(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 September 2022 (29.09.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/204340 A1

(51) International Patent Classification:
A61K 35/17 (2015.01) *A61P 35/00* (2006.01)
A61K 38/17 (2006.01)

(21) International Application Number:
PCT/US2022/021633

(22) International Filing Date:
24 March 2022 (24.03.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/166,550 26 March 2021 (26.03.2021) US

(71) Applicant: **ARCELLX, INC.** [US/US]; 25 West Watkins Mill Road, Suite A, Gaithersburg, MD 20878 (US).

(72) Inventor: **HILBERT, David, M.**; c/o of Arcellx, Inc., 25 West Watkins Mill Road, Suite A, Gaithersburg, MD 20878 (US).

(74) Agent: **GASZNER, Miklos**; Nixon & Vanderhye P.C., 901 North Glebe Road, 11th Floor, Arlington, VA 22203-1808 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(54) **Title:** MULTIFUNCTIONAL IMMUNE CELL THERAPIES

(57) **Abstract:** Provided herein are multi-functional chimeric antigen receptor (CAR)-based compositions and their use in directing immune responses to target cells. The compositions have uses that include treating hyperproliferative disorders such as cancer. The provided methods generally include the use of a CAR cell in combination with an Adapter. The Adapter confers the ability to modulate, alter, and/or redirect CAR cell- mediated immune response *in vitro* and *in vivo*. In some embodiments, the CAR cell comprises a genetic modification to reduce or eliminate the expression of a targeted antigenic determinant.

WO 2022/204340 A1

MULTIFUNCTIONAL IMMUNE CELL THERAPIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority of U.S. Provisional Application No. 63/166,550 filed March 26, 2021, which is incorporated herein in its entirety.

BACKGROUND

[0002] The disclosures of International Appl. Nos. PCT/US2018/060902 and PCT/US2018/060887, both filed November 14, 2018, are incorporated by reference herein in their entirety for all purposes.

[0003] The adoptive transfer of genetically modified T cells is a rapidly evolving innovative treatment for cancer. Chimeric antigen receptor (CAR) engineered T cells are renewable drugs with the capacity to provide sustained functional immunity. Clinical efficacy has been demonstrated with CD19 CAR T in a range of hematological cancers and encouraging early clinical data has been reported for other genetically modified CAR T in solid tumors. However, significant challenges must be met before CAR technology can more fully realize its substantial potential.

[0004] Current clinical trials with CAR T cells observe a high incidence of relapse in one year or less due to the inability of CAR T cells to address antigen escape and the inherent heterogeneity in the cancer or tumor phenotype. Moreover, current CAR technologies are not adaptive to such changes in cancer or tumor phenotype. In solid tumors, for example, current CAR technologies exhibit limited efficacy due to tumor target heterogeneity and the inability to reprogram CAR T cells to recognize an expanded set of antigenic targets expressed over time. In addition to improving the durability and sustainability of clinical responses, other key impediments to the use of current CAR cell-based technologies include the time required to generate CAR T cells, and the suboptimal specificity, efficacy, and safety of CAR cells for use in cancers beyond leukemia. Accordingly, there is a need for CAR cell-based technology that provides simultaneous and/or sequential target multispecificity and the ability to modulate, alter, or redirect CAR cell-mediated immune responses *in vivo*.

[0005] Bone marrow transplantation (BMT) and hematopoietic stem cell transplantation (HSCT) hold the promise of correcting any blood or immune disease. Czechowicz *et al.*, Blood 128 (22): 493 (2016). Despite their tremendous potential, the clinical use of BMT and HSCT remain fairly limited in part due to the severe safety and toxicity risks associated with current high dose chemotherapy/ irradiation conditioning regimens to prepare patients for transplant and subsequent donor HSC engraftment. The most common toxicities experienced by patients include neutropenia, infections, anemia, mucositis, infertility, organ damage particularly in the bone marrow compartment and secondary malignancies. Complete elimination of these

toxic conditioning regimens would dramatically improve the safety profile of BMT and HSCT and expand the potential applications to include many more non-malignant hematologic disorders, a wide variety of autoimmune disorders, as well as facilitate solid organ transplant. Accordingly, there is a need for the development of improved conditioning regimens that limit or eliminate toxicities associated with current high dose chemotherapy/ irradiation while also effectively treating the underlying disease state.

BRIEF SUMMARY

[0006] In some embodiments, the disclosure provides:

[1.] A composition comprising:

[1.] A method of treating a lymphoma or leukemia comprising administering to a subject in need thereof

a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA;

[2.] the method of [1], wherein the lymphoma or leukemia comprises cells expressing BCMA;

[3.] the method of [1] or [2], wherein the lymphoma or leukemia is a B cell lymphoma or leukemia;

[4.] the method of [1] or [2], wherein the lymphoma or leukemia is multiple myeloma;

[5.] a method of delivering an immune response to a multiple myeloma cell comprising administering to a subject in need thereof

a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA;

[6.] a method a method of killing a multiple myeloma cell comprising administering to a subject in need thereof

a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA;

[7.] a method of depleting multiple myeloma cells comprising administering to a subject in need thereof

a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA;

[8.] the method of any one of [[1] to [7], wherein the cells are immune effector cells;

[9.] the method of any one of [1] to [8], wherein the cells are T cells or NK cells;

[10.] the method of any one of [1] to [9], wherein the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201;

[11.] the method of any one of [1] to [10], wherein the CAR comprises the amino acid sequence of SEQ ID NO: 1164;

[12.] the method of any one of [1] to [11], wherein the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201;

[13.] the method of any one of [1] to [12], wherein the Adapter comprises the amino acid sequence of SEQ ID NO: 1165;

[14.] the method of any one of [1] to [13], wherein the Adapter is formulated for intravenous administration;

[15.] the method of any one of [1] to [13], wherein the Adapter is formulated for subcutaneous administration;

[16.] the method of any one of [1] to [15], wherein the cells and the Adapter are administered simultaneously;

[17.] the method of any one of [1] to [15], wherein the cells and the Adapter are administered consecutively;

[18.] the method of any one of [1] to [15], wherein the cells are administered before the Adapter;

[19.] the method of any one of [1] to [18], wherein the cells and the Adapter are administered on the same day;

[20.] the method of any one of [1] to [18], wherein the cells and the Adapter are administered on different days;

[21.] the method of [20], wherein the cells and the Adapter are administered on consecutive days;

[22.] the method of [20], wherein the cells and the Adapter are administered 1, 2, 3, 4, 5, 6, or 7 days apart;

[23.] the method of any one of [1] to [22], wherein the cells and the Adapter are administered on different days;

[24.] the method of any one of [1] to [23], comprising administering between about 20x106 and about 500x106 or between about 50x106 and about 200x106 cells expressing the CAR;

[25.] the method of any one of [1] to [23], comprising administering about 100x106 cells expressing the CAR;

[26.] the method of any one of [1 to 24], comprising administering one or more doses of about 1 □g/kg to about 10 mg/kg, about 5 □g/kg to about 5 mg/kg, about 10 □g/kg to about 2 mg/kg, about 20 □g/kg to about 1 mg/kg, or about 50 □g/kg to about 0.5 mg/kg of the Adapter;

[27.] the method of any one of [1] to [24], comprising administering one or more doses of about 20 □g/kg to about 1 mg/kg of the Adapter;

[28.] the method of any one of [1] to [24], comprising administering one or more doses of about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg of the Adapter;

[29.] the method of any one of [1] to [24], comprising administering one or more doses of about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, or about 0.3 mg/kg of the Adapter;

[30.] the method of any one of [1] to [24], comprising administering one or more doses of about 0.4 mg, about 0.8 mg, about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, about 20 mg, about 24 mg, about 28 mg, about 40 mg, or about 80 mg of the Adapter;

[31.] the method of any one of [1] to [24], comprising administering one or more doses of about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg of the Adapter;

[32.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered 3 times a day, twice a day, daily, every two days, twice a week, or weekly;

[33.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily;

[34.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered every two days;

[35.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for between about 1 to about 4 weeks, followed by administration every other day, twice a week, or weekly;

[36.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by every other day administration;

[37.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by twice weekly administration;

[38.] the method of any one of [1] to [31], comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by weekly administration;

[39.] the method of any one of [1] to [38], comprising administering the Adapter at different doses;

[40.] the method of any [36], comprising administering one or more loading doses of about 0.1 mg/kg to about 10 mg/kg of the Adapter, followed by the administration of one or more maintenance doses of about 0.01mg/kg to about 0.1 mg/kg;

[41.] the method of any [39], comprising administering one or more loading doses of about 4 mg to about 200 mg of the Adapter, followed by the administration of one or more maintenance doses of about 0.4 mg to about 10 mg;

[42.] the method of any [40] or [41], wherein the one or more loading doses are administered for about 1 day to about 3 weeks;

[43.] the method of any [40] or [41], wherein the one or more loading doses are administered for about 1 day to about 1 week;

[44.] the method of any [40] or [41], wherein the one or more loading doses are administered for 1 day, 2 days, 3 days, 4 days or about 1 week;

[45.] a method of treating a lymphoma or leukemia comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain;

[46.] the method of [45], wherein the lymphoma or leukemia comprises cells expressing BCMA;

[47.] the method of [45] or [46], wherein the lymphoma or leukemia is a B cell lymphoma or leukemia;

[48.] the method of [45] or [46], wherein the lymphoma or leukemia is multiple myeloma;

[49.] a method of delivering an immune response to a multiple myeloma cell comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain;

[50.] a method a method of killing a multiple myeloma cell comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracelular domain;

[51.] a method of depleting multiple myeloma cells comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0007] Provided herein are multi-functional chimeric antigen receptor (CAR)-based compositions and their use in directing immune responses to target cells. The compositions have uses that include treating hyperproliferative disorders such as cancer. The provided methods generally include the use of a CAR cell in combination with an Adapter. The Adapter confers the ability to modulate, alter, and/or redirect CAR cell-mediated immune response *in vitro* and *in vivo*.

[0008] The present disclosure relates to compositions comprising: (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises an antigenic determinant binding domain (ADBD), and (b) a soluble protein (an "Adapter") which comprises (i) an antigenic determinant (AD) and (ii) and an ADBD. The present disclosure also provides methods of killing a target cell with the compositions provided herein, including therapeutic applications of the compositions provided herein.

[0009] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises an (i) an ADBD that binds to a first AD on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0010] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0011] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an alternative scaffold binding domain (ASBD) that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell.

[0012] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD comprising an ASBD that binds to a second AD on a target cell.

[0013] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) a D domain that binds to a second AD on a target cell.

[0014] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) a D domain that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell.

[0015] In some embodiments, the disclosure provides a composition comprising: (a) a cell expressing a CAR, wherein the CAR comprises (i) a first D domain that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) a second D domain that binds to a second AD on a target cell.

[0016] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0017] In some embodiments, the disclosure provides a method of killing one or more target cells comprising contacting a composition comprising a first target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0018] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0019] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell

further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0020] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the first target cell further comprises an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on the target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0021] In some embodiments, the disclosure provides a method of killing one or more target cells comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the first target cell; (b) the composition comprising the first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0022] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0023] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0024] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0025] In some embodiments, the disclosure provides a method of delivering an immune response to one or more target cells comprising contacting a composition comprising a first target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0026] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0027] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0028] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the first target cell further comprises an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on the target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0029] In some embodiments, the disclosure provides a method of delivering an immune response to one or more target cells comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the first target cell; (b) the composition comprising the first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0030] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR

comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0031] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a CAR, wherein (a) a first antigenic determinant (AD) is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0032] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0033] In some embodiments, the disclosure provides a method of redirecting target cell killing in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0034] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0035] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0036] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD and a second AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to said second AD on said target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0037] In some embodiments, the disclosure provides a method of directing target cell killing in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) the patient has been treated with an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and (b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0038] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0039] In some embodiments, the disclosure provides a method of killing a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0040] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0041] In some embodiments, the disclosure provides a method of redirecting an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0042] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0043] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a

transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0044] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD and a second AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to said second AD on said target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0045] In some embodiments, the disclosure provides a method of directing an immune response to a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) the patient has been treated with an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and (b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0046] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0047] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with a an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0048] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0049] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular

domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0050] In some embodiments, the disclosure provides a method of redirecting treatment of a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0051] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0052] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0053] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD and a second AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to said second AD on said target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0054] In some embodiments, the disclosure provides a method of directing treatment of a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a CAR to the patient, wherein (a) the patient has been treated with an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and (b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0055] In some embodiments, the disclosure provides a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with an Adapter

comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0056] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with a an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0057] In some embodiments, the disclosure provides a method of treating hematological cancer comprising contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0058] In some embodiments, the disclosure provides a method of treating hematological cancer comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0059] In some embodiments, the disclosure provides a method of redirecting treatment of a hematological cancer comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0060] In some embodiments, the disclosure provides a method of treating hematological cancer comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0061] In some embodiments, the disclosure provides a method of treating hematological cancer comprising administering an Adapter to the patient, wherein (a) the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an ADBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an

intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0062] In some embodiments, the disclosure provides a method of treating hematological cancer comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD and a second AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to said second AD on said target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0063] In some embodiments, the disclosure provides a method of directing treatment of a hematological cancer comprising administering a cell expressing a CAR to the patient, wherein (a) the patient has been treated with an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and (b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0064] In some embodiments, the disclosure provides a method of treating hematological cancer comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0065] In some embodiments, the disclosure provides method of treating hematological cancer comprising administering a cell expressing a CAR to the patient, wherein (a) a first AD is present on the target cell; (b) the patient has been treated with a an Adapter comprising (i) an ADBD that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0066] In some embodiments, the disclosure provides an engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR) comprising (1) an antigenic determinant binding domain (ADBD) that specifically binds to a human CD45 antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of the human CD45 AD on the engineered cell, wherein the engineered cell is capable of directing an immune response to a CD45 AD expressing cell in an in vitro assay, and wherein the engineered cell does not express the CD45 AD.

[0067] In some embodiments, the disclosure provides a method of killing a human CD45 expressing target cell comprising contacting the target cell with an engineered human immune effector cell, wherein the engineered human immune effector cell comprises (a) a chimeric antigen receptor (CAR) comprising (1) an antigenic determinant binding domain (ADBD) that specifically binds to a human CD45 antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of the human CD45 AD on the engineered cell.

[0068] In some embodiments, the disclosure provides a method of delivering an immune response to a human CD45 expressing target cell comprising contacting the target cell with an engineered human immune effector cell, wherein the engineered human immune effector cell comprises (a) a chimeric antigen receptor (CAR) comprising (1) an antigenic determinant binding domain (ADBD) that specifically binds to a human CD45 antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of the human CD45 AD on the engineered cell.

[0069] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell, wherein the engineered human immune effector cell comprises (a) a chimeric antigen receptor (CAR) comprising (1) an antigenic determinant binding domain (ADBD) that specifically binds to a human CD45 antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of the human CD45 AD on the engineered cell.

[0070] In some embodiments, the disclosure provides an engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell, wherein the first AD is not the at least one human CD45 AD, wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a CD45 expressing cell in an in vitro assay, wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the at least one human CD45 AD, and wherein the engineered cell does not express the at least one human CD45 AD.

[0071] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting the target cell with an engineered human immune effector cell and an Adapter, wherein the target cell expresses CD45, wherein the engineered human immune effector cell comprises (a) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell, and wherein the Adapter comprises the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0072] In some embodiments, the disclosure provides a method of delivering an immune response to a target cell comprising contacting the target cell with an engineered human immune effector cell and an Adapter, wherein the target cell expresses CD45, wherein the engineered human immune effector cell comprises (a) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that

specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (b) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell, and wherein the Adapter comprises the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0073] In some embodiments, the disclosure provides a method of directing an immune response to a CD45 expressing target cell in a subject comprising (a) administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell; and (b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0074] In some embodiments, the disclosure provides a method of directing an immune response to a CD45 expressing target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell, wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0075] In some embodiments, the disclosure provides a method of directing an immune response to a CD45 expressing target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD, wherein the subject has been administered an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell.

[0076] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising (a) administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the

engineered cell; and (b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0077] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell, wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD.

[0078] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD, wherein the subject has been administered an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell.

[0079] In some embodiments, the disclosure provides an engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) a genetic modification that eliminates the expression of the first AD on the engineered cell, wherein the engineered cell does not express the first AD.

[0080] In some embodiments, the disclosure provides a method of killing a target cell comprising contacting the target cell with an engineered cell engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) a genetic modification that eliminates the expression of the first AD on the engineered cell.

[0081] In some embodiments, the disclosure provides a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an engineered cell engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an

intracellular domain; and (b) a genetic modification that eliminates the expression of the first AD on the engineered cell.

[0082] In some embodiments, the disclosure provides a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) a genetic modification that eliminates the expression of the first AD on the engineered cell.

[0083] In some embodiments, the disclosure provides a method of directing an immune response to a target cell in a subject comprising (a) administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR), wherein the CAR comprises (1) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of the first AD on the engineered cell; and (b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the target cell.

[0084] In some embodiments, the disclosure provides a engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) a genetic modification that eliminates the expression of a second AD on the engineered cell, wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a cell expressing the second AD in an in vitro assay, wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the engineered cell does not express the second AD.

[0085] In some embodiments, the disclosure provides a method of directing an immune response to a target cell in a subject comprising (a) administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR), wherein the CAR comprises (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of a second AD on the engineered cell; and (b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD recognized by the CAR and a second ADBD that is capable of binding the second AD, wherein the second AD is expressed on the target cell.

[0086] In some embodiments, the disclosure provides an engineered human immune effector cell comprising (a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that specifically binds to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) a genetic modification that eliminates the expression of a second AD on the engineered cell, wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a cell expressing the second AD in an in vitro assay, wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the engineered cell does not express the second AD.

[0087] In some embodiments, the disclosure provides a method of directing an immune response to a target cell in a subject comprising (a) administering to the subject in need thereof a therapeutically effective amount of an engineered human immune effector cell comprising (i) a chimeric antigen receptor (CAR), wherein the CAR comprises (1) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that specifically binds to a first antigenic determinants (AD), (2) a transmembrane domain, and (3) an intracellular domain; and (ii) a genetic modification that eliminates the expression of a second AD on the engineered cell; and (b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD recognized by the CAR and a second ADBD that is capable of binding the second AD, wherein the second AD is expressed on the target cell.

[0088] In some embodiments, the disclosure provides:

[1.] A composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[2.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[3.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an alternative scaffold binding domain (ASBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell;

[4.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) an ADBD comprising an ASBD that binds to a second AD on a target cell;

[5.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) a D domain that binds to a second AD on a target cell;

[6.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell;

[7.] a composition comprising:

(a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a first D domain that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) an Adapter which comprises (i) said first AD and (ii) a second D domain that binds to a second AD on a target cell;

[8.] the composition of any of [1]-[7], wherein CAR comprises a single-chain variable fragment (scFv) ADBD;

[9.] the composition of any of [1]-[7], wherein the CAR comprises an alternative scaffold binding domain (ASBD) ADBD;

[10.] the composition of [9], wherein the CAR comprises a D domain, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 17-26, and 27 or SEQ ID NO: 44-1078, and 1079;

[11.] the composition of any one of [1]-[10], wherein the CAR comprises 2 ADBDs;

[12.] the composition of [11], wherein the CAR comprises an ASBD and a scFv;

[13.] the composition of [11], wherein the CAR comprises a D domain and a scFv;

[14.] the composition of [11], wherein the CAR comprises 2 ASBDs;

[15.] the composition of [11], wherein the CAR comprises 2 D domains;

[16.] the composition of any of [1]-[15], wherein the CAR intracellular domain is a signaling domain;

[17.] the composition of [16], wherein the CAR intracellular domain comprises a primary signaling domain;

[18.] the composition of [16], wherein the CAR intracellular domain comprises a CD3ζ primary signaling domain;

[19.] the composition of [17] or [18], wherein the CAR intracellular domain further comprises a costimulatory signaling domain;

[20.] the composition of [19], wherein the CAR intracellular domain comprises a costimulatory signaling domain selected from: CD28, 41BB, CD27, and CD134;

[21.] the composition of [20], wherein the CAR intracellular domain comprises a 41BB costimulatory signaling domain;

[22.] the composition of any of [1]-[21], wherein the CAR binds to an antigen selected from: CD19, CD22, CD123, BCMA, CS1, HER2, TACI, BAFFR, and PDL1;

[23.] the composition of [22], wherein the CAR binds to BCMA, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 44-338, and 339;

[24.] the composition of [22], wherein the CAR binds to CD123, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 340-77and 773;

[25.] the composition of [22], wherein the CAR binds to CD19, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1030-1058, and 1059;

[26.] the composition of [22], wherein the CAR binds to CD22, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1060-1068, and 1069;

[27.] the composition of [22], wherein the CAR binds to CS1, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 780-794, and 795;

[28.] the composition of [22], wherein the CAR binds to HER2, optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 800-839, and 840;

[29.] the composition of [22], wherein the CAR binds to PDL1, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1010-1016, 1074-1078, and 1079;

[30.] the composition of any of [1]-[21], wherein the CAR binds to AFP p26, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 841-983, and 984;

[31.] the composition of any of [1]-[30], wherein the CAR comprises 2 ADBDs that bind to separate targets;

[32.] the composition of [31], wherein the CAR binds to CD19 and CD123;

[33.] the composition of [31], wherein the CAR binds to BCMA and CS1;

[34.] the composition of [31], wherein the CAR binds to CD22 and CD123;

[35.] the composition of [31], wherein the CAR binds to PDL1 and CD123;

[36.] the composition of [32], wherein the CAR comprises a first ASBD that binds to CD19 and a second ASBD that binds to CD123;

[37.] the composition of [36] wherein the CAR comprises a first D domain that binds to CD19 and a second D domain that binds to CD123;

[38.] the composition of [32], wherein the CAR comprises a D domain that binds to CD19 and a scFv that binds to CD123;

[39.] the composition of [33], wherein the CAR comprises a first ASBD that binds to BCMA and a second ASBD that binds to CS1;

[40.] the composition of [39] wherein the CAR comprises a first D domain that binds to BCMA and a second D domain that binds to CS1;

[41.] the composition of [33], wherein the CAR comprises a D domain that binds to CS1 and a scFv that binds to BCMA;

[42.] the composition of [39], wherein the CAR comprises a D domain that binds to BCMA and a scFv that binds to CS1;

[43.] the composition of [34], wherein the CAR comprises a first ASBD that binds to CD22 and a second ASBD that binds to CD123;

[44.] the composition of [43], wherein the CAR comprises a first D domain that binds to CD22 and a second D domain that binds to CD123;

[45.] the composition of [34], wherein the CAR comprises a D domain that binds to CD22 and a scFv that binds to CD123;

[46.] the composition of [35], wherein the CAR comprises a first ASBD that binds to PDL1 and a second ASBD that binds to CD123;

[47.] the composition of [46], wherein the CAR comprises a first D domain that binds to PDL1 and a second D domain that binds to CD123;

[48.] the composition of [35], wherein the CAR comprises a D domain that binds to PDL1 and a scFv that binds to CD123;

[49.] the composition of [32], wherein the CAR comprises an ASBD that binds to CD19 and a scFv that binds to CD123;

[50.] the composition of any of [1]-[49], wherein the Adapter comprises an AD of a tumor antigen, optionally wherein the tumor antigen is selected from the group: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1;

[51.] the composition of [1]-[50], wherein the Adapter comprises an AD that is an epitope of AFP p26 or AFP, and optionally comprises the amino acid residues of SEQ ID NO: 16 or 1117-1123-;

[52.] the composition of any of [1]-[51] wherein the Adapter comprises an ADBD that is a scFv;

[53.] the composition of any of [1]-[51], wherein the Adapter comprises an ADBD that is an ASBD;

[54.] the composition of [53], wherein the Adapter comprises a D domain, and optionally wherein the Adapter comprises a sequence selected from the group: SEQ ID NO: 17-26, and 27, or SEQ ID NO: 44-1078, and 1079;

[55.] the composition of any one of [1]-[54], wherein the Adapter comprises two ADBDs;

[56.] the composition of [55], wherein the two ADBDs (a) are the same, (b) bind to the same antigenic determinant, (c) bind to different ADs of the same antigen, or (d) bind to different antigens on the same cell, or (e) bind to different antigens on different cells;

[57.] the composition of [55] or [56], wherein the Adapter comprises two ASBDs;

[58.] the composition of any one of [55]-[57], wherein the Adapter comprises two D domains, and optionally wherein the Adapter comprises an amino acid sequence selected from the group: SEQ ID NO: 44-1079;

[59.] the composition of any one of [55] or [56], wherein the Adapter comprises an ADBD that is a scFv and an ADBD that is an ASBD;

[60.] the composition of [59], wherein the Adapter comprises an ADBD that is a scFv and an ADBD that is a D domain;

[61.] the composition of any of [1]-[60], wherein the Adapter comprises an ADBD that binds to a member selected from: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1;

[62.] the composition of [61], wherein the Adapter comprises an ADBD that binds to BCMA, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 44-338, and 339;

[63.] the composition of [61], wherein the Adapter comprises an ADBD that binds to CS1, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 780-794, and 795;

[64.] the composition of [61], wherein the Adapter comprises an ADBD that binds to CD123, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 340-772 and 773;

[65.] the composition of [61], wherein the Adapter comprises an ADBD that binds to CD19, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1030-1058, and 1059;

[66.] the composition of [61], wherein the Adapter comprises an ADBD that binds to binds to CD22, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1060-1068, and 1069;

[67.] the composition of [61], wherein the Adapter comprises an ADBD that binds to binds to binds to HER2, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 800-839, and 840;

[68.] the composition of [61], wherein the Adapter comprises an ADBD that binds to TACI or BAFFR;

[69.] the composition of [61], wherein the Adapter comprises an ADBD that binds to PDL1, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1010-1016, 1074-1078, and 1079;

[70.] the composition of any of [1]-[69], wherein the Adapter is bispecific;

[71.] the composition of [70], wherein the Adapter comprises an ADBD that binds to CD19 and an ADBD that binds to CD123;

[72.] the composition of [70], wherein the Adapter comprises an ADBD that binds to BCMA and an ADBD that binds to CS1;

[73.] the composition of [70], wherein the Adapter comprises an ADBD that binds to CD22 and an ADBD that binds to CD123;

[74.] the composition of [70], wherein the Adapter comprises an ADBD that binds to PDL1 and an ADBD that binds to CD123;

[75.] the composition of any of [1]-[74], wherein the target cell is a tumor cell;

[76.] the composition of [75], wherein the tumor cell is selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, myelodysplasia, breast cancer, and ovarian cancer;

[77.] the composition of [75], wherein the tumor cell is multiple myeloma;

[78.] the composition of [75], wherein at least one target cell is a tumor cell;

[79.] the composition of [75], wherein the first and second target cells are tumor cells;

[80.] the composition of [79], wherein the first and second tumor cells are of the same type;

[81.] the composition of [79], wherein the first and second tumor cells are of a different type;

[82.] the composition of [80] or [81], wherein the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, myelodysplasia, breast cancer, and ovarian cancer;

[83.] the composition of [82], wherein the tumor cells are multiple myeloma;

[84.] the composition of any of [1]-[83], wherein the cell expressing the CAR is an immune effector cell;

[85.] the composition of [84], wherein the immune effector cell is a T cell;

[86.] the composition of [84], wherein the immune effector cell is an NK cell;

[87.] the composition of any of [1]-[86], wherein the cell expressing the CAR kills the target cell;

[88.] the composition of any of [1]-[87], wherein binding of the Adapter to an antigenic determinant blocks the activity of the antigen comprising the AD;

[89.] a method of killing a target cell comprising contacting the target cell with the composition of any one of [1]-[88];

[90.] a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a CAR], wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[91.] a method of killing one or more target cells comprising contacting a composition comprising a first target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[92.] a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[93.] a method of killing a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[94.] a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the first target cell further comprises an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[95.] a method of killing one or more target cells comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first AD is present on the first target cell;

(b) the composition comprising the first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on a second target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[96.] a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[97.] a method of killing a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[98.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a CAR], wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[99.] a method of delivering an immune response to one or more target cells comprising contacting a composition comprising a first target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[100.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[101.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with an Adapter, wherein

(a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[102.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the first target cell further comprises an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[103.] a method of delivering an immune response to one or more target cells comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first AD is present on the first target cell;

(b) the composition comprising the first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on a second target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[104.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[105.] a method of delivering an immune response to a target cell comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[106.] a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[107.] a method of redirecting target cell killing in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[108.] a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[109.] a method of killing a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[110.] a method of killing a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) and a second AD is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to said second AD on said target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[111.] a method of directing target cell killing in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) the patient has been treated with an Adapter comprising (i) a first antigenic determinant (AD) and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[112.] a method of killing a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[113.] a method of killing a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with a an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[114.] a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[115.] a method of redirecting an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[116.] a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[117.] a method of delivering an immune response to a target cell in a patient comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[118.] a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) and a second AD is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to said second AD on said target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[119.] a method of directing an immune response to a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) the patient has been treated with an Adapter comprising (i) a first antigenic determinant (AD) and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[120.] a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[121.] a method of delivering an immune response to a target cell in a patient comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with a an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[122.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[123.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[124.] a method of redirecting treatment of a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[125.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[126.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[127.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) and a second AD is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to said second AD on said target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[128.] a method of directing treatment of a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) the patient has been treated with an Adapter comprising (i) a first antigenic determinant (AD) and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[129.] a method of treating proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[130.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with a an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[131.] the method of any one of [122]-[130], wherein the proliferative disorder or cancer is selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, myelodysplasia, breast cancer, and ovarian cancer ;

[132.] the method of any one of [122]-[130], wherein the proliferative disorder or cancer is multiple myeloma;

