Figure 2b provides amino acid sequences of various antibody variable light regions for use in the present invention. CDR regions LCDRl, LCDR2 and LCDR3 are designated from N- to C-terminus in boldface.

Figure 3 provides amino acid sequences of variable heavy regions of various consensus-based HuCAL antibody master gene sequences. CDR regions HCDRl, HCDR2 and HCDR3 are designated from N- to C-terminus in boldface.

Figure 4 provides amino acid sequences of variable light regions of various consensus-based HuCAL antibody master gene sequences. CDR regions LCDRl, LCDR2 and LCDR3 are designated from N- to C-terminus in boldface.

Figure 5 provides the amino acid sequence of CD38 (SWISS-PROT primary accession number P28907).

Figure 6 provides the nucleotide sequences of the heavy and light chains of chimeric OKT1O.

Figure 7 provides the DNA sequence of pMORPH®_h_IgGl_l (bp 601-2100) (SEQ ID NO: 74), encoding the IgG1 variable heavy chain (SEQ ID NOS: 129 and 138).÷ The vector is based on the pcDNA3.1+ vectors (Invitrogen). The amino acid sequence of the VH-stuffer sequence is indicated in bold, whereas the final reading frames of the VH-leader sequence and the constant region gene are printed in non-bold. Restriction sites are indicated above the sequence. The priming sites of the sequencing primers are underlined.

Figure 8 provides the DNA sequence of Ig kappa light chain expression vector pMORPH®_h_Igκ_l (bp 601-1400) (SEQ ID NO: 75), encoding the variable κ light chain (SEQ ID NO: 130).÷ The vector is based on the pcDNA3.1+ vectors (Invitrogen). The amino acid sequences of the Vκ-stuffer sequence is indicated in bold, whereas the final reading frames of the Vκ-leader sequence and of the constant region gene are

printed in non-bold. Restriction sites are indicated above the sequence. The priming sites of the sequencing primers are underlined.

Figure 9 provides the DNA sequence of HuCAL Ig lambda light chain vector pMORPH®_h_Igλ _1 (bp 601-1400) (SEQ ID NO: 76), encoding the variable λ light chain (SEQ ID NOS: 131 and 139).~~:~~ The amino acid sequence of the Vλ-stuffer sequence is indicated in bold, whereas the final reading frames of the Vλ-leader sequence and of the constant region gene are printed in non-bold. Restriction sites are indicated above the sequence. The priming sites of the sequencing primers are underlined.

Figure 10 provides different combinations of heavy and light chains in the Fab/IgG format for use in the present invention

Figure 11 provides CD38-expression analysis of Lymphocytes and Erythrocytes obtained by FACS. PBMCs and Erythrocytes were isolated from whole blood of cynomolgus, rhesus and marmoset by density gradient centrifugation followed by FACS-analysis using anti-CD38 Fab antibodies MOR03087 (A, right histograms, light arrow) and MOR03088 (B, right histograms; light arrow). An irrelevant Fab-antibody (A & B, left histograms; black arrow) was used as a negative control.

Figure 12 provides CD38 expression analysis of Lymphocytes and Erythrocytes obtained by FACS.

PBMCs and Erythrocytes were isolated from whole blood of human, cynomolgus and marmoset by density gradient centrifugation followed by FACS-analysis using anti-CD38 IgGl MOR03087 (right histograms; white arrow). An irrelevant IgGl control antibody (A & B, left histograms; black arrow) was used as a negative control.

Figure 13 provides a comparative overview of Cross-Reactivity of different anti-CD38 antibodies.

Figures 14(a) and 14(b) delineate the CDR and FR regions for certain antibodies for use in the invention and compare amino acids at agiven position to each other and to corresponding consensus sequences.

