ANTIBODIES TARGETING B-CELL MATURATION ANTIGEN AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Patent Application Serial No. 62/088,246, filed December 5, 2014, the content of which is incorporated by reference in its entirety, and to which priority is claimed.

FIELD OF THE INVENTION

The presently disclosed subject matter relates to antibodies that bind to B-cell maturation antigen (BCMA), and methods of using the same.

BACKGROUND

BCMA is involved in B cell differentiation and signaling and is known to be expressed on non-malignant differentiated B cells and plasma cells. Several groups have confirmed surface expression of BCMA on multiple myeloma (MM), with one group finding it as an alternative to CD138 as a FACS marker for malignant plasma cells from fresh or frozen patient bone marrow samples with mean relative mean fluorescence intensity (MFI) between 9-16 (n=35) (Frigyesi, I., et al. Robust isolation of malignant plasma cells in multiple myeloma. Blood 123, 1336-1340 (2014); Tai, Y.T., et al. Novel afucosylated anti-B cell maturation antigen-monomethyl auristatin F antibody-drug conjugate (GSK2857916) induces potent and selective anti-multiple myeloma activity. Blood (2014)). Given the significant role for BCMA in multiple myeloma, antibodies that recognize BCMA, and methods of using such agents, are desired.

SUMMARY

In one aspect, the present disclosure refers to an anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 167, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 168, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 169; and a light chain variable region comprising a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 170, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 171, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 172.

In another aspect, the present disclosure refers to an anti-B cell maturation antigen (BCMA) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3 of the heavy chain variable region sequence set forth in SEQ ID NO:53, and a light chain variable region comprising a CDR1, a CDR2, and a CDR3 of the light chain variable region sequence set forth in SEQ ID NO:54.

In another aspect, the present disclosure refers to a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, and a pharmaceutically acceptable carrier.

In another aspect, the present disclosure refers to an immunoconjugate comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, linked to a therapeutic agent.

In another aspect, the present disclosure refers to a composition comprising the immunoconjugate as described herein, and a pharmaceutically acceptable carrier.

In yet another aspect, the present disclosure refers to a bispecific molecule comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein, linked to a second functional moiety.

In yet another aspect, the present disclosure refers to a composition comprising the bispecific molecule as described herein, and a pharmaceutically acceptable carrier.

In yet another aspect, the present disclosure refers to a nucleic acid molecule that encodes an anti-BCMA antibody or antigen-binding fragment thereof as described herein.

In yet another aspect, the present disclosure refers to an expression vector comprising the nucleic acid molecule as described herein.

In yet another aspect, the present disclosure refers to a host cell comprising the expression vector as described herein.

In yet another aspect, the present disclosure refers to a method for detecting BCMA in a whole cell or tissue, comprising:

contacting a cell or tissue with the anti-BCMA antibody or antigen-binding fragment thereof of any one of claims 1-35, wherein the antibody or antigen-binding fragment thereof comprises a detectable label; and

determining the amount of the labeled antibody or antigen-binding fragment thereof bound to the cell or tissue by measuring the amount of detectable label associated with the cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of BCMA in the cell or tissue.

In yet another aspect, the present disclosure refers to a use of a composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein for the manufacture of a medicament for treating a tumor in a subject.

In yet another aspect, the present disclosure refers to a kit for treating a tumor, comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein.

In yet another aspect, the present disclosure refers to the composition comprising the anti-BCMA antibody or antigen-binding fragment thereof as described herein for use as a therapy.

The presently disclosed subject matter provides antibodies that bind to a B-cell maturation antigen (BCMA), and methods of using the same.

In certain examples, the presently disclosed subject matter provides an isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 5, 9, 13, 17, 21,