WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds to the human CD33 protein, wherein the antibody comprises three heavy chain complementarity determining regions (CDRs): heavy chain CDR1 consisting of SEQ ID NO:19, heavy chain CDR2 consisting of SEQ ID NO:20, and heavy chain CDR3 consisting of SEQ ID NO:21; and three light chain CDRs: light chain CDR1 consisting of SEQ ID NO:22, light chain CDR2 consisting of SEQ ID NO:23, and light chain CDR3 consisting of SEQ ID NO:24.

2. The antibody of claim 1, wherein the antibody is selected from a murine antibody, a chimeric antibody, and a humanized antibody.

3. The antibody of claim 2, wherein the antibody is a humanized 2H12 antibody.

4. The humanized antibody of claim 3, wherein the antibody comprises a mature heavy chain variable region having an amino acid sequence at least 90% identical to SEQ ID NO:18 provided that position H48 is occupied by I, position H66 is occupied by K, position H67 is occupied by A, position H69 is occupied by L, position H71 is occupied by A, and position H94 is occupied by S and a mature light chain variable region at least 90% identical to SEQ ID NO:8 provided position L22 is occupied by N, position L46 is occupied by T, position L69 is occupied by Q, and position L71 by Y, as determined by the Kabat numbering system.

5. The humanized antibody of claim 3, comprising a mature heavy chain variable region having an amino acid sequence at least 95% identical to SEQ ID NO:18 and a mature light chain variable region at least 95% identical to SEQ ID NO:8.

6. The humanized antibody of claim 3, wherein the mature heavy chain variable region is fused to a heavy chain constant region and the mature light chain variable region is fused to a light chain constant region.

7. The humanized antibody of claim 3, wherein the heavy chain constant region is a mutant form of natural human constant region which has reduced binding to an Fcγ receptor relative to the natural human constant region.

8. The humanized antibody of claim 2, wherein the heavy chain constant region is of IgG1 isotype.

9. The humanized antibody of claims 3-6, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:27 and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

10. The humanized antibody of claim 3, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:29 (S239C) and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

11. The humanized antibody of claim 3, wherein the mature heavy chain variable region has an amino acid sequence designated SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence designated SEQ ID NO: 8.

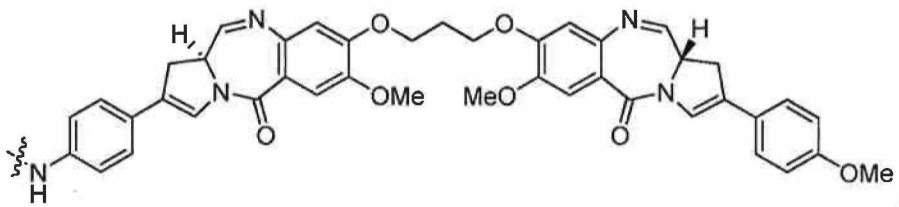
12. The antibody of any of the preceding claims, wherein the antibody is conjugated to a cytotoxic or cytostatic agent.

13. The antibody of claim 12, wherein the antibody is conjugated to a cytotoxic agent.

14. The antibody of claim 13, wherein the cytotoxic agent is conjugated to the antibody via an enzyme cleavable linker.

15. The antibody of claim 13 or 14, wherein the cytotoxic agent is a DNA minor groove binder.

16. The antibody of any of claims 13-15, wherein the cytotoxic agent has the formula



17. The antibody of claim 1 having an association constant for human or cynomolgus monkey CD33 of 0.5 to 2 x 10^9 M^{-1}.

18. A method of treating a patient having or at risk of having a cancer that expresses CD33, comprising administering to the patient an effective regime of a humanized antibody of any of the preceding claims.

19. The method of claim 18, wherein the cancer is acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), acute promyelocytic leukemia (APL), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), a chronic myeloproliferative disorders, precursor B-cell acute lymphoblastic leukemia (preB-ALL), precursor T-cell acute lymphoblastic leukemia (preT-ALL), multiple myeloma (MM), mast cell disease, or myeloid Sarcoma.

