multiple myeloma each year and almost 11,000 MM patients die each year. Despite advances in therapy, multiple myeloma remains an incurable disease, see Jemal A, *et al. CA Cancer J Clin.* 2008;58:71-96; Kyle RA, *et al. Mayo Clin Proc.* 2003;778:21-33; Bergsagel DE, *et al. Blood.* 1999, 94:1174-1182.

Summary

In a first aspect, the present invention refers to an isolated BCMA-binding antibody, or a BCMA-binding fragment thereof, a Vh-CDR1 comprising SEQ ID NO:4, a Vh-CDR2 comprising SEQ ID NO:5, a Vh-CDR3 comprising SEQ ID NO:6, a Vl-CDR1 comprising SEQ ID NO:106, a Vl-CDR2 comprising SEQ ID NO:107, and a Vl-CDR3 comprising SEQ ID NO:108. In a second aspect, the present invention refers to a pharmaceutical composition comprising the antibody or fragment of the present invention, a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, and/or a preservative. In a third aspect, the present invention refers to a use of a composition of the present invention in the manufacture of a medicament for treating a disease, wherein the disease is selected from the group consisting of: B-cell cancers, multiple myeloma, malignant plasma cell neoplasms, Kahler's disease and Myelomatosis; Plasma cell leukemia; Plasmacytoma; B-cell prolymphocytic leukemia; Hairy cell leukemia; B-cell non-Hodgkin's lymphoma (NHL); Acute myeloid leukemia (AML); Chronic myeloid leukemia (CML); Acute lymphocytic leukemia (ALL); Chronic lymphocytic leukemia (CLL); Follicular lymphoma (including follicular non-Hodgkin's lymphoma types); Burkitt's lymphoma (Endemic Burkitt's lymphoma; Sporadic Burkitt's lymphoma); Marginal zone lymphoma (Mucosa-Associated Lymphoid Tissue; MALT / MALToma; Monocytoid B cell lymphoma; Splenic lymphoma with villous lymphocytes); Mantle cell lymphoma; Large cell lymphoma (Diffuse large cell; Diffuse Mixed Cell; Immunoblastic Lymphoma; Primary Mediastinal B Cell Lymphoma; Angiocentric Lymphoma - pulmonary B cell); Small lymphocytic lymphoma (SLL); Precursor B-lymphoblastic lymphoma; Myeloid leukemia (granulocytic; myelogenous; Acute myeloid leukemia; Chronic myeloid leukemia; Subacute myeloid leukemia; Myeloid sarcoma; Chloroma; Granulocytic sarcoma; Acute promyelocytic leukemia; Acute myelomonocytic leukemia); Waldenstrom's macroglobulinemia, and other B-cell lymphoma. In a fourth aspect, the present invention refers to an isolated polynucleotide, wherein said polynucleotide encodes the light chain, the heavy chain, or the light chain and the heavy chain of the antibody or fragment of the present invention. In a fifth aspect, the present invention refers to a plasmid, comprising the polynucleotide of the present invention. In a sixth aspect, the present invention refers to an isolated cell, comprising said plasmid of claim 17, wherein said cell is a prokaryotic cell; a eukaryotic cell; a mammalian cell; an insect cell; or a CHO cell. In a seventh aspect, the present invention refers to a method of making a BCMA-binding antibody, or a BCMA-binding fragment thereof, comprising incubating said isolated cell of the present invention ~~under conditions that allow it to express said antibody or polypeptide~~. ~~In an eight aspect, the present invention refers to an isolated monoclonal antibody~~

~~that specifically binds to SEQ ID NO:285 and SEQ ID NO:286, but does not specifically bind SEQ ID NO:351. In a ninth aspect, the present invention refers to an isolated monoclonal antibody that specifically binds to SEQ ID NO:352, but does not specifically bind SEQ ID NO:351. In a tenth aspect, the present invention refers to an isolated monoclonal antibody that binds a neutralizing determinant comprising amino acids 1 though 20 (inclusive) of SEQ ID NO: 285. In an eleventh aspect, the present invention refers to an isolated monoclonal antibody that binds a neutralizing determinant comprising amino acids 1 through 11 (inclusive) of SEQ ID NO: 285. In a twelve aspect, the present invention refers to an isolated BCMA-binding antibody or BCMA-binding fragment thereof, wherein said antibody interacts with Gly6, Gln7, Phe14, Asp15, Ser16, Leu17, and His19 of human BCMA of SEQ ID NO:360 as defined by x-ray crystallography at a contact distance resolution of 0 to 3.4 Å (inclusive).~~

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 shows the amino acid sequence of human BCMA (SEQ ID NO:285) and cynomolgus (Macaca fascicularis) BCMA (SEQ ID NO:286).