The consensus sequences are VH1A (SEQ ID NO: 61), VH2 (SEQ ID NO: 63), VH3 (SEQ ID NO: 63), VH4 (SEQ ID NO: 64), VH5 (SEQ ID NO: 65), V1_λ1 (SEQ ID NO; 66), V1_λ2 (SEQ ID NO: 67), V1_ λ3 (SEQ ID NO: 68), V1_k1 (SEQ ID NO: 69) and V1_k3 (SEQ ID NO: 70), 3076 represents an antibody having a variable heavy region (VH) corresponding to SEQ ID NO: 16 and a variable light (VL) region corresponding to SEQ ID NO: 46. Likewise, 3078 VL (SEQ ID NO: 17) and VL (SEQ ID NO: 47); 3081 VL (SEQ ID NO: 18) and VL (SEQ ID NO: 48); 3085 VH (SEQ ID NO: 19) and VL (SEQ ID NO: 49); 3086 VH (SEQ ID NO: 20) and VL (SEQ ID NO: 50); 3087 VH (SEQ ID NO: 21) and VL (SEQ ID NO: 51); 3088 VH (SEQ ID NO: 22) and VL (SEQ ID NO: 52); 3089 VH (SEQ ID NO: 23) and VL (SEQ ID NO: 53); 3101 VH (SEQ ID NO: 24) and VL (SEQ ID NO: 54); 3102 VH (SEQ ID NO: 25) and VL (SEQ ID NO: 55); 3127 VH (SEQ ID NO: 26) and VL (SEQ ID NO: 56); 3128 VH (SEQ ID NO: 27) and VL (SEQ ID NO: 57); 3129 VH (SEQ ID NO: 28) and VL(SEQ ID NO: 58); 3130 VH (SEQ ID NO: 29) and VL (SEQ ID NO: 59); 3131 VH (SEQ ID NO: 30) and VL (SEQ ID NO: 60); 6183 VH (SEQ ID NO: 92); 6184 VH (SEQ ID NO: 93) 6185 VH (SEQ ID NO: 94); 6186 VH (SEQ ID NO: 95); 6187 VH (SEQ ID NO: 96); 6188 VH (SEQ ID NO: 97); 6189 VH (SEQ ID NO: 98); 6190 VH (SEQ ID NO: 99); 6192 VH (SEQ ID NO: 100); 6195 VH (SEQ ID NO: 101; 6197 VH (SEQ ID NO: 102); 6200 VH (SEQ ID NO: 103); 6201 VH (SEQ ID NO: 104); 6204 VH (SEQ ID NO: 105); 6214 VH (SEQ ID NO: 106); 6278 VL (SEQ ID NO: 109); and 6279 VL (SEQ ID NO: 110).

DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the discovery of novel antibodies and methods of using antibodies that are specific to or have a high affinity for CD38 and can deliver a therapeutic benefit to a subject. The antibodies, which may be human or humanized, can be used in many contexts, which are more fully described herein. Suitable antibodies for use in the present invention are disclosed in US 60/614,471, which hereby is incorporated by reference.

A "human" antibody or functional human antibody fragment is hereby defined as one that is not chimeric (e.g., not "humanized") and not from (either in whole or in part) a non-human species. A human antibody or functional antibody fragment can be derived from a human or can be a synthetic human antibody. A "synthetic human antibody" is defined herein as an antibody having a sequence derived, in whole or in part, *in silico* from synthetic sequences that are based on the analysis of known human antibody sequences. *In silico* design of a human antibody sequence or fragment thereof can be achieved, for example, by analyzing a database of human antibody or antibody fragment sequences and devising a polypeptide sequence utilizing the data obtained therefrom. Another example of a human antibody or functional antibody fragment, is one that is encoded by a nucleic acid isolated from a library of antibody sequences of human origin (*i.e.*, such library being based on antibodies taken from a human natural source).

A "humanized antibody" or functional humanized antibody fragment is defined herein as one that is (i) derived from a non-human source (e.g., a transgenic mouse which bears a

CLAIMS

1. An isolated antigen-binding region that is specific for CD38, which comprises (i) an H-CDR3 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 or (ii) an H-CDR3 region that has at least a sixty percent identity to an H-CDR3 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106.

