[0006] In some embodiments, an isolated antibody that binds to CD33 is provided. In some embodiments, the antibody binds to CD33 and has one or more of the following characteristics:

a) binds to recombinant human CD33;

b) binds to recombinant cynomolgus monkey CD33;

c) binds to endogenous CD33 on the surface of human peripheral blood mononucleocytes (PBMCs);

d) binds to endogenous CD33 on the surface of cynomolgus monkey PBMCs;

e) binds to endogenous CD33 on the surface of a cancer cell;

f) binds to endogenous CD33 on the surface of an AML cancer cell;

g) binds to endogenous CD33 on the surface of Molm-13 cells;

h) binds to CD33 comprising a R69G mutation;

i) binds to CD33 Ig V domain;

j) binds to CD33 that is void of N-linked glycosylation at N100;

k) binds to CD33 that is void of N-linked glycosylation at N113;

l) binds to CD33 comprising an S102A mutation;

m) binds to CD33 comprising an S115A mutation;

n) does not bind CD33 Ig C2 domain;

o) competes for human CD33 binding with My9.6 antibody;

p) competes for human CD33 binding with antibody 33H4;

q) competes for human CD33 binding with antibody 23E4;

r) binds to endogenous human CD33 with a Kd of less than 15 nM, less than 10 nM, less than 7 nM, less than 5 nM, or less than 3 nM;

s) binds to recombinant human CD33 with a Kd of less than 10 nM, less than 7 nM, less than 5 nM, or less than 3 nM; and/or

t) binds to recombinant cynomolgus monkey CD33 with a Kd of less than 10 nM, less than 7 nM, less than 5 nM, or less than 3 nM, less than 2 nM, or less than 1 nM.

[0007] Disclosed is an isolated antibody that binds to CD33 is provided, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:112; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:113; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:114; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:111; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7. In some embodiments, the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:115; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:116; (c) HVR-H3

comprising the amino acid sequence of SEQ ID NO:117; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7. In one aspect, there is provided an isolated antibody that binds to CD33, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:118; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:119; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:111; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

[0008] In some embodiments, an antibody that binds CD33 comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:20, SEQ ID NO:23, or SEQ ID NO:30; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:9, SEQ ID NO:12, SEQ ID NO:21, SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, or SEQ ID NO:35; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:10, SEQ ID NO:13, SEQ ID NO:22, or SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, or SEQ ID NO:29; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

[0009] In some embodiments, an antibody that binds CD33 comprises:

(i) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:8; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:9; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:10; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(ii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:11; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:12; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:13; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(iii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:21; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:22; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(iv) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid

g) a heavy chain variable region comprising the sequence of SEQ ID NO: 86 and a light chain variable region comprising the sequence of SEQ ID NO: 85;

h) a heavy chain variable region comprising the sequence of SEQ ID NO: 88 and a light chain variable region comprising the sequence of SEQ ID NO: 87;

i) a heavy chain variable region comprising the sequence of SEQ ID NO: 90 and a light chain variable region comprising the sequence of SEQ ID NO: 89;

j) a heavy chain variable region comprising the sequence of SEQ ID NO: 92 and a light chain variable region comprising the sequence of SEQ ID NO: 91;

k) a heavy chain variable region comprising the sequence of SEQ ID NO: 94 and a light chain variable region comprising the sequence of SEQ ID NO: 93;

l) a heavy chain variable region comprising the sequence of SEQ ID NO: 96 and a light chain variable region comprising the sequence of SEQ ID NO: 95;

m) a heavy chain variable region comprising the sequence of SEQ ID NO: 98 and a light chain variable region comprising the sequence of SEQ ID NO: 97; or

n) a heavy chain variable region comprising the sequence of SEQ ID NO: 100 and a light chain variable region comprising the sequence of SEQ ID NO: 99.

[00011] In some embodiments, an isolated antibody that binds to CD33 is provided. In some embodiments, the antibody binds to CD33 and has one or more of the following characteristics:

a) binds to recombinant human CD33;

b) binds to recombinant cynomolgus monkey CD33;

c) binds to endogenous CD33 on the surface of human peripheral blood mononucleocytes (PBMCs);

d) binds to recombinant human CD33 with a Kd of less than 10 nM, less than 7 nM, less than 5 nM, less than 3 nM, less than 2 nM, or less than 1 nM; and/or

e) binds to recombinant cynomolgus monkey CD33 with a Kd of less than 10 nM, less than 7 nM, less than 5 nM, less than 3 nM, less than 2 nM, or less than 1 nM.