20. A pharmaceutical composition comprising a humanized or chimeric antibody of claim 1.

21. A humanized antibody comprising a mature heavy chain variable region having an amino acid sequence at least 90% identical to HI (SEQ ID NO:18) and a mature light chain variable region at least 90% identical to LG (SEQ ID NO:8).

22. The humanized antibody of claim 21, comprising a mature heavy chain variable region having an amino acid sequence at least 95% identical to HI and a mature light chain variable region at least 95% identical to LG.

23. The humanized antibody of claim 21 or 22, provided that position H94 is occupied by S.

24. The humanized antibody of claim 21 or 22, provided that position H48, H66, H67, H69, H71 and H94 are occupied by I, K, A, L, A and S, and L22, L46, L69 and L71 are occupied by N, T, Q and Y.

25. The humanized antibody of any of claims 21-24, provided that any difference in the variable region frameworks of the mature heavy chain variable region and SEQ ID NO:18 are selected from the group consisting of position H48 occupied by I, position H66 occupied by K, position H67 occupied by A, position H69 occupied by L, position H71 occupied by A, position H94 occupied by S; and that any differences in the variable region frameworks of the mature light chain variable region and SEQ ID NO:8 are selected from the group consisting of position L22 occupied by N, position L46 occupied by T, position L69 occupied by Q, and position L71 occupied by Y.

26. The humanized antibody of any of claims 21-25, wherein the 3 CDRs of the mature heavy chain variable region are those of SEQ ID NO:18 and the 3 CDRs of the mature light chain variable region are those of SEQ ID NO:8.

27. The humanized antibody of any of claims 21-26, wherein the mature heavy chain variable region is fused to a heavy chain constant region and the mature light chain variable region is fused to a light chain constant region.

28. The humanized antibody of any of claims 21-27, wherein the heavy chain constant region is a mutant form of natural human constant region which has reduced binding to an Fcγ receptor relative to the natural human constant region.

29. The humanized antibody of any of claims 21-28, wherein the heavy chain constant region is of IgG1 isotype.

30. The humanized antibody of any of claims 21-27 or 29, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:27 and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

31. The humanized antibody of any of claims 21-27 or 29, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:29 (S239C) and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

32. The humanized antibody of any of claims 21-31 provided any differences in CDRs of the mature heavy chain variable region of SEQ ID NO:18 reside in positions H60-H65.

33. The humanized antibody of any of claims 21-32, wherein the mature heavy chain variable region has an amino acid sequence comprising SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence comprising SEQ ID NO:8.

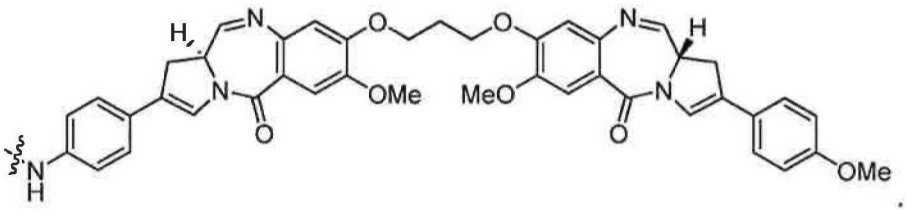
34. The humanized antibody of any of claims 21-33, wherein the antibody is conjugated to a cytotoxic or cytostatic agent.

35. The humanized antibody of claim 34, wherein the antibody is conjugated to a cytotoxic agent.

36. The humanized antibody of claim 35, wherein the cytotoxic agent is conjugated to the antibody via an enzyme cleavable linker.

