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(54) Title: ANTIBODIES AGAINST IMMUNE CHECKPOINT MOLECULES AND METHODS OF USE

(57) Abstract: Antibodies against the immune checkpoint molecules Erythroid membrane-associated protein (ERMAP/BTN5), TAP Binding Protein Like protein (TAPBPL), and CD300c are provided, and their use for treating cancer.

Antibodies against immune checkpoint molecules and methods of use

Statement of Government Support

This invention was made with government support under AG072234, AI175087, and AI123131 awarded by the National Institutes of Health. The government has certain rights in the invention.

Sequence Listing Statement

A computer readable form of the Sequence Listing is filed with this application by electronic submission and is incorporated into this application by reference in its entirety. The Sequence Listing is contained in the file created on June 11, 2024 having the file name "23-0840-WO.xml" and is 70,186 bytes in size.

Background

Tumor progression is often accompanied by profound immune suppression that interferes with an effective antitumor response and tumor elimination. Immune cells are regulated by checkpoint molecules. T lymphocytes (T cells) are the major component in the immune system. Many cancers protect themselves from the immune system attack by producing immune checkpoint molecules to inhibit the functions of T cells and/or other immune cells. In the past several years, several new drugs that target immune checkpoint molecules such as PD-L1/PD-1, CTLA-4 and LAG3 have been approved by the FDA for the treatment of cancer and autoimmune disease. Although targeting the existing immune checkpoint molecules has achieved some success, a complete and durable response was only seen in a fraction of treated patients. The results suggest that the immune system is regulated by additional checkpoint molecules.

Summary

In one aspect, the disclosure provides isolated anti-human BTN5 (ERMAP) antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SYYIH (SEQ ID NO: 1);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence WIYPGNVNTKYNEKFKG (SEQ ID NO: 2);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GDYDGGYAMDY (SEQ ID NO: 3).

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSKSLLHSNGNTYLY (SEQ ID NO: 4);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RMSNLAS (SEQ ID NO: 5); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence MQHLEYPLT (SEQ ID NO: 6).

In one embodiment, the anti-human BTN5 (ERMAP) antibody, or fragment thereof, comprises:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:1;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:2;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:3;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:4;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:5; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:6.

In another aspect, the disclosure provides isolated anti-human TAPBPL antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NYWIE (SEQ ID NO:9);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EILPGSGSTNYNEKFKG (SEQ ID NO:10);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence FTMARYWYFDV (SEQ ID NO:11);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSTGAVTTSNYAN (SEQ ID NO:12);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GTSNRAP (SEQ ID NO:13); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence ALWYSTH(F/Y)V (SEQ ID NO:14),;

wherein residues in parentheses are options at that position.

In one embodiment, the anti-human TAPBPL antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:9;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:10;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:11;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

In a further aspect, the disclosure provides isolated anti-human TAPBPL antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RYWMS (SEQ ID NO:18);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EINPDSSTINYTPSLKD (SEQ ID NO:19);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence VTTVVARDWYFDV (SEQ ID NO:20);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:12;

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:13; and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:14.

In one embodiment, the anti-human TAPBPL antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:18;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:19;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:20;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

In one aspect, the disclosure provides isolated anti-human CD300c antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GYNMN (SEQ ID NO:23);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NIDPYYGGTSYNQKFKG (SEQ ID NO:24);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SGYYYAMDY (SEQ ID NO:25);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQNVGTAVA (SEQ ID NO:26);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SASNRYT (SEQ ID NO:27); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQYSSYPYT (SEQ ID NO:28).

In one embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:23;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:24;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:25;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:26;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:27; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:28.

The disclosure also provides isolated anti-human CD300c antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMK (SEQ ID NO:31);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DINPNNGDTFYNQKFKG (SEQ ID NO:32);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGMVTTAMDY (SEQ ID NO:33);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RTITDIDDDMN (SEQ ID NO:34);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EGNTLRP (SEQ ID NO:35); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence LQSDNMPYT (SEQ ID NO:36).

In one embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:31;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:32;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:33;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:34;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:35; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:36.

In another aspect, the disclosure provides isolated anti-human CD300c antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMY (SEQ ID NO:39);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence TISNGGSYTYYPDSVKG (SEQ ID NO:40);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGDYYGNTYAY (SEQ ID NO:41);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQSVDYDGDSYIN (SEQ ID NO:42);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence AASNLES (SEQ ID NO:43); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQSNEDPYT (SEQ ID NO:44).

In one embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:39;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:40;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:41;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:42;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:43; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:44.

In embodiments of any aspect of the disclosure, the wherein the antibody comprises a monoclonal antibody, or fragment thereof, or the antibody comprises a humanized antibody, or fragment thereof.

In another embodiment, the antibody is a chimeric antibody. In one such embodiment, the heavy chain of any embodiment disclosed herein may further comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:47 and 70-72. In another embodiment, the light chain of any embodiment disclosed herein may further comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid

sequence selected from SEQ ID NO:48 and 73. In a further embodiment, the heavy chain or light chain comprises an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:50-61. In other embodiments, the antibodies or fragments thereof comprise a heavy chain and a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of a heavy chain-light chain pair selected from the group consisting of:

SEQ ID NO:50-51;

SEQ ID NO:52-53;

SEQ ID NO:54-55;

SEQ ID NO:56-57;

SEQ ID NO:58-59; and

SEQ ID NO:60-61.

The disclosure also provides nucleic acids encoding the antibody or fragment thereof of any embodiment; vectors comprising the nucleic acid operatively linked to a suitable control sequence, host cells comprising the antibody or fragment thereof, the nucleic acid and/or the expression vector of any embodiment, and pharmaceutical compositions, comprising the antibody or fragment thereof, the nucleic acid, the vector, and/or the host cell of embodiment; and a pharmaceutically acceptable carrier.

The disclosure also provides methods for treating cancer, comprising administering to a subject in need thereof the antibody or fragment thereof, the nucleic acid, the vector, the host cell, and/or the pharmaceutical composition of any embodiment herein, in an amount effective to treat the cancer.

Description of the Figures

Figure 1. Chimeric anti-hERMAP antibody (human IgG1) (SEQ ID NO:50-51) blocks the inhibitory activity of hERMAP protein on T cell activation (CD69 expression on CD4 and CD8 T cells). T cells were stimulated with anti-CD3 antibody in the presence of 8 ug/ml hERMAP protein and 25 ug/ml anti-hERMAP chimeric antibody (IgG) or control IgG. T cells were unstimulated as a negative control (blank). The percentage of $CD69^+$ on $CD4^+$ (A) or $CD8^+$ T cells (B) was analyzed by flow cytometry.

Figure 2. Anti-hERMAP monoclonal antibody (mAb) inhibits cancer growth in a leukemia animal model. (A) DBA/2J mice were injected subcutaneously (s.c.) with 1×10^5 P388 murine leukemia cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. (B) Tumors size was measured over time. The mean tumor diameter (mm^3) ± S.D. at the indicated time points is shown.

Figure 3. Anti-hERMAP mAb increases the survival of leukemia-bearing mice. DBA/2J mice were injected with 2×10^5 P388 murine leukemia cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The survival of the mice was monitored over time.

Figure 4. Anti-hERMAP mAb inhibits tumor growth in a colon cancer animal model. (A) BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. (B) Tumors size was measured over time. The mean tumor diameter (mm^3) ± S.D. at the indicated time points is shown.

Figure 5. Anti-hERMAP mAb increases the survival of colon cancer-bearing mice. BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The survival of the mice was monitored over time.

Figure 6. Anti-TAPBPL chimeric Ab (SEQ ID NO:62-63) inhibits tumor growth in (A) melanoma and (B) colon cancer animal models. C57BL/6 or BALB/c mice were injected subcutaneously (s.c.) with B16F10 melanoma cells or CT 26 colon cancer cells on day 0, followed by injection of the anti-TAPBPL chimeric Ab (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The melanomas and colon tumors were harvested on day 20 and 30, respectively. The photos show the sizes of the tumors.

Figure 7. Anti-hTAPBPL antibody (Ab) inhibits tumor growth in a melanoma model. (A) Syngeneic B57BL/6 mice were injected subcutaneously (s.c.) with melanoma cells. When cancers were visible and palpable, the mice were injected s.c. with graded doses of anti-hTAPBPL Ab (50, 100, and 200 μg) or control Ab. Cancer size (volume) was monitored over time. At the end of study, the cancer was analyzed for (B) CD4 and (C) CD8 T cells by flow cytometry.

Figure 8. Anti-hTAPBPL antibody (AB) treats established cancer in a P388 leukemia model. Syngeneic DBA/2J mice were injected subcutaneously (s.c.) with P388 leukemia cells. When cancers were visible and palpable, the mice were injected s.c. with graded doses

of anti-hTAPBPL Ab (50, 100, and 200 μg) or control Ab. Cancer size (volume) was monitored over time.

Figure 9. Anti-TAPBPL chimeric Ab (SEQ ID NO:62-63) treatment results in increased tumor infiltrating CD4 and CD8 T cells. BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti-TAPBPL chimeric Ab (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The colon cancers were harvested on day 30. Tumor infiltrating CD4 and CD8 T cells were examined by immunofluorescence.

Figure 10. Anti-TAPBPL Ab2 (murine precursor to SEQ ID NO:52-53) and Ab3 (murine precursor to SEQ ID NO:54-55) neutralize T cell inhibitory activity of TAPBPL-Ig *in vitro*. (A) T cells from splenocytes of C57BL/6 mice were stimulated with anti-CD3 Ab in the presence of control Ig or human TAPBPL-Ig with anti-TAPBPL Ab2 (left panel), anti-TAPBPL Ab3 (right panel), or their isotype Ab. T cells were then analyzed for the expression of CD69 (an early T cell activation marker) on CD4 and CD8 T cells 24 hours later. Figures show statistical analysis of the percentage of $CD69^{+}$ cells on CD4 and CD8 T cells. The data suggest that anti-TAPBPL Ab2 and Ab3 can neutralize the inhibitory activity of TAPBPL-Ig on T cell activation.

Figure 11. Anti-TAPBPL antibodies (Abs) inhibit tumor growth in a melanoma animal model. Syngeneic B57BL/6 mice were injected subcutaneously (s.c.) with B16F10 melanoma cells. When cancers were visible and palpable, the mice were injected with anti-TAPBPL Ab2, (murine precursor to SEQ ID NO:52-53) anti-TAPBPL Ab3 (murine precursor to SEQ ID NO:54-55) (100 μg), or control isotype Ab. Cancer size (volume) was monitored over time.

Figure 12. Anti-TAPBPL antibodies (Abs) inhibit tumor growth in a leukemia animal model. Syngeneic DBA/2J mice were injected s.c. with P388 leukemia cells. When cancers were visible and palpable, the mice were injected with anti-TAPBPL Ab2 (murine precursor to SEQ ID NO:52-53), anti-TAPBPL Ab3 (murine precursor to SEQ ID NO:54-55) (100 μg), or control isotype Ab. Cancer size (volume) was monitored over time.

Figure 13 Anti-CD300c Ab2 (murine precursor to SEQ ID NO:56-57), Ab3 (murine precursor to SEQ ID NO:58-59), and Ab4 (murine precursor to SEQ ID NO:60-61) neutralize T cell inhibitory activity of CD300c-Ig *in vitro*. (A) T cells from splenocytes of C57BL/6 mice were stimulated with anti-CD3 Ab in the presence of control Ig or human CD300c-Ig with anti-CD300c Ab2 (left panel), anti-CD300c Ab3 (middle panel), anti-CD300c Ab4 (right panel), or their isotype Ab. T cells were then analyzed for the expression of CD69 (an

early T cell activation marker) on CD4 and CD8 T cells 24 hours later. Figures show statistical analysis of the percentage of $CD69^+$ cells on CD4 and CD8 T cells. The data suggest that anti- CD300c Ab2, Ab3, and Ab4 can neutralize the inhibitory activity of CD300c-Ig on T cell activation.

Figure 14. Anti-CD300c antibodies (Abs) inhibit tumor growth in a melanoma animal model. Syngeneic B57BL/6 mice were injected subcutaneously (s.c.) with B16F10 melanoma cells. When cancers were visible and palpable, the mice were injected with anti-CD300c Ab2 murine precursor to SEQ ID NO:56-57), anti-CD300c Ab3 murine precursor to SEQ ID NO:58-59) (100 µg), or control isotype Ab. Cancer size (volume) was monitored over time.