[133.] a method of treating hematological cancer comprising contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[134.] a method of treating hematological cancer comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[135.] a method of redirecting treatment of a hematological cancer comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell;

[136.] a method of treating hematological cancer comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD

that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell;

[137.] a method of treating hematological cancer comprising administering an Adapter to the patient, wherein

(a) the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell;

[138.] a method of treating hematological cancer comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) and a second AD is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to said second AD on said target cell; and

(c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[139.] a method of directing treatment of a hematological cancer comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) the patient has been treated with an Adapter comprising (i) a first antigenic determinant (AD) and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and

(b) the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain;

[140.] a method of treating hematological cancer comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[141.] a method of treating hematological cancer comprising administering a cell expressing a chimeric antigen receptor (CAR) to the patient, wherein

(a) a first antigenic determinant (AD) is present on the target cell;

(b) the patient has been treated with a an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and

(c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain;

[142.] the method of any one of [133]-[141], wherein the hematological cancer is selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia;

[143.] the method of any one of [133]-[141], wherein the hematological cancer is multiple myeloma;

[144.] the method of any of [90]-[131], wherein CAR comprises a single-chain variable fragment (scFv) ADBD;

[145.] the method of any of [90]-[143], wherein the CAR comprises an alternative scaffold binding domain (ASBD) ADBD;

[146.] the method of [145], wherein the CAR comprises a D domain, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 17-26, and 27 or SEQ ID NO: 44-1078, and 1079;

[147.] the method of any one of [90]-[146], wherein the CAR comprises 2 ADBDs;

[148.] the method of [147], wherein the CAR comprises an ASBD and a scFv;

[149.] the method of [147], wherein the CAR comprises a D domain and a scFv;

[150.] the method of [147], wherein the CAR comprises 2 ASBDs;

[151.] the method of [147], wherein the CAR comprises 2 D domains;

[152.] the method of any one of [90]-[151], wherein the CAR intracellular domain is a signaling domain;

[153.] the method of [152], wherein the CAR intracellular domain comprises a primary signaling domain;

[154.] the method of [152], wherein the CAR intracellular domain comprises a CD3ζ primary signaling domain;

[155.] the method of [153] or [154], wherein the CAR intracellular domain further comprises a costimulatory signaling domain;

[156.] the method of [155], wherein the CAR intracellular domain comprises a costimulatory signaling domain selected from: CD28, 41BB, CD27, and CD134;

[157.] the method of [156], wherein the CAR intracellular domain comprises a 41BB costimulatory signaling domain;

[158.] the method of any one of [90]-[157], wherein the CAR binds to an antigen selected from: CD19, CD22, CD123, BCMA, CS1, HER2, TACI, BAFFR, and PDL1;

[159.] the method of [158], wherein the CAR binds to BCMA, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: SEQ ID NO: 44-338, and 339;

[160.] the method of [158], wherein the CAR binds to CS1, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 780-794, and 795;

[161.] the method of [158], wherein the CAR binds to CD123, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 340-772 and 773;

[162.] the method of [158], wherein the CAR binds to CD19, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1030-1058, and 1059;

[163.] the method of [158], wherein the CAR binds to CD22, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1060-1068, and 1069;

[164.] the method of [158], wherein the CAR binds to binds to HER2, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 800-839, and 840;

[165.] the method of [158], wherein the CAR binds to PDL1, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 1010-1016, 1074-1078, and 1079;

[166.] the method of any one of [90]-[157], wherein the CAR binds to AFP p26, and optionally wherein the CAR comprises a sequence selected from the group: SEQ ID NO: 841-983, and 984;

[167.] the method of any one of [90]-[166], wherein the CAR comprises 2 ADBDs that bind to separate targets;

[168.] the method of [167], wherein the CAR binds to CD19 and CD123;

[169.] the method of [167], wherein the CAR binds to CD22 and CD123;

[170.] the method of [167], wherein the CAR binds to PDL1 and CD123;

[171.] the method of [167], wherein the CAR binds to CS1 and BCMA;

[172.] the method of [168], wherein the CAR comprises a first ASBD that binds to CD19 and a second ASBD that binds to C123;

[173.] the method of [172], wherein the CAR comprises a first D domain that binds to CD19 and a second D domain that binds to CD123;

[174.] the method of [168], wherein the CAR comprises a D domain that binds to CD19 and a scFv that binds to CD123;

[175.] the method of [169], wherein the CAR comprises a first ASBD that binds to CD22 and a second ASBD that binds to CD123;

[176.] the method of [175], wherein the CAR comprises a first D domain that binds to CD22 and a second D domain that binds to CD123;

[177.] the method of [169], wherein the CAR comprises a D domain that binds to CD22 and a scFv that binds to CD123;

[178.] the method of [170], wherein the CAR comprises a first ASBD that binds to PDL1 and a second ASBD that binds to CD123;

[179.] the method of [178], wherein the CAR comprises a first D domain that binds to PDL1 and a second D domain that binds to CD123;

[180.] the method of [170], wherein the CAR comprises a D domain that binds to PDL1 and a scFv that binds to CD123;

[181.] the method of [168], wherein the CAR comprises an ASBD that binds to CD19 and a scFv that binds to CD123;

[182.] the method of [171], wherein the CAR comprises a first ASBD that binds to BCMA and a second ASBD that binds to CS1;

[183.] the method of [182], wherein the CAR comprises a first D domain that binds to BCMA and a second D domain that binds to CS1;

[184.] the method of [171], wherein the CAR comprises a D domain that binds to BCMA and a scFv that binds to CS1;

[185.] the method of [171], wherein the CAR comprises a D domain that binds to CS1 and a scFv that binds to BCMA;

[186.] the method of any one of [90]-[185], wherein the Adapter comprises an AD of a tumor antigen, optionally wherein the tumor antigen is selected from the group: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1;

[187.] the method of [90]-[186], wherein the Adapter comprises an AD that is an epitope of AFP p26 or AFP, and optionally comprises the amino acid residues of SEQ ID NO: 16 or 1117-1123;

[188.] the method of any one of [90]-[187], wherein the Adapter comprises an ADBD that is a scFv;

[189.] the method of any one of [90]-[187], wherein the Adapter comprises an ADBD that is an ASBD;

[190.] the method of [189], wherein the Adapter comprises a D domain, and optionally wherein the Adapter comprises a sequence selected from the group: SEQ ID NO: 17-26, and 27, or SEQ ID NO: 44-1078, and 1079;

[191.] the method of any one of [90]-[190], wherein the Adapter comprises two ADBDs;

[192.] the method of [191], wherein the two ADBDs (a) are the same, (b) bind to the same antigenic determinant, (c) bind to different ADs of the same antigen, or (d) bind to different antigens on the same cell, or (e) bind to different antigens on different cells;

[193.] the method of [191] or [192], wherein the Adapter comprises two ASBDs;

[194.] the method of any one of [191], [192], or [193], wherein the Adapter comprises two D domains, and optionally wherein the Adapter comprises an amino acid sequence selected from the group: SEQ ID NO: 44-1079;

[195.] the method of [191] or [192], wherein the Adapter comprises an ADBD that is a scFv and an ADBD that is an ASBD;

[196.] the method of [195], wherein the Adapter comprises an ADBD that is a scFv and an ADBD that is a D domain;

[197.] the method of any one of [90]-[196], wherein the Adapter comprises an ADBD that binds to a member selected from: BCMA, CS1, HER2, CD123, CD19, CD22, TACI, BAFFR, and PDL1;

[198.] the method of [197], wherein the Adapter comprises an ADBD that binds to BCMA, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 44-338, and 339;

[199.] the method of [197], wherein the Adapter comprises an ADBD that binds to CS1, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 780-794, and 795;

[200.] the method of [197], wherein the Adapter comprises an ADBD that binds to CD123, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 340-772, and 773;

[201.] the method of [197], wherein the Adapter comprises an ADBD that binds to CD19, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1030-1058, and 1059;

[202.] the method of [197], wherein the Adapter comprises an ADBD that binds to binds to CD22, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1060-1068, and 1069;

[203.] the method of [197], wherein the Adapter comprises an ADBD that binds to binds to HER2, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 800-839, and 840;

[204.] the method of [197], wherein the Adapter comprises an ADBD that binds to TACI or BAFFR;

[205.] the method of [197], wherein the Adapter comprises an ADBD that binds to PDL1, and optionally wherein the ADBD comprises a sequence selected from the group: SEQ ID NO: 1010-1016, 1074-1078, and 1079;

[206.] the method of any one of [90]-[205], wherein the Adapter is bispecific;

[207.] the method of [206], wherein the Adapter comprises an ADBD that binds to BCMA and an ADBD that binds to CS1;

[208.] the method of [206], wherein the Adapter comprises an ADBD that binds to CD19 and an ADBD that binds to CD123;

[209.] the method of [206], wherein the Adapter comprises an ADBD that binds to CD22 and an ADBD that binds to CD123;

[210.] the method of [206], wherein the Adapter comprises an ADBD that binds to PDL1 and an ADBD that binds to CD123;

[211.] the method of any one of [90]-[210], wherein the target cell is a tumor cell;

[212.] the method of [211], wherein the tumor cell is selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, myelodysplasia, breast cancer, and ovarian cancer;

[213.] the method of [211], wherein the tumor cell is multiple myeloma;

[214.] the method of [211], wherein at least one target cell is a tumor cell;

[215.] the method of [211], wherein the first and second target cells are tumor cells;

[216.] the method of [215], wherein the first and second tumor cells are of the same type;

[217.] the method of [215], wherein the first and second tumor cells are of a different type;

[218.] the method of [214] or [215], wherein the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, myelodysplasia, breast cancer, and ovarian cancer;

[219.] the method of [214] or [215], wherein the tumor cells are multiple myeloma;

[220.] the method of any one of [90]-[219], wherein the cell expressing the CAR is an immune effector cell;

[221.] the method of [220], wherein the immune effector cell is a T cell;

[222.] the method of [220], wherein the immune effector cell is an NK cell;

[223.] the method of any one of [90]-[222], wherein the cell expressing the CAR kills the target cell;

[224.] An engineered human immune effector cell comprising

(a) a chimeric antigen receptor (CAR) comprising (1) an antigenic determinant binding domain (ADBD) that specifically binds to a human CD45 antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and

(b) a genetic modification that eliminates the expression of the human CD45 AD on the engineered cell,

wherein the engineered cell is capable of directing an immune response to a CD45 AD expressing cell in an in vitro assay, and wherein the engineered cell does not express the CD45 AD;

[225.] a method of killing a target cell comprising contacting the engineered cell according to [224] with the target cell], wherein the target cell expresses human CD45;

[226.] a method of delivering an immune response to a target cell comprising contacting the engineered cell according to [224] with the target cell], wherein the target cell expresses human CD45;

[227.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [224];

[228.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [224];

[229.] a method of depleting lymphocytes comprising administering to a subject in need thereof an effective amount of the engineered cell according to [224];

[230.] a method of depleting memory T cell comprising administering to a subject in need thereof an effective amount of the engineered cell according to [224];

[231.] a method of treating an autoimmune disease or disorder comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [224];

[232.] a method of conditioning a subject for transplantation comprising administering to the subject in need thereof an effective amount of the engineered cell according to [224];

[233.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [224];

[234.] An engineered human immune effector cell comprising

(a) a chimeric antigen receptor (CAR) comprising (1) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain; and

(b) a genetic modification that eliminates the expression of at least one human CD45 AD on the engineered cell,

wherein the first AD is not the at least one human CD45 AD], wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a CD45 AD expressing cell in an in vitro assay], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the at least one human CD45 AD, and wherein the engineered cell does not express the at least one human CD45 AD;

[235.] a method of killing a target cell comprising contacting the engineered cell according to [234] with an Adapter and the target cell], wherein the target cell expresses CD45, and wherein the Adapter comprises the first AD and a second ADBD that specifically binds to a human CD45 AD;

[236.] a method of delivering an immune response to a target cell comprising contacting the engineered cell according to [234] with an Adapter and the target cell], wherein the target cell expresses CD45, and wherein the Adapter comprises the first AD and a second ADBD that specifically binds to a human CD45 AD;

[237.] a method of treating hematological cancer comprising contacting the engineered cell according to [234] with an Adapter and a cancer cell], wherein the cancer cell expresses CD45, and wherein the Adapter comprises the first AD and a second ADBD that specifically binds to a human CD45 AD;

[238.] a method of directing an immune response to a target cell in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[239.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [234], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[240.] a method of directing an immune response to a target cell in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[241.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[242.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [234], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[243.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[244.] a method of depleting lymphocytes comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[245.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[246.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[247.] a method of depleting memory T cell comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[248.] a method of depleting memory T cell comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[249.] a method of depleting memory T cell comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[250.] a method of treating an autoimmune disease or disorder comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[251.] a method of treating an autoimmune disease or disorder comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[252.] a method of treating an autoimmune disease or disorder comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[253.] a method of conditioning a subject for transplantation comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[254.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[255.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[256.] a method of treating a hematological cancer comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[257.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [234], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD;

[258.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to a human CD45 AD], wherein the subject has been administered the engineered cell according to [234];

[259.] An engineered human immune effector cell comprising:

(a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that bind to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) a genetic modification that eliminates the expression of the first AD on the engineered cell,

wherein the engineered cell does not express the first AD;

[260.] a method of killing a target cell comprising contacting the engineered cell according to [259] with the target cell;

[261.] a method of delivering an immune response to a target cell comprising contacting the engineered cell according to [259] with the target cell;

[262.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259];

[263.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259];

[264.] a method of depleting lymphocytes comprising administering to a subject in need thereof an effective amount of the engineered cell according to [259];

[265.] a method of conditioning a subject for transplantation comprising administering to the subject in need thereof an effective amount of the engineered cell according to [259];

[266.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259];

[267.] a method of killing a target cell comprising contacting the engineered cell according to [259] with an Adapter and the target cell], wherein the Adapter comprises an AD recognized by the CAR and a second ADBD;

[268.] a method of delivering an immune response to a target cell comprising contacting the engineered cell according to [259] with an Adapter and the target cell, and wherein the Adapter comprises an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the target cell;

[269.] a method of treating hematological cancer comprising contacting the engineered cell according to [259] with an Adapter and a cancer cell], wherein the Adapter comprises an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the cancer cell;

[270.] a method of directing an immune response to a target cell in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the target cell;

[271.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259], wherein the subject has been administered an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the target cell;

[272.] a method of directing an immune response to a target cell in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on the target cell], wherein the subject has been administered the engineered cell according to [259];

[273.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[274.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [259], wherein the subject has been administered an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[275.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell], wherein the subject has been administered the engineered cell according to [259];

[276.] a method of depleting lymphocytes comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[277.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259], wherein the subject has been administered an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[278.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell], wherein the subject has been administered the engineered cell according to [259];

[279.] a method of conditioning a subject for transplantation comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[280.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259], wherein the subject has been administered an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[281.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell], wherein the subject has been administered the engineered cell according to [259];

[282.] a method of treating a hematological cancer comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[283.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [259], wherein the subject has been administered an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell;

[284.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising an AD recognized by the CAR and a second ADBD that is capable of binding a second AD on a target cell], wherein the subject has been administered the engineered cell according to [259];

[285.] An engineered human immune effector cell comprising:

(a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a first antigenic determinant binding domain (ADBD) that specifically binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) a genetic modification that eliminates the expression of a second AD on the engineered cell,

wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a cell expressing the second AD in an in vitro assay], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the engineered cell does not express the second AD;

[286.] An engineered human immune effector cell comprising:

(a) a chimeric antigen receptor (CAR), wherein the CAR comprises (i) two or more antigenic determinant binding domains (ADBD) comprising a first ADBD that specifically binds to a first antigenic determinants (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and

(b) a genetic modification that eliminates the expression of a second AD on the engineered cell,

wherein the engineered cell used in combination with an Adapter is capable of directing an immune response to a cell expressing the second AD in an in vitro assay], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the engineered cell does not express the second AD;

[287.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286];

[288.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286];

[289.] a method of depleting lymphocytes comprising administering to a subject in need thereof an effective amount of the engineered cell according to [285] or [286];

[290.] a method of conditioning a subject for transplantation comprising administering to the subject in need thereof an effective amount of the engineered cell according to [285] or [286];

[291.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286];

[292.] a method of killing a target cell comprising contacting the engineered cell according to [285] or [286] with an Adapter and the target cell], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on the target cell;

[293.] a method of delivering an immune response to a target cell comprising contacting the engineered cell according to [285] or [286] with an Adapter and the target cell], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on the target cell;

[294.] a method of treating hematological cancer comprising contacting the engineered cell according to [285] or [286] with an Adapter and a cancer cell], wherein the Adapter comprises the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on the cancer cell;

[295.] a method of directing an immune response to a target cell in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the second AD is expressed on the target cell;

[296.] a method of directing an immune response to a target cell in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on the target cell;

[297.] a method of directing an immune response to a target cell in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the subject has been administered the engineered cell according to [285] or [286], and wherein the second AD is expressed on the target cell;

[298.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising

(a) administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the second AD is expressed on a target cell associated with the proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection;

[299.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to the subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on a target cell associated with the proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection;

[300.] a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a subject comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the subject has been administered the engineered cell according to [285] or [286], and wherein the second AD is expressed on a target cell associated with the proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection;

[301.] a method of depleting lymphocytes comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the second AD is expressed on a lymphocyte target cell;

[302.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on a lymphocyte target cell;

[303.] a method of depleting lymphocytes comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the subject has been administered the engineered cell according to [285] or [286], and wherein the second AD is expressed on a lymphocyte target cell;

[304.] a method of conditioning a subject for transplantation comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the second AD is expressed on a target cell associated with the transplantation;

[305.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on a target cell associated with the transplantation;

[306.] a method of conditioning a subject for transplantation comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the subject has been administered the engineered cell according to [285] or [286], and wherein the second AD is expressed on a target cell associated with the transplantation;

[307.] a method of treating a hematological cancer comprising

(a) administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]; and

(b) administering to the subject a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the second AD is expressed on a target cell associated with the hematological cancer;

[308.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of the engineered cell according to [285] or [286]], wherein the subject has been administered an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD, and wherein the second AD is expressed on a target cell associated with the hematological cancer;

[309.] a method of treating a hematological cancer comprising administering to a subject in need thereof a therapeutically effective amount of an Adapter comprising the first AD and a second ADBD that specifically binds to the second AD], wherein the subject has been administered the engineered cell according to [285] or [286], and wherein the second AD is expressed on a target cell associated with the hematological cancer;

[310.] an isolated Adapter polypeptide comprising (1) an antigenic determinant (AD) and (b) one or more antigenic determinant binding domain (ADBD),

wherein at least one ADBD specifically binds to a human CD45 AD, and wherein contacting the Adaptor with a CD45 AD expressing target cell in the presence of an engineered cell according to [234] is capable of directing an immune response by the engineered cell to the target cell in an in vitro assay.

BRIEF DESCRIPTION OF THE DRAWINGS/FIGURES

[0089] FIG. 1A-1D: The cytolytic activity of CD123-specific (cg06) and BCMA-specific (bc-40) CARs were compared to a CAR with no known target-specificity (α3D) on a panel of tumors using effector cell to target cell ratios ranging from 1: 4 to 1: 64. Briefly, 20,000 T cells expressing the bc40, cg06, or α3D CAR were incubated with increasing numbers of a $CD123^{+}/BCMA^{-}$ tumor target (MOLM13)(**FIG. 1A**); a $CD123^{-}$

/BCMA$^+$ tumor target (H929)(**FIG. 1B**); a CD123$^-$ tumor target (RAJI)(**FIG. 1C**); or a CD123$^+$/BCMA$^-$ tumor target (MOLM13)(**FIG. 1D**). After 16 hours, cells were washed and luciferase activity was assessed.

[0090] FIGS. 2A -2B: Adapter binding associates with the Adapter and CAR binding specificity. Jurkat NFAT-Luciferase reporter cells were transduced with a negative control CAR (α3D), an AFP (p26)-binding CAR (af03), or a BCMA-binding CAR (bc40). In **FIG. 2A**, CAR transduced Jurkat cells were incubated with 0.5μg of Adapter protein (4°C for 20 minutes), washed, and then stained with anti-HIS PE (clone J095G46, 4°C for 20 minutes). **FIG. 2B** shows CAR expression based on FLAG staining (clone L5) versus mock transduced Jurkat cells.

[0091] FIGS. 3A-3C show that the Adapter binding of matching CAR: Adapter and Target: Adapter specificity drives lysis of target cells. In **FIG. 3A**, 40,000 CD123$^+$BCMA$^-$ MOLM13-GFP/Luciferase cells were incubated with various Adapters in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D14-053017, Day 7) transduced with BCMA-binding CAR (bc40) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/ Luciferase cultured in the absence of T cells or Adapter protein. A control of CD123-specific CAR T cells (cg06) cultured at the same ratio was used as a positive control for lysis. In **FIG. 3B**, 40,000 CD123$^+$BCMA$^-$ MOLM13-GFP/Luciferase cells were incubated with CD123 (cg06)-AFP (p26) Adapter in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D16-061317, Day 7) transduced with AFP-binding CARs (Af03 or Af05) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/Luciferase cultured in the absence of T cells or Adapter protein. A control of CD123-specific CAR T cells (cg06) cultured at the same ratio was used as a positive control for lysis. In **FIG. 3C**, 40,000 BCMA$^+$ NCI H929-GFP/Luciferase cells were incubated with bc40-AFP (p26) Adapter in the presence or absence of 10,000 T cells (E: T ratio of 1: 4, donor D15-062017, Day 8) mock transduced or transduced with AFP-binding CARs (Af03 or Af05) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of NCI-H929-GFP/Luciferase cultured in the absence of T cells or Adapter protein.

[0092] FIGS. 4A – 4D show that Adapter binding of matching CAR: Adapter and Target: Adapter specificity drives cytokine production by CAR T cells. In **FIGS. 4A** and **4B**, donor D14-053017 T cells transduced with BCMA-binding CAR (bc40) were cultured overnight with various Adapters in the presence or absence of CD123$^+$BCMA$^-$ MOLM13 cells (25,000 T cells and target cells). Cultured supernatants were collected and assessed for the production of IL-2 (**FIG. 4A**) and IFN-γ (**FIG. 4B**). In **FIGS. 4C** and **4D**, donor D15-062017 T cells transduced with AFP-binding CARs (Af03 and Af05) were cultured overnight with cg06-AFP (p26) Adapter in the presence or absence of CD123$^+$BCMA$^-$ MOLM13 cells (25,000 T cells and

target cells). Cultured supernatants were collected and assessed for the production of IL-2 (**FIG. 4C**) and IFN-γ (**FIG. 4D**).

[0093] FIG. 5: Adapter binding of matching CAR: Adapter and Target: Adapter specificity drives proliferation of CAR T cells. Donor D16-062717 cells transduced with AFP-binding CAR (Af03) were CFSE labeled (10 minutes at 0.5μM), then cultured (25,000) in the presence of CD123-specific Adapter or BCMA-specific Adapter in the presence or absence of mitomycin-C treated $CD123^-$ $BCMA^+$ NCI-H929 cells (25,000) for 72 hours. At 72 hours, cells were stained for CD3, then analyzed for absolute numbers of $CD3^+$ cells via flow cytometry.

[0094] FIGS. 6A and **6B** show that Adapter binding of matching CAR: Adapter and Target: Adapter drives signaling by CAR-expressing Jurkat NFAT-Luciferase reporter cells. In **FIG. 6A**, 50,000 reporter cells previously transduced with a BCMA-binding CAR (bc40) were cultured for 5 hours in the presence of various Adapter proteins in the presence or absence of 50,000 $CD123^+BCMA^-$ MOLM14 cells, then assessed for luciferase activity. In **FIG. 6B**, 50,000 reporter cells previously transduced with an AFP (p26)-binding CAR (af03) were cultured for 5 hours in the presence of the aspecific α3D-Adapter or the BCMA-specific Bc40-Adapter protein in the presence or absence of 50,000 $BCMA^+$ NCI-H929 cells, then assessed for luciferase activity.

[0095] FIGS. 7A and 7B show that the CD123-specific Adapter with a BCMA antigenic determinant can function with either a BCMA-specific D domain CAR (bc40) or a BCMA-specific scFv CAR (c11D5-3). In **FIG. 7A**, 40,000 $CD123^+BCMA^-$ MOLM13-GFP/Luciferase cells were incubated with the Cg06-BCMA Adapter in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D14-062717, Day 9) transduced with a non-specific CAR (α3D), the BCMA-binding D domain CAR (bc40), or the BCMA-binding scFv CAR (c11D5-3) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/Luciferase cultured in the absence of T cells or Adapter protein. Solid lines indicate calculated 3-parameter non-linear curves, while the dashed line for c11D5-3 is present for illustrative purposes only. In **FIG. 7B**, $CD123^+BCMA^-$ MOLM13-GFP/Luciferase cells were cultured in the same experiment as in **FIG. 7A** with transduced T cells in the absence of Adapter protein.

[0096] FIGS. 8A and 8B show that AFP-specific CARs can simultaneously have CD123 and BCMA-binding capacity via incubation with multiple Adapter proteins. 10^5 Jurkat NFAT-Luciferase transduced with an AFP (p26)-binding CAR (af03) were incubated with a total of 0.5μg of Adapter proteins at various ratios of the BCMA- to CD123-specific Adapters (4°C for 20 minutes), washed, and then incubated with CD123-Fc and biotinylated BCMA (0.5μg of each) (4°C for 20 minutes), washed, then binding detected with Anti-Fc

A488 and Streptavidin-PE. **FIG. 8A** presents a flow cytometric analysis of CD123-binding and BCMA-binding to their respective target proteins, **FIG. 8B** provides a comparison of mean fluorescence intensity (MFI) of A488 MFI (CD123-binding, left axis) and PE MFI (BCMA-binding, right axis) flow cytometric data presented in **FIG. 8A**.

[0097] FIGS. 9A and 9B show that dual-binding domain adaptor proteins drive enhanced signaling by CAR-expressing Jurkat NFAT-Luciferase reporter cells over single-binding domain adaptor proteins. In **FIG. 9A**, 50,000 reporter cells previously transduced with an AFP (p26 domain)-binding CAR (af03) were cultured for 5 hours in the presence of the CD123-specific Cg06-adaptor (Cg06-p26) or the Cg06-dual adaptor protein (Cg06-p26-Cg06 in the presence of 50,000 $CD123^+$ MOLM13 or CD123-deficient MOLM13 cells, then assessed for luciferase activity. CD123 deficient cells were generated using CRISPR/Cas9 genetic engineering technology. In **FIG. 9B**, 50,000 reporter cells previously transduced with an AFP (p26 domain)-binding CAR (af03) were cultured for 5 hours in the presence of the BCMA-specific Bc40-adaptor (Bc40-p26) or the Bc40-dual adaptor protein (Bc40-p26-Bc40) in the presence or absence of 50,000 $BCMA^+$ U266 cells, then assessed for luciferase activity.

[0098] FIG. 10 shows that binding of truncated and full length p26 to human FcRn is pH dependent.

[0099] FIGS. 11A-11D show that adapters comprising CS1 (SLAMF7, CRACC, CD319) specific ADBD modulate intracellular signaling and killing of CS1 positive tumors. In **FIG.** 11A, the cc02 and cc08 ADBD displayed the most potent NFAT signaling when cultured in the presence of af59-CAR expressing JNL10 cells (**FIG. 11A**) and the CS1 positive tumor cell line, MM.1S. **FIG. 11B** shows that the bispecific bc98-p26-cc02 adapter capable of binding both CS1 and BCMA was more potent in its ability to signal than were the monospecific BCMA-binding bc98-p26-α3DQ19E adapter and the monospecific CS1-binding α3DQ19E-p26-cc02 adapter. **FIGS 11C and 11D** indicate the bispecific bc98-p26-cc02 is an effective adapter in killing HT929 (high expression of both BCMA and CS1; **FIG. 11C**) and MM.1S (high BCMA, low CS1; **FIG. 11D**).

[0100] FIGS. 12A-12C show that adapters comprising HER2 binding ADBD induce signaling in Af59-CAR expressing JNL10-cells cultured with HER2-positive SKBR3 tumor. **FIG. 12A** shows that the adapter comprising eb08 HER2-binding ABDB was the most potent stimulator in this assay. **FIG 12B** shows that the NFAT signaling in JNL10 cells mediated by the adapter comprising eb08 is greater than that of mediated by the adapter comprising zHERs:4, comparable to that of mediated by the adapter comprising 9.29, and less than that of G3 and zHER2:342. **FIG. 12C** demonstrates that adapters comprising the HER2-binding eb08 or eb04 modulate tumor lysis in a dose-dependent manner.

[0101] FIG. 13. T cells transduced with a p26-binding CAR ("ARC-T") in combination with a BCMA specific Adapter ("SPRX-BCMA") eliminate MM.1S tumor cells in vivo comparable to a BCMA-targeted CAR-T cells ("CART-ddBCMA"). Total flux measured by dorsal imaging of NGS mice engrafted with

MM.1S cells expressing GFP and luciferase following administration of BCMA-targeted CAR-T cells or a combination of T cells transduced cells with a p26-binding CAR and a BCMA specific Adapter.

[0102] FIG. 14. T cells transduced with a p26-binding CAR ("ARC-T") exhibit comparable activity in vivo with intermittent dosing of a BCMA specific Adapter ("SPRX-BCMA") in a disseminated model of BCMA+ B-cell leukemia (NALM6-BCMA). Total flux measured by dorsal imaging of NGS mice engrafted with NALM6-BCMA cells expressing GFP and luciferase following administration of 10^6 T cells transduced with a p26-binding CAR and a BCMA specific Adapter.

[0103] FIG. 15. In vivo residence time of a BCMA specific Adapter ("SPRX-BCMA") on NALM6-BCMA tumor cells in mice following I.V. administration.