37. The humanized antibody of claim 35 or 36, wherein the cytotoxic agent is a DNA minor groove binder.

38. The humanized antibody of claim 34-37, wherein the cytotoxic agent has the formula



39. A humanized antibody comprising a mature heavy chain variable region comprising the 3 CDRs of SEQ ID NO:18 and wherein positions H48, H66, H67, H69, H71 and H94 are occupied by I, K, A, L, A and S respectively, and a mature light chain variable region comprising the 3 CDRs of SEQ ID NO:8, and wherein positions L22, L46, L69 and L71 are occupied by N, T, Q and Y, respectively.

40. The humanized antibody of claim 39, having an association constant for human or cynomolgus monkey CD33 of 0.5 to 2 x 10^9 M^{-1}.

41. A nucleic acid encoding a mature heavy chain variable region and/or a mature light chain variable region as defined by any of claims 1-17 or claims 21-40.

42. A method of treating a patient having or at risk of cancer, comprising administering to the patient an effective regime of a humanized antibody of any of claims 21-40.

43. The method of claim 42, wherein the cancer is acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), acute promyelocytic leukemia (APL), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), a chronic myeloproliferative disorders, precursor B-cell acute lymphoblastic leukemia (preB-ALL), precursor T-cell acute lymphoblastic leukemia (preT-ALL), multiple myeloma (MM), mast cell disease, or myeloid Sarcoma.

44. A pharmaceutical composition comprising a humanized antibody of any preceding claim.

45. A method of treating a patient having or at risk of having acute myeloid leukemia (AML), comprising administering to the patient an effective regime of a humanized antibody humanized antibody of any of claims 1-17, 21-33 or 39-40.

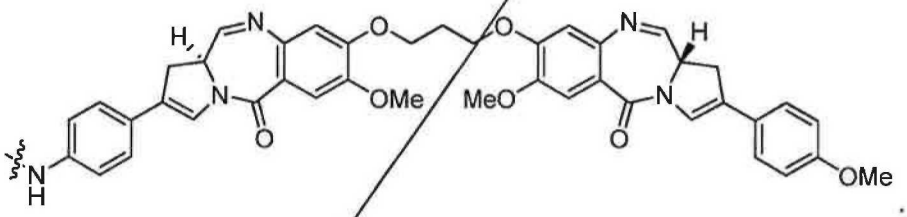
46. The method of claim 45, wherein the antibody is conjugated to a cytotoxic or cytostatic agent.

47. The method of claim 46, wherein the antibody is conjugated to a cytotoxic agent.

48. The method of claim 47, wherein the cytotoxic agent is conjugated to the antibody via an enzyme cleavable linker.

49. The method of claim 47 or 48, wherein the cytotoxic agent is a DNA minor groove binder.

50. The method of claims 47-49, wherein the cytotoxic agent has the formula



What is claimed is:

1. An isolated antibody that specifically binds to a human CD33 protein, wherein the antibody comprises a mature heavy chain variable region comprising three heavy chain complementarity determining regions (CDRs): heavy chain CDR1 consisting of SEQ ID NO:19, heavy chain CDR2 consisting of SEQ ID NO:20, and heavy chain CDR3 consisting of SEQ ID NO:21; and a mature light chain variable region comprising three light chain CDRs: light chain CDR1 consisting of SEQ ID NO:22, light chain CDR2 consisting of SEQ ID NO:23, and light chain CDR3 consisting of SEQ ID NO:24.

2. The antibody of claim 1, wherein the antibody is selected from a murine antibody, a chimeric antibody, and a humanized antibody.

3. The antibody of claim 2, wherein the antibody is a humanized antibody.

4. The humanized antibody of claim 3, wherein the antibody comprises a mature heavy chain variable region having an amino acid sequence at least 90% identical to SEQ ID NO:18 provided that position H48 is occupied by I, position H66 is occupied by K, position H67 is occupied by A, position H69 is occupied by L, position H71 is occupied by A, and position H94 is occupied by S and a mature light chain variable region at least 90% identical to SEQ ID NO:8 provided position L22 is occupied by N, position L46 is occupied by T, position L69 is occupied by Q, and position L71 by Y, as determined by the Kabat numbering system.