Detailed Description

As used herein and unless otherwise indicated, the terms "a" and "an" are taken to mean "one", "at least one" or "one or more". Unless otherwise required by context, singular terms used herein shall include pluralities and plural terms shall include the singular.

Unless the context clearly requires otherwise, throughout the description and the claims, the words 'comprise', 'comprising', and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of "including, but not limited to". Words using the singular or plural number also include the plural or singular number, respectively. Additionally, the words "herein," "above" and "below" and words of similar import, when used in this application, shall refer to this application as a whole and not to any particular portions of this application.

As used herein, the amino acid residues are abbreviated as follows: alanine (Ala; A), asparagine (Asn; N), aspartic acid (Asp; D), arginine (Arg; R), cysteine (Cys; C), glutamic acid (Glu; E), glutamine (Gln; Q), glycine (Gly; G), histidine (His; H), isoleucine (Ile; I), leucine (Leu; L), lysine (Lys; K), methionine (Met; M), phenylalanine (Phe; F), proline (Pro; P), serine (Ser; S), threonine (Thr; T), tryptophan (Trp; W), tyrosine (Tyr; Y), and valine (Val; V).

All embodiments of any aspect of the invention can be used in combination, unless the context clearly dictates otherwise.

In a first aspect, the disclosure provides isolated anti-human BTN5 (ERMAP) antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SYYIH (SEQ ID NO: 1);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence WIYPGNVNTKYNEKFKG (SEQ ID NO: 2);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GDYDGGYAMDY (SEQ ID NO: 3).

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSKSLLHSNGNTYLY (SEQ ID NO: 4);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RMSNLAS (SEQ ID NO: 5); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence MQHLEYPLT (SEQ ID NO: 6).

In one embodiment, the anti-human BTN5 (ERMAP) antibody, or fragment thereof, comprises:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:1;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:2;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:3;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:4;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:5; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:6.

As shown in the examples that follow, the disclosed anti-human Erythroid membrane-associated protein (BTN5 or ERMAP) antibodies, or fragments thereof, are the first antibodies shown to have the ability to neutralize the inhibitory effects of BTN5 (ERMAP) on T cells. The sequences of these antibodies have been determined, including the complementarity determining regions (CDRs) disclosed herein. As will be understood by those of skill in the art, the CDRs are the key factor in antigen-binding selectivity, and thus other regions of the antibody amino acid sequence may be substantially modified. In a further embodiment, the anti-human BTN5 (ERMAP) antibody, or antigen-binding fragment thereof comprises:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO 7; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:8.

QVQLQQSGPELVKPGASVRISCKASGYTFT**SYYIH**WVKQRPGQGLEWIG**WIYPGNVNTKYNE KFKG**KATLTADKSSSTAYMQLSSLTSEDSAVYFCAR**GDYDGGYAMDY**WGQGTSVTVSS
(SEQ ID NO:7; CDRs are highlighted)

DIVMTQAAPSVPVTPGESVSISC**RSSKSLLHSNGNTYLY**WFLQRPGQSPQLLIY**RMSNLAS**G VPDRFSGSGSGTAFTLRISRVEAEDVGVYYC**MQHLEYPLT**FGAGTKLELK
(SEQ ID NO:8; CDRs are highlighted).

In another embodiment, the disclosure provides isolated anti-human TAP Binding Protein Like protein (TAPBPL) antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NYWIE (SEQ ID NO:9);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EILPGSGSTNYNEKFKG (SEQ ID NO:10);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence FTMARYWYFDV (SEQ ID NO:11);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSTGAVTTSNYAN (SEQ ID NO:12);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GTSNRAP (SEQ ID NO:13); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence ALWYSTH(F/Y)V (SEQ ID NO:14), wherein residues in parentheses are options at that position.

In one embodiment, the anti-human TAPBPL antibody, or fragment thereof, comprises:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:9;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:10;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:11;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

In another embodiment, the L-CDR3 comprises the amino acid sequence of ALWYSTHFV (SEQ ID NO:15).

As shown in the examples that follow, the disclosed anti-human TAPBPL antibodies, or fragments thereof, have the ability to neutralize the inhibitory effects of TAPBPL on T cells. The sequences of these antibodies have been determined, including the complementarity determining regions (CDRs) disclosed herein. In a further embodiment, the anti-human TAPBPL antibody, or antigen-binding fragment thereof comprises:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:16; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17.

QVQLQQSGAELMKPGASVKISCKATGYTFS**NYWIE**WVKQRPGHGLEWIG**EILPGSGSTNYNE KFKG**KATFTADTSSNTAYMQLSSLTSEDSAVYYCAR**FTMARYWYFDV**WGAGTTVTVSS

(SEQ ID NO:16; CDRs are highlighted); and/or

QAVVTQESALTTSPGGTVILTC**RSSTGAVTTSNYAN**WVQEKPDHLFTGLIG**GTSNRAP**GVPV RFSGSLIGDKAALTITGAQTEDDAMYFC**ALWYSTHFV**FGGGTKVTVL

(SEQ ID NO:17; CDRs are highlighted).

In another embodiment, the isolated anti-human TAPBPL antibodies, or fragments thereof, comprise 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RYWMS (SEQ ID NO:18);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EINPDSSTINYTPSLKD (SEQ ID NO:19);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence VTTVVARDWYFDV (SEQ ID NO:20);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:12;

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:13; and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:14.

In one embodiment, the anti-human TAPBPL antibodies, or fragments thereof comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:18;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:19;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:20;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

In one embodiment, L-CDR3 comprises the amino acid sequence of ALWYSTHYV (SEQ ID NO:49).

In a further embodiment, the anti-human TAPBPL antibodies, or fragments thereof, comprise:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:21; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:22.

EVKLLQSGGGLVQPGGSLKLSCAASGFDFS**RYWMS**WVRQAPGKGLEWIG**EINPDSSTINYTP**
SLKDKFIISRDNAKNTLYLQMSKVRSEDTALYYCAS**VTTVVARDWYFDV**WGAGTTVTVSS
(SEQ ID NO:21; CDRs are highlighted); and/or

QAVVTQESALTTSPGGTVILTC**RSSTGAVTTSNYAN**WVQEKPDHLFTGLIG**GTSNRAP**GVPV
RFSGSLIGDKAALTITGAQTEDDAMYFC**ALWYSTHYV**FGGGTKVTVL
(SEQ ID NO:22; CDRs are highlighted).

In another aspect, the disclosure provides anti-human CD300c antibodies, or fragments thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GYNMN (SEQ ID NO:23);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NIDPYYGGTSYNQKFKG (SEQ ID NO:24);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SGYYYAMDY (SEQ ID NO:25);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQNVGTAVA (SEQ ID NO:26);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SASNRYT (SEQ ID NO:27); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQYSSYPYT (SEQ ID NO:28).

In one embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:23;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:24;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:25;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:26;
an L-CDR2 comprising the amino acid sequence of SEQ ID NO:27; and
an L-CDR3 comprising the amino acid sequence of SEQ ID NO:28.

As shown in the examples that follow, the disclosed anti-human CD300c antibodies, or fragments thereof, have the ability to neutralize the inhibitory effects of CD300c on T cells. The sequences of these antibodies have been determined, including the complementarity determining regions (CDRs) disclosed herein. In a further embodiment, the anti-human CD300c antibody, or antigen-binding fragment thereof comprises:

In one embodiment, the anti-human CD300c antibody, or fragment thereof, comprises:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:29; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:30).

EFQLQQSGPELEKPGASVKISCKASGYSFT**GYNMN**WVKQSNGKSLEWIG**NIDPYYGGTSYNQ**
KFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAR**SGYYYAMDY**WGQGTSVTVSS
(SEQ ID NO:29; CDRs are highlighted)

DIVMTQSQKFMSTSVGDRVSITC**KASQNVGTAVA**WYQQKPGQSPKLLIY**SASNRYT**GVPDRF
TGSGSGTDFTLTISNMQSEDLADYFC**QQYSSYPYT**FGGGTKLEIK (SEQ ID NO:30;
CDRs are highlighted).

In another embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMK (SEQ ID NO:31);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DINPNNGDTFYNQKFKG (SEQ ID NO:32);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGMVTTAMDY (SEQ ID NO:33);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RTITDIDDDMN (SEQ ID NO:34);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EGNTLRP (SEQ ID NO:35); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence LQSDNMPYT (SEQ ID NO:36).

In one embodiment, the anti-human CD300c antibodies, or fragment thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:31;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:32;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:33;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:34;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:35; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:36.

In a further embodiment, the anti-human CD300c antibody, or antigen-binding fragment thereof comprises:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:37; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:38.

EVQLQQSGPELVKPGASVKMSCKASGYTFT**DYYMK**WVKQSHGKSLEWIG**DINPNNGDTFYNQ KFKG**KATLTVDKSSSTAYMQLNSLTSEDSAVYYCAT**GGMVTTAMDY**WGQGTSVTVSS

(SEQ ID NO:37; CDRs are highlighted); and/or

ETTVTQSPASLSVATGEKVTIRC**RTITDIDDDMN**WYQQKPGEPPKLLIS**EGNTLRP**GVPSRF SSSGYGTDFVFTIENTLSEDVADYYC**LQSDNMPYT**FGGGTKLEIK

(SEQ ID NO:38; CDRs are highlighted).

In a further embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMY (SEQ ID NO:39);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence TISNGGSYTYYPDSVKG (SEQ ID NO:40);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGDYYGNTYAY (SEQ ID NO:41);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQSVDYDGDSYIN (SEQ ID NO:42);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence AASNLES (SEQ ID NO:43); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQSNEDPYT (SEQ ID NO:44).

In one embodiment, the anti-human CD300c antibodies, or fragments thereof, comprise:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:39;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:40;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:41;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:42;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:43; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:44.

In a further embodiment, the anti-human CD300c antibody, or antigen-binding fragment thereof comprises

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:45; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:46.

EVQLVESGGGLMKPGGSLKLSCAASGFTFS**DYYMY**WVRQTPEKRLEWVA**TISNGGSYTYYPD**
SVKGRFTISRDNAKNNLYLQMSSLKSEDTAMYYCAR**GGDYYGNTYAY**WGQGTLVTVSA
(SEQ ID NO:45; CDRs are highlighted)

DIVLTQSPASLAVSLGQRATISC**KASQSVDYDGDSYIN**WYQQKPGQPPKLLIY**AASNLES**GI
PARFSGSGSGTDFTLNIHPVEEEDAAAYYC**QQSNEDPYT**FGGGTKLEIK
(SEQ ID NO:46; CDRs are highlighted).

As used herein, the term "antibody includes antibodies having at least one antigen-binding domain and includes monoclonal antibodies fragments and/or variants thereof including recombinant polypeptides, fusion proteins, and immunoconjugates. Thus, the terms "antibody," "antibody fragment," and "antibody variant" are used interchangeably herein. Examples of antibody fragments of the invention include, but are not limited to, the Fab fragment, consisting of VL, VH, CL and CHI domains; the Fc fragment, consisting of the VH and CHI domains; the Fv fragment consisting of the VL and VH; the dAb fragment consisting of a VH domain; isolated CDR regions; $F(ab')_2$ a bivalent fragment comprising two linked Fab fragments; and single chain Fv molecules (scFv).. The antibodies may be chimeric, humanized, or fully human antibodies. In one specific embodiment, the antibody is a monoclonal antibody, or a fragment thereof.

In one embodiment, the antibodies may be chimeric, for example, including a human heavy chain and/or light chain constant region. Any human heavy chain constant region (such as IgG1, IgG2, IgG3, and IgG4) and/or light chain constant region (such as IgG kappa light chain or IgG lambda light chain) may be used. In one embodiment, the heavy chain of any embodiment disclosed herein may comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:47 and 70-72
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE

EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:47; Human IgG1 heavy chain constant region)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLT
VVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
LHNHYTQKSLSLSPGK (SEQ ID NO:70 Human IgG2 heavy chain constant region)

ASTKGPSVFPLAPCSRSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYTCNVNHKPSNTKVDKRVELKTPLGDTTHTCPRCPEPKSCDTPP
PCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQYNSTFRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE
WESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLS
LSPGK (SEQ ID NO: 71 Human IgG3 heavy chain constant region)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHE
ALHNHYTQKSLSLSLGK (SEQ ID NO:72 Human IgG4 heavy chain constant region)

In another embodiment, the light chain of any embodiment disclosed herein may comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:48 and 73.