2. An isolated antigen-binding region according to claim 1, further comprising (i) an H-CDR2 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 or (ii) an H-CDR2 region that has at least a sixty percent identity to an H-CDR2 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106.

3. An isolated antigen-binding region according to claim 2, further comprising (i) an H-CDR1 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 or (ii) an H-CDR1 region that has at least a sixty percent identity to an H-CDR1 region depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106.

4. An isolated antibody or functional fragment thereof that is specific for CD38, which comprises (i) a variable heavy chain depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 or (ii) a variable heavy chain that has at least a sixty percent identity to a

variable heavy chain depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106.

5. An isolated antigen-binding region that is specific for CD38, which comprises (i) an L-CDR3 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110 or (ii) an L-CDR3 region that has at least a sixty percent identity to an L-CDR3 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

6. An isolated antigen-binding region according to claim 5, further comprising (i) an L-CDR2 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110 or (ii) an L-CDR2 region that has at least a sixty percent identity to an L-CDR2 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

7. An isolated antigen-binding region according to claim 6, further comprising (i) an L-CDR1 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110 or (ii) an L-CDR1 region that has at least a sixty percent identity to an L-CDR1 region depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

8. An isolated antibody or functional fragment thereof, which comprises (i) a variable light chain depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110 or (ii) a variable light chain that has at least a sixty percent identity to a variable light chain depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

9. An isolated immunoglobulin according to claim 4 or 8, which is an IgG.

10. ~~An isolated immunoglobulin according to claim 9, which is an IgG1.~~

11. A variable heavy chain of an isolated antigen-binding region that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91, wherein said antigen-binding region is specific for CD38.

12. A variable light chain of an isolated antigen-binding region that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108, wherein said antibody or functional fragment thereof is specific for CD38.

13. An isolated nucleic acid sequence that encodes an antigen-binding region of a human antibody or functional fragment thereof that is specific for CD38.

14. A nucleic acid sequence encoding a variable heavy chain of an isolated antigen-binding region, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 and 91 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91, wherein said antigen-binding region is specific for CD38.

15. A nucleic acid sequence encoding a variable light chain of an isolated antigen-binding region, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 and 108 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108 wherein said antigen-binding region is specific for CD38.

16. A vector comprising a nucleic acid sequence according to any one of claims 13-15.

17. An isolated cell comprising a vector according to claim 16.

18. An isolated cell according to claim 17, wherein said cell is bacterial.

19. An isolated cell according to claim 17, wherein said cell is mammalian.

20. A pharmaceutical composition comprising an antibody or function fragment thereof according to claim 4 or 8and a pharmaceutically acceptable carrier or excipient therefor.

21. A method for treating a disorder or condition associated with the undesired presence of CD38+ cells, comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 20.

22. A method according to claim 21, wherein said disorder or condition is a haematological disease.

23. A method according to claim 22, wherein said haematological disease is taken from the list of multiple myeloma, chronic lymphocytic leukemia, chronic myelogenous leukemia, acute myelogenous leukemia and acute lymphocytic leukemia.

~~24. A method according to claim 21, wherein said disorder or condition is an~~ inflammatory disease.

25. A method according to claim 24, wherein said inflammatory disease is taken from the list of rheumatoid arthritis and systemic lupus erythematosus.

26. An isolated antigen-binding region according to any one of claims 1-3 and 5-7, wherein said sequence identity is at least 80%.

27. A method of inducing specific killing of tumor cells that express CD38, wherein said specific killing occurs by CD38 cross-linking, comprising the step of incubating said cells in the presence of a sufficient amount of an isolated human or humanized anti-CD38 antibody or a functional fragment thereof, wherein said human or humanized anti-CD38 antibody comprises (i) a nucleic acid sequence encoding a heavy chain depicted in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91, wherein said antibody or a functional fragment thereof is specific for CD38.