DETAILED DESCRIPTION

I. Definitions

[0104] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the disclosure pertains.

[0105] It is understood that wherever embodiments are described herein with the language "comprising" otherwise analogous embodiments described in terms of "consisting of" and/or "consisting essentially of" are also provided. However, when used in the claims as transitional phrases, each should be interpreted separately and in the appropriate legal and factual context (*e.g.,* "comprising" is considered more of an open-ended phrase while "consisting of" is more exclusive and "consisting essentially of" achieves a middle ground).

[0106] As used herein, the singular form "a", "an", and "the" includes plural references unless indicated otherwise.

[0107] The term "and/or" as used in a phrase such as "A and/or B" herein is intended to include both A and B; A or B; A (alone); and B (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following embodiments: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0108] "About" as the term is used herein, when referring to a measurable value such as an amount, a temporal duration, and other measurable values known in the art, is meant to encompass variations of ±20% or in some embodiments ±10%, or in some embodiments ±5%, or in some embodiments ±1%, or in some embodiments ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

[0109] The terms "protein" and "polypeptide" are used interchangeably herein to refer to a biological polymer comprising units derived from amino acids linked via peptide bonds; a protein can be composed of two or more polypeptide chains.

[0110] "Cell surface receptor" refers to molecules and complexes of molecules capable of receiving a signal and the transmission of such a signal across the plasma membrane of a cell. An example of a cell surface receptor provided herein is an activated integrin receptor, for example, an activated αvβ3 integrin receptor on a metastatic cell. As used herein, "cell surface receptor" also includes a molecule expressed on a cell surface that contains a CAR capable of binding an antigenic determinant target of interest. The term "receptor" denotes a cell-associated protein that binds to, or otherwise interacts with, a molecule (*e.g.,* a ligand) and mediates the effect of the ligand on the cell. In several embodiments, the molecule that interacts with a receptor is a bioactive molecule. Membrane-bound cell-surface receptors are characterized by a multi-domain structure comprising an extracellular ligand-binding domain, a membrane spanning domain, and an intracellular effector domain that is typically involved in signal transduction.

[0111] The term "Chimeric antigen receptor" or "CAR" or "CARs" as used herein refers to an engineered chimeric polypeptide that grafts an antigen or target specificity onto a cell such as an immune cell (*e.g.,* a T cell such as a naive T cell, central memory T cell, effector memory T cell, NK cell, NKT cell. or a plurality or combination thereof). CARs may also be referred to herein as artificial T cell receptors, chimeric T cell receptors or chimeric immunoreceptors. The CARs share structural or functional properties with a cell immune-function receptor or Adapter molecule. Upon binding to cognate antigen, a CAR can activate or inactivate the cytotoxic cell in which it is disposed, or modulate the cell's antitumor activity or otherwise modulate the cells immune response. In some embodiments, CARs comprise one or more element (*e.g.,* domain) from a T cell receptor (TCR, *e.g.,* the zeta chain associated with the T cell receptor complex) or a natural killer cell receptor (NKR). In some embodiments, CARs comprise (1) an antigenic determinant binding domain (ADBD) that specifically binds to antigenic determinant (AD), (2) a transmembrane domain, and (3) an intracellular domain. In some embodiments, CARs comprise more than one antigenic determinant binding domains. In some embodiments, CARs comprise more than one antigenic determinant binding domains that bind to different antigenic determinants of the same antigen, different antigenic determinants on different antigens, or antigenic determinants expressed by different target cells.

[0112] The term "immune cell" as used herein refers to the cells of the mammalian immune system including but not limited to antigen presenting cells, B-cells, basophils, cytotoxic T cells, dendritic cells, eosinophils, granulocytes, helper T cells, leukocytes, lymphocytes, macrophages, mast cells, memory cells, monocytes, natural killer cells, neutrophils, phagocytes, plasma cells and T cells.

[0113] The terms "T cell" and "T-lymphocyte" are interchangeable and used synonymously herein. Examples include but are not limited to naive T cells, central memory T cells, effector memory T cells or combinations thereof.

[0114] "Autologous" as the term is used herein refers to any material derived from the same individual to whom it is later to be re-introduced.

[0115] "Allogeneic" as the term is used herein refers to any material derived from a different animal of the same species as the individual to whom the material is introduced. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In some aspects, allogeneic material from individuals of the same species may be sufficiently unlike genetically to interact antigenically.

[0116] The term "effector cells" are leukocytes which express one or more FcRs and perform effector functions. Preferably, the cells express at least FcRIII and perform ADCC effector function. Examples of human leukocytes which mediate ADCC include peripheral blood mononuclear cells (PBMC), natural killer (NK) cells, monocytes, cytotoxic T cells and neutrophils; with PBMCs and NK cells being preferred in certain embodiments. The effector cells can be isolated from native source thereof, *e.g.,* from blood or PBMCs as described herein or otherwise known in the art. In a specific embodiment, the effector cells are human effector cells.

[0117] The term "effector function" refers to the specialized immune function of a differentiated cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

[0118] The term "immune response" as used herein refers to immunities including but not limited to innate immunity, humoral immunity, cellular immunity, immunity, inflammatory response, acquired (adaptive) immunity, autoimmunity and/or overactive immunity. Indicators of an immune response may include secretion of cytokines by immune cells, expansion of immune cell populations, production of antibodies, degranulation of cytotoxic cells, and killing of target cells. Such indicators may routinely be measured using readily available assays, *e.g.,* ELISA or ELISpot, known in the art.

[0119] The term "Adapter" as used herein refers to a multi-domain soluble protein that comprises an antigenic determinant (AD) and an antigenic determinant binding domain (ADBD), wherein the ADBD binds to a second AD. In addition to the AD and the ADBD, an Adapter can comprise additional AD, additional ADBD, and/or other additional domains.

[0120] The terms "antibody" or "immunoglobulin," as used interchangeably herein, includes whole antibodies. A whole antibody comprises at least two heavy (H) chains and two light (L) chains interconnected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2, and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, Cl. The VH and VL regions can be further subdivided into regions of hypervariability, termed Complementarity Determining Regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FW). Each VH and VL is composed of three CDRs and four FWs, arranged from amino-terminus to carboxy-terminus in the following order: FW1, CDR1, FW2, CDR2, FW3, CDR3, FW4. The variable regions of the heavy and

light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies can mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (*e.g.,* effector cells) and the first component (C1q) of the classical complement system.

[0121] The terms "antibody fragments" and the like as used herein, include any functional domain of an antibody such as an antigen-binding fragment or single chains thereof, an effector domain, salvage receptor binding epitope, or portion thereof. The antibody fragments described herein may exist in a variety of forms. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, and Fv fragments, an disulfide-linked Fv (sdFv), a Fd fragment consisting of VH and CH1 domains, an scFv, a minibody, a BiTE, a Tandab, a diabody ($(VL\text{-}VH)_2$ or $(VH\text{-}VL)_2$), a single domain antibody (*e.g.,* an sdAb such as a nanobody (either VL or VH)), and a camelid VHH domain), and multi-specific antibodies formed from antibody fragments. In some embodiments, an "antibody fragment" corresponds to an antigen-binding site or epitope binding site of an antibody. In other embodiments, an "antibody fragment" corresponds to other functional regions of an antibody such as, an effector domain or portion thereof, or a salvage receptor binding epitope, or portion thereof.

[0122] The terms "single chain variable fragment(s)," or "scFv" antibodies as used herein refer to forms of antibodies (*e.g.,* antibody fragments) comprising the variable regions of only the heavy and light chains, connected by a linker peptide. The scFv may comprise VL-linker-VH or may comprise VH-linker-VL. ScFv antibodies are generally 220-250 amino acids in length and contain linkers 10-25 amino acids in length.

[0123] As used herein, the term, "Fc region" or simply "Fc" is understood to mean the carboxyl-terminal portion of an immunoglobulin chain constant region, preferably an immunoglobulin heavy chain constant region, or a portion thereof. For example, an immunoglobulin Fc region may comprise (1) a CH1 domain, a CH2 domain, and a CH3 domain, (2) a CH1 domain and a CH2 domain, (3) a CH1 domain and a CH3 domain, (4) a CH2 domain and a CH3 domain, or (5) a combination of two or more domains and an immunoglobulin hinge region. In a preferred embodiment the immunoglobulin Fc region comprises at least an immunoglobulin hinge region a CH2 domain and a CH3 domain, and preferably lacks the CH1 domain. In one embodiment, the class of immunoglobulin from which the heavy chain constant region is derived is IgG (Igγ)(γ subclasses 1, 2, 3, or 4). Other classes of immunoglobulin, IgA (Igα), IgD (Igδ), IgE (Igε) and IgM (Igμ), may be used. The choice of appropriate immunoglobulin heavy chain constant region is discussed in detail in U.S. Pat. Nos. 5,541,087, and 5,726,044, each of which is incorporated by reference herein, in their entirety. The choice of particular immunoglobulin heavy chain constant region sequences from certain immunoglobulin classes and subclasses to achieve a particular result is considered to be within the level of skill in the art. The portion of the DNA construct encoding the immunoglobulin Fc region preferably comprises at least a portion of a hinge domain, and preferably at least a portion of a CH3 domain of Fc gamma or the homologous domains in any of IgA, IgD, IgE, or IgM. Furthermore, it is contemplated that

substitution or deletion of amino acids within the immunoglobulin heavy chain constant regions may be useful in the practice of the methods and compositions disclosed herein. One example would be to introduce amino acid substitutions in the upper CH2 region to create an Fc variant with reduced affinity for Fc receptors (Cole, J. Immunol. 159: 3613 (1997)).

[0124] "Antibody-dependent cell-mediated cytotoxicity" or "ADCC" refer to a cell-mediated reaction in which nonspecific cytotoxic cells that express Fc receptors (FcRs)(*e.g.,* Natural Killer (NK) cells, neutrophils, and macrophages) recognize bound antibody on a target cell and subsequently cause lysis (or other cytotoxic effects) of the target cell. To assess ADCC activity of a molecule of interest, any in vitro ADCC assay known in the art can be used, such as that described in U.S. Pat. Nos. 5,500,362 or 5,821,337. Useful effector cells for such assays include, but are not limited to, peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest can be assessed in vivo, *e.g.,* in an animal model such as that disclosed in Clynes *et al.*, PNAS 95: 652-656 (1998).

[0125] The term "antigenic determinant binding domain" or "ADBD" as the term is used herein, refers to a sequence of a polypeptide (*e.g.,* an Adapter or CAR) that is sufficient to confer recognition and specific binding to a target antigenic determinant (AD). In some embodiments, the ADBD is an antigen-binding antibody fragment, a scFv, or an antigen-binding peptide that is not based on an antibody or antibody fragment sequence (*e.g.,* a D domain or an affibody). In some embodiments, the ADBD comprises a non antibody-based binding scaffold (*e.g.,* a D domain, affibody, fibronectin domain, nanobody, lipocalin domain ankyrin domain, maxybody, Protein A domain, or affilin domain). In some embodiments the ADBD is a D domain. In some embodiments, the ADBD is an antibody-based binding sequence. In some embodiments the ADBD is a scFv or a domain antibody (dAb). In some embodiments, the ADBD has the ability to bind to a target antigen on the surface of a cell. In some embodiments, the ADBD has the ability to bind to a target antigen on the surface of an immune effector cell. In some embodiments, the ADBD has the ability to bind a growth factor receptor or a hormone receptor.

[0126] In particular embodiments, the ADBD is a non antibody-scaffold based polypeptide sequence that is sufficient to confer recognition and specific binding to a target antigenic determinant. In some embodiments, non-antibody based ADBD is a polypeptide that has the ability to bind to target antigen on the surface of a cell. In some embodiments, the non-antibody based ADBD has the ability to bind a growth factor receptor or a hormone receptor. In some embodiments, the ADBD is a D domain-based polypeptide. In particular embodiments, the ADBD is a D domain-based polypeptide that is sufficient to confer recognition and specific binding to a target antigenic determinant. In some embodiments, the ADBD is a D domain-based polypeptide that has the ability to bind to target antigen on the surface of a cell. In some embodiments, the ADBD is a D domain-based polypeptide that has the ability to bind a growth factor receptor or a hormone receptor. In some

embodiments, the ADBD is a D domain-based polypeptide that has the ability to bind a target antigen on a serum protein.

[0127] The terms "specifically binds" or "having selective affinity for" mean that a binding agent such as an Adapter or CAR, reacts or associates more frequently, more rapidly, with greater duration, with greater affinity, or with some combination of the above to the epitope, protein, or target molecule than with alternative substances, including proteins unrelated to the target epitope. Because of the sequence identity between homologous proteins in different species, specific binding can, in several embodiments, include a binding agent that recognizes a protein or target in more than one species. Likewise, because of homology within certain regions of polypeptide sequences of different proteins, specific binding can include a binding agent that recognizes more than one protein or target. It is understood that, in certain embodiments, a binding agent that specifically binds a first target may or may not specifically bind a second target. As such, "specific binding" does not necessarily require (although it can include) exclusive binding, *e.g.,* binding to a single target. Thus, a binding agent may, in certain embodiments, specifically bind more than one target. In certain embodiments, multiple targets may be bound by the same antigen-binding site on the binding agent.

[0128] The terms "linker," "spacer," and "hinge" are used interchangeably herein to refer to a peptide or other chemical linkage located between two or more otherwise independent functional domains of an Adapter or CAR. For example, a linker may be located between an antigenic determinant domain and an antigenic determinant binding domain of an Adapter. Similarly, a linker may be located between two antigenic determinant binding domains or an antigenic binding domain and a transmembrane domain of a CAR. Suitable linkers for coupling the two or more domains of an Adapter are described herein and/or will otherwise be clear to a person skilled in the art.

[0129] The term "operably linked," as used herein, indicates that two molecules are attached so as to each retain at least some level of functional activity that each molecule had alone (assuming that each molecule had a function activity). In embodiments when one molecule was without functional activity, it is operably linked with another molecule if the other molecule retains at least some level of its functional activity. Operably linked can also refer to linkage of two non-function molecules. Two molecules can be "operably linked" whether they are attached directly or indirectly (*e.g.,* via a linker).

[0130] "Target" refers to any molecule or combination of molecules that can be bound by an Adapter or CAR, or a component of the Adapter or CAR such as antigenic determinant binding domain.

[0131] The term "target cell" as used herein refers to cells which are involved in a disease and can be targeted by a CAR, an Adapter, and/or CAR/Adapter composition provided herein. Target cells include any cell in a subject (*e.g.,* a human or animal) that can be targeted by a CAR, an Adapter, and/or CAR/Adapter composition. The target cell can be a cell expressing or overexpressing a target specifically bound by a CAR, Adapter, and/or CAR/Adapter composition.

[0132] Expressions like "binding affinity for a target", "binding to a target" and analogous expressions known in the art refer to a property of a polypeptide which may be directly measured through the determination of the affinity constants, *e.g.,* the amount of Adapter that associates and dissociates at a given antigen concentration. Different methods can be used to characterize the molecular interaction, such as, but not limited to, competition analysis, equilibrium analysis and microcalorimetric analysis, and real-time interaction analysis based on surface plasmon resonance interaction (for example using a Biacore® instrument). These methods are well-known to the skilled person and are described, for example, in Neri *et al.*, Tibtech 14: 465-470 (1996), and Jansson *et al.*, J. Biol. Chem. 272: 8189-8197 (1997).

[0133] "The terms "antigenic determinant" and "epitope" are used interchangeably herein and refer to that portion of any molecule (*e.g.,* a target of interest, or an Adapter) capable of being recognized and specifically bound by a particular binding agent (*e.g.,* an Adapter or CAR). When the recognized molecule is a polypeptide, epitopes can be formed from contiguous amino acids and noncontiguous amino acids and/or other chemically active surface groups of molecules (such as carbohydrates) juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained upon protein denaturing, whereas epitopes formed by tertiary folding are typically lost upon protein denaturing. An epitope typically includes at least 3 amino acids, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

[0134] "Derived from" as that term is used herein, indicates a relationship between a first and a second molecule. It generally refers to structural similarity between the first molecule and a second molecule and does not connote or include a process or source limitation on a first molecule that is derived from a second molecule. For example, in the case of an intracellular signaling domain that is derived from a CD3zeta molecule, the intracellular signaling domain retains sufficient CD3zeta structure such that is has the required function, namely, the ability to generate a signal under the appropriate conditions. It does not connote or include a limitation to a particular process of producing the intracellular signaling domain, *e.g.,* it does not mean that, to provide the intracellular signaling domain, one must start with a CD3zeta sequence and delete unwanted sequence, or impose mutations, to arrive at the intracellular signaling domain.

[0135] The term "naturally occurring" when used in connection with biological materials such as a nucleic acid molecules, polypeptides, antigenic determinants, and host cells, refers to those which are found in nature and not modified by a human being. Conversely, "non-natural" or "synthetic" when used in connection with biological materials refers to those which are not found in nature and have been modified by a human being.

[0136] As used herein "modifications" with respect to a sequence of reference includes substitutions, deletions insertions and/or additions of a sequence when compared to the corresponding amino acid position(s) of the reference sequence.

[0137] A "substitution" with respect to a sequence of reference refers to a replacement of a particular amino acid residue with a different amino acid residue at a corresponding amino acid position of the reference sequence.

[0138] A "conservative" amino acid substitution is one in which one amino acid residue is replaced with another amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (*e.g.,* lysine (K), arginine (R), histidine (H)), acidic side chains (*e.g.,* aspartic acid (D), glutamic acid (E)), uncharged polar side chains (*e.g.,* glycine (G), asparagine (N), glutamine (Q), serine (S), threonine (T), tyrosine (Y), cysteine (C)), nonpolar side chains (*e.g.,* alanine (A), valine (V), leucine (L), isoleucine (I), proline (P), phenylalanine (F), methionine (M), tryptophan (W), beta-branched side chains (*e.g.,* threonine (T), valine (V), isoleucine (I)) and aromatic side chains (*e.g.,* tyrosine (Y), phenylalanine (F), tryptophan (W), histidine (H)). For example, substitution of a phenylalanine for a tyrosine is a conservative substitution. In one embodiment, conservative substitutions in the sequences of the Adapter or CAR results in a retained specific binding of the Adapter or CAR containing the substitution to the target of interest to which it binds. Methods of identifying nucleotide and amino acid conservative substitutions and non-conservative substitutions which confer, alter or maintain selective binding affinity are known in the art (*see*, *e.g.,* Brummell, Biochem. 32: 1180-1187 (1993); Kobayashi, Protein Eng. 12(10): 879-884 (1999); and Burks, PNAS 94: 412-417 (1997)).

[0139] A "non-conservative" amino acid substitution is one in which one amino acid residue is replaced with another amino acid residue having a dissimilar side chain. In one embodiment, non-conservative substitutions in the sequences of the Adapter or CAR result in a retained specific binding of the Adapter or CAR containing the substitution to the target of interest to which it binds.

[0140] "Non natural amino acids," "amino acid analogs" and "non-standard amino acid residues" are used interchangeably herein. Non-natural amino acids that can be substituted in an Adapter as provided herein are known in the art. In one embodiment the non-natural amino acid is 4-hydroxyproline which can be substituted for proline; 5-hydroxylysine which can be substituted for lysine; 3-methylhistidine which can be substituted for histidine; homoserine which can be substituted for serine; and ornithine which can be substituted for lysine. Additional examples of non-natural amino acids that can be substituted in an Adapter include, but are not limited to molecules such as: D-isomers of the common amino acids, 2,4-diaminobutyric acid, alpha-amino isobutyric acid, A-aminobutyric acid, Abu, 2-amino butyric acid, gamma-Abu, epsilon-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, beta-alanine, lanthionine, dehydroalanine, γ-aminobutyric acid, selenocysteine and pyrrolysine fluoro-amino acids, designer amino acids such as beta-methyl amino acids, C alpha-methyl amino acids, and N alpha-methyl amino acids, or combinations of non-natural amino acids. Still

additional non-natural amino acids can include 4-amino butyric acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, 2-thienyl alanine, and/or D-isomers of amino acids. As discussed herein, in several embodiments non-natural amino acids or amino acid analogs can include deletion of one or more amino acids from a sequence.

[0141] The terms "polynucleotide" and "nucleic acid," used interchangeably herein, refer to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. These terms include, but are not limited to, DNA, RNA, cDNA (complementary DNA), mRNA (messenger RNA), rRNA (ribosomal RNA), shRNA (small hairpin RNA), snRNA (small nuclear RNA), snoRNA (short nucleolar RNA), miRNA (microRNA), genomic DNA, synthetic DNA, synthetic RNA, and/or tRNA. In some embodiments, an isolated polynucleotide is a modified mRNA comprising non-naturally occurring nucleosides or nucleotides. In some embodiments, a modified mRNA comprises 2-thiouridine, pseudouridine, or 1-methylpseudouridine.

[0142] The term "naked DNA" as used herein refers to DNA (*e.g.,* histone free DNA) encoding a protein, such as an Adapter or a CAR, that is cloned in a suitable expression vector in proper orientation for expression (*e.g.,* a plasmid). Viral vectors which may be used include but are not limited to SIN lentiviral vectors, retroviral vectors, foamy virus vectors, adenovirus vectors, adeno-associated virus (AAV) vectors, hybrid vectors and/or plasmid transposons (for example sleeping beauty transposon system) or integrase based vector systems. Other vectors that can be used in connection with making and using Adapters and CARs are described herein or otherwise known in the art.

[0143] The terms "vector", "cloning vector" and "expression vector" as used herein refer to the vehicle by which a nucleic acid sequence (*e.g.,* an Adapter or CAR coding sequence) can be maintained or amplified in a host cell (*e.g.,* cloning vector) or introduced into a host cell, so as to transform the host and promote expression (*e.g.,* transcription and translation) of the introduced sequence. Vectors include plasmids, phages, viruses, etc.

[0144] A "host cell" includes an individual cell or cell culture which can be or has been a recipient of nucleic acids encoding an Adapter or CAR. Host cells include but are not limited to viral particles, phagemids, bacteria, yeast, plant, animal, and mammalian cells. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation and/or change. A host cell includes cells transfected or infected *in vivo*, *in vitro*, or *ex vivo* with nucleic acids encoding an Adapter or CAR. In some examples, the host cell is capable of expressing an Adapter. In some examples, the host cell is capable of expressing and secreting an Adapter. In some examples, the host cell is capable of expressing a CAR. In some examples, the host cell is capable of expressing and displaying a CAR on its surface. "Expression" includes transcription and/or translation.

[0145] As used herein, the terms "pharmaceutically acceptable," or "physiologically tolerable" and grammatical variations thereof, as they refer to compositions, carriers, diluents and reagents, are used interchangeably and represent that the materials are capable of administration to or upon a human without the production of therapeutically prohibitive undesirable physiological effects such as nausea, dizziness, gastric upset and other therapeutically prohibitive undesirable physiological effects known in the art.

[0146] "Parenteral" administration of an immunogenic composition includes, *e.g.,* subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, or infusion techniques.

[0147] The term "stimulate" or "stimulation" refers to a primary response induced by binding of a stimulatory molecule with its cognate ligand thereby mediating a signal transduction event, such as, but not limited to, signal transduction via the appropriate receptor, *e.g.,* T or NK receptor.

[0148] "Modulate" or "modulation" means adjustment or regulation of amplitude, frequency, degree, or activity. In another related aspect, such modulation may be positively modulated (*e.g.,* an increase in frequency, degree, or activity) or negatively modulated (*e.g.,* a decrease in frequency, degree, or activity). In several embodiments, modulation in a positive or negative direction is referenced as compared to the cell, tissue, or organ function prior to administration of a therapeutic. In additional embodiments, modulation in a positive or negative direction is referenced with respect to a normal, healthy cell, tissue or organ.

[0149] An "effective amount" of a CAR cell, Adapter, and/or CAR cell/Adapter composition as provided herein is an amount sufficient to carry out a specifically stated purpose such as to bring about an observable change in the level of one or more biological activities related to the target to which the CAR cell and/or Adapter binds. In certain embodiments, the change increases the level of target activity. In other embodiments, the change decreases the level of target activity. An "effective amount" can be determined empirically and in a routine manner, in relation to the stated purpose. The term "therapeutically effective amount" refers to an amount of a CAR cell and/or Adapter, or other therapeutic agent effective to "treat" (*e.g.,* reduce symptoms of) a disease or disorder in a subject (mammal). A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result.

[0150] "Patient," "subject," "animal" and "mammal" are used interchangeably and refer to mammals such as human patients and non-human primates, as well as experimental animals such as rabbits, rats, and mice, and other animals. Animals include all vertebrates, *e.g.,* mammals and non-mammals, such as chickens, amphibians, and reptiles. "Mammal" as used herein refers to any member of the class Mammalia, including, without limitation, humans and nonhuman primates such as chimpanzees and other apes and monkey species; farm animals such as cattle, sheep, pigs, goats and horses; domestic mammals such as dogs and cats; laboratory animals including rodents such as mice, rats and guinea pigs, and other members of the class Mammalia known in the art. In a particular embodiment, the patient is a human. The term does not denote a

particular age or sex. Thus, adult and newborn subjects, as well as embryos and fetuses, whether male or female, are intended to be included within the scope of this term.

[0151] The terms "treat," "treatment," and "treating," as used herein refer to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen or delay) the symptoms, complications, or biochemical indicia of a disease, condition, or disorder, alleviating the symptoms or arresting or inhibiting further development of the disease, condition, or disorder. Treatment can be prophylactic (to prevent or delay the onset of the disease, or to prevent the manifestation of clinical or subclinical symptoms thereof) or therapeutic suppression or alleviation of symptoms after the manifestation of the disease, condition, or disorder targeted pathologic condition, prevent the pathologic condition, pursue or obtain beneficial results, or lower the chances of the individual developing the condition even if the treatment is ultimately unsuccessful. Those in need of treatment include those already with the condition as well as those prone to have the condition or those in whom the condition is to be prevented. Treatment can be with a CAR cell, Adapter, and/or CAR cell/Adapter composition, alone or in combination with an additional therapeutic agent. In some embodiments, the terms "treat," "treatment," and "treating," are used herein to refer to therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen or delay) the symptoms, complications, or biochemical indicia of a proliferative disorder, or the amelioration of one or more symptoms (preferably, one or more discernible symptoms) of a proliferative disorder. In specific embodiments, the terms "treat", "treatment" and "treating" refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms "treat", "treatment" and "treating" refer to the inhibition of the progression of a proliferative disorder, either physically by, *e.g.,* stabilization of a discernible symptom, physiologically by, *e.g.,* stabilization of a physical parameter, or both. In other embodiments the terms "treat", "treatment" and "treating" refer to the reduction or stabilization of tumor size, tumor cell proliferation or survival, or cancerous cell count.

[0152] "Cancer," "tumor," or "malignancy" are used as synonymous terms and refer to any of a number of diseases that are characterized by uncontrolled, abnormal proliferation of cells, the ability of affected cells to spread locally or through the bloodstream and lymphatic system to other parts of the body (metastasize) as well as any of a number of characteristic structural and/or molecular features. "Tumor," as used herein refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. A "cancerous tumor," or "malignant cell" is understood as a cell having specific structural properties, lacking differentiation and being capable of invasion and metastasis. Cancers that can be treated using a CAR cell, Adapter, and/or CAR cell/Adapter composition provided herein include without limitation, breast, lung, brain, cervical, skin, bone, liver, pancreatic, colorectal, renal, head and neck, ovarian, hematopoietic (*e.g.,* leukemia), and prostate cancer, and lymphoma. Other types of cancer and tumors that

may be treated using a CAR cell, Adapter, and/or CAR cell/Adapter composition are described herein or otherwise known in the art. A reference to cancers, tumors, or tumor cells of a particular "type" is understood to mean cancer, tumors, or tumor cells characterized by a specific disease. For example, in some embodiments a first and second cancer of the same type is mixed cellularity Hodgkin's lymphoma and lymphocyte rich Hodgkin's lymphoma. In other embodiments a first and second cancer of the same type is precursor B cell acute lymphoblastic leukemia (ALL) and mature B cell ALL. Examples of a first and second cancer of a different type include, for example, Hodgkin's lymphoma and ALL.

[0153] The term "tumor antigen" refers to an antigen that is common to a specific hyperproliferative disorder such as cancer. The terms "tumor antigen" or "cancer antigen" are used interchangeably herein. In certain aspects, antigens are derived from cancers including but not limited to primary or metastatic melanoma, thymoma, lymphoma, sarcoma, lung cancer (*e.g.,* NSCLC or SCLC), liver cancer, non-Hodgkin's lymphoma, Hodgkin's lymphoma, leukemias, multiple myeloma, glioblastoma, neuroblastoma, uterine cancer, cervical cancer, renal cancer, thyroid cancer, bladder cancer, kidney cancer, mesothelioma, and adenocarcinomas such as breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, colon cancer and other cancers known in the art. In some embodiments, the cancer is B-cell acute lymphoid leukemia ("BALL"), T cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL), acute myelogenous leukemia (AML); one or more chronic leukemias including but not limited to chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia.