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD
STYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:48; Human IgG1 kappa light chain constant region)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHE
ALHNHYTQKSLSLSLGK (SEQ ID NO:73 Human immunoglobulin lambda light chain constant region)

In various further embodiments, the chimeric antibodies may comprise chimeric heavy chains and/or light chains comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:50-65, the sequences of which are provided in Table 1. In other embodiments, the antibody, or antigen-binding fragment thereof comprises a heavy chain and a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of a heavy chain-light chain pair selected from the group consisting of:

SEQ ID NO:50-51;

SEQ ID NO:52-53;

SEQ ID NO:54-55;

SEQ ID NO:56-57;

SEQ ID NO:58-59;

SEQ ID NO:60-61;

SEQ ID NO:62-63; and

SEQ ID NO:64-65.

Table 1

Name	SEQ ID NO	Sequence
BTN5 (ERMAP) Heavy	50	QVQLQQSGPELVKPGASVRISCKASGYTFT**SYYIH**WVKQRPGQGLEWIG**WIYPGN VNTKYNEKFKG**KATLTADKSSSTAYMQLSSLTSEDSAVYFCAR**GDYDGGYAMDY**W GQGTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK

BTN5 (ERMAP) light	51	DIVMTQAAPSVPVTPGESVSISC**RSSKSLLHSNGNTYLY**WFLQRPGQSPQLLIY**R MSNLAS**GVPDRFSGSGSGTAFTLRISRVEAEDVGVYYC**MQHLEYPLT**FGAGTKLE LKTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
TAPBPL heavy	52	QVQLQQSGAELMKPGASVKISCKATGYTFS**NYWIE**WVKQRPGHGLEWIG**EILPGS GSTNYNEKFKG**KATFTADTSSNTAYMQLSSLTSEDSAVYYCAR**FTMARYWYFDV**W GAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK
TAPBPL light	53	QAVVTQESALTTSPGGTVILTC**RSSTGAVTTSNYAN**WVQEKPDHLFTGLIG**GTSN RAP**GVPVRFSGSLIGDKAALTITGAQTEDDAMYFC**ALWYSTHFV**FGGGTKVTVLT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
TAPBPL heavy	54	EVKLLQSGGGLVQPGGSLKLSCAASGFDFS**RYWMS**WVRQAPGKGLEWIG**EINPDS STINYTPSLKD**KFIISRDNAKNTLYLQMSKVRSEDTALYYCAS**VTTVVARDWYFD V**WGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK
TAPBPL light	55	QAVVTQESALTTSPGGTVILTC**RSSTGAVTTSNYAN**WVQEKPDHLFTGLIG**GTSN RAP**GVPVRFSGSLIGDKAALTITGAQTEDDAMYFC**ALWYSTHYV**FGGGTKVTVLT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
CD300c heavy	56	EFQLQQSGPELEKPGASVKISCKASGYSFT**GYNMN**WVKQSNGKSLEWIG**NIDPYY GGTSYNQKFKG**KATLTVDKSSSTAYMQLKSLTSEDSAVYYCAR**SGYYYAMDY**WGQ GTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
CD300c Light	57	DIVMTQSQKFMSTSVGDRVSITC**KASQNVGTAVA**WYQQKPGQSPKLLIY**SASNRY T**GVPDRFTGSGSGTDFTLTISNMQSEDLADYFC**QQYSSYPYT**FGGGTKLEIKTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
CD300c heavy	58	EVQLQQSGPELVKPGASVKMSCKASGYTFT**DYYMK**WVKQSHGKSLEWIG**DINPNN GDTFYNQKFKG**KATLTVDKSSSTAYMQLNSLTSEDSAVYYCAT**GGMVTTAMDY**WG QGTSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQ KSLSLSPGK

CD300c Light	59	ETTVTQSPASLSVATGEKVTIRC**RTITDIDDDMN**WYQQKPGEPPKLLIS**EGNTLR PG**VPSRFSSSGYGTDFVFTIENTLSEDVADYYC**LQSDNMPYT**FGGGTKLEIKTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
CD300c heavy	60	EVQLVESGGGLMKPGGSLKLSCAASGFTFS**DYYMY**WVRQTPEKRLEWVA**TISNGG SYTYYPDSVKG**RFTISRDNAKNNLYLQMSSLKSEDTAMYYCAR**GGDYYGNTYAY**W GQGTLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK
CD300c Light	61	DIVLTQSPASLAVSLGQRATISC**KASQSVDYDGDSYIN**WYQQKPGQPPKLLIY**AA SNLES**GIPARFSGSGSGTDFTLNIHPVEEEDAAAYYC**QQSNEDPYT**FGGGTKLEI KTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQES VTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
TAPBPL Heavy	62	DVQLQESGPGLVKPSQTLSLTCSVTGYSLTSGYFWHWIRQFPGNKLEWMGYISYS GTTNYNPSLKNRISITHDSSKNQFFLNLNSVTAEDTATYFCAGDDWDWFAYWGQG TLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK
TAPBPL light	63	ENVLTQSPAIMSASPGEKVTMTCSASSSVNYMHWYQQKSSTSPKLWIYDTSKLAS GVPGRFSGSGSGNSYSLTISSMEAEDVATYYCFQGSGYPLTFGSGTKLEIKTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
CD300c Heavy	64	QIQLVQSGPELRKPGETVKISCKASGYTFTIYGMNWMKQAPGKGLKWMGWINTYT GEPTYADDFKGRFAFSLETSASTAFLQINNLTNEDTATYFCARSRFAYWGQGTLV TVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK
CD300c Light	65	DIVMTQSQKFMSTSVGDRVSVTCKASQNVGTNVAWYQQKPGQSPKALIYSASYRY SGVPDRFTGSRSGTDFTLTISNVQSEDLAEYVCQQYNSYPLTFGAGTKLELKTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

In one embodiment, variability compared to the reference sequence is present only outside the CDRs.

In some embodiments, the antibodies or fragments thereof are conjugated to one or more agents selected from the group including an additional therapeutic agent, such as a chemotherapeutic agent. A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include alkylating agents such as thiotepa and cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and

piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including the synthetic analogue topotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimustine; antibiotics such as the enediyne antibiotics (e. g., calicheamicin, especially calicheamicin gamma 11 and calicheamicin omega 11 (see, e.g., Agnew, Chem Intl. Ed. Engl., 33: 183-186 (1994)); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, carminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin (including morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfornithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine;

pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofiran; spirogermanium; tenuazonic acid; triaziquone; 2,2',22"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., paclitaxel, ABRAXANE® Cremophor-free, albumin-engineered nanoparticle formulation of paclitaxel (American Pharmaceutical Partners, Schaumberg, Ill.), and doxetaxel; chloranbucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Also included in the definition are proteasome inhibitors such as bortezomib (Velcade), BCL-2 inhibitors, IAP antagonists (e.g. Smac mimics/xIAP and cIAP inhibitors such as certain peptides, pyridine compounds such as (S)--N-{6-benzo[1,3]dioxol-5-yl-1-[5-(4-fluoro-benzoyl)-pyridin-3-ylmethy- l]-2-oxo-1,2-dihydro-pyridin-3-yl}-2-methylamino-propionamide, xIAP antisense), HDAC inhibitors (HDACI) and kinase inhibitors (Sorafenib).

In other embodiments, the antibodies or fragments thereof are linked to a detectable label, such as a radiolabel, an enzyme, a fluorescent label, a luminescent label, a bioluminescent label, a magnetic label, and/or biotin.

In some embodiments, the agent and/or detectable label is conjugated directly to the antibodies or fragments thereof. In other embodiments, the agent and/or detectable label is conjugated to the antibodies or fragments thereof via a linker.

In another aspect, the present disclosure provides nucleic acids encoding the antibodies or fragments thereof of any aspect or embodiment of the invention. The nucleic acid sequence may comprise RNA or DNA. Such nucleic acid sequences may comprise additional sequences useful for promoting expression and/or purification of the encoded protein, including but not limited to polyA sequences, modified Kozak sequences, and sequences encoding epitope tags, export signals, and secretory signals, nuclear localization signals, and plasma membrane localization signals. It will be apparent to those of skill in the art, based on the teachings herein, what nucleic acid sequences will encode the antibodies or fusion molecules disclosed herein.

In a further aspect, the present disclosure provides nucleic acid expression vectors comprising the nucleic acid of any embodiment of the disclosure operatively linked to a suitable control sequence. "Recombinant expression vector" includes vectors that operatively link a nucleic acid coding region or gene to any control sequences capable of effecting expression of the gene product. "Control sequences" operably linked to the nucleic acid sequences of the disclosure are nucleic acid sequences capable of effecting the expression of the nucleic acid molecules. The control sequences need not be contiguous with the nucleic acid sequences, so long as they function to direct the expression thereof. Thus, for example, intervening untranslated yet transcribed sequences can be present between a promoter sequence and the nucleic acid sequences and the promoter sequence can still be considered "operably linked" to the coding sequence. Other such control sequences include, but are not limited to, polyadenylation signals, termination signals, and ribosome binding sites. Such expression vectors can be of any type known in the art, including but not limited plasmid and viral-based expression vectors. The control sequence used to drive expression of the disclosed nucleic acid sequences in a mammalian system may be constitutive (driven by any of a variety of promoters, including but not limited to, CMV, SV40, RSV, actin, EF) or inducible (driven by any of a number of inducible promoters including, but not limited to, tetracycline, ecdysone, steroid-responsive. The expression vector must be replicable in the host organisms either as an episome or by integration into host chromosomal DNA. In one, the expression vector comprises a plasmid; in another embodiment a viral vector, including but not limited to adenoviral vectors or rAAV vectors.

In another aspect, the present disclosure provides recombinant host cells comprising the antibodies or fragments thereof, nucleic acids, and/or nucleic acid expression vectors of the disclosure. The host cells can be either prokaryotic or eukaryotic. The cells can be transiently or stably transfected or transduced. Such transfection and transduction of expression vectors into prokaryotic and eukaryotic cells can be accomplished via any suitable technique. A method of producing the antibodies or fragments thereof is also provided herein. The method comprises the steps of (a) culturing a host according to this aspect of the disclosure under conditions conducive to the expression of the antibodies or fragments thereof, and (b) optionally, recovering the expressed antibodies or fragments thereof. The expressed antibodies or fragments thereof can be recovered from the cell free extract, cell pellet, or recovered from the culture medium.

In a further aspect, the present disclosure provides pharmaceutical compositions, comprising the antibodies or fragments thereof, nucleic acids, nucleic acid expression

vectors, or recombinant host cells, of any aspect or embodiment of the disclosure, and a pharmaceutically acceptable carrier. The pharmaceutical compositions of the disclosure can be used, for example, in the methods of the disclosure. The pharmaceutical composition may comprise in addition to the antibodies or fragments thereof, nucleic acids, etc. of the disclosure (a) a lyoprotectant; (b) a surfactant; (c) a bulking agent; (d) a tonicity adjusting agent; (e) a stabilizer; (f) a preservative and/or (g) a buffer.

In some embodiments, the buffer in the pharmaceutical composition is a Tris buffer, a histidine buffer, a phosphate buffer, a citrate buffer or an acetate buffer. The pharmaceutical composition may also include a lyoprotectant, e.g. sucrose, sorbitol or trehalose. In certain embodiments, the pharmaceutical composition includes a preservative e.g. benzalkonium chloride, benzethonium, chlorohexidine, phenol, m-cresol, benzyl alcohol, methylparaben, propylparaben, chlorobutanol, o-cresol, p-cresol, chlorocresol, phenylmercuric nitrate, thimerosal, benzoic acid, and various mixtures thereof. In other embodiments, the pharmaceutical composition includes a bulking agent, like glycine. In yet other embodiments, the pharmaceutical composition includes a surfactant e.g., polysorbate-20, polysorbate-40, polysorbate- 60, polysorbate-65, polysorbate-80 polysorbate-85, poloxamer-188, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan monooleate, sorbitan trilaurate, sorbitan tristearate, sorbitan trioleaste, or a combination thereof. The pharmaceutical composition may also include a tonicity adjusting agent, e.g., a compound that renders the formulation substantially isotonic or isoosmotic with human blood. Exemplary tonicity adjusting agents include sucrose, sorbitol, glycine, methionine, mannitol, dextrose, inositol, sodium chloride, arginine and arginine hydrochloride. In other embodiments, the pharmaceutical composition additionally includes a stabilizer, e.g., a molecule which, when combined with a protein of interest substantially prevents or reduces chemical and/or physical instability of the protein of interest in lyophilized or liquid form. Exemplary stabilizers include sucrose, sorbitol, glycine, inositol, sodium chloride, methionine, arginine, and arginine hydrochloride.