[00012] Disclosed is an isolated antibody that binds to CD33 is provided, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:17; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:18; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:19; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:16.

[00013] In some embodiments, an antibody that binds CD33 comprises:

a) a heavy chain variable region comprising the sequence of SEQ ID NO: 70 and a light chain variable region comprising the sequence of SEQ ID NO: 69;

b) a heavy chain variable region comprising the sequence of SEQ ID NO: 72 and a light chain variable region comprising the sequence of SEQ ID NO: 71;

c) a heavy chain variable region comprising the sequence of SEQ ID NO: 74 and a light chain variable region comprising the sequence of SEQ ID NO: 73; or

d) a heavy chain variable region comprising the sequence of SEQ ID NO: 76 and a light chain variable region comprising the sequence of SEQ ID NO: 75.

[00014] In one aspect, an isolated antibody that binds to CD33 is provided, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

[00015] In one aspect, an isolated antibody that binds to CD33 is provided, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:26; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

[00016] Disclosed is an isolated antibody that binds to CD33 is provided, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:17; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:18; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:19; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:16.

[00017] 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 CD33. In some embodiments, CD33 is human CD33 has the sequence of SEQ ID NO: 1, with or without a signal sequence (*e.g.*, with or without amino acids 1-17).

[00018] In one aspect, an isolated nucleic acid encoding an antibody described herein is provided. In one aspect, a host cell comprising the nucleic acid is provided. In one aspect, a method of producing an antibody comprising culturing the host cell so that the antibody is produced is provided.

described herein under conditions permissive for binding of the immunoconjugate to CD33 on the surface of the cell, thereby inhibiting proliferation of the cell. In some embodiments, the cell is an AML cancer cell. In one aspect, an *in vitro* method of inhibiting proliferation of a CD33-positive cell is provided, the method comprising exposing the cell to the immunoconjugate described herein under conditions permissive for binding of the immunoconjugate to CD33 on the surface of the cell, thereby inhibiting proliferation of the cell. Disclosed is use of the immunoconjugate described herein in the manufacture of a medicament for inhibiting proliferation of a CD33-positive cell is provided, wherein the cell is to be exposed to the immunoconjugate under conditions permissive for binding of the immunoconjugate to CD33 on the surface of the cell, thereby inhibiting proliferation of the cell.

[0010] In one aspect, a method of detecting human CD33 in a biological sample is provided, comprising contacting the biological sample with an anti-CD33 antibody described herein under conditions permissive for binding of the anti-CD33 antibody to a naturally occurring human CD33, and detecting whether a complex is formed between the anti-CD33 antibody and a naturally occurring human CD33 in the biological sample. In some embodiments, an anti-CD33 antibody is an antibody described herein. In some embodiments, the biological sample is an AML cancer sample.

[0011] In another aspect, there is provided the antibody described herein for detecting a CD33-positive cancer in a subject having or suspected of having a CD33-positive cancer. In some embodiments, an anti-CD33 antibody is an antibody described herein. In some such embodiments, the labeled anti-CD33 antibody comprises an anti-CD33 antibody conjugated to a positron emitter. In some embodiments, the positron emitter is ^{89}Zr.

BRIEF DESCRIPTION OF THE FIGURES

[0012] **Figure 1A-B** shows alignment of the light chain variable region sequences (A) and heavy chain variable region sequences (B) of 7A1, 9C2, 10D3, and 15G15.

[0013] **Figure 2A-B** shows alignment of the light chain variable region sequences (A) and heavy chain variable region sequences (B) of 15G15, 15G15.33, 15G15.37, 15G15.83, 15G15.88, 15G15.7, 15G15.17, 15G15.30, 15G15.31, 15G15.39, and 15G15.84.

[0014] **Figure 3A-B** shows alignment of the light chain variable region sequences (A) and heavy chain variable region sequences (B) of 23E4, 27C6, 33F3, 33F9, and 33H4.

[0015] **Figure 4A-B** shows alignment of the light chain variable region sequences (A) and heavy chain variable region sequences (B) of 9C3, 9C3.2, 9C3.3, and 9C3.4.

[0016] **Figure 5A-D** show species cross-reactivity of anti-CD33 antibodies to recombinant CD33. Anti-CD33 antibody binding to 293 cells expressing recombinant human (hu) CD33 (A, C) and cynomolgus (cyno) CD33 (B, D) is shown.