5. The humanized antibody of claim 3, comprising a mature heavy chain variable region having an amino acid sequence at least 95% identical

to SEQ ID NO:18 and a mature light chain variable region at least 95% identical to SEQ ID NO:8.

6. The humanized antibody of claim 3, wherein the mature heavy chain variable region is fused to a heavy chain constant region and the mature light chain variable region is fused to a light chain constant region.

7. The humanized antibody of claim 6, wherein the heavy chain constant region is a mutant form of natural human constant region which has reduced binding to an Fcγ receptor relative to the natural human constant region.

8. The humanized antibody of claim 6, wherein the heavy chain constant region is of IgG1 isotype.

9. The humanized antibody of claim 6, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:27 and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

10. The humanized antibody of claim 6, wherein the heavy chain constant region has an amino acid sequence comprising SEQ ID NO:29 (S239C) and the light chain constant region has an amino acid sequence comprising SEQ ID NO:25.

11. The humanized antibody of claim 3, wherein the mature heavy chain variable region has an amino acid sequence designated SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence designated SEQ ID NO: 8.

12. The antibody of claim 1, wherein the antibody is conjugated to a cytotoxic or cytostatic agent.

13. The antibody of claim 12, wherein the antibody is conjugated to a cytotoxic agent.

14. The antibody of claim 13, wherein the cytotoxic agent is conjugated to the antibody via an enzyme cleavable linker.

15. The antibody of claim 13, wherein the cytotoxic agent is a DNA minor groove binder.

16. The antibody of claim 13, wherein the cytotoxic agent is a pyrrolobenzodiazepine.

17. The antibody of claim 1 having an association constant for human or cynomolgus monkey CD33 of 0.5 to 2 x 10^9 M^{-1}.

18. A pharmaceutical composition comprising the antibody of claim 1.

19. The humanized antibody of claim 3 comprising a mature heavy chain variable region having an amino acid sequence at least 90% identical to HI (SEQ ID NO:18) and a mature light chain variable region at least 90% identical to LG (SEQ ID NO:8).

20. The humanized antibody of claim 19, provided that position H94 is occupied by S.

21. A humanized antibody comprising a mature heavy chain variable region comprising 3 CDRs of SEQ ID NO:18 and wherein positions H48, H66, H67, H69, H71 and H94 are occupied by I, K, A, L, A and S respectively, and a mature light chain variable region comprising 3 CDRs of SEQ ID NO:8, and wherein positions L22, L46, L69 and L71 are occupied by N, T, Q and Y, respectively.

22. An antibody that specifically binds to a human CD33 protein comprising a mature heavy chain variable region having the amino acid sequence of SEQ ID NO:18 linked to a heavy chain constant region having the amino acid sequence of SEQ ID NO: 27 or 29, and a mature light chain variable region having the amino acid sequence designated SEQ ID NO:8 linked to a light chain constant region having the amino acid sequence of SEQ NO:25, wherein the antibody is conjugated to a pyrrolobenzodiazepine.

23. The antibody of claim 22, wherein the mature heavy chain variable region is linked to a mature heavy chain constant region having an amino acid sequence comprising SEQ ID NO:29 (S239C).

24. A pharmaceutical composition comprising the antibody of claim 22.

25. A pharmaceutical composition comprising the antibody of claim 22.

26. A pharmaceutical composition comprising the antibody of claim 19 conjugated to a cytotoxic agent, which is a pyrrolobenzodiazepine.

27. The pharmaceutical composition of claim 26, wherein the antibody comprises a mature heavy chain variable region having an amino acid sequence designated SEQ ID NO:18 and a mature light chain variable region having an amino acid sequence designated SEQ ID NO:8.

28. The pharmaceutical composition of claim 27, wherein the mature heavy chain variable region is linked to a mature heavy chain constant region having an amino acid sequence comprising SEQ ID NO:29 (S239C) and the mature light chain variable region is linked to a light chain constant region having an amino acid sequence comprising SEQ ID NO:25.