FIGURE 2 is a schematic of one embodiment of an antibody drug conjugate showing the structures of an exemplary linker and toxin.

FIGURE 3 shows that BCMA mRNA is expressed on >99% of multiple myeloma patient samples.

FIGURES 4A and B are schematics of the monoclonal antibody generation, screening, and characterization for the two campaigns.

FIGURES 5A-C are data tables for the monoclonal antibody generation, screening, and characterization for the two campaigns.

FIGURE 6 shows binding of the 2A1 and 1E1 mAbs to the myeloma cell line H929.

FIGURE 7 shows the 2A1 mAb bound BCMA on various myeloma and B-cell lines.

FIGURE 8 is a graph of the ADCC activity for the 2A1 and 1E1 antibodies (EC_{50} of 11 ng/ml for 2A1 and 76 ng/ml for 1E1).

FIGURE 9 shows that the 2A1 antibody was readily internalized following binding to BCMA on H929 cells.

FIGURE 10 is various 2A1-MCC-DM1 ADCs analyzed by mass spectrometry.

FIGURE 11 depicts two different antibodies (2A1 and 1E) that were conjugated with different linkers and maytansine molecules and analyzed for their capacity to kill myeloma cells.

FIGURES 12A-F shows 2A1-MCC-DM1 ADC was tested against various multiple myeloma cell lines, including H929, U266, MMIR, MMIS, the EW36 B-cell lymphoma cell line, and the RAMOS Burkitt's lymphoma cell line.

a. a Vh-CDR1 comprising SEQ ID NO:1, a Vh-CDR2 comprising SEQ ID NO:2, and a Vh-CDR3 comprising SEQ ID NO:3,; and/or

b. a Vl-CDR1 comprising SEQ ID NO:103, a Vl-CDR2 comprising SEQ ID NO:104, and a Vl-CDR3 comprising SEQ ID NO:105.

15. The polynucleotide of claim 13, wherein said polynucleotide sequence comprises an Ab-1Vl comprising SEQ ID NO:239 and/or an Ab-1Vh comprising SEQ ID NO:205.

16. The polynucleotide of claim 13, wherein said polynucleotide sequence comprises a light chain comprising SEQ ID NO:279 and/or a heavy chain comprising SEQ ID NO:273.

17. A plasmid, comprising the polynucleotide of claim 13.

18. The plasmid of claim 13, wherein said plasmid is an expression vector.

19. An isolated cell, comprising said plasmid of claim 17, wherein said cell is:

a. a prokaryotic cell;

b. a eukaryotic cell;

c. a mammalian cell;

d. an insect cell; or

e. a CHO cell.

20. A method of making a BCMA-binding antibody, or a BCMA-binding fragment thereof, comprising incubating said isolated cell of claim 19 ~~under conditions that allow it~~ to express said antibody or polypeptide.

~~21. An isolated monoclonal antibody that specifically binds to SEQ ID NO:285 and SEQ ID NO:286, but does not specifically bind SEQ ID NO:351.~~

~~22. An isolated monoclonal antibody that specifically binds to SEQ ID NO:352, but does not specifically bind SEQ ID NO:351.~~

~~23. An isolated monoclonal antibody that binds a neutralizing determinant comprising amino acids 1 though 20 (inclusive) of SEQ ID NO: 285.~~

24. An isolated monoclonal antibody that binds a neutralizing determinant comprising amino acids 1 through 11 (inclusive) of SEQ ID NO: 285.

25. An isolated BCMA-binding antibody or BCMA-binding fragment thereof, wherein said antibody interacts with Gly6, Gln7, Phe14, Asp15, Ser16, Leu17, and His19 of human BCMA of SEQ ID NO:360 as defined by x-ray crystallography at a contact distance resolution of 0 to 3.4 Å (inclusive).

26. The antibody or fragment thereof of claim 25, wherein said antibody interacts with Gly6, Gln7, Cys8, Tyr,13, Phe14, Asp15, Ser16, Leu17, Leu18, His19, and Ala20 of human BCMA of SEQ ID NO:360 as defined by x-ray crystallography at a contact distance resolution of 3.4 to 5.0 Å (inclusive).

27. The antibody or fragment thereof of claim 25, wherein said antibody forms a hydrogen bond with Gln7, Asp15, Ser16, Leu17, and His19 of human BCMA of SEQ ID NO:360 as defined by x-ray crystallography at a contact distance resolution of 0 to 3.4 Å (inclusive).