The antibodies or fragments thereof, nucleic acids, etc. of the disclosure may be the sole active agent in the pharmaceutical composition, or the composition may further comprise one or more other active agents suitable for an intended use.

The pharmaceutical compositions described herein generally comprise a combination of a therapeutic described herein and a pharmaceutically acceptable carrier, diluent, or excipient. Such compositions are substantially free of non-pharmaceutically acceptable components, *i.e.*, contain amounts of non-pharmaceutically acceptable components lower

than permitted by US regulatory requirements at the time of filing this application. In some embodiments of this aspect, if the compound is dissolved or suspended in water, the composition further optionally comprises an additional pharmaceutically acceptable carrier, diluent, or excipient.

In another aspect, the disclosure provides methods for treating cancer, comprising administering to a subject in need thereof the antibody or fragment thereof, the nucleic acid, the vector, the host cell, and/or the pharmaceutical composition of any embodiment or combination of embodiments herein, in an amount effective to treat the cancer.

The methods may be used to treat any suitable cancer. In various non-limiting embodiments, the cancer may be selected from the group consisting of breast cancer, lung cancer, colon cancer, melanoma, prostate cancer, leukemia, neuroblastoma, liver, lymphoma, cervical cancer, ovarian cancer, gastric cancer, and esophageal cancer, etc.

Tumor progression is often accompanied by profound immune suppression that interferes with an effective antitumor response and tumor elimination. In order to elicit protective immunity to cancer, and to prevent an overactive immune system, immune responses need to be tightly controlled by immune cell stimulatory and inhibitory molecules. Many cancers protect themselves from the immune system by producing inhibitory molecules to inhibit T cell function. The inventors have identified CD300c, BTN5, and TAPBPL, as targets for treating cancer.

As used herein, the term "treat," "treatment," or "treating," means to reverse, alleviate, ameliorate, inhibit, slow down or stop the progression or severity of a symptom or condition of the disorder being treated. The term "treating" includes reducing or alleviating at least one adverse effect or symptom of a condition. Treatment is generally "effective" if one or more symptoms are reduced. Alternatively, treatment is "effective" if the progression of a condition is reduced or halted. That is, "treatment" may include not just the improvement of symptoms, but also a cessation or slowing of progress or worsening of symptoms that would be expected in the absence of treatment. Beneficial or desired clinical results include, but are not limited to, alleviation of one or more symptom(s), diminishment of extent of the deficit, stabilized (i.e., not worsening) state of a tumor or malignancy, delay or slowing of tumor growth and/or metastasis, and an increased lifespan as compared to that expected in the absence of treatment.

As used herein, the term "administering," refers to the placement of a therapeutic into a subject by a method or route deemed appropriate. The therapeutic can be administered by any appropriate route which results in an effective treatment in the subject including orally,

parentally, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants, and vehicles. The term parenteral as used herein includes, subcutaneous, intravenous, intra-arterial, intramuscular, intrasternal, intratendinous, intraspinal, intracranial, intrathoracic, infusion techniques or intraperitoneal administration. Dosage regimens can be adjusted to provide the optimum desired response (e.g., a therapeutic response). A suitable dosage range may, for instance, be 0.1 ug/kg-100 mg/kg body weight; alternatively, it may be 0.5 ug/kg to 50 mg/kg; 1 ug/kg to 25 mg/kg, or 5 ug/kg to 10 mg/kg body weight. The therapeutic can be delivered in a single bolus, or may be administered more than once (e.g., 2, 3, 4, 5, or more times) as determined by attending medical personnel.

As used herein, the phrase "amount effective" or "the like refers to an amount that provides a therapeutic benefit in the treatment, of cancer or autoimmune disease. Determination of a therapeutically effective amount is well within the capability of those skilled in the art. Generally, a therapeutically effective amount can vary with the subject's history, age, condition, sex, as well as the severity and type of the medical condition in the subject, and administration of other pharmaceutically active agents.

Examples

Generation of human and mouse chimeric antibodies (Abs) against human ERMAP, TAPBPL and CD300c.

Murine monoclonal antibodies (mAbs) of the disclosure were generated against human ERMAP, TAPBPL and CD300c, and shown to enhance antitumor immunity and inhibit tumor growth in animal models (Figures 10-14). The hybridomas that produce the murine mAbs were sequenced, and chimeric Abs in which the murine variable domains of each mAb are linked to human constant regions were generated (SEQ ID NO:50-65). Genes for the murine heavy chain variable domains were cloned into a pFUSEss-CHIg-hG1 vector (from InvivoGen) that contains the heavy chain constant regions of human IgG1. Genes for the murine light chain variable domains were cloned into a pFUSEss-CLg-hk vector (from InvivoGen) that contains the light chain constant regions of human IgG. The two vectors were then co-transfected into HEK-293 cells to produce each chimeric Ab, which was then purified from the supernatant of the cells by Protein G Sepharose™ 4.

Anti-hERMAP and Anti-TAPBPL promote an antitumor T cell response.

Functional studies were performed for the chimeric Abs. The anti-ERMAP chimeric Ab (SEQ ID NO:50-51) was demonstrated to neutralize the inhibitory activity of ERMAP-Ig on T cell activation (reduced CD69 expression on CD4 and CD8 T cells) (**Figure 1**). T cells were stimulated with anti-CD3 antibody in the presence of 8 μg/ml hERMAP protein and 25 μg/ml anti-hERMAP chimeric antibody or control IgG. Flow cytometry analysis quantification (**Figure 1A**) demonstrated reduced CD69 expression on $CD4^+$ T cells. Flow cytometry analysis quantification (**Figure 1B**) demonstrated reduced CD69 expression on $CD8^+$ T cells.

$CD4^+$ T cells and $CD8^+$ T cells infiltrate tumors to mediate an antitumor immune response (Tay et al. Cancer Gene Ther 28: 5-17 (2021)). Anti-TAPBPL chimeric Ab (SEQ ID NO: 62-63) treatment increased tumor infiltrating $CD4^+$ T cells and $CD8^+$ T cells (**Figure 9**). BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti-TAPBPL chimeric Ab (100μg) or control (isotype) Ab (100μg) on days 3, 5, 7, 9, and 12. The colon cancers were harvested on day 30. Immunofluorescent staining for tumor infiltrating $CD4^+$ T cells and $CD8^+$ T cells demonstrated increases in both cell types over control with anti-TAPBPL chimeric Ab treatment.

Anti-hERMAP inhibits tumor growth and increase survival.

Anti-hERMAP monoclonal antibody was tested in a leukemia animal model (**Figure 2**). DBA/2J mice were injected subcutaneously (s.c.) with 1×10^5 P388 murine leukemia cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12 (**Figure 2A**). Tumors size was measured over time. The mean tumor diameter (mm^3) $\pm$ S.D. at the indicated time points is shown in **Figure 2B**. Treatment with anti-hERMAP inhibited tumor growth compared with control starting at day 9 and through day 15.

Survival of leukemia-bearing mice treated with anti-hERMAP was compared with control (**Figure 3**). DBA/2J mice were injected with 2×10^5 P388 murine leukemia cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The graph shows a Kaplan-Meier curve for the survival of control treated versus anti-hERMAP treated leukemia-bearing mice. The survival of the mice was monitored over time. Treatment with anti-hERMAP increased the survival of leukemia-bearing mice compared to control with 100% mortality in the control mice by day 22 and about 40% mortality at the same time point for anti-hERMAP treated mice.

Anti-hERMAP mAb was tested in a colon cancer animal model (**Figure 4**). BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12 (**Figure 4A**). Tumors size was measured over time. The mean tumor diameter (mm^3) ± S.D. at the indicated time points is shown (**Figure 4B**). Treatment with anti-hERMAP mAb inhibited tumor growth compared with control starting at day 9 and through day 24 (**Figure 4B**).

Additionally, we assessed survival of colon cancer-bearing mice treated with anti-hERMAP compared with control (**Figure 5**). BALB/c mice were injected subcutaneously (s.c.) with CT 26 colon cancer cells on day 0, followed by injection of the anti- hERMAP mAb (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The survival of the mice was monitored over time. Treatment with anti-hERMAP increased survival of colon cancer-bearing mice compared to control with 100% mortality at day 30 for the control mice and 5% mortality at the same time point for the anti-hERMAP treated mice.

Antibodies against TAPBPL inhibits tumor growth and promotes tumor infiltration.

The impact of anti-TAPBPL on malignancy growth/progression was also assessed. Anti-TAPBPL chimeric Ab (SEQ ID NO:62-63) inhibited tumor growth in melanoma (**Figure 6A**) and colon cancer animal models (**Figure 6B**). C57BL/6 or BALB/c mice were injected subcutaneously (s.c.) with B16F10 melanoma cells or CT 26 colon cancer cells on day 0, followed by injection of the anti-TAPBPL chimeric Ab (100μg) or control (isotype) Ab (100 μg) on days 3, 5, 7, 9, and 12. The melanomas and colon cancers were harvested on day 20 and 30, respectively. The top photo shows reduced melanoma tumor sizes with anti-TAPBPL chimeric Ab treatment compared to control. The bottom photo shows reduced colon tumor sizes with anti-TAPBPL chimeric Ab treatment compared to control.

Additionally, anti-hTAPBPL was tested in a melanoma model (**Figure 7**). Syngeneic B57BL/6 mice were injected subcutaneously (s.c.) with melanoma cells. When cancers were visible and palpable, the mice were injected s.c. with graded doses of anti-hTAPBPL Ab (50, 100, and 200 μg) or control Ab. Anti-hTAPBPL inhibited tumor growth, as seen by the tumor volume over time, in a dose dependent fashion (**Figure 7A**). At the end of study, the tumors were analyzed for CD4 and CD8 T cells by flow cytometry. Anti-hTAPBPL increased both $CD4^+$ T cells (**Figure 7B**) and $CD8^+$ T cells (**Figure 7C**) in the tumors, which are involved in tumor infiltration, compared with control.

Anti-hTAPBPL was then tested in an established cancer leukemia model (**Figure 8**). Syngeneic DBA/2J mice were injected subcutaneously (s.c.) with P388 leukemia cells. When cancers were visible and palpable, the mice were injected s.c. with graded doses of anti-hTAPBPL Ab (50, 100, and 200 μg) or control Ab. The data demonstrated that anti-hTAPBPL treats established cancer in a leukemia model as shown by the slowing in growth of tumor volume over time.

I claim

1. An isolated anti-human BTN5 (ERMAP) antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SYYIH (SEQ ID NO: 1);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence WIYPGNVNTKYNEKFKG (SEQ ID NO: 2);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GDYDGGYAMDY (SEQ ID NO: 3).

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSKSLLHSNGNTYLY (SEQ ID NO: 4);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RMSNLAS (SEQ ID NO: 5); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence MQHLEYPLT (SEQ ID NO: 6).

2. The anti-human BTN5 (ERMAP) antibody, or fragment thereof, of claim 1, comprising:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:1;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:2;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:3;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:4;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:5; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:6.

3. The anti-human BTN5 (ERMAP) antibody, or fragment thereof, of claim 1 or 2, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO 7; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:8.

4. The anti-human BTN5 (ERMAP) antibody, or fragment thereof, of claim 1 or 2, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO 7; and

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:8.

5. An isolated anti-human TAPBPL antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NYWIE (SEQ ID NO:9);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EILPGSGSTNYNEKFKG (SEQ ID NO:10);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence FTMARYWYFDV (SEQ ID NO:11);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RSSTGAVTTSNYAN (SEQ ID NO:12);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GTSNRAP (SEQ ID NO:13); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence ALWYSTH(F/Y)V (SEQ ID NO:14),;

wherein residues in parentheses are options at that position.

6. The anti-human TAPBPL antibody, or fragment thereof, of claim 5, comprising:
an H-CDR1 comprising the amino acid sequence of SEQ ID NO:9;
an H-CDR2 comprising the amino acid sequence of SEQ ID NO:10;
an H-CDR3 comprising the amino acid sequence of SEQ ID NO:11;
an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;
an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and
an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

7. The anti-human TAPBPL antibody, or fragment thereof, of claim 5 or 6, wherein the L-CDR3 comprises the amino acid sequence ALWYSTHFV (SEQ ID NO:15).