[0017] **Figure 6A-D** shows anti-CD33 antibody binding to endogenous huCD33 expressed in Molm-13 (A, C) and AML (B, D) cells.

[0018] **Figure 7A-D** shows species cross-reactivity of anti-CD33 antibodies to endogenous CD33. Anti-CD33 antibody binding to huCD33+ (A, C) and cynoCD33+ (B, D) myeloid cells.

WHAT IS CLAIMED IS:

1. An isolated antibody that binds to CD33, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:118; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:119; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:111; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

2. The antibody of claim 1, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23 or SEQ ID NO:30; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, or SEQ ID NO:35; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, or SEQ ID NO:29; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

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

(i) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(ii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:26; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(iii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:27; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(iv) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:28; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(v) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:29; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(vi) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:30; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(vii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:31; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(viii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:32; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(ix) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:33; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7;

(x) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:34; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7; or

(xi) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:35; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

4. The antibody of any one of the preceding claims, wherein the antibody comprises:

(a) a heavy chain variable region comprising the sequence of SEQ ID NO: 80 and a light chain variable region comprising the sequence of SEQ ID NO: 79;

(b) a heavy chain variable region comprising the sequence of SEQ ID NO: 82 and a light chain variable region comprising the sequence of SEQ ID NO: 81;

(c) a heavy chain variable region comprising the sequence of SEQ ID NO: 84 and a light chain variable region comprising the sequence of SEQ ID NO: 83;

(d) a heavy chain variable region comprising the sequence of SEQ ID NO: 86 and a light chain variable region comprising the sequence of SEQ ID NO: 85;

(e) a heavy chain variable region comprising the sequence of SEQ ID NO: 88 and a light chain variable region comprising the sequence of SEQ ID NO: 87;

(f) a heavy chain variable region comprising the sequence of SEQ ID NO: 90 and a light chain variable region comprising the sequence of SEQ ID NO: 89;

(g) a heavy chain variable region comprising the sequence of SEQ ID NO: 92 and a light chain variable region comprising the sequence of SEQ ID NO: 91;

(h) a heavy chain variable region comprising the sequence of SEQ ID NO: 94 and a light chain variable region comprising the sequence of SEQ ID NO: 93;

(i) a heavy chain variable region comprising the sequence of SEQ ID NO: 96 and a light chain variable region comprising the sequence of SEQ ID NO: 95;

(j) a heavy chain variable region comprising the sequence of SEQ ID NO: 98 and a light chain variable region comprising the sequence of SEQ ID NO: 97; or

(k) a heavy chain variable region comprising the sequence of SEQ ID NO: 100 and a light chain variable region comprising the sequence of SEQ ID NO: 99.

5. The antibody of any one of the preceding claims, wherein the antibody has one or more of the following characteristics:

a) binds to recombinant human CD33;

b) binds to recombinant cynomolgus monkey CD33;

c) binds to endogenous CD33 on the surface of human peripheral blood mononucleocytes (PBMCs);

d) binds to endogenous CD33 on the surface of cynomolgus monkey PBMCs;

e) binds to endogenous CD33 on the surface of a cancer cell;

f) binds to endogenous CD33 on the surface of an AML cancer cell;

g) binds to endogenous CD33 on the surface of Molm-13 cells;

h) binds to CD33 comprising a R69G mutation;

i) binds to CD33 Ig V domain;

j) binds to CD33 that is void of N-linked glycosylation at N100;

k) binds to CD33 that is void of N-linked glycosylation at N113;

l) binds to CD33 comprising an S102A mutation;

m) binds to CD33 comprising an S115A mutation;

n) does not bind CD33 Ig C2 domain;

o) binds to endogenous human CD33 with a Kd of less than 15 nM, less than 10 nM, less than 7 nM, less than 5 nM, or less than 3 nM;

p) binds to recombinant human CD33 with a Kd of less than 10 nM, less than 7 nM, less than 5 nM, or less than 3 nM; and/or

q) binds to recombinant cynomolgus monkey CD33 with a Kd of less than 2 nM or less than 1 nM.

6. The antibody of any one of the preceding claims, which is a monoclonal antibody.

7. The antibody of any one of the preceding claims, which is a humanized or chimeric antibody.

8. The antibody of any one of the preceding claims, which is an antibody fragment that binds CD33.

9. The antibody of any one of the preceding claims, wherein CD33 is human CD33 comprising amino acids 18 to 364 of SEQ ID NO: 1.