28. A method of inducing specific killing of tumor cells that express CD38, wherein said specific killing occurs by CD38 cross-linking, comprising the step of incubating said cells in the presence of a sufficient amount of an isolated human or humanized anti-CD38 antibody or a functional fragment thereof, wherein said human or humanized anti-CD38 antibody comprises (i) a nucleic acid sequence encoding a light chain depicted in SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ

~~ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108, wherein said~~ antibody or a functional fragment thereof is specific for CD38.

29. A method of inducing specific killing of tumor cells that express CD38, wherein said specific killing occurs by CD38 cross-linking, comprising the step of incubating said cells in the presence of a sufficient amount of an isolated human or humanized anti-CD38 antibody or a functional fragment thereof, wherein said human or humanized anti-CD38 antibody or said functional fragment thereof comprises (i) a heavy chain amino acid sequence depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 or (ii) a variable heavy chain that has at least a sixty percent identity to a variable heavy chain depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106.

30. A method of inducing specific killing of tumor cells that express CD38, wherein said specific killing occurs by CD38 cross-linking, comprising the step of incubating said cells in the presence of a sufficient amount of an isolated human or humanized anti-CD38 antibody or a functional fragment thereof, wherein said human or humanized anti-CD38 antibody comprises (i) and/or a light chain amino acid sequence depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110 or (ii) a variable light chain that has at least a sixty percent identity to a variable light chain depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

31. A method of detecting specific killing of tumor cells that express CD38, by CD38 cross-linking, comprising the steps of:

~~(i) administering to a subject in need thereof an effective amount of a human or humanized~~ anti-CD38 antibody or a functional fragment thereof, and

(ii) detecting the specific killing activity of said human or humanized anti-CD38 antibody or said functional fragment thereof.

32. A method according to claim 31, wherein said tumor cells are of human, minipig or rabbit origin.

33. A method of detecting the presence of CD38 in a tissue or a cell of minipig origin, comprising the steps of:

(i) allowing a human or humanized anti-CD38 antibody or a functional fragment thereof to come into contact with said CD38, and

(ii) detecting the specific binding of said human or humanized anti-CD38 antibody or functional fragment thereof to said CD38 minipig cells, wherein said antibody or functional fragment thereof is also able to specifically bind to CD38 of human origin.

34. A method according to claim 33, wherein said CD38 of minipig origin is comprised within an isolated cell type selected from the group consisting of peripheral blood monocyte, erythrocyte, lymphocyte, thymocyte, muscle cell, cerebellum cell, pancreas cell, lymph-node cell, tonsil cell, spleen cell, prostate cell, skin cell and a cell of the retina.

35. A method according to claim 34, wherein said human or humanized anti-CD38 antibody or functional fragment thereof comprises (i) a nucleic acid sequence encoding a heavy chain depicted in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91 and/or a nucleic acid sequence encoding a light chain depicted in SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108 or (ii) a sequence having at least 60 percent identity in the heavy chain regions depicted in SEQ ID

~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88,~~ 89, 90 or 91 and/or a sequence having at least 60 percent identity in the light chain regions depicted in SEQ ID NO 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108.

36. A method of detecting CD38 in a CD38-expressing erythrocyte, comprising the steps of:

(i) allowing a human or humanized anti-CD38 antibody or a functional fragment thereof to come into contact with said CD38-expressing erythrocyte, and

(ii) detecting the specific binding of said human or humanized anti-CD38 antibody or functional fragment thereof to said CD38-expressing erythrocytes, wherein said antibody or functional fragment thereof is also able to specifically bind to human CD38 from a cell or tissue other than human erythrocytes.

37. A method according to claim 36, wherein said antibody or functional fragment thereof is also able to specifically bind to human CD38 from a cell that is a human lymphocyte.