8. The anti-human TAPBPL antibody, or fragment thereof, of any one of claims 5-7, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:16; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17.

9. The anti-human TAPBPL antibody, or fragment thereof, of any one of claims 5-7, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:16; and

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17.

10. An isolated anti-human TAPBPL antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDRs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RYWMS (SEQ ID NO:18);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EINPDSSTINYTPSLKD (SEQ ID NO:19);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence VTTVVARDWYFDV (SEQ ID NO:20);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:12;

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:13; and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence of SEQ ID NO:14.

11. The anti-human TAPBPL antibody, or fragment thereof, of claim 10, comprising:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:18;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:19;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:20;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:12;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:13; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:14.

12. The anti-human TAPBPL antibody, or fragment thereof, of claim 10 or 11, wherein the L-CDR3 comprises the amino acid sequence ALWYSTHYV (SEQ ID NO:49).

13. The anti-human TAPBPL antibody, or fragment thereof, of any one of claims 10-12, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:21; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:22.

14. The anti-human TAPBPL antibody, or fragment thereof, of any one of claims 10-12, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:21; and

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:22.

15. An isolated anti-human CD300c antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GYNMN (SEQ ID NO:23);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence NIDPYYGGTSYNQKFKG (SEQ ID NO:24);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SGYYYAMDY (SEQ ID NO:25);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQNVGTAVA (SEQ ID NO:26);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence SASNRYT (SEQ ID NO:27); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQYSSYPYT (SEQ ID NO:28).

16. The anti-human CD300c antibody, or fragment thereof, of claim 15, comprising:
an H-CDR1 comprising the amino acid sequence of SEQ ID NO:23;
an H-CDR2 comprising the amino acid sequence of SEQ ID NO:24;
an H-CDR3 comprising the amino acid sequence of SEQ ID NO:25;
an L-CDR1 comprising the amino acid sequence of SEQ ID NO:26;
an L-CDR2 comprising the amino acid sequence of SEQ ID NO:27; and
an L-CDR3 comprising the amino acid sequence of SEQ ID NO:28.

17. The anti-human CD300c antibody, or fragment thereof, of claim 15 or 16, comprising
(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:29; and/or
(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:30).

18. The anti-human CD300c antibody, or fragment thereof, of claim 15 or 16, comprising
(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:29; and
(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:30.

19. An isolated anti-human CD300c antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:
Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMK (SEQ ID NO:31);
Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DINPNNGDTFYNQKFKG (SEQ ID NO:32);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGMVTTAMDY (SEQ ID NO:33);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence RTITDIDDDMN (SEQ ID NO:34);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence EGNTLRP (SEQ ID NO:35); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence LQSDNMPYT (SEQ ID NO:36).

20. The anti-human CD300c antibody, or fragment thereof, of claim 19, comprising:
an H-CDR1 comprising the amino acid sequence of SEQ ID NO:31;
an H-CDR2 comprising the amino acid sequence of SEQ ID NO:32;
an H-CDR3 comprising the amino acid sequence of SEQ ID NO:33;
an L-CDR1 comprising the amino acid sequence of SEQ ID NO:34;
an L-CDR2 comprising the amino acid sequence of SEQ ID NO:35; and
an L-CDR3 comprising the amino acid sequence of SEQ ID NO:36.

21. The anti-human CD300c antibody, or fragment thereof, of claim 19 or 20, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:37; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:38.

22. The anti-human CD300c antibody, or fragment thereof, of claim 19 or 20, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:37; and

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:38.

23. An isolated anti-human CD300c antibody, or fragment thereof, comprising 1, 2, 3, 4, 5, or all 6 complementarity determining regions (CDs) selected from the group consisting of:

Heavy chain CDR1 (H-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence DYYMY (SEQ ID NO:39);

Heavy chain CDR2 (H-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence TISNGGSYTYYPDSVKG (SEQ ID NO:40);

Heavy chain CDR3 (H-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence GGDYYGNTYAY (SEQ ID NO:41);

Light chain CDR1 (L-CDR1) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence KASQSVDYDGDSYIN (SEQ ID NO:42);

Light chain CDR2 (L-CDR2) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence AASNLES (SEQ ID NO:43); and

Light chain CDR3 (L-CDR3) comprising an amino acid sequence at least 80%, 85%, 90%, 95%, or 100% identical to the amino acid sequence QQSNEDPYT (SEQ ID NO:44).

24. The anti-human CD300c antibody, or fragment thereof, of claim 23, comprising:

an H-CDR1 comprising the amino acid sequence of SEQ ID NO:39;

an H-CDR2 comprising the amino acid sequence of SEQ ID NO:40;

an H-CDR3 comprising the amino acid sequence of SEQ ID NO:41;

an L-CDR1 comprising the amino acid sequence of SEQ ID NO:42;

an L-CDR2 comprising the amino acid sequence of SEQ ID NO:43; and

an L-CDR3 comprising the amino acid sequence of SEQ ID NO:44.

25. The anti-human CD300c antibody, or fragment thereof, of claim 23 or 24, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:45; and/or

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:46.

26. The anti-human CD300c antibody, or fragment thereof, of claim 23 or 24, comprising:

(a) a heavy chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:45; and

(b) a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO:46.

27. The antibody or fragment thereof of any preceding claim, wherein the antibody comprises a monoclonal antibody, or fragment thereof.

28. The antibody or fragment thereof of any preceding claim, wherein the antibody comprises a humanized antibody, or fragment thereof.

29. The antibody or fragment thereof of any preceding claim, wherein the antibody is a chimeric antibody.

30. The antibody or fragment thereof of claim 29, wherein the heavy chain of any embodiment disclosed herein may further comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:47 and 70-72.

31. The antibody or fragment thereof of claim 29, wherein the light chain of any embodiment disclosed herein may further comprise an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:48 and 73.

32. The antibody or fragment thereof of any preceding claim, wherein the heavy chain or light chain comprises an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected from SEQ ID NO:50-61.

33. The antibody or fragment thereof of any preceding claim, comprising a heavy chain and a light chain comprising an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of a heavy chain-light chain pair selected from the group consisting of:

SEQ ID NO:50-51;

SEQ ID NO:52-53;

SEQ ID NO:54-55;

SEQ ID NO:56-57;

SEQ ID NO:58-59; and

SEQ ID NO:60-61.

34. The antibody or fragment thereof of any preceding claim, further comprising a therapeutic agent, including but not limited to a chemotherapeutic, conjugated to the antibody or fragment thereof.

35. A nucleic acid encoding the antibody or fragment thereof of any preceding claim.

36. A vector comprising the nucleic acid of claim 35 operatively linked to a suitable control sequence, such as a promoter.

37. A host cell comprising the antibody or fragment thereof, the nucleic acid and/or the expression vector of any preceding claim.

38. A pharmaceutical composition, comprising

(a) the antibody or fragment thereof, the nucleic acid, the vector, and/or the host cell of any preceding claim; and

(b) a pharmaceutically acceptable carrier.

39. A method for treating cancer, comprising administering to a subject in need thereof the antibody or fragment thereof, the nucleic acid, the vector, the host cell, and/or the pharmaceutical composition of any preceding claim, in an amount effective to treat the cancer.

40. The method of claim 37 wherein the cancer is selected from the group consisting of breast cancer, lung cancer, colon cancer, melanoma, prostate cancer, leukemia, neuroblastoma, liver, lymphoma, cervical cancer, ovarian cancer, gastric cancer, and esophageal cancer.

Figure 1A

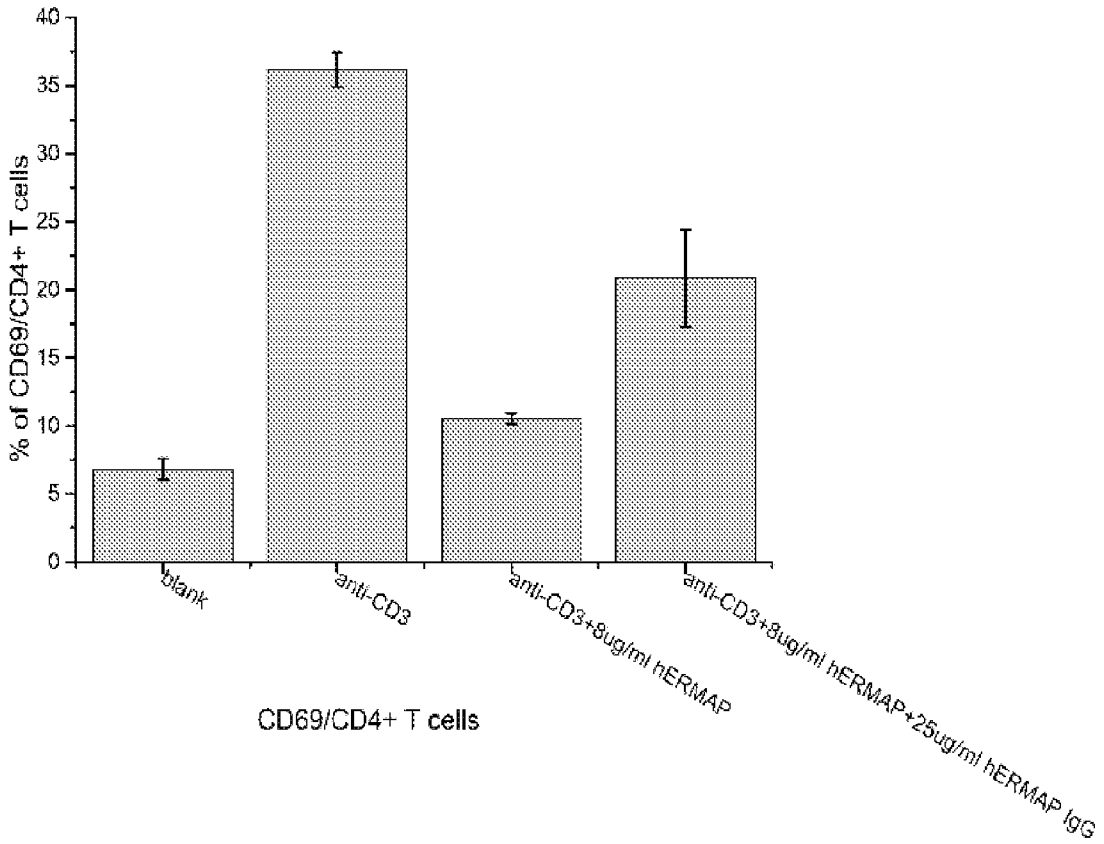

% of CD69/CD4+ T cells
40
35
30
25
20
15
10
5
0
blank
anti-CD3
anti-CD3+8ug/ml hERMAP
anti-CD3+8ug/ml hERMAP+25ug/ml hERMAP IgG
CD69/CD4+ T cells