10. An isolated antibody that binds to CD33, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:6; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

11. An isolated antibody that binds to CD33, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:23; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:24; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:25; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:5; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:26; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:7.

12. An isolated nucleic acid encoding the antibody of any one of the preceding claims.

13. A host cell comprising the nucleic acid of claim 12.

14. A method of producing an antibody comprising culturing the host cell of claim 13 so that the antibody is produced.

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

16. The immunoconjugate of claim 15 having the formula Ab-(L-D)p, wherein:

(a) Ab is the antibody of any one of claim 1 to 11;

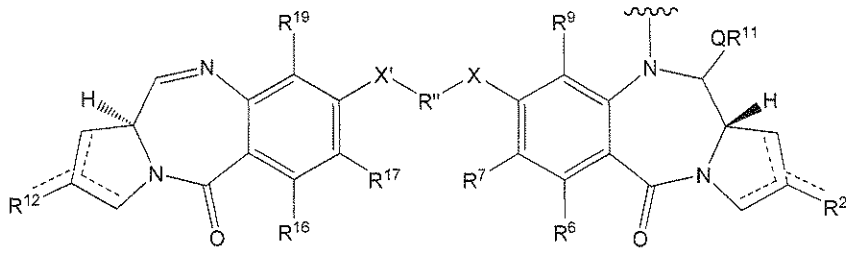
(b) L is a linker;

(c) D is a cytotoxic agent; and

(d) p ranges from 1-8.

17. The immunoconjugate of claim 15 or claim 16, wherein the cytotoxic agent is selected from a maytansinoid, a calicheamicin, a pyrrolobenzodiazepine, and a nemorubicin derivative.

18. The immunoconjugate of claim 16, 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, $=CH\text{-}R^D$, $=C(R^D)_2$, $O\text{-}SO_2\text{-}R$, 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;

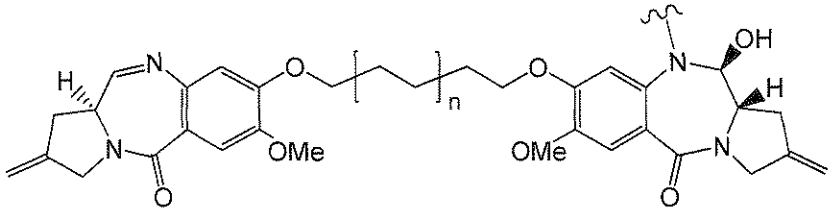
R and R' are each independently selected from optionally substituted C_{1-8} alkyl, C_{3-8} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered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

19. The immunoconjugate of claim 18, wherein D has the structure:

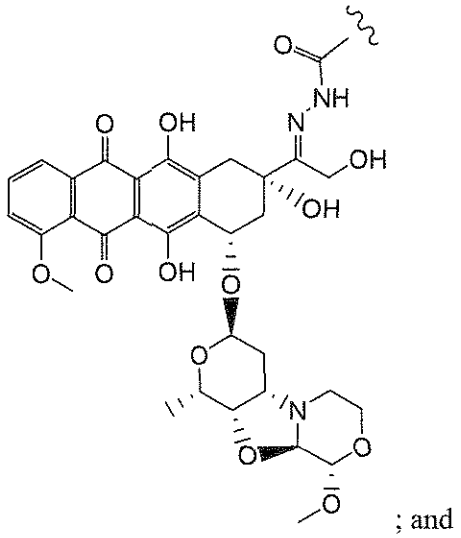


;

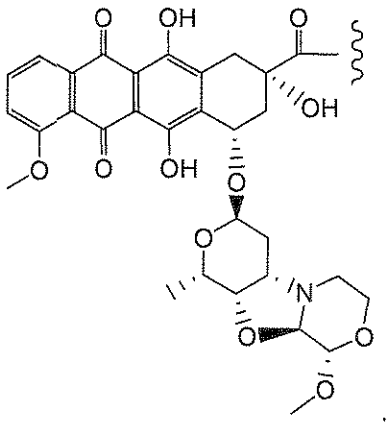
wherein n is 0 or 1.