[0154] Tumor and cancer antigens may be further defined as "tumor-specific antigens (TSA)", "cancer-specific antigens (CSA)", "tumor-associated antigens (TAA)", or "cancer-associated antigens (CAA)". A TSA is an antigen that is unique to tumor cells and does not occur on other cells in the body. A TAA is an antigen that is found on both tumor and some normal cells. A TAA may be expressed on normal cells under conditions that fail to induce a state of immunologic tolerance to the antigen. The expression of the TAAs on the tumor may occur under conditions that enable the immune system to respond to the antigen. TAAs may be expressed on normal cells during fetal development when the immune system is immature and unable to respond or may be normally present at extremely low levels on normal cells but which are expressed at much higher levels on tumor cells. Because of the dynamic nature of tumors, in some instances, tumor cells may express unique antigens at certain stages, and at others also express antigens that are also expressed on non-tumor cells. Thus, inclusion of a certain marker as a TAA does not preclude it being considered a TSA. In

some embodiments, the TAA and/or TSA that contains an antigenic determinant specifically bound by a CAR cell, Adapter, and/or CAR cell/Adapter composition provided herein, is selected from: BCMA, CD19, CD20, CD22, CD30, CD33/lL3Ra, CD70, CD123, CD171 (L1-CAM), CS1, EGFRvIII, GD2, Lewis^{Y}, ROR 1, mesothelin, IL13Ra2, cMet, PSMA, folate receptor alpha (FR-alpha), CEA, ErbB2 (HER-2/neu); EGFR (HER), PSCA, PSA, MUC1, MUC16, CD44v6, CD44v6/7, CD44v7/8, CD55, IL11Ra, EphA2, EGP40, TAG72, CAIX, HMW-MAA (CSPG4), MAGEA4, NKG2D ligands, beta-HCG, Glycolipid F77, HLA-A2 (NY-ESO- 1), HMW-MAA, GD3, TCR, MAGE A3, MARTI, WT1, thyroglobulin, gp100 (Pmel 17), tyrosinase, TRP1, TRP2, HLA-A1, MAGE1, MAGE3, BAGE, GAGE1, GAGE2, pi5, p53, Ras, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR; VEGFR2, FAP, FAR, EBVA, HPV antigen E6, HPV antigen E7, TSP-180, MAGE4, MAGE5, MAGE6, RAGE, pl85erbB2, pl80erbB3, nm-23Hl, CA 19-9, CA72-4, CAM 17.1, NuMa, K-ras, beta-Catenin, CDK4, Mum-1, p15, p16, 43-9F, alpha-fetoprotein, BCA225, BTAA, CA125, CA 15-3, CA 27.29(BCAA), CA195, CA242, CA50, CAM43, CD68, CO-029, FGF5, G250, HTgp-175, M344, MA50, MG7-Ag, NB/70K, NY-CO-1, RCAS1, SDCCAG16, M2BP, TAAL6, TLP, and TPS.

[0155] The term "CS1" as used herein refers to an NK cell receptor regulating immune functions that is also expressed on B cells, T cells, dendritic cells, NK-T cells, and monocytes. CS1 is overexpressed in multiple myeloma and has been successfully targeted for immunotherapy multiple myeloma. Malaer & Mathew, Am J Cancer Res. 7(8): 1637–1641 (2017). CS1 is also known as SLAM7, protein 19A, CRACC, and CD319. The term "CS1" includes variants, isoforms, homologues, orthologs and paralogs. CS1 is a transmembrane protein with various differentially spliced isoforms. In some embodiments, the amino acid sequence of human CS1, comprising a 22 amino acid residue N-terminal signal sequence (MAGSPTCLTLIYILWQLTGSAA, SEQ ID NO: 1119) and an extracellular domain comprising the 226 N-terminal residues (SEQ ID NO: 1120), has Genbank Accession No. NP_067004 (SEQ ID NO: 1121). In some embodiments, the amino acid sequence of human CS1 has Genbank Accession No. NP_001269517, NP_001269518, NP_001269519, NP_001269520, NP_001269521, NP_001269522, NP_001269523, NP_001269524, or NP_001269525.

[0156] The term "autoimmune disease" as used herein is defined as a disorder that results from an autoimmune response. An autoimmune disease is the result of an inappropriate and excessive response to a self-antigen. Examples of autoimmune diseases include but are not limited to, Addison's disease, alopecia areata, ankylosing spondylitis, autoimmune hepatitis, autoimmune parotitis, Crohn's disease, diabetes (Type I), dystrophic epidermolysis bullosa, epididymitis, glomerulonephritis, Graves' disease, Guillain-Barr syndrome, Hashimoto's disease, hemolytic anemia, systemic lupus erythematosus, multiple sclerosis, myasthenia gravis, pemphigus vulgaris, psoriasis, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, spondyloarthropathies, thyroiditis, vasculitis, vitiligo, myxedema, pernicious anemia, ulcerative colitis, among others.

[0157] The term "transduction" as used herein refers to the introduction of a foreign nucleic acid into a cell using a viral vector. "Transfection" as used herein refers to the introduction of a foreign nucleic acid into a cell using recombinant DNA technology. The term "transformation" means the introduction of a "foreign" (*e.g.,* extrinsic, extracellular, or otherwise non-endogenous) nucleic acid (DNA or RNA) sequence to a host cell, so that the host cell will express the introduced nucleic acid to produce a desired substance, such as a protein or enzyme coded by the introduced coding sequence. The introduced nucleic acid sequence can also be called a "cloned" or "foreign" gene or sequence, can include regulatory or control sequences, such as start, stop, promoter, signal, secretion, or other sequences used by a cell's genetic machinery. The nucleic acid sequence can include nonfunctional sequences or sequences with no known function. A host cell that receives and expresses introduced nucleic acid (*e.g.,* DNA or RNA) has been "transformed" and is a "transformant" or a "clone." The DNA or RNA introduced to a host cell can come from any source, including cells of the same genus or species as the host cell, or cells of a different genus or species or may be non-naturally occurring.

[0158] The term "D domain" refers to a target binding polypeptide sharing certain sequence and certain structural features of the reference scaffold sequence: MGSWAEFKQRLAAIK TRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEALRK EAAAIRDELQAYRHN (SEQ ID NO: 1) (*see* WO 2016/164305 and WO 2016/164308, each of which is incorporated by reference herein in its entirety). The reference scaffold is a variant of a non-naturally occurring and targetless antiparallel three helical bundle reference polypeptide originally engineered as an exercise in protein folding (*see*, Walsh *et al.*, PNAS 96: 5486-5491 (1999) incorporated by reference herein in its entirety). It has been discovered that polypeptides containing modifications of the targetless reference scaffold having the amino acid sequence of SEQ ID NO: 1 are able to specifically bind targets of interest. Thus, a D domain, or a molecule comprising a D domain, can specifically (non-randomly) bind to a target molecule. While not wishing to be bound by theory, it is believed that in designing the D domain, the structural constraints of surface-exposed residues (that can be modified) confer the ability of the surface exposed residues to specifically bind a target of interest.

[0159] "Co-express" as used herein refers to expression of two or more protein coding sequences by the same cell or cell population. The coding sequences may be for example, nucleic acids that each encode a single protein or a chimeric protein as a single polypeptide chain.

[0160] "Antigen loss escape variants" as used herein refer to cells which exhibit reduced or loss of expression of the target antigen, which antigenic determinants are targeted by an Adapter or CAR provided herein.

II. Antigenic Determinants (ADs)

[0161] Antigenic determinants (ADs) are epitopes that are capable of being recognized and specifically bound by an antigenic determinant binding regions (ADBDs) (*e.g.,* antigen-binding fragments of an antibody

or alternative scaffold binding domains (ASBDs) (*e.g.*, D domains)). The ADs in the Adapters and on the target cells provided herein can be bound by the CARs discussed below.

[0162] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an AD that is present in a naturally occurring protein or other molecule. In some embodiments, the AD is an AD that is endogenous to humans.

[0163] In some embodiments, the AD in the Adapter is an AD that is present on a target cell.

[0164] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an AD that is present in a transmembrane protein, *e.g.,* an AD that is present in the extracellular portion of a transmembrane protein. In some embodiments, the AD is a tumor antigen. In some embodiments, the AD is a tumor-associated antigen. In some embodiments, the AD is a tumor-specific antigen.

[0165] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is a cancer antigen. In some embodiments, the AD is a cancer-associated antigen. In some embodiments, the AD is a cancer-specific antigen.

[0166] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of BCMA. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 5.

[0167] In some embodiments, the AD is an epitope of CD19. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 3.

[0168] In some embodiments, the AD is an epitope of CD20. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 6-9, or 10.

[0169] In some embodiments, the AD is an epitope of CD22. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 41.

[0170] In some embodiments, the AD is an epitope of CD123. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 11.

[0171] In some embodiments, the AD is an epitope of CD37. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 12 or 13.

[0172] In some embodiments, the AD is an epitope of CS1. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the

amino acid residues of SEQ ID NO: 1139. In further embodiments, the AD is an epitope of CS1 that is bound by elotuzumab.

[0173] In some embodiments, the AD is an epitope of HER2. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 42.

[0174] In some embodiments, the AD is an epitope of AFP. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 15.

[0175] In some embodiments, the AD is an epitope of AFP p26. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 16. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 1117. In further embodiments, the AD comprises the amino acid residues of SEQ ID NO: 16, 1117, 1118, 1119, 1120, 1121, 1122, or 1123.

[0176] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is expressed on the surface of an immune effector cell.

[0177] In some embodiments, the AD is an epitope of the extracellular domain (ECD) of human CD45. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 29-766 of SEQ ID NO: 1106.

[0178] In some embodiments, the AD is an epitope of human CD45 that is bound by the UCHL-1, A6, or ODP4 antibody. In some embodiments, the AD is an epitope of human CD45 that is bound by the 4KB5, MB1, KiB3, 2H4, or MT2 antibody.

[0179] In some embodiments, the AD is an epitope of CD26. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 29-766 of SEQ ID NO: 1113.

[0180] In some embodiments, the AD is an epitope of CD30. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 19-379 of SEQ ID NO: 1114.

[0181] In some embodiments, the AD is an epitope of CD33. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 18-259 of SEQ ID NO: 1115.

[0182] In some embodiments, the AD is an epitope of CD38. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 43-300 of SEQ ID NO: 1116.

[0183] In some embodiments, the AD is an epitope of a human intracellular protein. In further embodiments, the AD is an epitope of an intracellular portion of a membrane associated receptor protein selected from the group: cytokine receptor, chemokine receptor, T cell receptor, B cell receptor, NK cell receptor, myeloid cell receptor, endothelial cell receptor, and epithelial cell receptor. In some embodiments, the AD is an epitope of the intracellular portion of CD3, CD137, CD279, CD223, CD152, CD28, and VEGFR-2. In some embodiments, the AD is an epitope of a human nuclear protein.

[0184] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a tumor antigen associated with a malignant tumor. In some embodiments, the AD is an epitope of a tissue-specific antigen from a melanoma. In some embodiments, the AD is an epitope of a tissue-specific melanoma antigen selected from: MART-1, tyrosinase, and GP 100. In some embodiments, the AD is an epitope of a tissue-specific antigen from a prostate cancer. In some embodiments, the tissue-specific prostate cancer antigen is selected from: prostatic acid phosphatase (PAP) and prostate-specific antigen (PSA). In some embodiments, the AD is an epitope of a transformation-related molecule. In further embodiments, the AD is an epitope of ErbB2 (HER2). In some embodiments, the AD is an epitope of an onco-fetal antigen. In some embodiments, the AD is an epitope of carcinoembryonic antigen (CEA). In some embodiments, the AD is an epitope of a B-cell lymphoma-specific idiotype immunoglobulin. In some embodiments, the AD is an epitope of a B-cell differentiation antigen. In some embodiments, the AD is an epitope of a B-cell differentiation antigen selected from: CD19, CD20, and CD37. In some embodiments, the AD is an epitope of an antigen on myeloid cells. In some embodiments, the AD is an epitope of a myeloid cell antigen selected from: TSLPR and IL-7R. In some embodiments, the AD is an epitope of a cancer testis (CT) antigen. In some embodiments, the AD is an epitope of a cancer testis (CT) selected from: NY-ESO-1 and LAGE-1a. In some embodiments, the AD is an epitope of an antigen selected from: CS1, CD38, CD138, MUC1, HM1.24, CYP1B1, SP17, PRAME, Wilms' tumor 1 (WT1), and heat shock protein gp96 on multiple myeloma cells.

[0185] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a TSA or TAA. In some embodiments, the AD is an epitope of a tumor differentiation antigen. In some embodiments, the AD is an epitope of a tumor differentiation antigen selected from: MART1/MelanA, gp100 (Pmel 17), tyrosinase, TRP1, and TRP2. In some embodiments, the AD is an epitope of a tumor-specific multilineage antigen. In some embodiments, the AD is an epitope of a tumor-specific multilineage antigen selected from: MAGE1, MAGE3, BAGE, GAGE1, GAGE2, and p15. In some embodiments, the AD is an epitope of an overexpressed embryonic antigen. In some embodiments, the AD is an epitope of CEA. In some embodiments, the AD is an epitope of an overexpressed oncogene or mutated tumor-suppressor gene product. In some embodiments, the AD is an epitope of an overexpressed oncogene or mutated tumor-suppressor gene product selected from: p53, Ras, and HER2/neu. In some embodiments, the AD is an epitope of a unique tumor antigen resulting from chromosomal translocations. In some embodiments, the AD is an epitope of a

unique tumor antigen resulting from a chromosomal translocation selected from: BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, and MYL-RAR. In some embodiments, the AD is an epitope of a viral antigen. In some embodiments, the AD is an epitope of the Epstein Barr virus antigen EBVA. In other embodiments, the AD is an epitope of the human papillomavirus (HPV) antigen E6 or E7. In some embodiments, the AD is an epitope of a large, protein-based antigen.

[0186] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a hematological tumor antigen. In some embodiments, the AD is an epitope of an antigen selected from: BCMA, CD19, CD20, CD22, CD30, CD138, CD33, CD38, CD123, CS1, ROR1, $Lewis^Y$, Ig kappa light chain, TCR, BCMA, TACI, BAFFR (CD268), and a NKG2DL ligand.

[0187] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a solid tumor antigen. In some embodiments, the AD is an epitope of an antigen selected from: disialoganglioside (GD2), o-acetyl GD2, EGFRvIII, HER2 (ErbB2), VEGFR2, FAP, mesothelin, IL13Ra2 (glioma), cMET, PSMA, folate receptor alpha, L1CAM, carcinoembryonic antigen (CEA), and EGFR.

[0188] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of an antigen selected from the group: CD137, PDL1, CTLA4, CD47, KIR, TNFRSF10B (DR5), TIM3, PD1, cMet, Glycolipid F77, EGFRvIII, HLAA2 (NY-ESO-1), LAG3, CD134 (OX40), HVEM, BTLA, TNFRSF25 (DR3), CD133, MAGE A3, PSCA, MUC1, CD44v6, CD44v6/7, CD44v7/8, IL11Ra, ephA2, CAIX, MNCAIX, CSPG4, MUC16, EPCAM (EGP2), TAG72, EGP40, ErbB receptor family, ErbB2 (HER2), ErbB3/4, RAGE1, GD3, FAR, $Lewis^Y$, NCAM, HLAA1/MAGE1, MAGEA1, MAGEA3, MAGE-A4, B7H3, WT1, MelanA (MART1), HPV E6, HPV E7, thyroglobulin, tyrosinase, PSA, CLL1GD3, Tn Ag, FLT3, KIT, PRSS21, CD24, PDGFR-beta, SSEA4, prostase, PAP, ELF2M, ephB2, IGF1, IGFII, IGFI receptor, LMP2, gp100, bcr-ab1, Fucosyl GM1, sLe, GM3, TGS5, folate receptor beta, TEM1 (CD248), TEM7R, CLDN6, TSHR, GPRC5D, CXORF61, CD97, CD7a, HLE, CD179a, ALK, Plysialic acid, PLAC1, GloboH, NY—BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, LAGE1a, legumain, E7, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT1, MAD-CT2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin, telomerase, PCTA1 (Galectin 8), Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP4, SSX2, reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, neutrophil elastase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRLS, IGLL1, TSP-180, MAGE4, MAGE5, MAGE6, VEGFR1, IGF1R, hepatocyte growth factor receptor, p185ErbB2, p180ErbB-3, nm-23H1, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras, beta-Catenin, CDK4, Mum1, p15, p16, 43-9F, 5T4, 791Tgp72, β-human chorionic gonadotropin, BCA225, BTAA, CA125, CA15-3, CA 27.29 (BCAA), CA195, CA242, CA-50, CAM43, CD68, CO-029, FGF5, G250, HTgp-175, M344, MA50, MG7-Ag, MOV18, NB/70K, NY-CO1,

RCAS1, SDCCAG16, M2BP, TAAL6, TLP, and TPS, glioma-associated antigen, alpha-fetoprotein (AFP), a p26 fragment of AFP, or variants thereof, lectin-reactive AFP, and TLR4.

[0189] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a TSA or TAA. In some embodiments the AD is an epitope of an antigen selected from: PTGER4, ITGA4, CD37, CD52, CD62L (L-selectin), CXCR4, CD69, EVI2B (CD361), SLC39A8, MICB, LRRC70, CLELC2B, HMHA1, LST1, and CMTM6 (CKLFSF6). In some embodiments the AD is an epitope of BCMA. In some embodiments the AD is an epitope of CS1.

[0190] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of an antigen selected from: PDGFRA, VEGFR1, VEGFR3, neuropilin 1 (NRP1), neuropilin 2 (NRP2), betacellulin, PLGF, RET (rearranged during transfection), TIE1, TIE2 (TEK), CA125, CD3, CD4, CD7, CD10, CD13, CD25 CD32, CD32b, CD44 (*e.g.,* CD44v6), CD47, CD49e (integrin alpha 5), CD54 (ICAM), CD55, CD64, CD74, CD80, CD90, CD200, CD147, CD166, CD200, ESA, SHH, DHH, IHH, patched 1 (PTCH1), smoothened (SMO), WNT1, WNT2B, WNT3A, WNT4, WNT4A, WNT5A, WNT5B, WNT7B, WNT8A, WNT10A, WNT10B, WNT16B, LKP5, LRP5, LRP6, FZD1, FZD2, FZD4, FZD5, FZD6, FZD7, FZD8, Notch, Notch1, Notch3, Notch4, DLL4, Jagged, Jagged1, Jagged2, Jagged3, TNFRSF1A (TNFR1, p55, p60), TNFRSF1B (TNFR2), TNFRSF6 (Fas, CD95), TNFRSF6B (DcR3), TNFRSF7 (CD27), TNFSF9 (41BB Ligand), TNFRSF8 (CD30), TNFRSF10A (TRAILRl, DR4), TNFRSF11A (RANK), TNFRSF12 (TWEAKR), TNFRSF19L (KELT), TNFRSF19 (TROY), TNFRSF21 (DR6), ILIRI, 1L1R2, IL2R, IL5R, IL6R, 1L8R, IL10R, IL12R, IL13R, IL15R, IL18R, IL19R, IL21R, IL23R, XAG1, XAG3, REGIV, FGFR1, FGFR2, FGFR3, ALK, ALK1, ALK7, ALCAM, Axl, TGFb, TGFb2, TGFb3, TGFBR1, IGFIIR, BMPRI, N-cadherin, E-cadherin, VE-cadherin, ganglioside GM2, ganglioside GD3, PSGR, DCC, CDCP1, CXCR2, CXCR7, CCR3, CCR4, CCR5, CCR7, CCR10, Claudin1, Claudin2, Claudin3, Claudin4, TMEFF2, neuregulin, MCSF, CSF, CSFR (fms), GCSF, GCSFR, BCAM, BRCA1, BRCA2, HLA-DR, ABCC3, ABCB5, HM 1.24, LFA1, LYNX, S100A8, S100A9, SCF, Von Willebrand factor, Lewis Y6 receptor, CA G250 (CA9), CRYPTO, VLA5, HLADR, MUCl8, mucin CanAg, EGFL7, integrin avb3, integrin α5β activin Bl alpha, leukotriene B4 receptor (LTB4R), neurotensin NT receptor (NTR), 5T4 oncofetal antigen, Tenascin C, MMP, MMP2, MMP7, MMP9, MMP12, MMP14, MMP26, cathepsin G, SULF1, SULF2, MET, CA9, TM4SF1, syndecan (SDCl), Ephrin B4, TEM1, TGFbeta 1, and TGFBRII.

[0191] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of an antigen associated with an autoimmune disorder, associated with an inflammatory or other disorder of the immune system, or is associated with regulating an immune response.

[0192] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of an immunoinhibitory target. In another embodiment, the AD is an epitope of an immunoinhibitory target selected from: IL1Ra, IL6R, CD26L, CD28, CD80, FcGamma RIIB. In another embodiment, the AD in the Adapter is

an epitope of an immunostimulatory target selected from: CD25, CD28, CTLA4, PD1, B7H1 (PDL1), B7H4 TGFbeta, TNFRSF4 (OX40), TNFRSF5 (CD40), TNFRSF9 (41BB, CD137), TNFRSF14 (HVEM), TNFRSF25 (DR3), and TNFRSF18 (GITR).

[0193] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a target selected from: IL1Rb, C3AR, C5AR, CXCR1, CXCR2, CCR1, CCR3, CCR7, CCR8, CCR9, CCR10, ChemR23, MPL, GP130, TLR2, TLR3, TLR4, TLR5, TLR7, TLR8, TLR9, TREM1, TREM2, CD49a (integrin alpha 1), integrin a5b3, alpha4 integrin subunit, A4B7 integrin, cathepsin G, TNFRSF3 (LTBR), TNFRSF6 (Fas, CD95), TNFRSF6B (DcR3), TNFRSF8 (CD30), TNFRSF11A (RANK), TNFRSF16 (NGFR), TNFRSF19L (RELT), TNFRSF19 (TROY), TNFRSF21 (DR6), CD14, CD23, CD36, CD36L, CD39, CD91, CD153, CD164, CD200, CD200R, B71 (CD80), B72 (CD86), B7h, B7DC (PDL2), ICOS, ICOSL, MHC, CD, B7H2, B7H3, B7x, SLAM, KIM1, SLAMF2, SLAMF3, SLAMF4, SLAMF5, SLAMF6, SLAMF7, TNFRSF1A (TNFR1, p55, p60), TNFRSF1B (TNFR2), TNFRSF7 (CD27), TNFRSF12 (TWEAKR), TNFRSF5 (CD40), IL1R, IL2R, IL4Ra, IL5R, IL6RIL15R, IL17R, IL17Rb, IL17RC, IL22RA, IL23R, TSLPR, B7RP1, cKit, GMCSF, GMCSFR, CD2, CD4, CD11a, CD18, CD30, CD40, CD86, CXCR3, CCR2, CCR4, CCR5, CCR8, RhD, IgE, and Rh.

[0194] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of an antigen associated with a neurological disorder.

[0195] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an epitope of a target selected from: amyloid beta (Abeta), beta amyloid, PLP, ROBO4, ROBO, LINGO, gpIIB, gpIIIa, integrin a2bB3, AOC3, TNFRSF19L (RELT), TNFRSF19 (TROY), and sclerostin.

[0196] The above targets and those otherwise described herein are intended to be illustrative and not limiting.

[0197] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is bound by a chimeric antigen receptor (CAR). In some embodiments, the AD is bound by a cell expressing a chimeric antigen receptor. In some embodiments, the AD is bound by a scFv. In some embodiments, the AD is bound by an alternative scaffold binding domain (ASBD). In some embodiments, the AD is bound by a D domain. In some embodiments, the AD is bound by an antibody or an antigen-binding fragment thereof.

III. Antigenic Determinant Binding Domains (ADBDs)

[0198] A protein domain that binds to an antigenic determinant (AD) (*e.g.,* as described in Section II) is referred to herein as an "antigenic-determinant binding domain" or "ADBD." In some embodiments, the ADBD is sufficient to confer recognition and specific binding to a target of interest. The ADBD described

herein can be present in an Adapter (*e.g.,* as described in Section V) and/or in a chimeric antigen receptor (CAR) (*e.g.,* as described in Section VI).

[0199] The target of interest specifically bound by the ADBD (*e.g.,* of an Adapter and/or CAR) can be any molecule for which it is desirable for an Adapter and/or CAR to bind, *e.g.,* any of the ADs described herein (*e.g.,* as described in Section II). In some embodiments, the target(s) specifically bound by the ADBD can be any target of purification, manufacturing, formulation, therapeutic, diagnostic, or prognostic relevance or value. In some embodiments, the target of the ADBD can be naturally occurring or synthetic. In some embodiments, the target of the ADBD can be an extracellular component, an intracellular component, a soluble factor (*e.g.,* an enzyme, hormone, cytokine, growth factor, toxin, venom, pollutant, etc.), or a transmembrane protein (*e.g.,* a cell surface receptor).

[0200] In some embodiment, the ADBD (*e.g.,* of an Adapter and/or CAR) specifically binds a target of interest on the surface of a target cell. In some embodiments, the ADBD specifically binds a cell surface receptor. In some embodiments, the ADBD specifically binds a target of interest that is a member of a family selected from: a phosphatase receptor, growth factor receptor, a tyrosine kinase receptor, a TNF family receptor, a G-protein-coupled receptor, and a chemokine receptor. In some embodiments, the ADBD binds multiple members of the same family (*e.g.,* the TNF receptors TRAILR1 and TRAILR2). In some embodiments, the ADBD binds members from different families. Thus, for example, in some embodiments, the ADBD can bind to a growth factor receptor and a TNF receptor or a G-protein-coupled receptor and a chemokine receptor.

[0201] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) binds to a tumor antigen. In some embodiments, the ADBD binds to a tumor-associated antigen. In some embodiments, the ADBD binds to a tumor-specific antigen.

[0202] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) binds a cancer antigen. In some embodiments, the ADBD binds to a cancer-associated antigen. In some embodiments, the ADBD binds to a cancer-specific antigen.

[0203] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) binds an antigen expressed on the surface of an immune effector cell.

[0204] In some embodiments, a target of interest bound by the ADBD (*e.g.,* of an Adapter and/or CAR) is a human protein. In one embodiment, the ADBD binds a human protein target of interest and its monkey (*e.g.,* cynomolgous monkey), mouse, rabbit, hamster and/or a rabbit ortholog.

[0205] In another embodiment, the ADBD (*e.g.,* of an Adapter and/or CAR) binds a peptide tag present on a target of interest. Such peptide tags provide a useful means by which to detect, monitor, and/or attach one or more additional moieties to the Adapter. In one embodiment, the ADBD specifically binds a peptide tag

selected from: a hexahistidyl (His6) tag, a myc tag, and a FLAG tag. Other peptide tags are described herein or otherwise known in the art.

[0206] Affinity requirements for a given ADBD binding event are contingent on a variety of factors including, but not limited to: the composition and complexity of the binding matrix, the valency and density of both the ADBD and target molecules, and the functional application of the ADBD. In one embodiment, the ADBD binds a target of interest with a dissociation constant (KD) of less than or equal to 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, or 10^{-5} M. In an additional embodiment, the ADBD binds a target of interest with a KD of less than or equal to 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, or 10^{-8} M. In additional embodiments, a the ADBD binds a target of interest with a KD less than or equal to 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M. In several embodiments, the ADBD generated by the methods disclosed herein have a dissociation constant selected from the group: between 10^{-4} M and 10^{-5} M, between 10^{-5} M and 10^{-6} M, between 10^{-6} M and 10^{-7} M, between 10^{-7} M and 10^{-8} M, between 10^{-8} M and 10^{-9} M, between 10^{-9} M and 10^{-10} M, between 10^{-10} M and 10^{-11} M and between 10^{-11} M and 10^{-12} M.

[0207] In one embodiment the ADBD binds a target of interest in active form. In one embodiment the ADBD reversibly binds a target of interest in active form and also releases the bound target in active form. In one embodiment the ADBD binds a target of interest in the native form. In specific embodiments, the ADBD bind targets of interest with off-rates or Koff of greater than or equal to 10^{-10} sec^{-1}, 5×10^{-9} sec^{-1}, 10^{-9} sec^{-1}, 5×10^{-8} sec^{-1}, 10^{-8} sec^{-1}, 5×10^{-7} sec^{-1}, 10^{-7} sec^{-1}, 5×10^{-6} sec^{-1}, 10^{-6} sec^{-1}, 5×10^{-5} sec^{-1}, 10^{-5} sec^{-1}, 5×10^{-4} sec^{-1}, 10^{-4} sec^{-1}, 5×10^{-3} sec^{-1}, 10^{-3} sec^{-1}, 5×10^{-2} sec^{-1}, 10^{-2} sec^{-1}, 5×10^{-1} sec^{-1}, or 10^{-1} sec^{-1}.

[0208] Binding experiments to determine KD and off-rates can be performed in a number of conditions including, but not limited to, [pH 6.0, 0.01% Tween 20], [pH 6.0, 0.1% gelatin], [pH5.0, 0.01% Tween 20], [pH9.0, 0.1% Tween 20], [pH6.0, 15% ethylene glycol, 0.01% Tween 20], [pH5.0, 15% ethylene glycol, 0.01% Tween 20], and [pH9.0, 15% ethylene glycol, 0.01% Tween 20]. The buffers in which to make these solutions can readily be determined by one of skill in the art, and depend largely on the desired pH of the final solution. Low pH solutions (<pH 5.5) can be made, for example, in citrate buffer, glycine-HCl buffer, or in succinic acid buffer. High pH solutions can be made, for example, in Tris-HCl, phosphate buffers, or sodium bicarbonate buffers. A number of conditions may be used to determine KD and off-rates for the purpose of determining, for example, optimal pH and/or salt concentrations.

[0209] In one embodiment, the ADBD specifically binds a target of interest with a KOff ranging from 0.1 to 10^{-7} sec^{-1}, 10^{-2} to 10^{-7} sec^{-1}, or 0.5 X 10^{-2} to 10^{-7} sec^{-1}. In a specific embodiment, the ADBD binds a target of interest with an off rate (KOff) of less than 5 X 10^{-2} sec^{-1}, 10^{-2} sec^{-1}, 5 X 10^{-3} sec^{-1}, or 10^{-3} sec^{-1}. In an additional embodiment, the ADBD binds a target of interest with an off rate (K_{Off}) of less than 5 X 10^{-4} sec^{-1}, 10^{-4} sec^{-1}, 5 X 10^{-5} sec^{-1}, or 10^{-5} sec^{-1}, 5 X10^{-6} sec^{-1}, 10^{-6} sec^{-1}, 5 X 10^{-7} sec^{-1}, or 10^{-7} sec^{-1}.