38. A method according to claim 36, wherein said human or humanized anti-CD38 antibody or functional fragment thereof comprises (i) a nucleic acid sequence encoding a heavy chain depicted in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91 and/or a nucleic acid sequence encoding a light chain depicted in SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 or 45, 107 or 108 or (ii) a sequence having at least 60 percent identity in the heavy chain regions depicted in SEQ ID NO 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91 and a sequence having at least 60 percent identity in the light chain regions depicted in SEQ ID NO: 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 107 or 108.

~~39. A method according to claim 36, wherein said human or humanized anti-~~ CD38 antibody or functional fragment thereof comprises (i) a heavy chain amino acid sequence depicted in SEQ ID NO: 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 and/or a light chain amino acid sequence depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110; or (ii) a sequence having at least 60 percent identity in the heavy chain regions depicted in SEQ ID NO 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105 or 106 and a sequence having at least 60 percent identity in the light chain regions depicted in SEQ ID NO: 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 109 or 110.

40. A diagnostic composition comprising an antibody or functional fragment thereof according to claim 4 or 8; and an acceptable carrier or excipient.

41. An isolated antibody or functional fragment thereof according to claim 1, which comprises (i) an H-CDR3 region depicted in SEQ ID NO: 21 or 22 or (ii) an H-CDR3 region at least a sixty percent identity thereto, and that is specific for human CD38 and marmoset CD38.

42. An isolated antibody or functional fragment thereof according to claim 5, which comprises (i) an L-CDR3 region depicted in SEQ ID NO: 51 or 52 or (ii) an L-CDR3 region at least a sixty percent identity thereto, that is specific for human CD38 and marmoset CD38.

43. A variable heavy chain of an isolated antigen-binding region according to claim 11, that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 6 or 7 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to a complementary strand thereof, which antigen-binding region is specific for human CD38 and marmoset CD38.

~~44. A variable light chain of an isolated antigen-binding region according to claim 12, that is~~ encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 36 or 37 or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to a complementary strand thereof, which antigen-binding region is specific for human CD38 and marmoset CD38.

CLAIMS

The invention claimed is:

1. An isolated antibody or antigen-binding fragment thereof that binds to CD38, which comprises the three variable heavy chain complementarity determining regions (H-CDRs) and the three variable light-chain complementarity determining regions (L-CDRs) that are in the variable heavy chain and variable light chain pairs selected from:

(i) SEQ ID NO: 18 and 48,

(ii) SEQ ID NO: 20 and 50,

(iii) SEQ ID NO: 21 and 51,

(iv) SEQ ID NO: 22 and 52, and

(v) SEQ ID NO: 25 and 55.

2. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises the three H-CDRs in SEQ ID NO: 18 and the three L-CDRs depicted in SEQ ID NO: 48.

3. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises the three H-CDRs in SEQ ID NO: 20 and the three L-CDRs depicted in SEQ ID NO: 50.

4. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises the three H-CDRs in SEQ ID NO: 21 and the three L-CDRs depicted in SEQ ID NO: 51.

5. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises the three H-CDRs in SEQ ID NO: 22 and the three L-CDRs depicted in SEQ ID NO: 52.

6. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises the three H-CDRs in SEQ ID NO: 25 and the three L-CDRs depicted in SEQ ID NO: 55.

7. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a variable heavy chain at least eighty percent identical to that depicted in SEQ ID NO: 18, 20, 21, 22, or 25.

8. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 7, which comprises a variable heavy chain at least ninety percent identical to that depicted in SEQ ID NO: 18, 20, 21, 22, or 25.

9. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 8, which comprises a variable heavy chain depicted in SEQ ID NO: 18, 20, 21, 22, or 25.

10. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a variable light chain at least eighty percent identical to that depicted in SEQ ID NO: 48, 50, 51, 52, or 55.

11. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 10, which comprises a variable light chain at least ninety percent identical to that depicted in SEQ ID NO: 48, 50, 51, 52, or 55.

12. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 11, which comprises a variable light chain depicted in SEQ ID NO: 48, 50, 51, 52, or 55.

13. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 4, which comprises a variable heavy chain at least 80% identical to that depicted in SEQ ID NO: 21.

14. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 13, which comprises a variable heavy chain at least 90% identical to that depicted in SEQ ID NO: 21.

15. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 14, which comprises a variable heavy chain depicted in SEQ ID NO: 21.

16. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 15, which comprises a variable heavy chain at least 80% identical to that depicted in SEQ ID NO: 22.

17. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 16, which comprises a variable heavy chain at least 90% identical to that depicted in SEQ ID NO: 22.

18. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 17, which comprises a variable heavy chain depicted in SEQ ID NO: 22.

19. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 4, which comprises a variable light chain at least 80% identical to that depicted in SEQ ID NO: 51.

20. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 19, which comprises a variable light chain at least 90% identical to that depicted in SEQ ID NO: 51.

21. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 20, which comprises a variable light chain depicted in SEQ ID NO: 51.

22. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 5, which comprises a variable light chain at least 80% identical to that depicted in SEQ ID NO: 52.

23. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 22, which comprises a variable light chain at least 90% identical to that depicted in SEQ ID NO: 52.

24. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 23, which comprises a variable light chain depicted in SEQ ID NO: 52.

25. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy and light chain pair that has at least eighty percent identity to those depicted in the heavy and light chain pairs selected from:

(i) SEQ ID NO: 18 and 48,

(ii) SEQ ID NO: 20 and 50,

(iii) SEQ ID NO: 21 and 51,

(iv) SEQ ID NO: 22 and 52, and

(v) SEQ ID NO: 25 and 55.

26. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy and light chain pair that has at least ninety percent identity to those depicted in the heavy and light chain pairs selected from:

(i) SEQ ID NO: 18 and 48,

(ii) SEQ ID NO: 20 and 50,

(iii) SEQ ID NO: 21 and 51,

(iv) SEQ ID NO: 22 and 52, and

(v) SEQ ID NO: 25 and 55.

27. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy chain depicted in SEQ ID NO: 18, and a light chain depicted in SEQ ID NO: 48.

28. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy chain depicted in SEQ ID NO: 20, and a light chain depicted in SEQ ID NO: 50.

29. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 25, which comprises a heavy chain at least 80% identical to that depicted in SEQ ID NO: 21, and a light chain at least 80% identical to that depicted in SEQ ID NO: 51.

30. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 26, which comprises a heavy chain at least 90% identical to that depicted in SEQ ID NO: 21, and a light chain at least 90% identical to that depicted in SEQ ID NO: 51.

31. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy chain depicted in SEQ ID NO: 21, and a light chain depicted in SEQ ID NO: 51.

32. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 25, which comprises a heavy chain at least 80% identical to that depicted in SEQ ID NO: 22 and a light chain at least 80% identical to that depicted in SEQ ID NO: 52.

33. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 26, which comprises a heavy chain at least 90% identical to that depicted in SEQ ID NO: 22 and a light chain at least 90% identical to that depicted in SEQ ID NO: 52.

34. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy chain depicted in SEQ ID NO: 22 and a light chain depicted in SEQ ID NO: 52.

35. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which comprises a heavy chain depicted in SEQ ID NO: 25 and a light chain depicted in SEQ ID NO: 55.

36. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which is an scFv, Fab or $F(ab')_2$ fragment.

37. The isolated antibody or antigen binding fragment thereof that binds to CD38 according to claim 1, which is an IgG.

38. The isolated antibody according to claim 37, which is an IgG1.

39. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof that binds to CD38 according to claim 1, and a pharmaceutically acceptable carrier or excipient therefor.

40. A diagnostic composition comprising an antibody or antigen-binding fragment thereof that binds to CD38 according to claim 1, and an acceptable carrier or excipient therefor.