Figure 1B

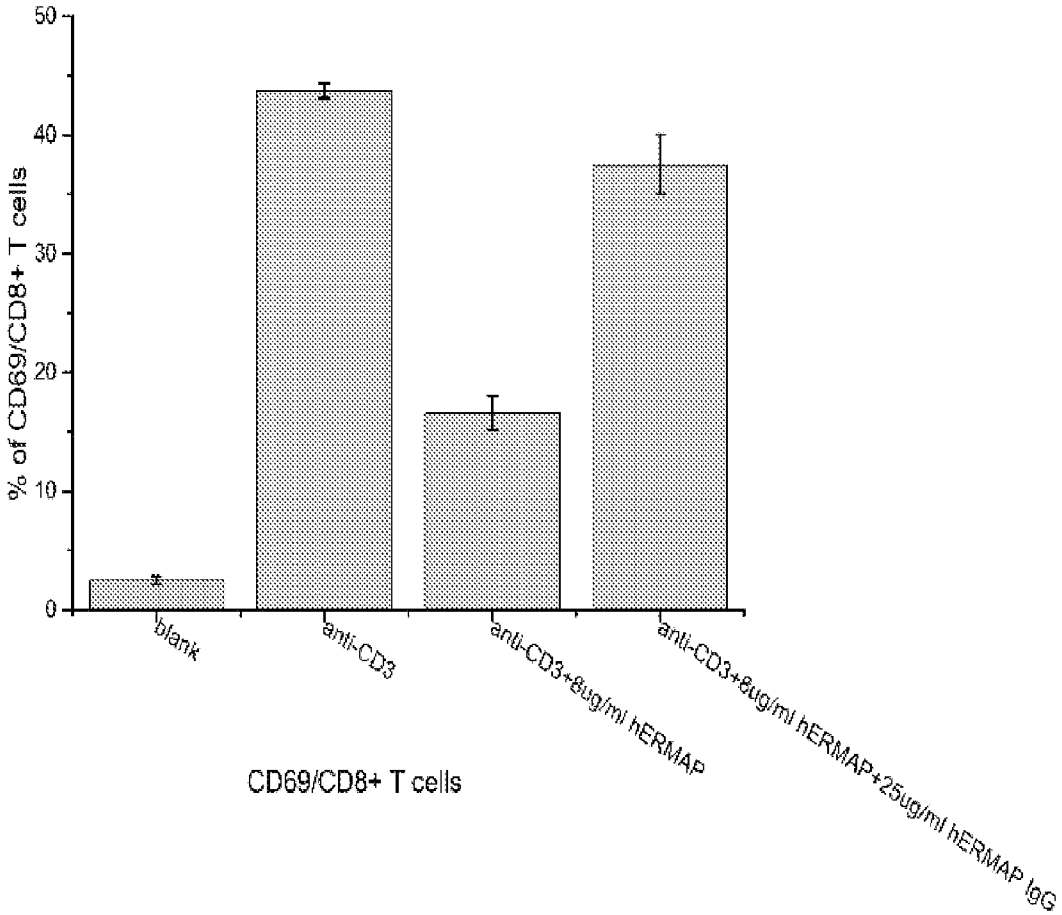
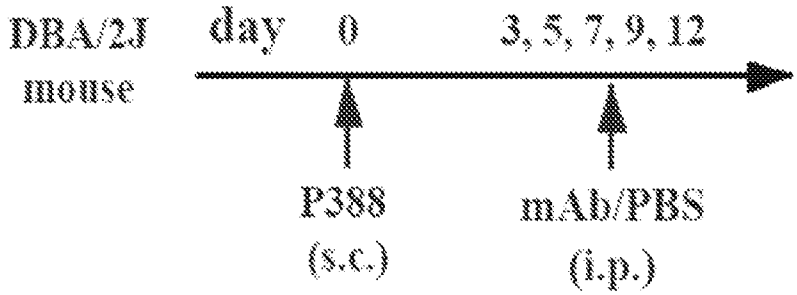

50
40
30
20
10
0
% of CD69/CD8+ T cells
blank
anti-CD3
anti-CD3+8ug/ml hERMAP
anti-CD3+8ug/ml hERMAP+25ug/ml hERMAP IgG
CD69/CD8+ T cells

Figure 2A



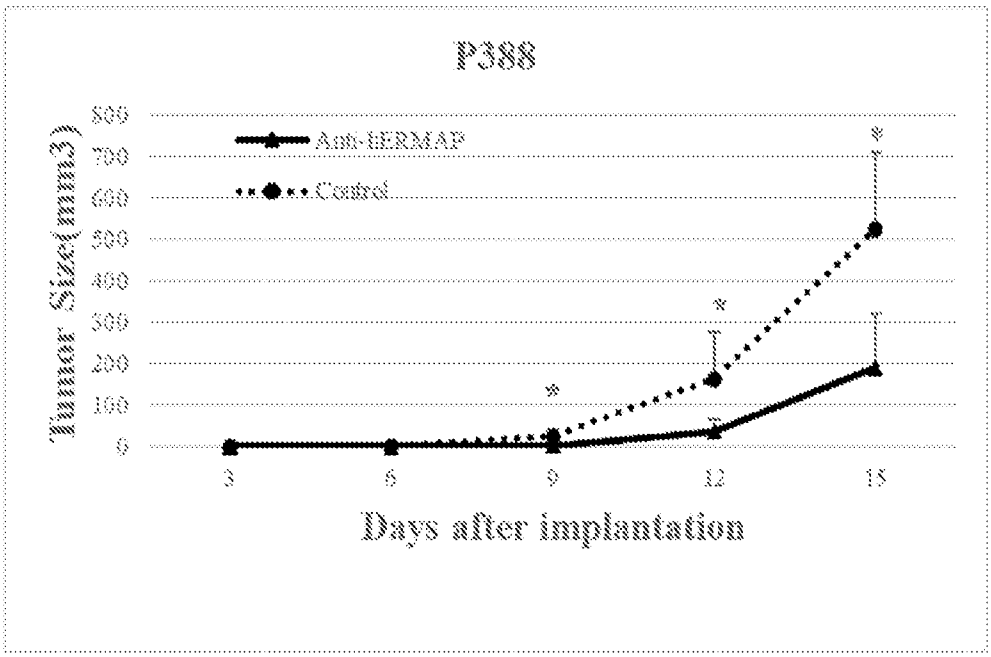


Figure 2B

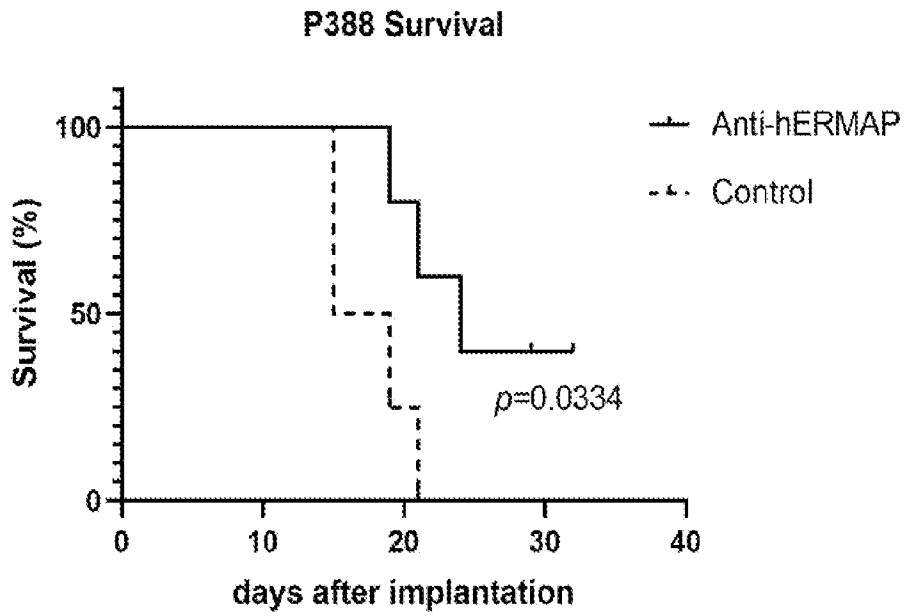
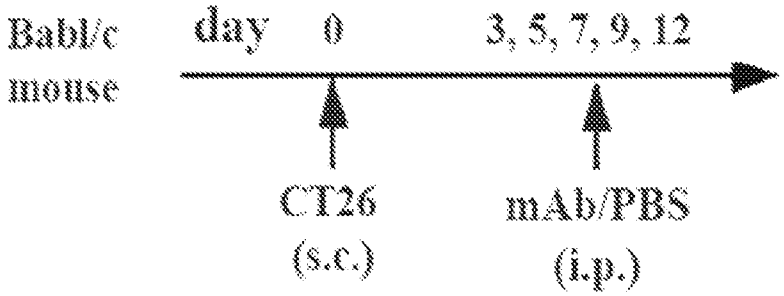

P388 Survival
Anti-hERMAP
Control
Survival (%)
100
50
0
0
10
20
30
40
days after implantation
p=0.0334

Figure 3

Figure 4A



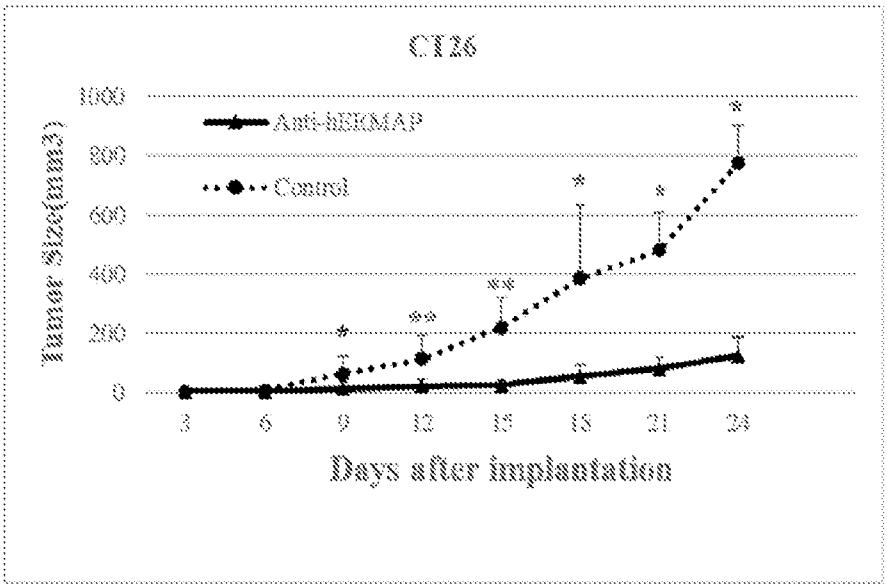


Figure 4B

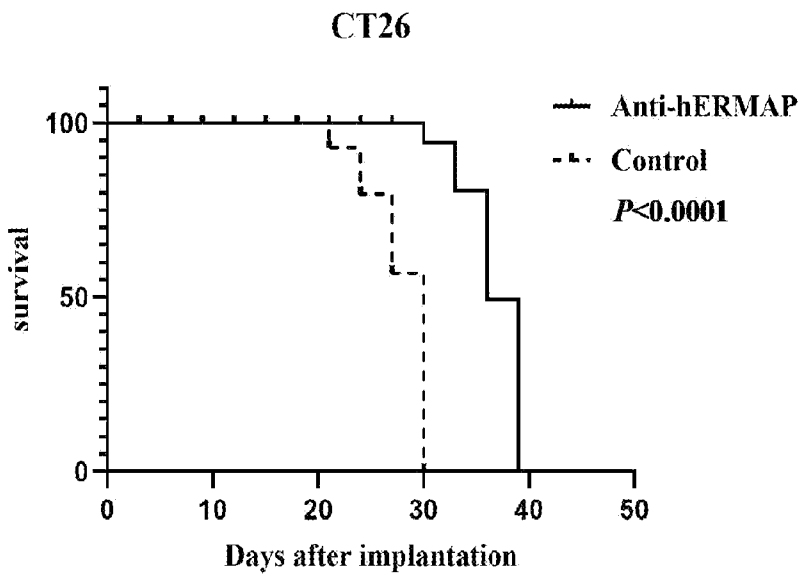

CT26
Anti-hERMAP
Control
P<0.0001
survival
100
50
0
0
10
20
30
40
50
Days after implantation