[0210] In one embodiment, the ADBD specifically binds a target of interest with a KOn ranging from 10^3 to 10^7 $M^{-1}sec^{-1}$, 10^3 to 10^6 $M^{-1}sec^{-1}$, or 10^3 to 10^5 $M^{-1}sec^{-1}$. In other specific embodiments, the ADBD binds the target of interest its target of interest with an on rate (KOn) of greater than 10^3 $M^{-1}sec^{-1}$, 5 X 10^3 $M^{-1}sec^{-1}$, 10^4 $M^{-1}sec^{-1}$, or 5 X 10^4 $M^{-1}sec^{-1}$. In an additional embodiment, the ADBD binds a target of interest with a KOn of greater than 10^5 $M^{-1}sec^{-1}$, 5 X 10^5 $M^{-1}sec^{-1}$, 10^6 M^{-1} sec^{-1}, or 5 X 10^6 $M^{-1}sec^{-1}$, or 10^7 M^{-1} sec^{-1}.

[0211] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) is an antibody or an antigen-binding fragment thereof. In some embodiments, the ADBD is a scFv. In some embodiments, the ADBD is an alternative scaffold binding domain. In some embodiments, the ADBD is a D domain.

IIIa. Antibody-derived Antigenic Determinant Binding Domains (ADBD)

[0212] In some embodiments, one or more ADBDs (*e.g.,* of an Adapter and/or CAR) can be derived from an antibody molecule, *e.g.,* one or more of monoclonal antibodies, polyclonal antibodies, recombinant antibodies, human antibodies, humanized antibodies, single-domain antibodies *e.g.,* a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) from, *e.g.,* human or camelid origin. In some embodiments, the ADBD is derived from the same species in which the Adapter or CAR will ultimately be used, *e.g.,* for use in humans. It may be beneficial for Adapter and/or CAR to comprise a human or a humanized ADBD. Compositions and techniques for routinely generating such ADBDs are known in the art.

[0213] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) comprises a fragment of an antibody that is sufficient to confer recognition and specific binding to the target antigen. Examples of an antibody fragment include, but are not limited to, an Fab, Fab', $F(ab')_2$, or Fv fragment, an scFv antibody fragment, a linear antibody, single domain antibody such as an sdAb (either VL or VH), a camelid VHH domain, and multi-specific antibodies formed from antibody fragments.

[0214] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) is a "scFv," which can comprise a fusion protein comprising a VL chain and a VH chain of an antibody, wherein the VH and VL are, *e.g.,* linked via a short flexible polypeptide linker, *e.g.,* a linker described herein. scFvs can routinely be prepared according to methods known in the art (*see, e.g.,* Bird *et al.*, Science 242: 423-426 (1988) and Huston *et al.*, Proc. Natl. Acad. Sci. USA 85: 5879-5883 (1988)).

[0215] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) is a single domain antigen binding (SDAB) molecule. A SDAB molecule includes molecules containing complementary determining regions that are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain variable domains, binding molecules naturally devoid of light chains, single domains derived from conventional 4-chain antibodies, engineered domains and single domain scaffolds other than those derived from antibodies. SDAB molecules can be derived from any species including, but not limited to mouse,

human, camel, llama, fish, shark, goat, rabbit, and bovine. This term also includes naturally occurring single domain antibody molecules from species other than Camelidae and sharks.

[0216] In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) comprises a human antibody or a fragment thereof. In some embodiments, the ADBD (*e.g.,* of an Adapter and/or CAR) comprises a humanized antibody or a fragment thereof.

[0217] Humanization of antibodies is well-known in the art and can essentially be performed following the method of Winter and co-workers (Jones *et al.*, Nature 321: 522-525 (1986); Riechmann *et al.*, Nature 332: 323-327 (1988); Verhoeyen *et al.*, Science 239: 1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody, *i.e.*, CDR-grafting (EP 239,400; Intl. Appl. Publ. No. WO 91/09967; and U.S. Pat. Nos. 4,816,567; 6,331,415; 5,225,539; 5,530,101; 5,585,089; and 6,548,640; the contents of which are incorporated herein by reference herein in their entirety). Humanization of antibodies can also be achieved by veneering or resurfacing (EP 592,106; EP 519,596; Padlan, 1991, Molecular Immunology, 28(4/5): 489-498; Studnicka *et al.*, Protein Engineering 7(6): 805-814 (1994); and Roguska *et al.*, PNAS 91: 969-973 (1994)) or chain shuffling (U.S. Pat. No. 5,565,332), the contents of which are incorporated herein by reference herein in their entirety.

IIIb. Alternative scaffold binding domains

[0218] In some embodiments, the ADBD(s) (*e.g.,* of an Adapter and/or CAR) is an alternative scaffold binding domain (ASBD). An "alternative scaffold binding domain" or "ASBD" as used herein, is an antigen determinant binding domain that is derived from, or corresponds to, a non-antibody-based binding scaffold.

[0219] In some embodiments, the disclosure provides a CAR comprising an ADBD that is an ASBD. In some embodiments, the disclosure provides a cell comprising a CAR that comprises an ADBD that is an ASBD. In further embodiments, an immune effector cell that comprises a CAR comprising and ASBD is provided. In some embodiments, the disclosure provides an Adapter comprising an ADBD that is an ASBD.

[0220] In further embodiments, the disclosure provides a composition comprising an Adapter and a CAR that each comprise an ASBD.

[0221] In some embodiments, the binding of the ASBD (*e.g.,* of an Adapter and/or CAR) to the target AD is mediated by secondary structures of the binding scaffold, such as alpha helices or beta sheets. In some embodiments, the ASBD is a three-helix bundle-based binding domain. In some embodiments, the ASBD is a D domain-based binding domain. In other embodiments, the ASBD is a Z-domain (Affibody)-based binding domain.

[0222] In some embodiments, the ASBD (*e.g.,* of an Adapter and/or CAR) is a D domain (*de novo* binding domain)-based AD binding domain. The D domain scaffold-based binding domain generally consists of 70-75 amino acid residues in which substitutions of up to 20 positions corresponding to structurally constrained surface-exposed residues in a non-naturally occurring antiparallel three helical bundle reference scaffold

(SEQ ID NO: 1) confer target recognition and binding specificity for the target (AD) of interest. D domain scaffold-based binding domains are further disclosed in Intl. Appl. Publ. No. WO2016164308, the contents of which are herein incorporated by reference in their entirety. In one embodiment, the D domain comprises an amino acid sequence that differs (*e.g.,* due to amino acid modifications) from that of a reference scaffold having the sequence of SEQ ID NO: 1 by up to 20 substitutions. In some embodiments, the D domain comprises a sequence selected from the group: SEQ ID NO: 17, 18, and 19. In some embodiments, the D domain comprises a sequence selected from the group: SEQ ID NO: 20-26, and 27. In further embodiments, the D domain comprises a sequence selected from the group: SEQ ID NO: 44-1078 and 1079.

[0223] In some embodiments the ASBD (*e.g.,* of an Adapter and/or CAR) is a Z-domain scaffold (Affibody)-based AD binding domain. Z-domain scaffold-based binding domains generally consist of 58 amino acid residues in which substitutions of up to 13 positions located in the first and second of three alpha helices, confer binding confer target (AD) recognition and binding specificity for the target (AD) of interest. In further embodiments, the Z-domain ASBD comprises a sequence selected from SEQ ID NO: 28 and 29. Z-domain (Affibody) scaffold-based binding domains are further described in U.S. Pat. No. 5,831,012, the entire contents of which are herein incorporated by reference in their entirety.

[0224] Additional examples of ASBDs that display secondary structure-mediated target binding include DARPins, affilins, and armadillo repeat-based binding scaffolds.

[0225] In some embodiments, the ASBD (*e.g.,* of an Adapter and/or CAR) is a DARPin-based AD binding domain. DARPin-based binding domains generally contain 2-3 repeats of the sequence of SEQ ID NO: 30 positioned between N- and C- terminal capping repeats (*e.g.,* the sequence MRGSHHHHHHGSDLGKKLLEAARAGQDDEVRILMANGA DVNAX_{33} (SEQ ID NO: 31) and the sequence QDKFGKTAFDISIDNGNEDLAEILQ (SEQ ID NO: 32), respectively, wherein the first Gln corresponds to consensus repeat position X_{33} of the preceding repeat). Each internal repeat consists of 27 framework residues and up to 6 substituted non-framework residues that that form a β-turn followed by two antiparallel helices and a loop that connects to the β-turn of the next repeat. The collective substitutions and structure of the DARPin confers target (AD) recognition and binding specificity.

Table 1. Exemplary secondary structure-based ASBD Sequences

ADBD	Sequence
D-domain F1	MGSWX_5X_6FKX_9X_{10}LAX_{13}IK$X_{16}X_{17}$LEALGGSEAELAX_{30}FE$X_{33}X_{34}$IAX_{37}FE$X_{40}X_{41}$LQ X_{44}YKGKGNPEVEALRKEAAAIRDELQAYRHN **(SEQ ID NO: 17)**
D-domain F2	MGSWAEFKQRLAAIKTRLEALGGSEAELAAF$X_{32}X_{33}$EIX_{36}AF$X_{39}X_{40}$ELX_{43}AYKGKG NPEVEAL$X_{57}X_{58}$EAX_{61}AI$X_{64}X_{65}$ELX_{68}AYRHN **(SEQ ID NO: 18)**
D-domain F3	MGSWX_5EFX_8X_9RLX_{12}AI$X_{15}X_{16}$RLX_{19}ALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEX_{55}LR$X_{58}X_{59}$AAX_{62}IR$X_{65}X_{66}$LQAYRHN **(SEQ ID NO: 19)**
D-domain C1	MGSWX_5X_6FKX_9X_{10}LAX_{13}IK$X_{16}X_{17}$LEALGGSEAELAAF$X_{32}X_{33}$EIX_{36}AF$X_{39}X_{40}$ ELX_{43}A YKGKGNPEVEX_{55}LR$X_{58}X_{59}$AAX_{62}IR$X_{65}X_{66}$LQAYRHN **(SEQ ID NO: 20)**
D-domain C2	MGSWX_5EFX_8X_9RLX_{12}AI$X_{15}X_{16}$RLX_{19}ALGGSEAELAX_{30}FE$X_{33}X_{34}$IAX_{37}FEX_{40} X_{41}LQ X_{44}YKGKGNPEVEAL$X_{57}X_{58}$EAX_{61}AI$X_{64}X_{65}$ELX_{68}AYRHN **(SEQ ID NO: 21)**

D-domain FlLpx	MGSWX$_5$X$_6$FKX$_9$X$_{10}$LAX$_{13}$IKX$_{16}$X$_{17}$LEALZ$_1$EAELAX$_{28}$FEX$_{31}$X$_{32}$IAX$_{35}$FEX$_{38}$X$_{39}$LQ X$_{42}$Y Z$_2$NPEVEALRKEAAAIRDELQAYRHN **(SEQ ID NO: 22)**
D-domain F2Lpx	MGSWAEFKQRLAAIKTRLEALZ$_1$EAELAAFX$_{30}$X$_{31}$EIX$_{34}$AFX$_{37}$X$_{38}$ELX$_{41}$AYZ$_2$NPEV EALX$_{52}$X$_{53}$EAX$_{56}$AIX$_{59}$X$_{60}$ELX$_{63}$AYRHN **(SEQ ID NO: 23)**
D-domain F3Lpx	MGSWX$_5$EFX$_8$X$_9$RLX$_{12}$AIX$_{15}$X$_{16}$RLX$_{19}$ALZ$_1$EAELAAFEKEIAAFESELQAY Z$_2$NPEVE X$_{50}$LRX$_{53}$X$_{54}$AAX$_{57}$IRX$_{60}$X$_{61}$LQAYRHN **(SEQ ID NO: 24)**
D-domain C1Lpx	MGSWX$_5$X$_6$FKX$_9$X$_{10}$LAX$_{13}$IKX$_{16}$X$_{17}$LEALZ$_1$EAELAAFX$_{30}$X$_{31}$EIX$_{34}$AFX$_{37}$X$_{38}$ELX$_{41}$ AYZ$_2$ NPEVEX$_{50}$LRX$_{53}$X$_{54}$AAX$_{57}$IRX$_{60}$X$_{61}$LQAYRHN **(SEQ ID NO: 25)**
D-domain C2Lpx	MGSWX$_5$EFX$_8$X$_9$RLX$_{12}$AIX$_{15}$X$_{16}$RLX$_{19}$ALZ$_1$EAELAX$_{28}$FEX$_{31}$X$_{32}$IAX$_{35}$FEX$_{38}$X$_{39}$L QX$_{42}$Y Z$_2$NPEVEALX$_{52}$X$_{53}$EAX$_{56}$AIX$_{59}$X$_{60}$ELX$_{63}$AYRHN **(SEQ ID NO: 26)**
D-domain DD-WTF	MGSWX$_5$EFX$_8$X$_9$RLX$_{12}$X$_{13}$IX$_{15}$X$_{16}$RLX$_{19}$ALGGSEAELAAFEKEIX$_{36}$AFX$_{39}$X$_{40}$ELX$_{43}$AYK GKGNPEVEALRX$_{58}$EAX$_{61}$X$_{62}$IRX$_{65}$ELX$_{68}$X$_{69}$YRX$_{72}$X$_{73}$ **(SEQ ID NO: 27)**
Z-Domain AFFa	VDNKFNKEX$_9$X$_{10}$X$_{11}$AX$_{13}$X$_{14}$EIX$_{17}$X$_{18}$LPNLNX$_{24}$X$_{25}$QX$_{27}$X$_{28}$AFIX$_{32}$SLX$_{35}$DDPSQSANLL AEAKKLNDAQAPK (SEQ ID NO: 28)
Z-Domain AFFb	NKEX$_4$X$_5$X$_6$AX$_8$X$_9$EIX$_{12}$X$_{13}$LPNLNX$_{19}$X$_{20}$QX$_{22}$X23AFIX27SLX30DDP (SEQ ID NO: 29)
DARPin	DX$_2$X$_3$GX$_5$TPLHLAAX$_{13}$X$_{14}$GHLEIVEVLLKZ$_{26}$GADVNAX$_{33}$ (SEQ ID NO: 30) wherein X is any amino acid but C, R or P and Z is H, N, or Y.
X = all amino acid residues, including natural and non-natural amino acids Z = amino acid sequence corresponding to loop1 (Z$_1$) or loop2 (Z$_2$) as described herein, comprising between about 2 to about 30 natural or non-natural amino acids	

[0226] In some embodiments, the binding specificity of the ASBD (*e.g.,* of an Adapter and/or CAR) to the target AD is mediated by amino acids in exposed loops on the ASBD. Examples of scaffolds having these binding properties include, adnectins, lipocalins, avimers, knottins, fynomers, atrimers, kunitz domain-based binders, and CTLA4-based binding scaffolds.

[0227] In some embodiments, the ASBD is an adnectin-based AD binding domain. The adnectin-based binding domain is derived from the tenth domain of fibronectin type III (10Fn3). This ADBD is generally a 94 amino acid binding domain that adopts a beta sandwich fold containing seven strands that are connected by six loops. Substitutions in three surface-exposed loops on one side of the adnectin domain generate target (AD) specific binding moieties.

[0228] In some embodiments, the ASBD (*e.g.,* of an Adapter and/or CAR) is a lipocalin-, affilin-, or anticalin-based AD-binding domain. The anticalin scaffold displays a conserved β-barrel structure made up of eight anti-parallel β-strands and generally consists of 160–180 amino acids. The ligand binding pocket of the anticallin-based binding scaffold is composed of four loops, each containing up to 24 substitutions, that collectively confer target (AD) recognition and binding specificity.

[0229] In some embodiments, the ASBD (*e.g.,* of an Adapter and/or CAR) is an Avimer scaffold-based AD-binding domain. Avimer scaffold-based binding domains are derived from the A-domain of cell surface receptors and are generally 35 amino acids in length. The structure of the Avimer-based binding domain is maintained by 12 conserved amino acids. Substitutions of up to all of the remaining 23 residues of the binding domain confer target (AD) recognition and binding specificity. In some embodiments, the Avimer

scaffold-based binding domain comprises the sequence $EFX_3CX_5NGX_8CIPX_{12}X_{13}WX_{15}CDGX_{19}DDCGDX_{25}SDE$, wherein X is any amino acid (SEQ ID NO: 33). Avimer scaffold-based binding domains are further described in U.S. Appl. Publ. Nos. 20040175756, 20050053973, 20050048512, and 20060008844, the entire contents of each of which are herein incorporated by reference in their entireties.

[0230] In some embodiments, the ASBD (*e.g.,* of an Adapter and/or CAR) is a fynomer scaffold-based AD binding domain. The fynomer binding domain is generally 60-75 amino acids in length and is composed of a pair of anti-parallel beta sheets joined by two flexible loops. Substitutions/insertions in the loops confer AD target recognition and binding specificity. In some embodiments, the fynomer-based AD binding domain comprises the sequence GVTLFV $ALYDYX_{12}X_{13}X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ $X_{22}LSFHKGEKFQILSTHEYEX_{41}X_{42}X_{43}X_{44}X_{45}X_{46}X_{47}X_{48}WEARSLTTGETGX_{61}IPSNYVAPVDSIQ$, wherein X is any amino acid residue and X_{13}-X_{21} and X_{42}-X_{46}, are optionally absent (SEQ ID NO: 34). In some embodiments, the fynomer-based AD binding domain comprises the sequence $GVTLFVALYDYX_{12}X_{13}X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}X_{22}$ LSFHKGEKFQILSTHEYEDWWEARSLTTGETGYIPSNYVAPVDSIQ, wherein X is any amino acid residue and X_{16}-X_{21} and are optionally absent (SEQ ID NO: 35).

[0231] In some embodiments the ASBD (*e.g.,* of an Adapter and/or CAR) is a knottin scaffold-based AD binding domain. Knottin scaffold-based binding domains correspond to a 30-amino-acid protein fold composed of three anti-parallel β-strands connected by loops of variable length and multiple disulfide bonds.

[0232] In some embodiments the ASBD (*e.g.,* of an Adapter and/or CAR) is a Kunitz domain-based AD binding domain. Kunitz domain-based binding domains are derived from the active motif of Kunitz-type protease inhibitors and are generally about 60 amino acids in length. The hydrophobic core of this ADBD is composed of a twisted two-stranded antiparallel β-sheet and two α-helices stabilized by three pairs of disulfide bonds. Substitutions and insertions in the three loops confer AD target recognition and binding specificity. In some embodiments, the Kunitz domain-based AD binding domain comprises the sequence $MHSFCAFKADX_{11}GX_{13}C\ X_{15}$ $X_{16}X_{17}X_{18}X_{19}RFFFNIFTRQCEEFX_{34}YGGCX_{39}X_{40}NQNRFESLEECKKMCTRDGA$ (SEQ ID NO: 36) sequence that is at least 85% identical to at positions other than X; X_{11} is one of: A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y; X_{13} is one of: A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y; X_{15} is one of: A, D, E, F, G, H, I, K, L, M, N, Q, R, S, T, V, W, Y; X_{16} is one of: A, G, E, D, H, T; X_{17} is one of: A, D, E, F, G, H, I, K, L, M, N, Q, R, S, T, V, W, Y; X_{18} is one of: A, D, E, F, G, H, I, K, L, M, N, Q, R, S, T, V, W, Y; X_{19} is one of: A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y; X_{34} is one of: A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y; X_{39} is one of: A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y; and

X_{40} is one of: G, and A. Kunitz scaffold-based binding domains are further described in Intl. Appl. Publ. No. WO 2004063337, the entire contents of which are herein incorporated by reference in their entirety.

[0233] In some embodiments the ASBD (*e.g.,* of an Adapter and/or CAR) is a WW domain-based AD-binding domain. WW domain-based binding scaffolds are generally 30-35 amino acids in length. In some embodiments, the WW domain-based AD binding scaffold comprises the sequence KLPPGWX_7KX_9WS$X_{12}X_{13}X_{14}$GRVX_{18}YX_{20}NX_{22}ITX$_{25}$AX_{27}QWERP (SEQ ID NO: 37), wherein X_7,X_9,X_{12}, X_{13}, X_{14}, X_{18}, X_{20}, X_{22}, X_{25}, and X_{27} represent any amino acid, and X_{14} is optionally absent.

[0234] In some embodiments, the WW domain-based AD binding scaffold comprises the sequence KLPPGWX_7KX_9WS$X_{12}X_{13}$GRVX_{17} YX_{19}NX_{21}ITX$_{24}$AX_{26}QWERP (SEQ ID NO: 38), wherein X_7,X_9,X_{12}, X_{13}, X_{17}, X_{19}, X_{21}, X_{24}, and X_{26} represent any amino acid, and X_{14} is optionally absent.

Table 2. Exemplary loop-based ASBDs

ASBD	Sequence
Avimer1	EFX$_3$CX$_5$NGX$_8$CIPX$_{12}$X$_{13}$WX$_{15}$C DGX$_{19}$DDCGDX$_{25}$SDE (SEQ ID NO: 33)
Fynomer1	GVTLFVALYDYX$_{12}$X$_{13}$X$_{14}$X$_{15}$X$_{16}$X$_{17}$X$_{18}$X$_{19}$X$_{20}$X$_{21}$X$_{22}$LSFHKGEK FQILSTHEYEX$_{41}$X$_{42}$ X$_{43}$X$_{44}$X$_{45}$X$_{46}$X$_{47}$ X$_{48}$WEARSLTTGETGX$_{61}$IPSNY VAPVDSIQ wherein X= any amino acid residue and X$_{13}$-X$_{21}$ and X$_{42}$-X$_{46}$, are optionally absent (SEQ ID NO: 34)
Fynomer2	GVTLFVALYDYX$_{12}$X$_{13}$X$_{14}$X$_{15}$X$_{16}$X$_{17}$X$_{18}$X$_{19}$X$_{20}$X$_{21}$X$_{22}$LSFHKGEKFQILSTHEYEDWWE ARSLTTGETGYIPSNYVAPVDSIQ, wherein X$_{16}$-X$_{21}$ are optionally absent (SEQ ID NO: 35)
Kunitz1	MHSFCAFKADX$_{11}$GXi3CX$_{15}$ X$_{16}$X$_{17}$X$_{18}$X$_{19}$RFFFNIFTRQCEEFX$_{34}$ YGGCX$_{39}$X$_{40}$NQNR FES LEECKK MCTRDGA (SEQ ID NO: 36)
WW1	KLPPGWX$_7$KX$_9$WSX$_{12}$X$_{13}$X$_{14}$GRVX$_{18}$ YX$_{20}$NX$_{22}$ITX$_{25}$AX$_{27}$QWERP (SEQ ID NO: 37)
WW2	KLPPGWX$_7$KX$_9$WSX$_{12}$X$_{13}$GRVX$_{17}$ YX$_{19}$NX$_{21}$ITX$_{24}$AX$_{26}$QWERP (SEQ ID NO: 38)
X = all amino acid residues	

IV. Linkers

[0235] Linkers are peptide or other chemical linkages located between two or more otherwise independent functional domains of the Adapter or CAR.

[0236] Suitable linkers for operably linking two or more functional domains of the Adapter in a single-chain amino acid sequence include but are not limited to, polypeptide linkers such as glycine linkers, serine linkers, mixed glycine/serine linkers, glycine- and serine-rich linkers or linkers composed of largely polar polypeptide fragments.

[0237] In one embodiment, the linker is made up of a majority of amino acids selected from glycine, alanine, proline, asparagine, glutamine, and lysine. In one embodiment, one or more linkers in the Adapter or CAR is made up of a majority of amino acids selected from glycine, alanine, proline, asparagine, aspartic acid, threonine, glutamine, and lysine. In one embodiment, one or more linkers in the Adapter or CAR is made up of one or more amino acids selected from glycine, alanine, proline, asparagine, aspartic acid, threonine, glutamine, and lysine. In another embodiment, one or more linkers in the Adapter or CAR is made up of a

majority of amino acids that are sterically unhindered. In another embodiment, a linker in which the majority of amino acids are glycine, serine, and/or alanine. In some embodiments, one or more linkers in an Adapter or CAR linker comprises polyglycines (such as $(Gly)_5$ (SEQ ID NO:1099), and $(Gly)_8$ (SEQ ID NO:1100), poly(Gly-Ala), and polyalanines. In some embodiments, the peptide linker contains the sequence of Gly-Gly-Gly-Gly-Thr-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 39). In some embodiments, one or more linkers in the Adapter or CAR comprises the sequence of Gly-Gly-Gly-Gly-Asp-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 40).

[0238] In one embodiment, the Adapter or CAR comprises an ADBD directly attached (*i.e.*, without a linker) to another component of the Adapter or CAR, respectively. In one embodiment, the Adapter or CAR contains at least 2, at least 3, at least 4, or at least 5 ADBDs directly attached to another domain of the Adapter or CAR, respectively.

[0239] In another embodiment, an ADBD can be operably linked to another component of the Adapter or CAR through a linker. Adapters or CARs can contain a single linker, multiple linkers, or no linkers. In one embodiment, the Adapter or CAR comprises an ADBD operably linked to another component of the Adapter or CAR, respectively, through a linker peptide. In one embodiment, the Adapter or CAR contains at least 2, at least 3, at least 4, or at least 5 ADBDs operably linked to another domain of the Adapter or CAR, respectively, through the same or different linkers.

[0240] Linkers can be of any size or composition so long as they are able to operably link a functional domain of the Adapter or CAR in a manner that enables the functional domain to function (*e.g.*, the ability of an antigenic determinant binding domain to bind a target of interest). In some embodiments, linker(s) are about 1 to about 100 amino acids, about 1 to 50 amino acids, about 1 to 20 amino acids, about 1 to 15 amino acids, about 1 to 10 amino acids, about 1 to 5 amino acids, about 2 to 20 amino acids, about 2 to 15 amino acids, about 2 to 10 amino acids, or about 2 to 5 amino acids. It should be clear that the length, the degree of flexibility and/or other properties of the linker(s) may have some influence on the properties of the final polypeptide of the invention, including but not limited to the affinity, specificity or avidity for a target of interest, or for one or more other target proteins of interest. When two or more linkers are used in the Adapter or CAR, these linkers may be the same or different. In the context and disclosure provided herein, a person skilled in the art will be able to routinely determine the optimal linker composition and length for the purpose of operably linking the functional domains of an Adapter or CAR.

[0241] The linker can also be a non-peptide linker such as an alkyl linker, or a PEG linker. For example, alkyl linkers such as -NH-(CH2)s-C(0)-, wherein s=2-20 can be used. These alkyl linkers may further be substituted by any non-sterically hindering group such as lower alkyl *e.g.,* C1-C6) lower acyl, halogen (*e.g.,* CI, Br), CN, NH2, phenyl, etc. An exemplary non- peptide linker is a PEG linker. In certain embodiments, the PEG linker has a molecular weight of about 100 to 5000 kDa, or about 100 to 500 kDa.

[0242] Suitable linkers for coupling Adapter or CAR functional domains by chemical cross-linking include, but are not limited to, homo-bifunctional chemical cross-linking compounds such as glutaraldehyde, imidoesters such as dimethyl adipimidate (DMA), dimethyl suberimidate (DMS) and dimethyl pimelimidate (DMP) or N-hydroxysuccinimide (NHS) esters such as dithiobis(succinimidylpropionate)(DSP) and dithiobis (sulfosuccini- midylpropionate)(DTSSP). Examples of suitable linkers for coupling Adapter or CAR functional domains include but are not limited to cross-linkers with one amine-reactive end and a sulfhydryl-reactive moiety at the other end, or with a NHS ester at one end and an SH-reactive group (*e.g.,* a maleimide or pyridyl).

[0243] In additional embodiments, one or more of the linkers in the Adapter or CAR is cleavable. Examples of cleavable linkers include, include but are not limited to a peptide sequence recognized by proteases (in vitro or in vivo) of varying type, such as Tev, thrombin, factor Xa, plasmin (blood proteases), metalloproteases, cathepsins (*e.g.,* GFLG, etc.), and proteases found in other corporeal compartments.

[0244] In some embodiments, the linker is a "cleavable linker" that facilitates the release of an Adapter functional domain or cytotoxic agent in a cell or at the cell surface. For example, an acid-labile linker (*e.g.,* hydrazone), protease-sensitive (*e.g.,* peptidase-sensitive) linker, photolabile linker, dimethyl linker or disulfide-containing linker (*see, e.g.,* Chari, Can. Res. 52: 127-131 (1992); U.S. Pat. No. 5,208,020; and U.S. Appl. Pub. No. 20090110753; the contents of each of which is herein incorporated by reference in its entirety) can be used wherein it is desirable that the covalent attachment between an Adapter or a cytotoxic agent is intracellularly cleaved when the composition is internalized into the cell. The terms "intracellularly cleaved" and "intracellular cleavage" refer to a metabolic process or reaction inside a cell on an Adapter drug conjugate whereby the covalent attachment, *i.e.*, linked via a linker between the Adapter and cytotoxic agent is broken, resulting in the free Adapter and/or cytotoxic agent dissociated inside the cell.

[0245] In additional embodiments, one or more of the linkers in the CAR is cleavable. Examples of cleavable linkers include, include but are not limited to a peptide sequence recognized by proteases (in vitro or in vivo) of varying type, such as Tev, thrombin, factor Xa, plasmin (blood proteases), metalloproteases, cathepsins (*e.g.,* GFLG, etc.), and proteases found in other corporeal compartments.

[0246] In some embodiments, a short oligo- or polypeptide linker, from about 1 to 100 amino acids in length, is used to link together any of the domains of a CAR. Linkers can be composed of flexible residues like glycine and serine (or any other amino acid) so that the adjacent protein domains are free to move relative to one another. The amino acids sequence composition of the linker may be selected to minimize potential immunogenicity of the CAR. Longer linkers can be used when it is desirable to ensure that two adjacent domains do not sterically interfere with one another.