20. The immunoconjugate of claim 19, wherein D is a nemorubicin derivative.

21. The immunoconjugate of claim 20, wherein D has a structure selected from:



; and



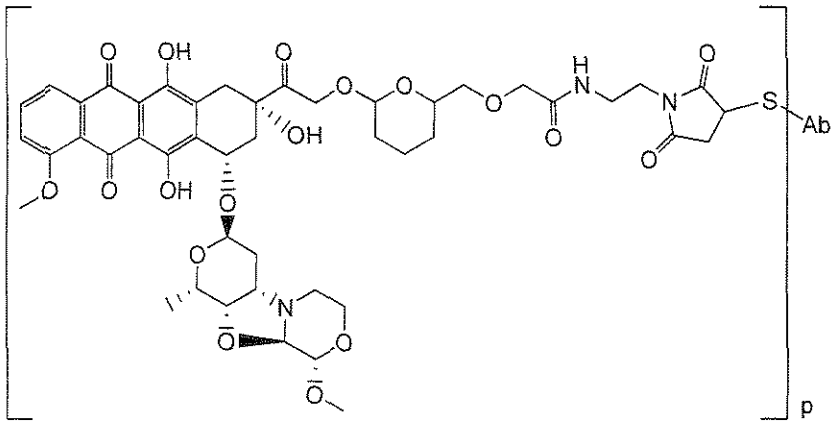
.

22. The immunoconjugate of any one of claims 16 to 21, wherein the linker is cleavable by a protease.

23. The immunoconjugate of any one of claims 16 to 21, wherein the linker is acid-labile.

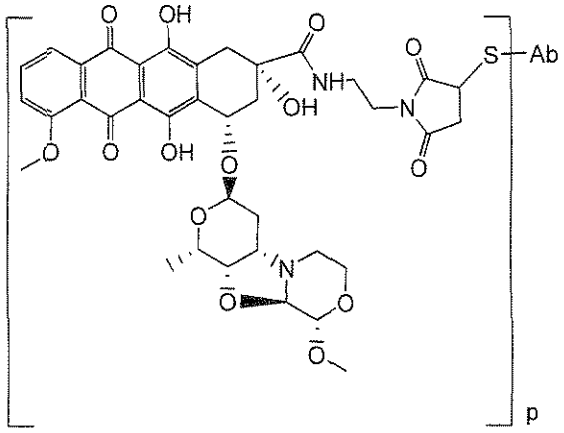
24. The immunoconjugate of claim 23, wherein the linker comprises hydrazone.

25. The immunoconjugate of claim 21 having a formula selected from:



;

and



.

26. The immunoconjugate of any one of claims 16 to 25, wherein p ranges from 2-5.

27. The immunoconjugate of any one of claims 16 to 26, comprising an antibody of claim 10 or claim 11.

28. A pharmaceutical formulation comprising the immunoconjugate of any one of claims 16 to 27 and a pharmaceutically acceptable carrier.

29. The pharmaceutical formulation of claim 28, further comprising an additional therapeutic agent.

30. Use of the immunoconjugate of any one of claims 16 to 27 or the pharmaceutical formulation of claim 28 in the manufacture of a medicament for treating an individual having a CD33-positive cancer.

31. The use of claim 30, wherein the CD33-positive cancer is AML.

32. The use of claim 30 or claim 31, wherein the medicament is to be administered with an additional therapeutic agent.

33. An *in vitro* method of inhibiting proliferation of a CD33-positive cell, the method comprising exposing the cell to the immunoconjugate of any one of claims 16 to 27 under conditions permissive for binding of the immunoconjugate to CD33 on the surface of the cell, thereby inhibiting proliferation of the cell.

34. The method of claim 33, wherein the cell is an AML cancer cell.

35. The antibody of any one of claims 1 to 11 conjugated to a label.

36. The antibody of claim 26, wherein the label is a positron emitter.

37. The antibody of claim 28, wherein the positron emitter is ^{89}Zr.

38. A method of detecting human CD33 in a biological sample comprising contacting the biological sample with the anti-CD33 antibody of any one of claims 1 to 11 under conditions permissive for binding of the anti-CD33 antibody to a naturally occurring human CD33, and detecting whether a complex is formed between the anti-CD33 antibody and a naturally occurring human CD33 in the biological sample.

39. The method of claim 38, wherein the anti-CD33 antibody is an antibody as in claim 10 or claim 11.

40. The method of claim 39, wherein the biological sample is a AML endometrial cancer sample.

41. The antibody of any one of claims 35 to 37 for detecting a CD33-positive cancer in a subject having or suspected of having a CD33-positive cancer.

42. The antibody of claim 41, wherein the antibody is an antibody of claim 10 or claim 11 conjugated to a label.