Figure 5

Figure 6A

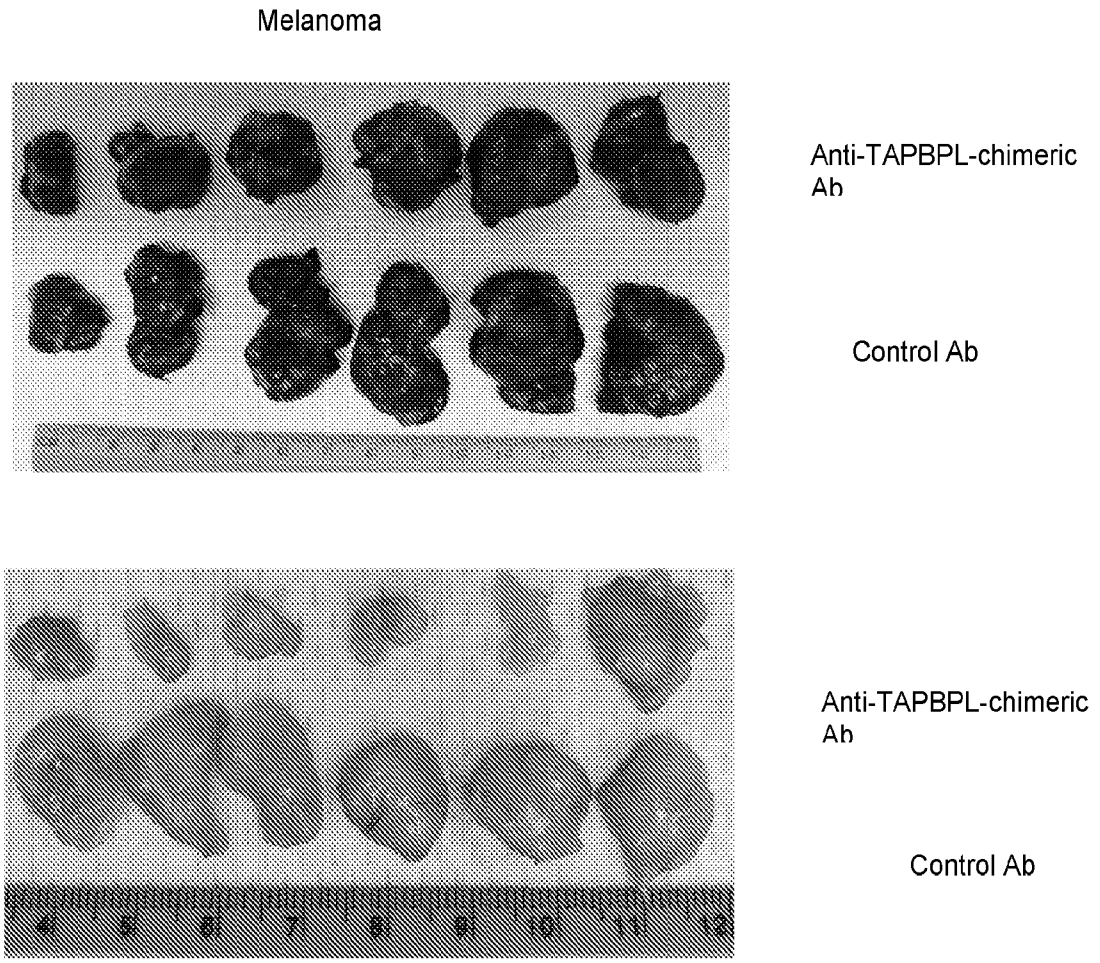


Figure 6B

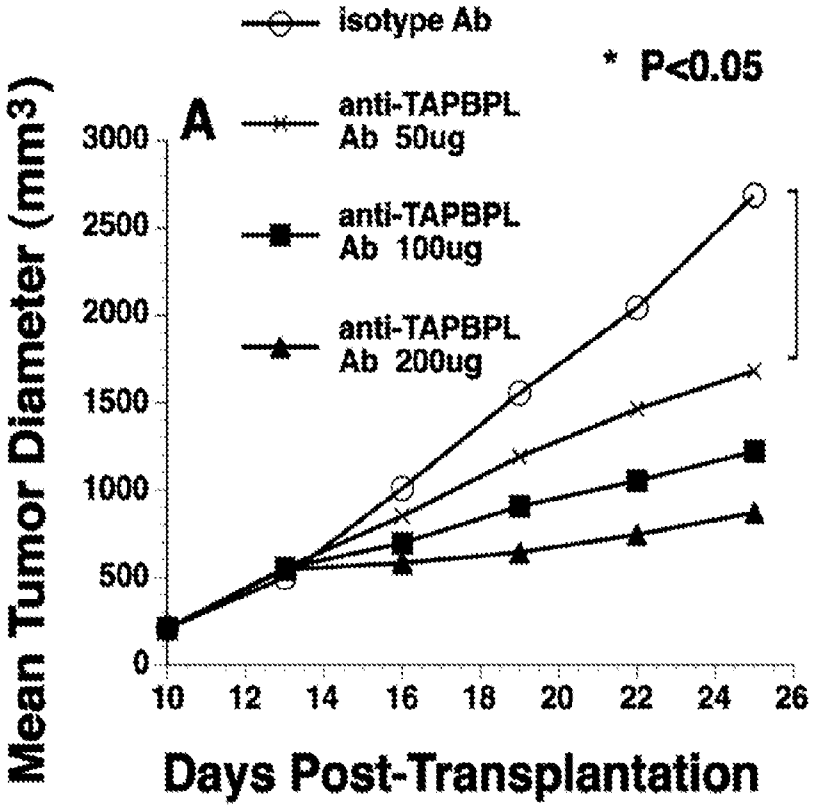

isotype Ab
* P<0.05
A
anti-TAPBPL Ab 50ug
anti-TAPBPL Ab 100ug
anti-TAPBPL Ab 200ug
Mean Tumor Diameter (mm3)
3000
2500
2000
1500
1000
500
0
10
12
14
16
18
20
22
24
26
Days Post-Transplantation

Figure 7A

Figure 7B

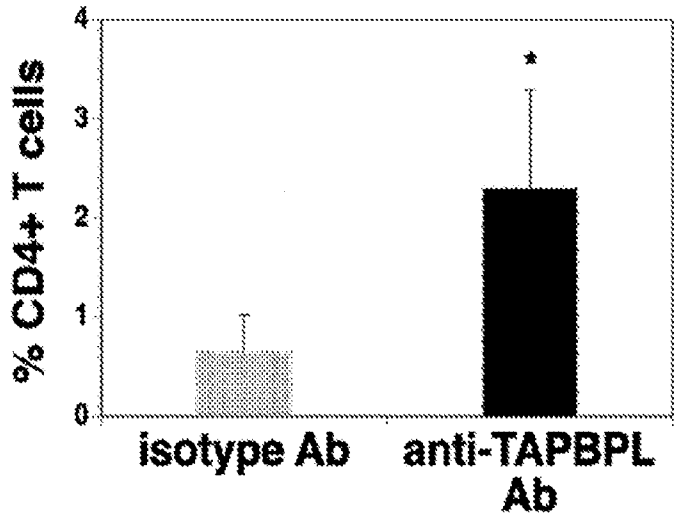
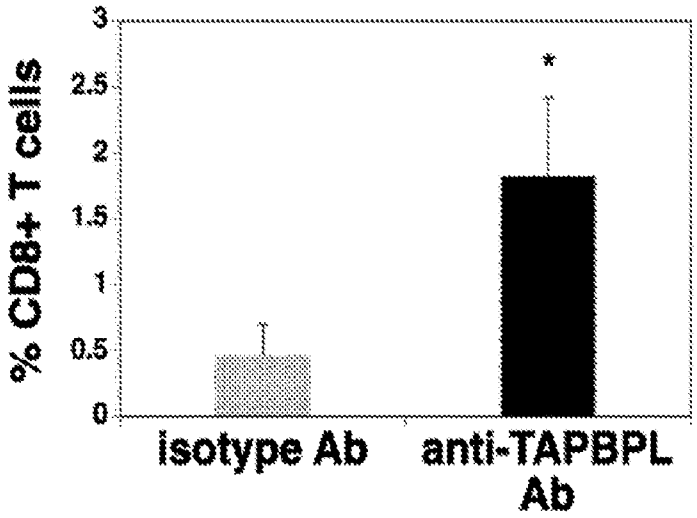


Figure 7C



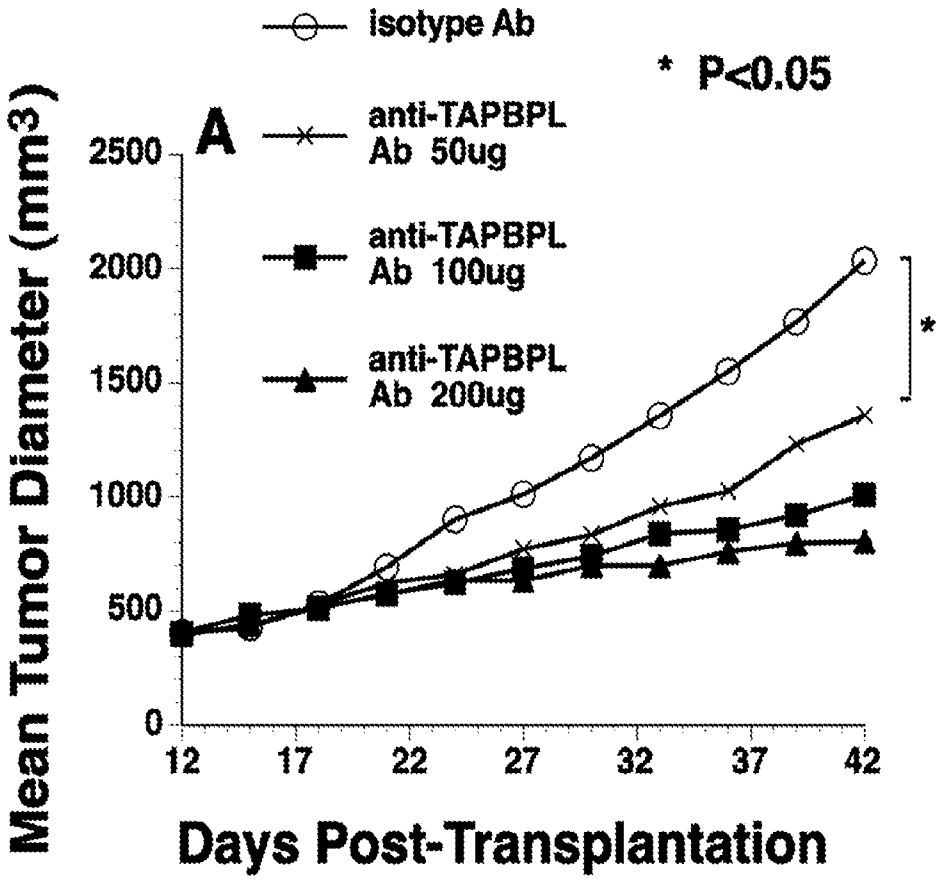
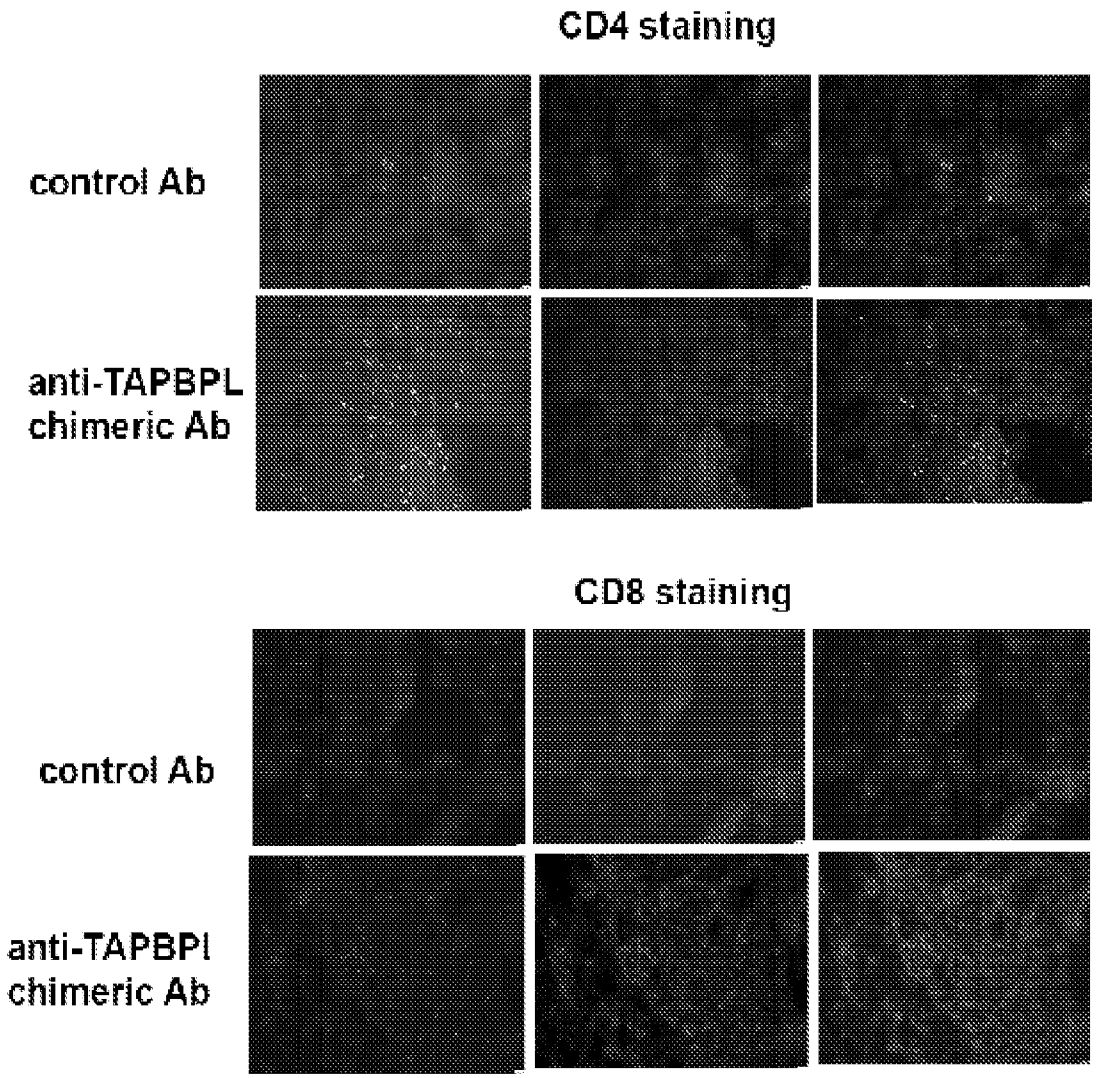

isotype Ab
anti-TAPBPL Ab 50ug
anti-TAPBPL Ab 100ug
anti-TAPBPL Ab 200ug
* P<0.05
A
Mean Tumor Diameter (mm3)
2500
2000
1500
1000
500
0
12
17
22
27
32
37
42
Days Post-Transplantation
*