[0247] In some embodiments, preferably between 2 and 10 amino acids in length forms the linkage between the transmembrane domain and the cytoplasmic signaling domain of the CAR. In further embodiments, the

linker is between 10 and 15 amino acids in length, or between 15 and 20, or between 20 and 30, or between 30 and 60, or between 60 and 100 amino acids in length (or any range in between those listed). In further embodiments, the linker is a glycine-serine doublet sequence. In some embodiments, the ESD corresponds to the human T cell surface glycoprotein CD8 alpha-chain ESD region (*e.g.,* amino acid residues 138 to 182 CD8 alpha chain; Swiss-Prot Acc. No. P01732). In some embodiments, the ESD corresponds to the CD8 ESD region that has been further modified, through amino acid substitution, to improve expression function or immunogenicity. In further embodiments, the ESD corresponds to the CD28 ESD or sequences containing modifications of the CD28 ESD that confer improved expression function or immunogenicity.

[0248] Linker optimization can be evaluated using techniques described herein and/or otherwise known in the art. In some embodiments, linkers do not disrupt the ability of an Adapter or CAR to bind a target antigenic determinant and/or another Adapter or CAR functional domain to function appropriately (*e.g.,* the ability of an effector functional domain in the Adapter to elicit an effector function or the ability of an FcRn binding domain in the Adapter to bind FcRn).

V. Adapters - Soluble Proteins

[0249] Provided herein are multi-domain soluble Adapter proteins. The Adapter comprises an antigenic determinant (AD) (*e.g.,* as described in Section II) and an antigenic determinant binding domain (ADBD) (*e.g.,* as described in Section III). The Adapter can further comprise additional ADs, additional ADBDs, and/or other additional domains.

[0250] In an Adapter provided herein, the AD can be N-terminal to ADBD. Alternatively, the ADBD can be N-terminal to the AD. In some embodiments, the AD and ADBD are directly fused. In some embodiments, the AD and the ADBD are fused via a linker (a protein linker or chemical linker) or another protein domain (*e.g.,* a functional domain).

[0251] In some embodiments, the Adapter comprises a linker located between an ADBD and another functional domain of the Adapter. In some embodiments, the linker is located between two ADBDs of the Adapter. In some embodiments, the linker is located between the AD and an ADBD of the Adapter. Suitable linkers for coupling the two or more functional domains of the Adapter will be clear to persons skilled in the art and may generally be any linker used in the art to link peptides, proteins or other organic molecules. Exemplary linkers are provided in Section IV. In particular embodiments, the linker(s) is suitable for constructing proteins or polypeptides that are intended for pharmaceutical use.

[0252] In addition to the AD (or multiple ADs) and the ADBD (or multiple ADBDs), an Adapter provided herein can further comprise an additional domain or additional domains, *e.g.,* a domain that confers an extended half-life.

[0253] In some embodiments, the Adapter, or the ADBD in the Adapter, is deimmunized.

[0254] The Adapters provided herein have uses that include but are not limited to diagnostic, analytic, and therapeutic applications. In particular embodiments, the Adapters are used in combination with chimeric antigen receptors (CARs) (*e.g.,* as described in Section VI) expressed on the surface of cells (*e.g.,* as described in Section VII), *e.g.,* to kill a target cell.

Va. Antigenic Determinants (ADs)

[0255] An Adapter provided herein comprises at least one antigenic determinant (AD). In some embodiments, the Adapter comprises a single AD. In some embodiments, the Adapter comprises two or more ADs. Where an Adapter comprises two or more ADs, the ADs can be the same or different.

[0256] In an Adapter provided herein, the AD can be any AD or combination of ADs (*e.g.,* as described in Section II).

[0257] In some embodiments, the Adapter comprises the extracellular domain of BCMA (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 5. In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 5.

[0258] In some embodiments, Adapter comprises the extracellular domain of CD123 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 11. In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 11.

[0259] In some embodiments, the Adapter comprises the extracellular domain of CD19 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 2 or 3. In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 2 or 3.

[0260] In some embodiments, the Adapter comprises the extracellular domain of CD20. In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 6-9, or 10.

[0261] In some embodiments, the Adapter comprises the extracellular domain of CD22 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 41). In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 41.

[0262] In some embodiments, the Adapter comprises the extracellular domain of CD37 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 12 or 13). In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 12 or 13.

[0263] In some embodiments, the Adapter comprises the extracellular domain of CS1 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 1138). In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 1138.

[0264] In some embodiments, the Adapter comprises the extracellular domain of HER2 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 42). In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 42.

[0265] In some embodiments, the Adapter comprises the extracellular domain of CD45 (*e.g.,* a polypeptide comprising the sequence of residues 29-766 of SEQ ID NO: 1106). In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of residues 29-766 of SEQ ID NO: 1106.

[0266] In some embodiments, the Adapter comprises the extracellular domain of CD26, CD30, CD33, or CD38. In some embodiments, the Adapter comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of the extracellular domain of CD26, CD30, CD33, or CD38.

[0267] In some embodiments, the AD is an epitope of AFP. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 15.

[0268] In some embodiments, the AD is an epitope of AFP p26. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 16. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of SEQ ID NO: 1117. In further embodiments, the AD comprises the amino acid residues of SEQ ID NO: 16, 1117, 1118, 1119, 1120, 1121, 1122, or 1123.

[0269] In some embodiments, Adapter comprises a p26 protein (*e.g.*, having the sequence of SEQ ID NO: 16, 1117, 1118, 1119, 1120, 1121, 1122, or 1123). Such fusion proteins containing p26 sequences have been discovered herein to have surprisingly long serum half-life. In some embodiments, the Adapter has a plasma half-life *in vivo* of at least 1 hour, at least 2 hours, at least 4 hours, at least 8 hours, at least 16 hours, at least 32 hours, at least 64 hours, or more. In some embodiments, the Adapter has an *in vivo* plasma half-life of at least 1 hour, at least 2 hours, at least 4 hours, at least 8 hours, at least 16 hours, at least 32 hours, at least 64 hours, or more hours 65 hours, or 1-10 hours, 2-10 hours, 4-10 hours, 6-10 hours, or 6-9 hours in a mouse. In some embodiments, the Adapter has an *in vivo* plasma half-life of at least 1 hour, at least 2 hours, at least 4

hours, at least 8 hours, at least 16 hours, at least 32 hours, at least 64 hours, or more hours 65 hours, or 1-10 hours, 2-10 hours, 4-10 hours, 6-10 hours, or 6-9 hours, in a human.

[0270] In some embodiments, the disclosure provides a method for modifying the *in vivo* half-life (*e.g.*, in a mouse or human) of an Adapter comprising a p26 protein (*e.g.*, having the sequence of SEQ ID NO: 16, 1117, 1118, 1119, 1120, 1121, 1122, or 1123). In some embodiments, the Adapter comprises one or more target-binding DDpp. In some embodiments, the half-life of the Adapter is increased or decreased by substituting or deleting one or more amino acid residues normally found in the human p26 protein, or by inserting one or more amino acid residues not normally found in the human p26 protein. In another embodiment, the p26 sequence of the Adapter is modified through 1, 2, 3, 5, 5, 10, or 1-20, 1-10, 3-10, or 3-5, amino acid substitutions (conservative and/or nonconservative substitutions), deletions, and/or insertions so as to increase or decrease the *in vivo* half-life of the Adapter. In a particular embodiment, the amino acid residue corresponding to the glutamine (Gln, Q) at position 217 of p26 (SEQ ID NO: 16) is substituted with another amino acid residues. In a futher embodiment, the substitution is Gln217Pro. In another embodiment, the p26 sequence of the Adapter is modified through deletion of 1-150, 1-100, 1-50, 1-25 or 1-10 amino acid residues so as to increase or decrease the *in vivo* half-life of the Adapter. In additional embodiments, the p26 sequence of the Adapter is modified through 1, 2, 3, 5, 5, 10 or 1-20, 1-10, 3-10, or 3-5, amino acid substitutions (conservative and/or nonconservative substitutions), deletions, and/or insertions so as to increase or decrease the interaction of the Adapter with FcRn.

[0271] In some embodiments, the AD (*e.g.,* in an Adapter and/or on a target cell) is an AD that is present in a naturally occurring protein or other molecule. In some embodiments, the AD is an AD that is endogenous to humans.

[0272] In some embodiments, the AD is an epitope of a human intracellular protein. In further embodiments, the AD is an epitope of a human intracellular protein selected from: elastinTyk2, Jak1, Jak2, Jak3, LCK, ZAP-70, and GRB2. In further embodiments, the AD comprises 5-25, 5-50, 5-75, 5-100, 5-125, or 5-150 amino acid residues, more than 150 amino acid residues, or all of the amino acid residues of the intracellular protein.

[0273] In some embodiments, the target of interest specifically bound by the ADBD of an Adapter is itself an AD of another Adapter, having a different sequence.

Vb. Antigenic Determinant Binding Domains (ADBDs)

[0274] An Adapter provided herein comprises at least one antigenic determinant binding domain (ADBD). In some embodiments, the Adapter contains one ADBD. In some embodiments, the Adapter contains at least 2, 3, 4, or 5, or more than 5 ADBDs. In some embodiments, the Adapter contains 1-3, 1-4, 1-5, or more than 5 different ADBDs. In some embodiments, the Adapter contains at least 2, 3, 4, or 5, or more than 5 different ADBDs. Thus, an Adapter can comprise a monomeric ADBD (*i.e.*, containing one antigenic determinant

binding domain) or multimeric ADBDs (*i.e.*, containing more than one antigenic determinant binding domains in tandem optionally operably connected by a linker). In some embodiments, the use of a multimeric Adapter provides enhanced (*e.g.,* synergistic) target binding. In additional embodiments, the use of a multimeric Adapter allows for targeting of more than one target using a single Adapter construct (*e.g.,* bi-, tri-specific, etc.).

[0275] The multimeric Adapter is homo-multimeric (*i.e.*, containing more than one of the same ADBD optionally connected by linker(s)(*e.g.,* homodimers, homotrimers, homotetramers etc.) or Adapter hetero-multimeric (*i.e.*, containing two or more antigenic determinant binding domains in which there are at least two different antigenic determinant binding domains). The number of ADBDs included in any particular Adapter may vary, depending on the embodiment, and may be defined, at least in part, by the expression system in which the Adapter is produced. In several embodiments, however, the fusion proteins may comprise multimers of about 5 to about 10 ADBDs, about 10 to about 15 ADBDs, about 15 to about 20 ADBDs, about 20 to about 25 ADBDs, or about 25 to about 30 ADBDs (including numbers in between those listed as well as endpoints). Moreover, multiple domains of an Adapter can contain the same or different ADBD(s). In some embodiments, 2, 3, 4, 5, or more than 5 domains are in tandem.

[0276] In one embodiment, the Adapter comprises two or more ADBDs that are operably linked. In one embodiment, the Adapter comprises two ADBDs that bind to the same or different ADs on a target antigen. The linkage of two or more identical ADBDs that bind to the same target antigen results in a multivalent molecule that provides distinct advantages (*e.g.,* increased binding avidity, target clustering and receptor activation) over compositions that only contain one ADBD for a target antigen. In another embodiment the Adapter comprises two ADBDs that bind to different antigens. In some embodiments the Adapter comprises two ADBDs that bind to different antigens on the same cell. In some embodiments the Adapter comprises two ADBDs that bind to different antigens on different cells. The linkage of two or more ADBDs results in a multivalent and multi-specific Adapter that has the potential to bind more than one target antigen, either independently or simultaneously. In some embodiments, the multivalent Adapter is able to bind the same target antigen simultaneously. In some embodiments, the multivalent Adapter is able to bind different target antigens simultaneously. In some embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an Antigenic Determinant. In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant. In further

embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD26, CD30, CD33, or CD38 Antigenic Determinant.

[0277] An ADBD in the Adapter provided herein can bind to any AD (*e.g.,* as described in Section II). In some embodiments, the ADBD binds to BCMA (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 5). In some embodiments, the ADBD binds to CD123 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 11). In some embodiments, the ADBD binds to CD22 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 41). In some embodiments, the ADBD binds to CD19 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 3). In some embodiments, the ADBD binds to CD20 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 6-9 or 10). In some embodiments, the ADBD binds to CD37 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 12 or 13). In some embodiments, the ADBD binds to CS1 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 1138). In some embodiments, the ADBD binds to HER2 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 42). In some embodiments, the ABDB binds to CD45. In some embodiments, the ABDB in the Adapter provided herein specifically binds to an AD of human CD26, CD30, CD33, or CD38.An Adapter can be "monospecific" or "multi-specific." An Adapter that is "multi-specific" (*e.g.,* bispecific, trispecific or of greater multi-specificity) recognizes and binds to two or more different epitopes present on one or more different molecules.

[0278] In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of BCMA (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO 4). In some embodiments, Adapter comprises a domain (*e.g.,* the extracellular domain) of CD123 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 11). In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of CD22 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 24). In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of CD19 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 3). In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of CS1 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 1138). In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of HER2 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 42). In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of CD45. In some embodiments, the Adapter comprises a domain (*e.g.,* the extracellular domain) of CD26, CD30, CD33, or CD38. In some embodiments, the Adapter comprises a fragment of a domain. In further embodiments, the Adapter comprises a fragment of a domain having an amino acid sequence selected from the group: SEQ ID NO: 4 or 5, SEQ ID NO: 11, SEQ ID NO: 24, and SEQ ID NO: 3. In some embodiments, the Adapter comprises a fragment of a domain that is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-

200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150, amino acids in length.

[0279] In some embodiments, the Adapter contains at least two ADBDs that bind and cross-link one or more target antigens bound by the ADBDs and/or complexes containing the target antigen(s). In some embodiments, the cross-linked antigen(s) is on the same cell. In some embodiments, the cross-linked antigen(s) is on different cells. In some embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an Antigenic Determinant (*e.g.,* a domain described above). In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD26, CD30, CD33, or CD38 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant.

[0280] In some embodiments, the Adapter contains at least two of the same ADBDs (*i.e.*, is multivalent). In some embodiments, the multivalent Adapter is able to bind two or more of the same target antigens simultaneously. In some embodiments, the Adapter is multivalent and is able to bind the same target antigen simultaneously. In some embodiments, the multi-multivalent Adapter comprises two or more operably linked ADBDs that are separated by an Antigenic Determinant. In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the multivalent Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the multivalent Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the multivalent Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant.

[0281] In some embodiments, the Adapter contains at least two ADBDs that bind to different antigens (*i.e.*, is multispecific). In some embodiments, the multi-specific Adapter is able to bind the different target antigens simultaneously. In some embodiments, the Adapter is also multivalent and is able to bind the same target antigen simultaneously. In some embodiments, the multi-specific Adapter comprises two or more operably

linked ADBDs that are separated by an Antigenic Determinant. In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant.

[0282] In one embodiment, a multi-specific Adapter contains at least two ADBDs that bind to at least two different epitopes on a single target of interest (*i.e.*, is multiepitotic for the same target antigen). In additional embodiments, a multi-specific Adapter comprises at least one ADBD that specifically binds one epitope on a target of interest and at least one other ADBD that specifically binds to a different epitope on the same target antigen. In one embodiment, a multi-specific Adapter comprises at least one ADBD that specifically binds to an epitope on a first target antigen and at least one ADBD that specifically binds to an epitope on a second antigen. In some embodiments, the Adapter comprises at least one ADBD that specifically binds to an epitope on a first target antigen on a cell and at least one ADBD that specifically binds to an epitope on a second antigen on the same cell. In some embodiments, the Adapter comprises at least one ADBD that specifically binds to an epitope on a first target antigen on a cell and at least one ADBD that specifically binds to an epitope on a second antigen on a different cell.

[0283] In a further embodiment, the Adapter comprises 2 or more ADBDs that are operably linked with other heterologous proteins (or their subdomains) and in so doing, impart the multivalent, multi-specific, and/or functional properties (*e.g.,* pharmacokinetics such as increased half-life) of the fusion partner to the Adapter fusion protein. Examples of fusion partners of an Adapter include but are not limited to, antibodies, antibody subdomains (*e.g.,* scFv or Fc domains), serum albumin, serum albumin subdomains, cell surface receptors, an alpha chain of a T cell receptor (TCR), a beta chain of a T cell receptor, cell surface receptor subdomains, peptides, peptide tags (*e.g.,* FLAG or myc). The number and location of ADBDs and their respective positions within the Adapter can vary. For example, ADBDs can be located at one or all termini of a fusion partner and/or interspersed within heterologous subunits within the Adapter fusion partner. In some embodiments the Adapter comprises 2 or more ADBDs that are separated by a heterologous protein (*e.g.,* Antigenic Determinant). In some embodiments, the heterologous protein is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the heterologous protein is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length.

[0284] In one embodiment, the Adapter is bispecific and contains ADBDs that specifically bind to two different target antigens. In further embodiments, the bispecific Adapter specifically binds to two different target antigens expressed on the surface of two different cell types. In further embodiments, the bispecific Adapter specifically binds to two different target antigens expressed on the surface of a tumor cell. In further embodiments, the bispecific Adapter specifically binds to two different target antigens expressed on the surface of a multiple myeloma cell (e.g., BCMA and CS1). In one embodiment, the bispecific Adapter binds to target antigens expressed on different cells. In a further embodiment, the bispecific Adapter binds to target antigens expressed on different cells of a tumor. In another embodiment, the bispecific Adapter binds to target antigens expressed on different cells within a tumor vasculature or tumor microenvironment. In one embodiment, the bispecific Adapter specifically binds to a cancer cell target and an immune effector cell target. In one embodiment the bispecific Adapter specifically binds a target expressed on a cancer cell (*e.g.* CD19) and a target expressed on the surface of a T lymphocyte (*e.g.,* CD3 or CD45).). In some embodiments, the bispecific Adapter is able to bind the different target antigens simultaneously. In some embodiments, the bispecific Adapter comprises two or more operably linked ADBDs that are separated by an Antigenic Determinant. In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant.

[0285] In some embodiments where the Adapter comprises more than one ADBD, the ADBD can be any of the types of ADBD discussed herein (*e.g.,* any ADBD described in Section III above and in). For example, an ADBD can be an antibody, an antigen-binding fragment thereof, a ScFv, an alternative scaffold binding domain, a D domain, a T cell receptor, or an antigen-binding fragment thereof.

[0286] In some embodiments, where an Adapter comprises more than one ADBD, those ADBD can be the same types of antigen-binding molecules or can be different. For example, an Adapter can comprise two ADBD that are D domains. The two ADBD that are D domains can be the same or different. An Adapter can also comprise an ADBD that is a D domain and an ADBD that is a scFv. An Adapter can also comprise an ADBD that is a T cell receptor or antigen-binding fragment thereof and an ADBD that is a scFv. In some embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an Antigenic Determinant. In some embodiments, the Antigenic Determinant is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, or 500 amino acids in length. In some embodiments, the Antigenic Determinant is 5-500, 5-

400, 10-300, 5-200, 50-100, 5-50, 10-500, 10-400, 10-300, 10-200, 10-100, 10-50, 50-500, 50-400, 50-300, 50-200, 50-100 50-75, 100-500, 100-400, 100-300, 100-200, or 100-150 amino acids in length. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a BCMA Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by a CD45 Antigenic Determinant. In further embodiments, the Adapter comprises two or more operably linked ADBDs that are separated by an AFP P26 Antigenic Determinant.

[0287] In some embodiments, the ADBD of the Adapter is deimmunized.

[0288] In some embodiments, the Adapter comprises an ABDB that binds to an antigen target containing an AD of interest, and has no discernable impact on the function of the target. Alternatively, in some embodiments, the Adapter comprises an ADBD that binds to an antigen target containing an AD of interest and completely or partially inhibits, antagonizes, agonizes, blocks, increases, stimulates, or interferes with the biological activity of the target. Binding can be identified as agonistic or antagonistic and determined using or routinely modifying assays, bioassays, and/or animal models known in the art for evaluating such activity.

[0289] An Adapter agonist refers to an Adapter that in some way increases or enhances the biological activity of the Adapter target or has biological activity comparable to a known agonist of the Adapter target. In another embodiment, the Adapter is an antagonist of the target it binds. An Adapter antagonist refers to an Adapter that completely or partially blocks or in some way interferes with the biological activity of the Adapter target or has biological activity comparable to a known antagonist or inhibitor of the Adapter target.

[0290] In one embodiment an Adapter specifically binds a target of interest that is a serum protein. In one embodiment, an Adapter specifically binds a serum protein selected from: serum albumin (*e.g.,* human serum albumin (HSA)), thyroxin-binding protein, transferrin, fibrinogen, and an immunoglobulin (*e.g.,* IgG, IgE and IgM). Without being bound by theory, the binding of an Adapter to a carrier protein is believed to confer upon the Adapter an improved pharmacodynamic profile that includes, but is not limited to, improved tumor targeting, tumor penetration, diffusion within the tumor, and enhanced therapeutic activity compared to the Adapter in which the carrier protein binding sequence is missing (*see*, *e.g.,* WO 01/45746, the contents of which are herein incorporated by reference in its entirety).

[0291] In one embodiment the target of interest specifically bound by an Adapter is a disease-related antigen. The antigen can be an antigen characteristic of a cancer, and/or of a particular cell type (*e.g.,* a hyperproliferative cell), and/or of a pathogen (*e.g.,* a bacterial cell (*e.g.,* tuberculosis, smallpox, and anthrax), a virus (*e.g.,* HIV and H), a parasite (*e.g.,* malaria and leishmaniosis), a fungal infection, a mold, a mycoplasm, a prion antigen, or an antigen associated with a disorder of the immune system.

[0292] In an additional embodiment, the target of interest bound by an Adapter (is a bacterial antigen, a viral antigen, a fungal antigen, a mycoplasm antigen, a prion antigen, or a parasite antigen (*e.g.,* one infecting a mammal). In one embodiment, the target of an Adapter is human papillomavirus anthrax, hepatitis b, rabies,

Nipah virus, west Nile virus, a meningitis virus, or CMV. In an additional embodiment, an Adapter specifically binds a pathogen.

Vc. Adapter functional domain(s)

[0293] In some embodiments, the Adapter comprises a first antigenic determinant (an AD), a domain that binds to a second antigenic determinant (an ADBD), and further comprises a functional domain that confers one or more additional desirable properties (*e.g.,* improved manufacturing) and/or pharmacokinetic properties (*e.g.,* improved half-life). The functional domain of the Adapter can be located between the AD and the ADBD. The Adapter can also be located N-terminal to both the AD and ADBD or C-terminal to both the AD and ADBD. In some embodiments, where the Adapter comprises two or more ADs, the functional domain of the Adapter can be located between two or more ADs, N-terminal to two or more ADs, or C-terminal to two or more ADs. In some embodiments, where the Adapter comprises two or more ADBDs, the functional domain of the Adapter can be located between two or more ADBDs, N-terminal to two or more ADBDs, or C-terminal to two or more ADBDs.

[0294] In some embodiments, the Adapter comprises a functional domain selected from: an Fc or variant Fc (*e.g.,* a human Fc or variant Fc domain) or a fragment thereof, a serum protein (*e.g.,* human serum albumin) or a fragment thereof; an FcRn binding domain; a serum protein binding domain; a cytokine, growth factor, hormone, or enzyme; an imaging agent; a labeling agent; and a peptide tag.

[0295] The functional domain(s) of the Adapter can be naturally derived or the result of recombinant engineering (*e.g.,* phage display, xenomouse, or synthetic). In certain embodiments, the functional domain of the Adapter enhances half-life, increases or decreases antibody dependent cellular cytotoxicity (ADCC), and/or increases or decreases complement dependent cytotoxicity (CDC) activity.

[0296] In some embodiments, the Adapter comprises a functional domain selected from: an Fc or variant Fc (*e.g.,* a human Fc or variant human Fc domain) or a fragment or derivative thereof, a serum protein (*e.g.,* human serum albumin) or a fragment or derivative thereof (*e.g.,* a serum protein binding domain); an FcRn binding domain; and a serum protein binding domain.

[0297] In one embodiment, an Adapter comprises a functional domain that comprises an antibody effector domain or derivative of an antibody effector domain that confers one or more effector functions to the Adapter, such as the ability to bind to one or more Fc receptors. In some embodiments, the functional domain comprises one or more CH2 and or CH3 domains of an antibody having effector function provided by the CH2 and CH3 domains. In some embodiments, the functional domain comprises one or more derivatives of CH2 and/or CH3 domains of an antibody having effector function provided by the CH2 and CH3 domains. Other sequences that can be included in the Adapter to provide an effector function and that are encompassed by the invention will be clear to those skilled in the art and can routinely be chosen and designed into an Adapter encompassed herein on the basis of the desired effector function(s).

[0298] In one embodiment, the Adapter comprises a functional domain that increases the antibody dependent cellular cytotoxicity (ADCC) conferred by the Adapter (*see*, *e.g.,* Bruhns *et al.*, Blood 113: 3716-3725 (2009); Shields *et al.*, J. Biol. Chem. 276: 6591-6604 (2001); Lazar *et al.*, PNAS 103: 4005-4010 (2006); Stavenhagen *et al.*, Cancer Res. 67: 8882-8890 (2007); Horton *et al.*, Cancer Res. 68: 8049-8057 (2008); Zalevsky *et al.*, Blood 113: 3735-3743 (2009); Bruckheimer, Neoplasia 11: 509-517 (2009); WO2006/020114; Strohl, Curr. Op. Biotechnol. 20: 685-691 (2009); and WO2004/074455, each of which is herein incorporated by reference in its entirety). Examples of fragment engineering modifications of effector function conferring portions of an Fc contained in the functional domain of an Adapter that increases ADCC include one or more modifications corresponding to: IgGl- S298A, E333A, K334A; IgGl-S239D, I332E; IgGl-S239D, A330L, I332E; IgGl-P247I, A339D or Q; IgGl-D280H, K290S with or without S298D or V; IgGl-F243L, R292P, Y300L; IgGl-F243L, R292P, Y300L, P396L; and IgGl-F243L, R292P, Y300L, V305I, P396L; wherein the numbering of the residues in the Fc region is that of the EU index of Kabat *et al.* (Kabat *et al.*, Sequences of proteins of Immunological Interest, 1991 Fifth edition).

[0299] Accordingly, in some embodiments, the Adapter comprises a functional domain that comprises an antibody fragment that confers upon the Adapter a biological or biochemical characteristic of an immunoglobulin. In some embodiments, the antibody fragment confers a characteristic selected from: the ability to non-covalently dimerize, the ability to localize at the site of a tumor, and an increased serum half-life when compared to an Adapter without the antibody fragment. In certain embodiments, the Adapter is at least as stable as the corresponding antibody fragment without the Adapter. In certain embodiments, the Adapter is more stable than the corresponding antibody fragment without the Adapter. Adapter protein stability can be measured using established methods, including, for example, ELISA techniques. In some embodiments, the Adapter is stable in whole blood (*in vivo* or *ex vivo*) at 37° C for at least about 10 hours, at least about 15 hours, at least about 20 hours, at least about 24 hours, at least about 25 hours, at least about 30 hours, at least about 35 hours, at least about 40 hours, at least about 45 hours, at least about 48 hours, at least about 50 hours, at least about 55 hours, at least about 60 hours, at least about 65 hours, at least about 70 hours, at least about 72 hours, at least about 75 hours, at least about 80 hours, at least about 85 hours, at least about 90 hours, at least about 95 hours, or at least about 100 hours (including any time between those listed). In one embodiment, the Adapter contains an immunoglobulin effector domain or half-life influencing domain that corresponds to an immunoglobulin domain or fragment in which at least a fraction of one or more of the constant region domains has been altered so as to provide desired biochemical characteristics such as reduced or increased effector functions, the ability to non-covalently dimerize, increased ability to localize at the site of a tumor, reduced serum half-life, or increased serum half-life when compared with an immunoglobulin fragment having the corresponding unaltered immunoglobulin sequence. These alterations of the constant region domains can be amino acid substitutions, insertions, or deletions.

[0300] In one embodiment, the Adapter comprises a functional domain that comprises an amino acid sequence of an immunoglobulin effector domain or a derivative of an immunoglobulin effector domain that confers antibody dependent cellular cytotoxicity (ADCC) to the Adapter. In additional embodiments, the Adapter comprises a sequence of an immunoglobulin effector domain that has been modified to increase ADCC (*see, e.g.,* Bruhns, Blood 113: 3716-3725 (2009); Shields, J. Biol. Chem. 276: 6591-6604 (2001); Lazar, PNAS 103: 4005-4010 (2006); Stavenhagen, Cancer Res. 67: 8882-8890 (2007); Horton, Cancer Res. 68: 8049-8057 (2008); Zalevsky, Blood 113: 3735-3743 (2009); Bruckheimer, Neoplasia 11: 509-517 (2009); WO 06/020114; Strohl, Curr. Op. Biotechnol. 20: 685-691 (2009); and WO 04/074455, the contents of each of which is herein incorporated by reference in its entirety). Examples of immunoglobulin fragment engineering modifications contained in an amino acid sequence in the Adapter that increases ADCC include immunoglobulin effector domain sequences having one or more modifications corresponding to: IgG1-S298A, E333A, K334A; IgG1-S239D, I332E; IgG1-S239D, A330L, I332E; IgG1-P247I, A339D or Q; IgG1-D280H, K290S with or without S298D or V; IgG1-F243L, R292P, Y300L; IgG1-F243L, R292P, Y300L, P396L; and IgG1-F243L, R292P, Y300L, V305I, P396L; wherein the numbering of the residues in the Fc region is that of the EU index of Kabat *et al.* (Kabat *et al.*, Sequences of proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference).

