically acceptable carrier.

40. The pharmaceutical formulation of claim 39, further comprising an additional therapeutic agent.

41. The pharmaceutical formulation of claim 40, wherein the additional therapeutic agent is Avastin® (bevacizumab).

42. Use of the immunoconjugate of any one of claims 21 to 38 in the manufacture of a medicament for treating an individual having a B7-H4-positive cancer.

43. The use of claim 42, wherein the B7-H4-positive cancer is selected from breast cancer, ovarian cancer, and endometrial cancer.

44. The use of claim 43, further comprising administering an additional therapeutic agent to the individual.

45. The use of claim 44, wherein the additional therapeutic agent is Avastin® (bevacizumab).

46. A method of inhibiting proliferation of an B7-H4-positive cell, the method comprising exposing the cell to the immunoconjugate of any one of claims 21 to 38 under

conditions permissive for binding of the immunoconjugate to B7-H4 on the surface of the cell, thereby inhibiting proliferation of the cell.

47. The method of claim 46, wherein the cell is a breast, ovarian, or endometrial cancer cell.

48. The antibody of any one of claims 1 to 16 conjugated to a label.

49. The antibody of claim 48, wherein the label is a positron emitter.

50. The antibody of claim 49, wherein the positron emitter is ^{89}Zr.

51. A method of detecting human B7-H4 in a biological sample comprising contacting the biological sample with the anti-B7-H4 antibody of any one of claims 1 to 16 under conditions permissive for binding of the anti-B7-H4 antibody to a naturally occurring human B7-H4, and detecting whether a complex is formed between the anti-B7-H4 antibody and a naturally occurring human B7-H4 in the biological sample.

52. The method of claim 51, wherein the anti-B7-H4 antibody is an antibody as in claim 9 or claim 15.

53. The method of claim 51, wherein the biological sample is a breast cancer sample, ovarian cancer sample, or endometrial cancer sample.

54. A method for detecting an B7-H4-positive cancer comprising (i) administering a labeled anti-B7-H4 antibody to a subject having or suspected of having a B7-H4-positive cancer, wherein the labeled anti-B7-H4 antibody comprises the anti-B7-H4 antibody of any one of claims 1 to 16, and (ii) detecting the labeled anti-B7-H4 antibody in the subject, wherein detection of the labeled anti-B7-H4 antibody indicates a B7-H4-positive cancer in the subject.

55. The method of claim 54, wherein the labeled anti-B7-H4 antibody is an antibody as in claim 8 or claim 14 that is labeled.

56. The method of claim 54 or claim 55, wherein the labeled anti-B7-H4 antibody comprises an anti-B7-H4 antibody conjugated to a positron emitter.

57. The method of claim 56, wherein the positron emitter is ^{89}Zr.