Figure 8

Figure 9


CD4 staining
control Ab
anti-TAPBPL
chimeric Ab
CD8 staining
control Ab
anti-TAPBPl
chimeric Ab

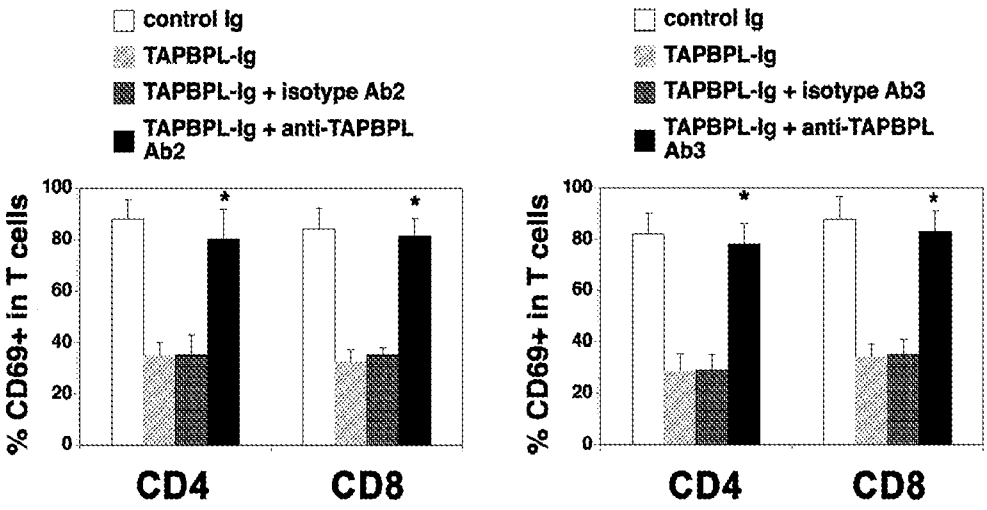

control Ig
TAPBPL-Ig
TAPBPL-Ig + isotype Ab2
TAPBPL-Ig + anti-TAPBPL Ab2
% CD69+ in T cells
100
80
60
40
20
0
*
*
CD4
CD8
control Ig
TAPBPL-Ig
TAPBPL-Ig + isotype Ab3
TAPBPL-Ig + anti-TAPBPL Ab3
% CD69+ in T cells
100
80
60
40
20
0
*
*
CD4
CD8

Figure 10

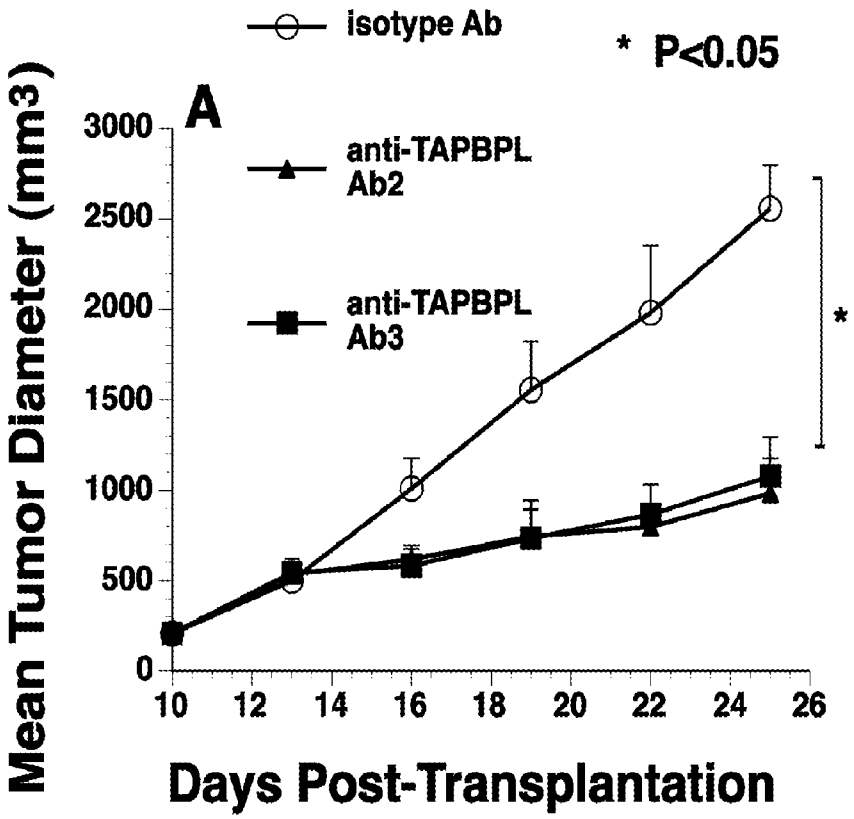

isotype Ab
* P<0.05
A
anti-TAPBPL Ab2
anti-TAPBPL Ab3
Mean Tumor Diameter (mm3)
3000
2500
2000
1500
1000
500
0
10
12
14
16
18
20
22
24
26
Days Post-Transplantation
*

Figure 11

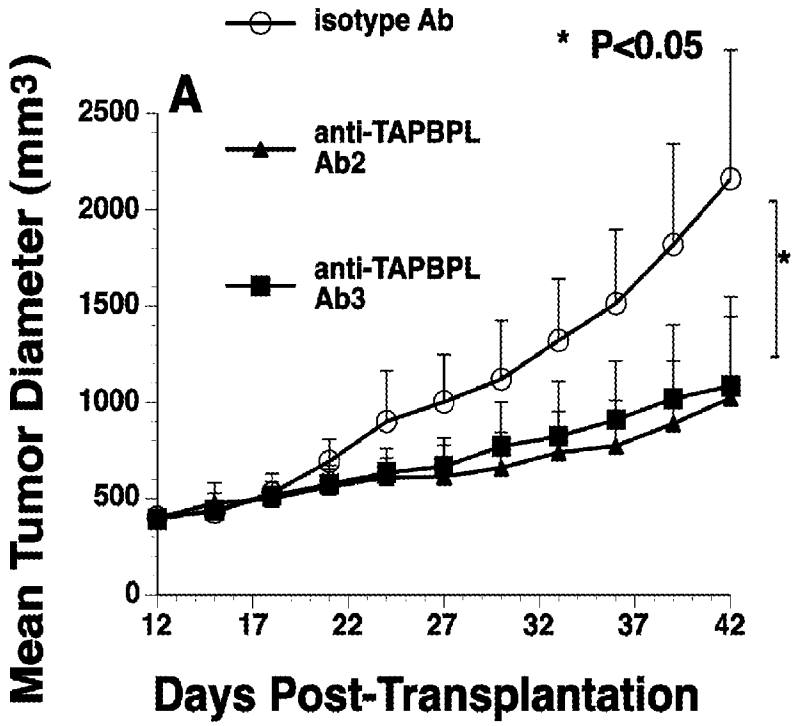

isotype Ab
* P<0.05
A
anti-TAPBPL Ab2
anti-TAPBPL Ab3
Mean Tumor Diameter (mm3)
2500
2000
1500
1000
500
0
12
17
22
27
32
37
42
Days Post-Transplantation
*

Figure 12

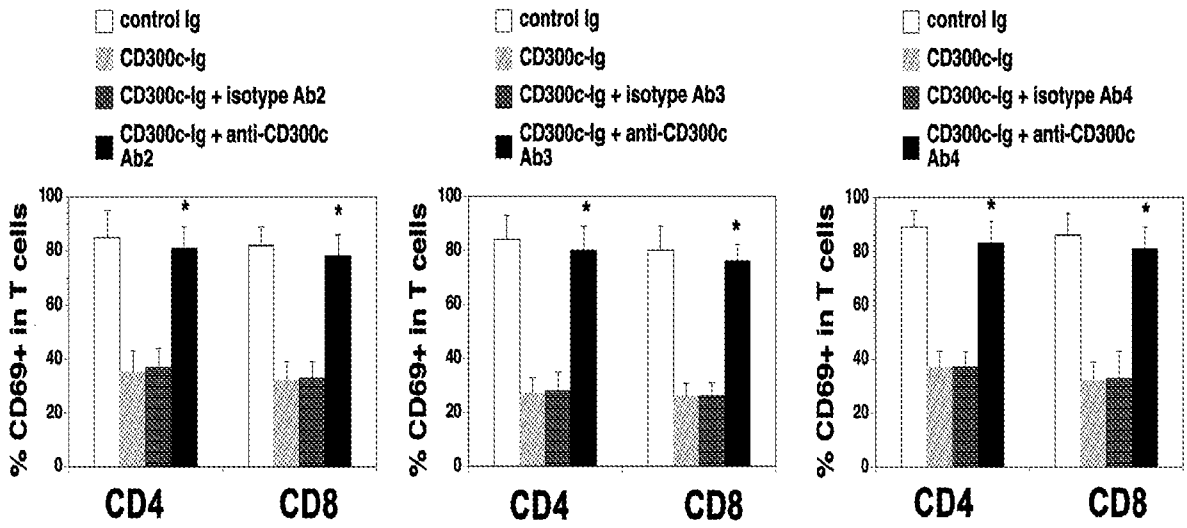

control Ig
CD300c-Ig
CD300c-Ig + isotype Ab2
CD300c-Ig + anti-CD300c Ab2
% CD69+ in T cells
100
80
60
40
20
0
*
*
CD4
CD8
control Ig
CD300c-Ig
CD300c-Ig + isotype Ab3
CD300c-Ig + anti-CD300c Ab3
% CD69+ in T cells
100
80
60
40
20
0
*
*
CD4
CD8
control Ig
CD300c-Ig
CD300c-Ig + isotype Ab4
CD300c-Ig + anti-CD300c Ab4
% CD69+ in T cells
100
80
60
40
20
0
*
*
CD4
CD8

Figure 13

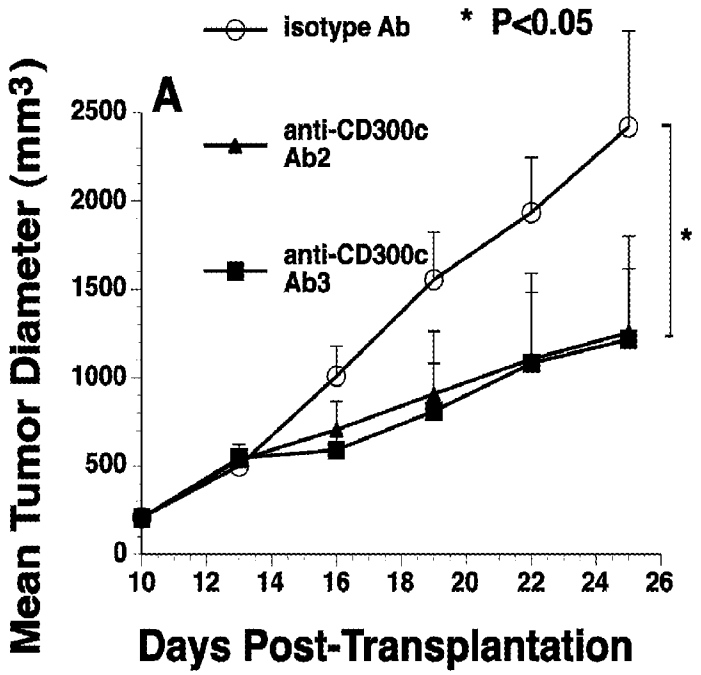

isotype Ab
* P<0.05
A
anti-CD300c Ab2
anti-CD300c Ab3
Mean Tumor Diameter (mm3)
2500
2000
1500
1000
500
0
10
12
14
16
18
20
22
24
26
Days Post-Transplantation
*

Figure 14