[0301] In additional embodiments, the Adapter comprises a functional domain that comprises the amino acid sequence of an immunoglobulin effector domain, or a derivative of an immunoglobulin effector domain, that confers antibody-dependent cell phagocytosis (ADCP) to the Adapter. In additional embodiments, the Adapter comprises a sequence of an immunoglobulin effector domain that has been modified to increase antibody-dependent cell phagocytosis (ADCP); (*see, e.g.,* Shields *et al.*, J. Biol. Chem. 276: 6591-6604 (2001); Lazar *et al.*, PNAS 103: 4005-4010 (2006); Stavenhagen *et al.*, Cancer Res. 67: 8882-8890 (2007); Richards *et al.*, Mol. Cancer Ther. 7: 2517-2527 (2008); Horton *et al.*, Cancer Res. 68: 8049-8057 (2008), Zalevsky *et al.*, Blood 113: 3735-3743 (2009); Bruckheimer *et al.*, Neoplasia 11: 509-517 (2009); WO 06/020114; Strohl, Curr. Op. Biotechnol. 20: 685-691 (2009); and WO 04/074455, the contents of each of which is herein incorporated by reference in its entirety). Examples of immunoglobulin fragment engineering modifications contained in an amino acid sequence in the Adapter that increases ADCP include immunoglobulin effector domain sequences having one or more modifications corresponding to: IgG1-S298A, E333A, K334A; IgG1-S239D, I332E; IgG1-S239D, A330L, I332E; IgG1-P247I, A339D or Q; IgG1-D280H, K290S with or without S298D or V; IgG1-F243L, R292P, Y300L; IgG1-F243L, R292P, Y300L, P396L; IgG1-F243L, R292P, Y300L, V305I, P396L; and IgG1-G236A, S239D, I332E; wherein the numbering of the residues is that of the EU index of Kabat *et al.* (Kabat *et al.*, Sequences of proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference).

[0302] In additional embodiments, the Adapter comprises a functional domain that comprises an amino acid sequence of an immunoglobulin effector domain, or a derivative of an immunoglobulin effector domain, that confers complement-dependent cytotoxicity (CDC) to the Adapter. In additional embodiments, the Adapter comprises a sequence of an immunoglobulin effector domain that has been modified to increase complement-dependent cytotoxicity (CDC) (*see*, *e.g.,* Idusogie *et al.*, J. Immunol. 166: 2571-2575 (2001); Strohl, Curr. Op. Biotechnol. 20: 685-691 (2009); and Natsume *et al.*, Cancer Res. 68: 3863-3872 (2008), the contents of each of which is herein incorporated by reference in its entirety). By way of example, Adapters can contain an antibody fragment or domain that contains one or more of the following modifications that increase CDC: IgG1-K326A, E333A; IgG1-K326W, E333S, IgG2-E333S; wherein the numbering of the residues is that of the EU index of Kabat *et al.* (Sequences of proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference).

[0303] In additional embodiments, the Adapter comprises a functional domain that comprises an amino acid sequence of an immunoglobulin effector domain, or a derivative of an immunoglobulin effector domain, that confers the ability to bind FcgammaRIIb receptor to the Adapter. In additional embodiments, the Adapter comprises a sequence of an immunoglobulin effector domain that has been modified to increase inhibitory binding to FcgammaRIIb receptor (*see*, *e.g.,* Chu *et al.*, Mol. Immunol. 45: 3926-3933 (2008)). An example of an immunoglobulin fragment engineering modification contained in an amino acid sequence in the Adapter that increases binding to inhibitory FcgammaRIIb receptor is IgG1- S267E, L328F.

[0304] The half-life of an IgG is mediated by its pH-dependent binding to the neonatal receptor FcRn. In certain embodiments the Adapter contains a functional domain that comprises an amino acid sequence of an immunoglobulin effector domain, or a derivative of an immunoglobulin effector domain, that confers the ability to bind neonatal receptor FcRn to the Adapter. In certain embodiments the Adapter contains a functional domain that comprises a sequence of an immunoglobulin FcRn binding domain that has been modified to enhance binding to FcRn (*see*, *e.g.,* Petkova *et al.*, Int. Immunol. 18: 1759-1769 (2006); Dall'Acqua *et al.*, J. Immunol.169: 5171-5180 (2002); Oganesyan *et al.*, Mol. Immunol. 46: 1750-1755 (2009); Dall'Acqua *et al.*, J. Biol. Chem. 281: 23514-23524 (2006), Hinton *et al.*, J. Immunol. 176: 346-356 (2006); Datta-Mannan *et al.*, Drug Metab. Dispos. 35: 86-94 (2007); Datta-Mannan *et al.*, J. Biol. Chem. 282: 1709-1717 (2007); WO 06/130834; Strohl, Curr. Op. Biotechnol. 20: 685-691 (2009); and Yeung *et al.*, J. Immunol. 182: 7663-7671 (2009), the contents of each of which is herein incorporated by reference in its entirety).

[0305] In additional embodiments, the Adapter comprises a functional domain that comprises a sequence of an immunoglobulin effector domain that has been modified to have a selective affinity for FcRn at pH 6.0, but not pH 7.4. By way of example, the Adapter functional domain can contain an antibody fragment or domain that contains one or more of the following modifications that increase half-life: IgG1-M252Y, S254T, T256E;

IgG1-T250Q, M428L; IgG1-H433K, N434Y; IgG1-N434A; and IgG1-T307A, E380A, N434A; wherein the numbering of the residues is that of the EU index of Kabat *et al.* (Kabat *et al.*, Sequences of Proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference).

[0306] According to another embodiment, the Adapter comprises a functional domain that comprises an amino acid sequence corresponding to a immunoglobulin effector domain that has been modified to contain at least one substitution in its sequence corresponding to the Fc region (*e.g.,* Fc gamma) position selected from: 238, 239, 246, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, 276, 278, 280, 283, 285, 286, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, 309, 312, 315, 320, 322, 324, 326, 327, 329, 330, 331, 332, 333, 334, 335, 337, 338, 340, 360, 373, 376, 378, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438, and 439, wherein the numbering of the residues in the Fc region is according to the EU numbering system; of Kabat *et al.* (Sequences of proteins of Immunological Interest, 1991 Fifth edition, herein incorporated by reference). In a specific embodiment, the Adapter contains a functional domain that comprises a sequence of an immunoglobulin effector domain derivative wherein at least one residue corresponding to position 434 is a residue selected from: A, W, Y, F and H. According to another embodiment, the Adapter comprises a sequence of an immunoglobulin effector fragment derivative having the following respective substitutions S298A/E333A/K334A. In an additional embodiment, the Adapter comprises an immunoglobulin effector domain derivative having a substitution corresponding to K322A. In another embodiment, the Adapter comprises a sequence of an immunoglobulin effector domain derivative having one or any combination of the following substitutions K246H, H268D, E283L, S324G, S239D and I332E. According to yet another embodiment, the Adapter comprises a sequence of an immunoglobulin effector domain derivative having substitutions corresponding to D265A/N297A.

[0307] In certain embodiments, the Adapter comprises a functional domain that comprises a sequence of an immunoglobulin effector domain that has been glycoengineered or mutated to increase effector function using techniques known in the art. For example, the inactivation (through point mutations or other means) of a constant region domain sequence contained in the Adapter may reduce Fc receptor binding of the circulating Adapter thereby increasing tumor localization. In other cases it may be that constant region modifications consistent with certain embodiments of the instant invention moderate complement binding and thus reduce the serum half-life and nonspecific association of a conjugated cytotoxin. Yet other modifications of the constant region may be used to modify disulfide linkages or oligosaccharide moieties that allow for enhanced localization due to increased antigen specificity or antibody flexibility. The resulting physiological profile, bioavailability and other biochemical effects of the modifications, such as tumor localization, biodistribution and serum half-life, can easily be measured and quantified using well know immunological techniques without undue experimentation.

Adapter as Chemical Conjugates

[0308] Adapter that promote specific binding to targets of interest can be chemically conjugated with a variety of compound such as fluorescent dyes, radioisotopes, chromatography compositions (*e.g.,* beads, resins, gels, etc.) and chemotherapeutic agents. Adapter conjugates have uses that include but are not limited to purification, diagnostic, analytic, manufacturing and therapeutic applications.

[0309] The inherent lack of cysteines in the Adapter sequence provides the opportunity for introduction of unique cysteines for purposes of site-specific conjugation.

[0310] In some embodiments, the Adapter contains at least one reactive residue. Reactive residues are useful, for example, as sites for the attachment of conjugates such as chemotherapeutic drugs. The reactive residue can be, for example, a cysteine, a lysine, or another reactive residue. Thus, a cysteine can be added to an Adapter at either the N- or C- terminus, or within the Adapter sequence. A cysteine can be substituted for another amino acid in the sequence of an Adapter. In addition, a lysine can be added to an Adapter at either end or within the Adapter sequence and/or a lysine can be substituted for another amino acid in the sequence of an Adapter. In one embodiment, a reactive residue (*e.g.,* cysteine, lysine, etc.,) is located in a loop sequence of an ADBD (*e.g.,* Z1 and Z2 of SEQ ID NOS: 22-25, or 26). In one embodiment, a reactive residue is located between components of an Adapter, *e.g.,* in a linker located between an ADBD and other component of an Adapter fusion protein. The reactive residue (*e.g.,* cysteine, lysine, etc.) can also be located within the sequence of an Adapter. In one embodiment, an Adapter comprises at least one, at least two, at least three reactive residues. In one embodiment, an Adapter comprises at least one, at least two, or at least three, cysteine residues.

Vd. Production of Adapters

[0311] The production of the Adapter, useful in practicing the provided methods, may be carried out using a variety of standard techniques for chemical synthesis, semi-synthetic methods, and recombinant DNA methodologies known in the art. Also provided is a method for producing the Adapter, individually or as part of multi-domain fusion protein, as soluble agents and cell associated proteins.

[0312] In several embodiments, the overall production scheme for the Adapter comprises obtaining a reference protein scaffold and identifying a plurality of residues within the scaffold for modification. Depending on the embodiment, the reference scaffold may comprise a protein structure with one or more alpha-helical regions, or other tertiary structure. Once identified, the plurality of residues can be modified, for example by substitution of an amino acid. In some embodiments substitution is conservative, while in other embodiments non-conservative substitutions are made. In some embodiments a natural amino acid (*e.g.,* one of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine) is substituted into the reference scaffold at the targeted position for modification. In certain embodiments, the modifications do not include substituting in either a cysteine or a proline. After

modifications have been made at all the identified positions desired in a particular embodiment, the resulting modified polypeptides (*e.g.,* candidate Adapter) can be recombinantly expressed, for example in a plasmid, bacteria, phage, or other vector (*e.g.* to increase the number of each of the modified polypeptides). The modified polypeptides can then be purified and screened to identify those modified polypeptides that have specific binding to a particular target of interest. In several embodiments, certain modified polypeptides will show enhanced binding specificity for a target of interest vis-à-vis the reference scaffold, which in some embodiments may exhibit little or no binding to a given target of interest. In additional embodiments, depending on the target of interest the reference scaffold may show some interaction (*e.g.* nonspecific interaction) with a target of interest, while certain modified polypeptides will exhibit at least about two fold, at least about five fold, at least about 10 fold, at least about 20 fold, at least about 50 fold, or at least about 100 fold (or more) increased binding specificity for the target of interest. Optionally, the reference sequence and/or the modified polypeptides (*e.g.,* Adapter) can be de-immunized. For example, residues or motifs that are potentially immunogenic can be identified and modified in order to reduce or eliminate potential immune responses to the Adapter. Additional details regarding various embodiments of the production, selection, and isolation of Adapter are provided in more detail below.

Ve. Recombinant expression of Adapters

[0313] In some embodiments, the Adapter is "recombinantly produced," (*i.e.*, produced using recombinant DNA technology). Exemplary recombinant methods available for synthesizing Adapter fusion proteins, include, but are not limited to polymerase chain reaction (PCR) based synthesis, concatemerization, seamless cloning, and recursive directional ligation (RDL)(*see*, *e.g.,* Meyer *et al.*, Biomacromolecules 3: 357-367 (2002), Kurihara *et al.*, Biotechnol. Lett. 27: 665-670 (2005), Haider *et al.*, Mol. Pharm. 2: 139-150 (2005); and McMillan *et al.*, 32: 3643-3646 (1999), the contents of each of which is herein incorporated by reference in its entirety).

[0314] Nucleic acids comprising a polynucleotide sequence encoding the Adapter are also provided. Such polynucleotides optionally further comprise, one or more expression control elements. For example, the polynucleotide can comprise one or more promoters or transcriptional enhancers, ribosomal binding sites, transcription termination signals, and polyadenylation signals, as expression control elements. The polynucleotide can be inserted within any suitable vector, which can be contained within any suitable host cell for expression.

[0315] The expression of nucleic acids encoding the Adapter is typically achieved by operably linking a nucleic acid encoding the Adapter to a promoter in an expression vector. Typical expression vectors contain transcription and translation terminators, initiation sequences, and promoters useful for regulation of the expression of the desired nucleic acid sequence. Methods known in the art can be used to routinely construct expression vectors containing the nucleic acid sequence encoding an Adapter along with appropriate

transcriptional/ translational control signals. These methods include, but are not limited to in vitro recombinant DNA techniques, synthetic techniques and in vivo recombination/genetic recombination. The expression of the polynucleotide can be performed in any suitable expression host known in the art including, but not limited to bacterial cells, yeast cells, insect cells, plant cells or mammalian cells. In one embodiment, a nucleic acid sequence encoding the Adapter is operably linked to a suitable promoter sequence such that the nucleic acid sequence is transcribed and/or translated into the Adapter in a host. Promoters useful for expression in *E. coli*, include but are not limited to, the T7 promoter.

[0316] In one embodiment, a vector comprising the Adapter encoding nucleic acid is introduced into a host cell (*e.g.,* phagemid) for expression of the Adapter. The vector can remain episomal or become chromosomally integrated, as long as the insert encoding therapeutic agent can be transcribed. Vectors can be constructed by standard recombinant DNA technology. Vectors can be plasmids, phages, cosmids, phagemids, viruses, or any other types known in the art, which are used for replication and expression in prokaryotic or eukaryotic cells. It will be appreciated by one of skill in the art that a wide variety of components known in the art (such as expression control elements) can be included in such vectors, including a wide variety of transcription signals, such as promoters and other sequences that regulate the binding of RNA polymerase onto the promoter. Any promoter known or demonstrated to be effective in the cells in which the vector will be expressed can be used to initiate expression of the Adapter. Suitable promoters can be inducible (*e.g.,* regulated) or constitutive. Non-limiting examples of suitable promoters include the SV40 early promoter region, the promoter contained in the 3' long terminal repeat of Rous sarcoma virus, the HSV-1 (herpes simplex virus-1) thymidine kinase promoter, the regulatory sequences of the metallothionein gene, etc., as well as the following animal transcriptional control regions, which exhibit tissue specificity and have been utilized in transgenic animals: elastase I gene control region which is active in pancreatic acinar cells; insulin gene control region which is active in pancreatic beta cells, mouse mammary tumor virus control region which is active in testicular, breast, lymphoid and mast cells, albumin gene control region which is active in liver, alpha-fetoprotein gene control region which is active in liver, alpha 1-antitrypsin gene control region which is active in the liver, beta-globin gene control region which is active in erythroid cells, myelin basic protein gene control region which is active in oligodendrocyte cells in the brain, myosin light chain-2 gene control region which is active in skeletal muscle, and gonadotropin releasing hormone gene control region which is active in the hypothalamus. In a particular embodiment, the promoter is an immunoglobulin gene control region which is active in lymphoid cells.

[0317] In one embodiment, one or several nucleic acids encoding the Adapter is expressed under the control of a constitutive promoter or, alternately, a regulated expression system. Suitable regulated expression systems include, but are not limited to, a tetracycline-regulated expression system, an ecdysone inducible expression system, a lac-switch expression system, a glucocorticoid-inducible expression system, a

temperature-inducible promoter system, and a metallothionein metal-inducible expression system. If several different nucleic acids encoding the Adapter are contained within the host cell system, some of the nucleic acids may be expressed under the control of a constitutive promoter, while others may be expressed under the control of a regulated promoter. Expression levels may be determined by methods known in the art, including Western blot analysis and Northern blot analysis.

[0318] A variety of host-expression vector systems can be utilized to express a nucleic acid encoding the Adapter. Vectors containing the nucleic acids encoding the Adapter or portions or fragments thereof, include plasmid vectors, a single and double-stranded phage vectors, as well as single and double-stranded RNA or DNA viral vectors. Phage and viral vectors may also be introduced into host cells in the form of packaged or encapsulated virus using known techniques for infection and transduction. Moreover, viral vectors may be replication competent or alternatively, replication defective. Alternatively, cell-free translation systems may also be used to produce the protein using RNAs derived from the DNA expression constructs (*see*, *e.g.,* WO86/05807 and WO89/01036; and U.S. Pat. No. 5,122,464, each incorporated in its entirety by reference herein).

[0319] Generally, any type of cells or cultured cell line can be used to express the Adapter provided herein. In some embodiments the background cell line used to generate an engineered host cells is a phage, a bacterial cell, a yeast cell or a mammalian cell. A variety of host-expression vector systems may be used to express the coding sequence of the Adapter. Mammalian cells can be used as host cell systems transfected with recombinant plasmid DNA or cosmid DNA expression vectors containing the coding sequence of the target of interest and the coding sequence of the Adapter.

[0320] The cells can be primary isolates from organisms (including human), cultures, or cell lines of transformed or transgenic nature. In some embodiments the host cell is a human cell. In some embodiments, the host cell is human T cell. In some embodiments, the host cell is derived from a human patient.

[0321] Useful host cells include but are not limited to microorganisms such as, bacteria (*e.g., E. coli* and *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing Adapter coding sequences; yeast (*e.g.,* Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing Adapter coding sequences; insect cell systems infected with recombinant virus expression vectors (*e.g.,* Baculovirus) containing Adapter coding sequences; plant cell systems infected with recombinant virus expression vectors (*e.g.,* cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.,* Ti plasmid) containing Adapter coding sequences. In particular embodiments, the mammalian cell systems are used to produce the Adapter. Mammalian cell systems typically utilize recombinant expression constructs containing promoters derived from the genome of mammalian cells (*e.g.,* metallothionein promoter) or from mammalian viruses (*e.g.,* the adenovirus late promoter; the vaccinia virus 7.5K promoter).

[0322] Prokaryotes useful as host cells in producing the Adapter, include gram negative or gram positive organisms such as, *E. coli* and *B. subtilis*. Expression vectors for use in prokaryotic host cells generally contain one or more phenotypic selectable marker genes (*e.g.,* genes encoding proteins that confer antibiotic resistance or that supply an autotrophic requirement). Examples of useful prokaryotic host expression vectors include the pKK223-3 (Pharmacia, Uppsala, Sweden), pGEMl (Promega, Wis., USA), pET (Novagen, Wis., USA) and pRSET (Invitrogen, Calif., USA) series of vectors (*see*, *e.g.,* Studier, J. Mol. Biol. 219: 37 (1991) and Schoepfer, Gene 124: 83 (1993)). Exemplary promoter sequences frequently used in prokaryotic host cell expression vectors include T7, (Rosenberg *et al.*, Gene 56: 125-135 (1987)), beta-lactamase (penicillinase), lactose promoter system (Chang *et al.*, Nature 275: 615 (1978)); and Goeddel *et al.*, Nature 281: 544 (1979)), tryptophan (trp) promoter system (Goeddel *et al.*, Nucl. Acids Res. 8: 4057, (1980)), and tac promoter (Sambrook *et al.*, 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.).

[0323] In one embodiment, a eukaryotic host cell systems is used, including yeast cells transformed with recombinant yeast expression vectors containing the coding sequence of an Adapter, such as, the expression systems taught in U.S. Appl. No. 60/344,169 and WO03/056914 (methods for producing humanlike glycoprotein in a non-human eukaryotic host cell)(the contents of each of which are incorporated by reference in their entirety). Exemplary yeast that can be used to produce compositions of the invention, such as, DBD, include yeast from the genus Saccharomyces, Pichia, Actinomycetes and Kluyveromyces. Yeast vectors typically contain an origin of replication sequence from a 2mu yeast plasmid, an autonomously replicating sequence (ARS), a promoter region, sequences for polyadenylation, sequences for transcription termination, and a selectable marker gene. Examples of promoter sequences in yeast expression constructs include, promoters from metallothionein, 3-phosphoglycerate kinase (Hitzeman, J. Biol. Chem. 255: 2073 (1980)) and other glycolytic enzymes, such as, enolase, glyceraldehyde-3 -phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phospho glycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. Additional suitable vectors and promoters for use in yeast expression as well as yeast transformation protocols are known in the art. *See*, *e.g.,* Fleer, Gene 107: 285-195 (1991) and Hinnen, PNAS 75: 1929 (1978).

[0324] Insect and plant host cell culture systems are also useful for producing the compositions of the invention. Such host cell systems include for example, insect cell systems infected with recombinant virus expression vectors (*e.g.,* baculovirus) containing the coding sequence of a DBD; plant cell systems infected with recombinant virus expression vectors (*e.g.,* cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.,* Ti plasmid) containing the coding sequence of a DBD, including, but not limited to, the expression systems taught in U.S. Pat. No. 6,815,184;

U.S. Publ. Nos. 60/365,769, and 60/368,047; and WO2004/057002, WO2004/024927, and WO2003/078614, the contents of each of which is herein incorporated by reference in its entirety.

[0325] In an additional embodiment the host cell systems may be used, including animal cell systems infected with recombinant virus expression vectors (*e.g.,* adenoviruses, retroviruses, adeno-associated viruses, herpes viruses, lentiviruses) including cell lines engineered to contain multiple copies of the DNA encoding an Adapter either stably amplified (CHO/dhfr) or unstably amplified in double-minute chromosomes (*e.g.,* murine cell lines). In one embodiment, the vector comprising the polynucleotide(s) encoding the Adapter is polycistronic. Exemplary mammalian cells useful for producing these compositions include 293 cells (*e.g.,* 293T and 293F), CHO cells, BHK cells, NS0 cells, SP2/0 cells, YO myeloma cells, P3X63 mouse myeloma cells, PER cells, PER.C6 (Crucell, Netherlands) cells VERY, Hela cells, COS cells, MDCK cells, 3T3 cells, W138 cells, BT483 cells, Hs578T cells, HTB2 cells, BT20 cells, T47D cells, CRL7O30 cells, HsS78Bst cells, hybridoma cells, and other mammalian cells. Additional exemplary mammalian host cells that are useful in practicing the invention include but are not limited, to T cells. Some examples of expression systems and selection methods are described in the following references and references cited therein: Borth *et al.*, Biotechnol. Bioen. 71(4): 266-73 (2000), in Werner *et al.*, Arzneimittelforschung/Drug Res. 48(8): 870-80 (1998), Andersen *et al.*, Curr. Op. Biotechnol. 13: 117-123 (2002), Chadd *et al.*, Curr. Op. Biotechnol. 12: 188-194 (2001), and Giddings, Curr. Op. Biotechnol. 12: 450-454 (2001). Additional examples of expression systems and selection methods are described in Logan *et al.*, PNAS 81: 355-359 (1984), Birtner *et al.* Methods Enzymol. 153: 51-544 (1987)). Transcriptional and translational control sequences for mammalian host cell expression vectors are frequently derived from viral genomes. Commonly used promoter sequences and enhancer sequences in mammalian expression vectors include, sequences derived from Polyoma virus, Adenovirus 2, Simian Virus 40 (SV40), and human cytomegalovirus (CMV). Exemplary commercially available expression vectors for use in mammalian host cells include pCEP4 (Invitrogen) and pcDNA3 (Invitrogen).

[0326] Physical methods for introducing a nucleic acid into a host cell (*e.g.,* a mammalian host cell) include calcium phosphate precipitation, lipofection, particle bombardment, microinjection, electroporation, and other methods known in the art. Methods for producing cells comprising vectors and/or exogenous nucleic acids are well-known in the art. *See*, for example, Sambrook *et al.* (2001, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York).

[0327] Biological methods for introducing a polynucleotide of interest into a host cell include the use of DNA and RNA vectors. Viral vectors, and especially retroviral vectors, have become the most widely used method for inserting genes into mammalian (*e.g.,* human) cells. Other viral vectors can be derived from lentivirus, poxviruses, herpes simplex virus I, adenoviruses and adeno-associated viruses, and other viral

vectors known in the art. *See*, for example, U.S. Pat, Nos. 5,350,674 and 5,585,362, the contents of each of which is herein incorporated by reference in its entirety.

[0328] Methods for introducing a DNA and RNA polynucleotides of interest into a host cell include electroporation of cells, in which an electrical field is applied to cells in order to increase the permeability of the cell membrane, allowing chemicals, drugs, or polynucleotides to be introduced into the cell. Adapter encoding DNA or RNA constructs may be introduced into mammalian or prokaryotic cells using electroporation.

[0329] In a preferred embodiment, electroporation of cells results in the expression of a CAR on the surface of T cells, NK cells, NKT cells. Such expression may be transient or stable over the life of the cell. Electroporation may be accomplished with methods known in the art including MaxCyte GT® and STX® Transfection Systems (MaxCyte, Gaithersburg, MD, USA).

[0330] Chemical means for introducing a polynucleotide into a host cell include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. An exemplary colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (*e.g.,* an artificial membrane vesicle). In the case where a non-viral delivery system is utilized, an exemplary delivery vehicle is a liposome. The use of lipid formulations is contemplated for the introduction of the nucleic acids into a host cell (in vitro, ex vivo or in vivo). In another aspect, the nucleic acid can be associated with a lipid. The nucleic acid associated with a lipid can be encapsulated in the aqueous interior of a liposome, interspersed within the lipid bilayer of a liposome, attached to a liposome via a linking molecule that is associated with both the liposome and the oligonucleotide, entrapped in a liposome, complexed with a liposome, dispersed in a solution containing a lipid, mixed with a lipid, combined with a lipid, contained as a suspension in a lipid, contained or complexed with a micelle, or otherwise associated with a lipid. Lipid, lipid/DNA or lipid/expression vector associated compositions are not limited to any particular structure in solution. For example, they can be present in a bilayer structure, as micelles, or with a "collapsed" structure. They can also simply be interspersed in a solution, possibly forming aggregates that are not uniform in size or shape. Lipids are fatty substances which can be naturally occurring or synthetic lipids. For example, lipids include the fatty droplets that naturally occur in the cytoplasm as well as the class of compounds which contain long-chain aliphatic hydrocarbons and their derivatives, such as fatty acids, alcohols, amines, amino alcohols, and aldehydes.

[0331] Lipids suitable for use can be obtained from commercial sources. For example, dimyristoyl phosphatidylcholine ("DMPC") can be obtained from Sigma, St. Louis, MO; dicetyl phosphate ("DCP") can be obtained from K & K Laboratories (Plainview, NY); cholesterol ("Choi") can be obtained from Calbiochem-Behring; dimyristoyl phosphatidylglycerol ("DMPG") and other lipids may be obtained from Avanti Polar Lipids, Inc. (Birmingham, AL). Stock solutions of lipids in chloroform or chloroform/methanol

can be stored at about -20°C. Chloroform may be used as the only solvent since it is more readily evaporated than methanol. "Liposome" is a generic term encompassing a variety of single and multilamellar lipid vehicles formed by the generation of enclosed lipid bilayers or aggregates. Liposomes can be characterized as having vesicular structures with a phospholipid bilayer membrane and an inner aqueous medium. Multilamellar liposomes have multiple lipid layers separated by aqueous medium. They form spontaneously when phospholipids are suspended in an excess of aqueous solution. The lipid components undergo self-rearrangement before the formation of closed structures and entrap water and dissolved solutes between the lipid bilayers (Ghosh *et al.*, Glycobiology 5: 505-510 (1991)). However, compositions that have different structures in solution than the normal vesicular structure are also encompassed. For example, the lipids can assume a micellar structure or merely exist as non-uniform aggregates of lipid molecules. Also contemplated are lipofectamine-nucleic acid complexes.

[0332] Regardless of the method used to introduce exogenous nucleic acids into a host cell, or the presence of the recombinant nucleic acid sequence in the host cell can routinely be confirmed through a variety of assays known in the art. Such assays include, for example, "molecular biological" assays known in the art, such as Southern and Northern blotting, RT-PCR and PCR; "biochemical" assays, such as detecting the presence or absence of a particular peptide, *e.g.,* by immunological means (ELISAs and Western blots) or by assays described herein to identify agents falling within the scope of the invention.

[0333] Reporter genes are used for identifying potentially transfected cells and for evaluating the functionality of regulatory sequences. In general, a reporter gene is a gene that is not present in or expressed by the recipient organism, tissue, or cell and that encodes a polypeptide whose expression is manifested by some easily detectable property, *e.g.,* enzymatic activity. Expression of the reporter gene is assayed at a suitable time after the DNA has been introduced into the recipient cells. A non-limiting list of suitable reporter genes can include genes encoding luciferase, beta-galactosidase, chloramphenicol acetyl transferase, secreted alkaline phosphatase, or the green fluorescent protein gene (*e.g.,* Ui-Tei *et al.*, FEBS Lett. 479: 79-82 (2000)). Suitable expression systems are known in the art and can be prepared using known techniques or obtained commercially. In general, the construct with the minimal 5' flanking region showing the highest level of expression of reporter gene is identified as the promoter. Such promoter regions can routinely be linked to a reporter gene and used to evaluate agents for the ability to modulate promoter-driven transcription.

[0334] A number of selection systems can be used in mammalian host-vector expression systems, including, but not limited to, the herpes simplex virus thymidine kinase, hypoxanthine-guanine phosphoribosyltransferase and adenine phosphoribosyltransferase (Lowy *et al.*, Cell 22: 817 (1980)) genes, which can be employed in tk^-, $hgprt^-$ or $aprt^-$ cells, respectively. Additionally, antimetabolite resistance can be used as the basis of selection for *e.g.,* dhfr, gpt, neo, hygro, trpB, hisD, ODC (ornithine decarboxylase), and the glutamine synthase system.

Vf. Adapter purification

[0335] Once an Adapter has been produced by recombinant expression, it can be purified by any method known in the art for purification of a recombinant protein, for example, by chromatography (*e.g.,* ion exchange, affinity, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In additional embodiments, the Adapter is optionally fused to a heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification. More particularly, it is envisioned that ligands (*e.g.,* antibodies and other affinity matrices) for Adapter affinity columns for affinity purification and that optionally, the Adapter or other components of the Adapter fusion composition that are bound by these ligands are removed from the composition prior to final preparation of the Adapter using techniques known in the art.

Vg. Chemical Synthesis of Adapters

[0336] In addition to recombinant methods, Adapter production may also be carried out using organic chemical synthesis of the desired polypeptide using a variety of liquid and solid phase chemical processes known in the art. Various automatic synthesizers are commercially available and can be used in accordance with known protocols. *See*, for example, Tam *et al.*, J. Am. Chem. Soc. 105: 6442 (1983); Merrifield, Science 232: 341-347 (1986); Barany and Merrifield, The Peptides, Gross and Meienhofer, eds, Academic Press, New York, 1- 284; Barany *et al.*, Int. J. Pep. Protein Res. 30: 705-739 (1987); Kelley *et al.* in Genetic Engineering Principles and Methods, Setlow, J. K., ed. Plenum Press, NY. 1990, vol. 12, pp. 1-19; Stewart *et al.*, Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, 1989. One advantage of these methodologies is that they allow for the incorporation of non-natural amino acid residues into the sequence of the Adapter.

[0337] The Adapters that are used in the methods of the present invention may be modified during or after synthesis or translation, *e.g.,* by glycosylation, acetylation, benzylation, phosphorylation, amidation, pegylation, formylation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, ubiquitination, etc. (*see, e.g.,* Creighton, Proteins: Structures and Molecular Properties, 2d Ed. (W.H. Freeman and Co., N.Y., 1992); Postranslational Covalent Modification of Proteins, Johnson, ed. (Academic Press, New York, 1983), pp. 1-12; Seifter, Meth. Enzymol. 182: 626-646 (1990); Rattan, Ann. NY Acad. Sci. 663: 48-62 (1992).) In specific embodiments, the peptides are acetylated at the N-terminus and/or amidated at the C-terminus.

[0338] Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to acetylation, formylation, etc. Additionally, the derivative may contain one or more non-classical amino acids.

VI. Chimeric Antigen Receptors

[0339] As provided herein, chimeric antigen receptors (CARs) are multi-domain proteins that comprise an extracellular domain comprising an ADBD, a transmembrane domain, and an intracellular signaling domain. Such CARs can be expressed on the surface of cells (*e.g.,* as described in Section VII) and used in combination with Adapters (*e.g.,* as described in Section V), for example, to kill a target cell. In several embodiments, the ADBD is made up of, at least in part, a target-binding polypeptide as disclosed herein. In several embodiments, the intracellular signaling domain is selected from the group: a human CD3 zeta domain, 41BB domain, a CD28 domain and any combination thereof. Depending on the embodiment, the costimulatory signaling region comprises the intracellular domain of a costimulatory molecule selected from the group: CD27, CD28, 4lBB, OX40, CD30, CD40, PD1, lymphocyte function-associated antigen-1 (LFA1), CD2, CD7, LIGHT, NKG2C, B7H3, a ligand that specifically binds with CD83, and any combination thereof. In several embodiments, the CAR comprises a fusion protein that includes an additional target-binding polypeptide. Also provided for are isolated nucleic acid sequences encoding CARs that include the target-binding polypeptides as part (or all) of the targeting region.

[0340] In some embodiments, the ADBD of a CAR comprises at least one alternative scaffold binding domain (*e.g.,* a D domain or affibody) designed to impart binding specificity to a membrane bound CAR. A receptor comprising an alternative scaffold binding domain may be expressed by any cell type.

[0341] In one embodiment, the CAR is composed of the following elements: an extracellular domain, a transmembrane domain and a cytoplasmic domain wherein the cytoplasmic domain comprises the signaling domain. In another embodiment the CAR is composed of an extracellular domain and a transmembrane domain. In a further embodiment the CAR is comprised of an extracellular domain composed of one or more ADBDs with the same or different specificities. In one embodiment, the intracellular domain (*e.g.,* the cytoplasmic domain) of the CAR comprises the intracellular domain of CD3 zeta chain. In another embodiment the intracellular signaling domain of the CAR is comprised of part of the intracellular domain of CD3 zeta chain. In a further embodiment, the intracellular domain of the CAR comprises the intracellular domain of CD3 zeta chain and a costimulatory signaling region. The costimulatory signaling region refers to a portion of the CAR comprising all or part of the intracellular domain of a costimulatory molecule. Costimulatory molecules and portions of these molecules that are able to confer costimulatory properties to a CAR are known in the art and can routinely be incorporated into the CAR. In addition, truncations or mutation to these intracellular signaling and costimulatory domains may be incorporated to further enhance or reduce receptor signaling. In preferred embodiments, a T cell is genetically modified to stably express a CAR. In such embodiments the cytoplasmic domain of the CAR can be designed to comprise the CD28 and/or 41BB signaling domain by itself or be combined with any other desired cytoplasmic domain(s) useful in the context of the invention. In one embodiment, the cytoplasmic domain of the CAR can be designed to further comprise the signaling domain of CD3-zeta. In one embodiment, the CAR comprises an extracellular domain,

an extracellular protein linker with a transmembrane domain that passes through the cellular membrane (such as found in T cells or NK cells), and a cytoplasmic domain, optionally comprising multiple signaling modules. In several embodiments, the CAR may also comprise an epitope tag. In several embodiments, the cytoplasmic domain of the CAR can include but is not limited to CD3-zeta, 41BB and CD28 signaling modules and combinations thereof.

VIa. CAR Extracellular Antigenic Determinant Binding Domain

[0342] The CARs provided herein comprise one or more antigenic determinant binding domains (ADBDs). The ADBD of the CAR can be any ADBD described herein (*e.g.,* as described in Section III). An exemplary ADBD comprises a polypeptide, *e.g.,* an antibody molecule (which includes an antibody, and antigen binding fragments thereof, *e.g.,* an immunoglobulin, single domain antibody (sdAb), and a scFv), or a non-antibody scaffold (*e.g.,* a D domain, or affibody).

[0343] Depending on the desired antigen(s) to be targeted, the extracellular domain of the CAR can be engineered to include one or more antigenic determinant binding domains (ADBDs) that specifically bind the desired antigen target(s). For example, in one embodiment, the CAR is engineered to target CD19 and a CD19-binding ADBD is incorporated into the extracellular domain of the CAR. Alternatively, an extracellular domain of a CAR may include more than one ADBD, thereby imparting multi-specificity or multi-valency to the CAR.

[0344] The choice of ADBDs in the extracellular domain of the CAR depends upon the identity of the cell or cells to be targeted. For example, the extracellular domain of the CAR may be engineered to specifically bind to cell surface proteins, such as a receptor, on the same cell or another cell. In other embodiments, the extracellular domain of the CAR is engineered to specifically bind to a soluble molecule, such as an immunoglobulin. In other embodiments the targets of interest bound by the CAR include those associated with viral, bacterial and parasitic infections, diseases and disorders of the immune system (*e.g.,* autoimmune disease).

[0345] In other embodiments, the extracellular domain of the CAR contains one or more ADBDs that bind a ligand that acts as a cell surface marker on target cells associated with a cancer. In some embodiments, ADBD(s) target and bind a tumor or cancer antigen (*e.g.,* a TAA, TSA, CAA, CSA or other tumor antigen described herein or otherwise known in the art). Accordingly, provided herein are methods for creating CAR, their use in creating chimeric cells such as, human T cells and natural killer cells, and the use of these chimeric T and NK cells in adoptive immunotherapy.

[0346] The choice of an ADBD can depend upon the type and number of ligands or receptors that define the surface of a target cell. For example, the ADBD may be chosen to recognize a ligand or receptor that acts as a cell surface marker on target cells associated with a particular disease state. Examples of cell surface markers that may act as ligands or receptors include a cell surface marker associated with a particular disease state,

e.g., cell surface makers for viral diseases, bacterial diseases parasitic infections, autoimmune diseases and disorders associated with unwanted cell proliferation, *e.g.,* a cancer, such as, a cancer described herein.

[0347] The target of interest specifically bound by the ADBD of the CAR can be any molecule for which it is desirable for a CAR or an Adapter to bind, *e.g.,* any of the ADs described in Section IIa.

[0348] In some embodiments, the ADBD binds to a target listed in Table 4. In further embodiments, the ADBD comprises 1, 2, 3, 4, 5, 1-5, 1-10, or more than 10, D domain sequences listed in Table 3 (*e.g.,* SEQ ID NO: 44-1078, or 1079). In some embodiments, the ADBD comprises 1, 2, 3, 4, 5, 1-5, 1-10, or more than 10, different D domain sequences listed in Table 3.

[0349] In some embodiments, the ADBD binds to BCMA (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 5). In some embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 44-338, and 339.

[0350] In some embodiments, the ADBD binds to CS1 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 1138). In some embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 780-794, and 795

[0351] In some embodiments, the ADBD binds to HER2 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 42). In some embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 800-839, and 840

[0352] In some embodiments, the ADBD binds to CD123 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 11). In some embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 340-772 and 773.

[0353] In some embodiments, the ADBD binds to AFP (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 14 or 15). In some embodiments, the ADBD binds to AFP p26 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 16, 1117, 1118, 1119, 1120, 1121, 1122, or 1123). In some embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 841-983and 984.

[0354] In some embodiments, the ADBD binds to CD137 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 1081). In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 985-990 and 991.

[0355] In some embodiments, the ADBD binds to CD47. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 992-995 and 996.

[0356] In some embodiments, the ADBD binds to CTLA4. In further embodiments, the ADBD comprises a DD sequence of SEQ ID NO: 997.

[0357] In some embodiments, the ADBD binds to DR5. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 998-1006, 1070-1072, and 1073.

[0358] In some embodiments, the ADBD binds to KIR. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 1007, 1008, and 1009.

[0359] In some embodiments, the ADBD binds to PDL1. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 1010-1016, 1074-1078, and 1079.

[0360] In some embodiments, the ADBD binds to TIM3. In further embodiments, the ADBD comprises the DD sequence of SEQ ID NO: 1017.

[0361] In some embodiments, the ADBD binds to PD1. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 1018, 1019, and 1020.

[0362] In some embodiments, the ADBD binds to CD137. In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 985-990 and 991.

[0363] In some embodiments, the ADBD binds to CD19 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 3). In some embodiments, the ADBD binds to CD20 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 6-9 or 10). In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 1030-1058, and 1059.

[0364] In some embodiments, the ADBD binds to CD22 (*e.g.,* a polypeptide comprising the sequence of SEQ ID NO: 41). In further embodiments, the ADBD comprises a DD sequence selected from the group: SEQ ID NO: 1060-1068, and 1069.

[0365] In some embodiments, the ADBD binds an intracellular protein. In further embodiments, the ADBD comprises a DD sequence that binds an intracellular protein selected from the group: elastin, Tyk2, Jak1, Jak2, Jak3, LCK, ZAP-70, and GRB2.

[0366] In some embodiments, the ADBD binds to the extracellular domain (ECD) of human CD45 (*e.g.*, residues 29-766 of SEQ ID NO: 1106).

[0367] In some embodiments, the ADBD binds to CD26 (*e.g.*, residues 29-766 of SEQ ID NO: 1113).

[0368] In some embodiments, the ADBD binds to CD30 (*e.g.*, residues 19-379 of SEQ ID NO: 1114).

[0369] In some embodiments, the ADBD binds to CD33 (*e.g.*, residues 18-259 of SEQ ID NO: 1115).

[0370] In some embodiments, the ADBD binds to CD38 (*e.g.*, residues 43-300 of SEQ ID NO: 1116).

[0371] In some embodiments, the ADBD binds a tumor antigen or cancer antigen that comprises one or more antigenic cancer epitopes immunologically recognized by tumor infiltrating lymphocytes (TIL) derived from a cancer or tumor of a mammal.

[0372] In some embodiments, the ADBD binds an AD expressed on the surface of an immune effectore cell.

[0373] In some embodiments, the CAR binds to an AD (*e.g.,* in an Adapter and/or on a target cell) that is present in a naturally occurring protein or other molecule. In some embodiments, the CAR binds to an AD that is endogenous to humans.

[0374] In some embodiments, a CAR provided herein comprises an ADBD (*e.g.,* an antibody fragment or ASBD) that binds to a MHC presented-peptide. Normally, peptides derived from endogenous proteins fill the pocket of Major histocompatibility complex (MHC) class I molecules, and are recognized by T cell receptors (TCRs) on CD8+T lymphocytes. The MHC class I complexes are constitutively expressed by all nucleated cells. In cancer, virus-specific and/or tumor-specific peptide/MHC complexes represent a unique class of cell surface targets for immunotherapy. TCR-like antibodies targeting peptides derived from viral or tumor antigenic determinants in the context of human leukocyte antigen (HLA)-A1 or HLA-A2 have been described (*see, e.g.,* Sastry *et al.*, J. Virol. 85(5): 1935-1942 (2011); Sergeeva *et al.*, Blood 117(16): 4262-4272 (2011); Verma *et al.*, J. Immunol. 184(4): 2156-2165(2010); Willemsen *et al.*, Gene Ther. 8(21): 1601-1608 (2001); Dao *et al.*, Sci. Transl. Med. 5(176): 176ra33 (2013); Tassev *et al.*, Cancer Gene Ther. 19(2): 84-100 (2012)). For example, TCR-like antibody can be identified from screening a library, such as a human scFv phage displayed library. Accordingly, in some embodiments, the disclosure provides a CAR that comprises an ADBD that binds to a MHC presented peptide of a molecule selected from any tumor antigen described above that is expressed intracellularly, *e.g.,* p53, BCR-Ab1, Ras, K-ras, NY-ESO-1, and c-met.

[0375] In some embodiments, the CAR comprises an ADBD that is an antibody or an antigen-binding fragment thereof. In some embodiments, the CAR comprises an ADBD that is a scFv. In some embodiments, the CAR comprises an ADBD that is an alternative scaffold binding domain. In some embodiments, the CAR comprises an ADBD that is a D domain. In some embodiments, the CAR comprises a T cell receptor, or an antigen-binding fragment thereof.

[0376] Also provided herein are CAR wherein the CAR comprises a plurality of ADBDs. In some embodiments, the CAR comprises a plurality of the same ADBD. In some embodiments, the CAR comprises a plurality of different ADBDs. In some embodiments, the CAR comprises a plurality of ADBDs that bind the same antigenic determinant. In some embodiments, the CAR comprises a plurality of ADBDs, wherein the binding domains bind to different ADs. In some embodiments, the CAR comprises a plurality of ADBDs, wherein the binding domains bind to different ADs on the same cell. In some embodiments, the CAR comprises a plurality of ADBDs, wherein the binding domains bind to different ADs on different cells.

[0377] In some embodiments, a CAR comprises a plurality of, *e.g.,* 2, 3, 4, 5, or more than 5, ADBDs (*e.g.,* D domains, affibodies, or scFvs), wherein each ADBD(s) are able to bind to a target antigen. In one embodiment, two or more of the ADBDs of a CAR can bind to different ADs. In an additional embodiment, two or more of the ADBDs of the CAR can bind to the same antigen, *e.g.,* the same or different epitopes on the same antigen. In one embodiment, a plurality of ADBDs of the CAR are linked to each other, *e.g.,* the C-terminus of a first ADBD is linked to the N-terminus of a second ADBD. In an embodiment, the C-terminus of a first ADBD is linked to the N-terminus of a second ADBD by a covalent bond, *e.g.,* a peptide bond.

[0378] In some embodiments, a linker or hinge region is contained between one or more of the ADBDs, *e.g.*, a linker or hinge region is located between the C-terminus of a first ADBD and the N-terminus of a second ADBD. By way of example, an antigen binding member comprising two ADBDs (*e.g.*, $ADBD_1$ and $ADBD_2$) can be arranged in the following configuration: [$ADBD_1$]-[linker/hinge]-[$ADBD_2$]. Additional ADBDs can be added in a similar manner, optionally with linker or hinge regions located between the C-terminus of an ADBD and the N-terminus of the next ADBD. Linkers or hinge regions suitable for use in linking a plurality of antigen binding members are flexible, non-cleavable, and allow near-free motion of each ADBD independent from the other ADBDs to encourage binding with multiple target ADs simultaneously. Any flexible linker or hinge region known in the art can be used. Examples of linkers include peptide linkers comprising glycine and serine residues, *e.g.*, (GGGGS)n, where n is a positive integer equal to or greater than 1, *e.g.*, n=1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 (SEQ ID NO: 43).

VIb. Extracellular Spacer Domain

[0379] In some embodiments, the CARs comprise an extracellular spacer domain. As used herein, the term "extracellular spacer domain" or "ESD" refers to a polypeptide sequence of a CAR disposed between the ADBD and the transmembrane domain. In an embodiment the extracellular spacer domain allows sufficient distance from the outer surface of the cell and the ADBD as well as flexibility to minimize steric hindrance between the cell and the ADBD.

[0380] In particular embodiments, the extracellular spacer domain is sufficiently short or flexible that it does not interfere with engagement of the cell that includes the CAR with a cell bearing an AD, *e.g.*, a target cell. In an embodiment, the extracellular spacer domain is from 2 to 20, 5 to 15, 7 to 12, or 8 to 10 amino acids in length. In some embodiments, the ESD domain includes at least 50, 20, or 10 residues. In some embodiments the ESD is 10 to 300, 10 to 250, or 10 to 200 residues in length.

[0381] In some embodiments the distance from which the ESD extends from the cell is sufficiently short that the hinge does not hinder engagement of the CAR ADBD with the surface of a target cell. In some embodiment the ESD extends less than 20, 15, or 10 nanometers from the surface of the cytotoxic cell. Thus, suitability for an ESD can be influenced by both linear length, the number of amino acid residues and flexibility of the ESD. By way of example, an IgG4 ESD can be as long as 200 amino acids in length, but the distance it extends from the surface of the cytotoxic cell is smaller due to Ig-domain folding. A CD8 alpha ESD, which is ~43 amino acids at ~8 nm in length. In contrast, the IgG4 C2 & C3 ESD is ~ 200 amino acids in length, but has a distance from the cytotoxic cell surface that is comparable to that of the CD8 alpha ESD. While not wishing to be bound by theory, the similarity in extension is influenced by flexibility.

[0382] In some embodiments, the extracellular spacer domains include but are not limited to Fc fragments of antibodies or fragments or derivatives thereof, hinge regions of antibodies or fragments or derivatives thereof, CH2 regions of antibodies, CH3 regions of antibodies, artificial spacer sequences or combinations thereof.

Additional examples of extracellular spacer domains include but are not limited to CD8a hinge, and artificial spacers made of polypeptides which may be as small as, for example, Gly3 or CH1 and CH3 domains of IgGs (such as human IgG4). In some embodiments, the extracellular spacer domain is any one or more of (i) a hinge, CH2 and CH3 regions of IgG4, (ii) a hinge region of IgG4, (iii) a hinge and CH2 of IgG4, (iv) a hinge region of CD8a, (v) a hinge, CH2 and CH3 regions of IgGl, (vi) a hinge region of IgGl or (vi) a hinge and CH2 region of IgGl. Other extracellular spacer domains will be apparent to those of skill in the art and may be used in connection with alternate embodiments provided herein.

[0383] In some embodiments, the ESD is a naturally occurring sequence. In some embodiments, the ESD of the CAR corresponds to an ESD from a human protein, a fragment thereof, or a short oligo- or polypeptide linker. In some embodiments, the CAR ESD corresponds to a human Ig (immunoglobulin) ESD (hinge), or fragment thereof. In one embodiment, the ESD comprises (*e.g.,* consists of) the amino acid sequence of the IgG4 ESD. In one embodiment, for example, the hinge comprises (*e.g.,* consists of) the amino acid sequence of the IgD hinge. In some embodiments, the hinge can be a human CD8 hinge, or fragment thereof. In one embodiment, for example, the hinge comprises (*e.g.,* consists of) the amino acid sequence of the CD8 hinge.

[0384] In some embodiments, the ESD is an artificial sequence. In one embodiment, the ESD is a short oligopeptide linker comprising a glycine-serine doublet.

[0385] In some embodiments, the CARs do not contain an extracellular spacer domain.

VIc. Transmembrane domain

[0386] The term "transmembrane domain" (TMD) as used herein refers to the region of a cell surface expressed protein, such as a CAR, which spans the plasma membrane. In some embodiments, the TMD links an extracellular sequence, *e.g.,* an extracellular ADBD, and an intracellular sequence, such as an intracellular signaling domain. In some embodiments, the transmembrane domain of the CAR is the transmembrane region of a transmembrane protein (for example Type I transmembrane proteins), an artificial hydrophobic sequence or a combination thereof. Other transmembrane domains will be apparent to those of skill in the art and may be used in connection with alternate embodiments of the invention.

[0387] The CAR can be designed to contain a transmembrane domain that is fused to the extracellular domain of the receptor. As described above, the fusion of the extracellular and transmembrane domains can be accomplished with or without a linker. In one embodiment, the transmembrane domain that is naturally associated with one of the domains in the CAR is used. In a specific embodiment, the transmembrane domain in the CAR is the CD8 transmembrane domain. In some instances, the transmembrane domain of the CAR comprises the CD8 hinge domain. In some embodiments, the transmembrane domain is selected or modified by amino acid substitution to promote or inhibit association with other surface membrane proteins.

[0388] The transmembrane domain can be derived either from a natural or from a synthetic source. Where the source is natural, the domain can be derived from any membrane-bound or transmembrane protein.

Transmembrane regions of particular use for the purposes herein may be derived from (*i.e.*, comprise at least the transmembrane region(s) of) a member selected from the group: the alpha, beta or zeta chain of the T cell receptor; CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, and CD154. In some embodiments, the transmembrane domain is derived from the transmembrane region(s) of a NKR. In further embodiments, the transmembrane domain is derived from the transmembrane region of a molecule selected from the group consisting of, KIRDS2, OX40, TNFR2, LFA1 (CD11a, CD18), ICOS, 41BB, GITR, LTBR, BAFFR, HVEM, NKp80 (KLRF1), IL2R beta, IL2R gamma, IL7R α, ITGA1, ITGA4, ITGA6, ITGAD, ITGAE, ITGAL, ITGAM, ITGB7, VLA1, VLA6, IA4, ITGAX, CD11c, ITGB1 CD27, CD29, ITGB2, CD2, CD11a, CD11b, CD11d, CD18, CD19, CD40, CD49a, CD49d, CD49f, CD84, CD96, CD100, CD103, CD160, CD162, CD226, CD229, CEACAM1, CRTAM, PSGL1, SLAM (SLAMF1), SLAMF4, SLAMF6 (NTB-A, Ly108), SLAMF7, SLAMF8, SELPLG, and PAG/Cbp. Alternatively, the transmembrane domain can be synthetic, and preferably predominantly comprises hydrophobic residues such as leucine and valine. In further embodiments, the transmembrane domain comprises the triplet of FWV (phenylalanine, tryptophan and valine) at each end of the transmembrane domain.

[0389] Exemplary NKR domains, *e.g.,* transmembrane, hinge or stem, or intracellular (*e.g.,* cytoplasmic) domains (identified by the NKR from which the domain is derived) Killer immunoglobulin KIR2DL1 receptors (KIRs) include KIR2DL2/L3, KIR2DL4, KIR2DL5A, KIR2DL5B, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DL1/S1, KIR3DL2, KIR3DL3, KIR2DP1, KIR2DP1, NCRs: , NKp30, NKp44, NKp46, SLAM; Receptors SLAM, CD48, CD229, 2B4, CD84, NTB-A, CRACC, BLAME, CD2F-10, SLAMF6, SLAMF7; Fc-binding Receptors CD16, FcgRIII, CD64, Ly49; Receptors Ly49, Lectin-related NK Ly49A cell receptor, Ly49C; other NK receptors NKG2D, CD160 (TM containing splice variant(s)) DNAM1, CRTAM, CD27, PSGL1, CD96, CD100, NKp80, CEACAM1, and CD244.

VId. Intracellular signaling domain

[0390] Described herein are intracellular signaling domains that can be used in a chimeric antigen receptor (CAR) according to the present invention.

[0391] "Intracellular signaling domain" (ISD) or "cytoplasmic domain" as used herein refer to the portion of the CAR which transduces the effector function signal and directs the cell to perform its specialized function (*e.g.,* cytolytic activity and helper activity, including cytokine secretion).

[0392] The cytoplasmic domain (*i.e.*, intracellular signaling domain) of a CAR is responsible for activation of at least one of the normal effector functions of an immune cell engineered to express a CAR. The term "effector function" refers to a specialized function of a cell. The effector function of a T cell, for example, includes cytolytic activity and helper activity including the secretion of cytokines. Thus the term "intracellular signaling domain" refers to the portion of a CAR protein which transduces the effector function signal and

directs the cell to perform a specialized function. While typically the entire intracellular signaling domain corresponding to a naturally occurring receptor can be employed, in many cases it is not necessary to use the entire chain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion can be used in place of the intact chain as long as it transduces the effector function signal. The term intracellular signaling domain is thus meant to include any truncated portion of the intracellular signaling domain sufficient to transduce the effector function signal. In one embodiment, an intracellular signaling domain in the CAR includes the cytoplasmic sequences of the T cell receptor (TCR) and also the sequence of co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, or any derivative or variant of these sequences that has functional capability. Examples of domains that transduce an effector function signal include but are not limited to the ζ chain of the T cell receptor complex or any of its homologues (*e.g.,* η chain, FcsRly and β chains, MB 1 (Iga) chain, B29 (Ig) chain, etc.), human CD3 zeta chain, CD3 polypeptides (Δ, δ and ε), syk family tyrosine kinases (Syk, ZAP 70, etc.), src family tyrosine kinases (Lck, Fyn, Lyn, etc.) and other molecules involved in T cell transduction, such as CD2, CD5 and CD28.

[0393] In some embodiments, the intracellular signaling domain of the CAR produces an intracellular signal when an extracellular domain (*e.g.,* an ADBD) to which it is fused, binds a cognate AD. The Intracellular signaling domains of the CAR can include primary intracellular signaling domains and costimulatory signaling domains. In one embodiment, the CAR is constructed for expression in an immune cell (*e.g.,* a T or NK cell), such that the expressed CAR comprises a domain such as a primary intracellular signaling domain and/or costimulatory signaling domain, that is derived from a polypeptide typically associated with the immune cell. For example, in some embodiments, the CAR is for expression in a T cell and comprises a 41BB domain and a CD3 zeta domain. In another embodiment, the CAR molecule is constructed for expression in an immune cell such that the expressed CAR comprises a domain that is derived from a polypeptide that is not typically associated with the immune cell. For example, in some embodiments the CAR for expression in a T cell comprises a KIR domain derived from a NK cell. In an alternative embodiment, the CAR for expression in an NK cell comprises a 41BB domain and a CD3 zeta domain derived from a T cell (*See e.g.* WO2013/033626, incorporated herein by reference).

[0394] The intracellular signaling domain of the CAR comprises sufficient primary stimulatory molecule sequence to produce an intracellular signal, *e.g.,* when an ADBD to which it is fused binds a cognate AD. In particular embodiments, the intracellular signal of the CAR mediates a T cell response selected from the group: proliferation, cytokine secretion, killing, activation, and differentiation.

[0395] In one embodiment, the intracellular signaling region of the CAR comprises a domain that contains an immunoreceptor tyrosine-based activation motif (ITAM). In a further embodiment, the CAR intracellular signaling region comprises ITAM containing domain from a molecule selected from: TCR zeta (CD3 zeta),

FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (FCER1B), CD3 gamma, CD3 delta, CD3 epsilon, CD3 gamma, CD5, CD22, CD79a, CD79b, DAP10, DAP12, CD32 (Fc gamma RIIa), CD79a, and CD79b. In a specific embodiment, the intracellular signaling domain of the CAR comprises a CD3 zeta signaling domain. In another specific embodiment, the intracellular signaling domain of the CAR comprises a DAP12 signaling domain. In some embodiments, the ITAM containing signaling domain has at least 70, 75, 80, 85, 90, 95, 98, or 99% sequence identity with, or differs by no more than 30, 25, 20, 15, 10, 5, 4, 3, 2, or 1 amino acid residues from the corresponding residues of a naturally occurring ITAM containing domain.

[0396] Examples of ITAM containing primary cytoplasmic signaling sequences that are of particular use in the invention include those derived from TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD22, CD79a, CD79b, and CD66d. It is particularly preferred that a cytoplasmic signaling molecule in the CAR comprises a cytoplasmic signaling sequence derived from CD3 zeta.

[0397] In a preferred embodiment, the cytoplasmic domain of the CAR comprises the CD3-zeta signaling domain by itself or combined with any other desired cytoplasmic domain(s) useful in the context of the CAR. For example, the cytoplasmic domain of the CAR can comprise a CD3 zeta chain portion and a costimulatory signaling region. The costimulatory signaling region refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. A costimulatory molecule is a cell surface molecule other than an antigen receptor or their ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 41BB (CD 137), OX40, CD30, CD40, PD1, ICOS, lymphocyte function-associated antigen-1 (LFA1), CD2, CD7, LIGHT, NKG2C, B7H3, TIM1, and LAG3.

[0398] "Co-stimulatory domain" (CSD) as used herein refers to the portion of the CAR which enhances the proliferation, survival and/or development of memory cells. The CAR may comprise one or more co-stimulatory domains. Each co-stimulatory domain comprises the costimulatory domain of any one or more of, for example, a member of the TNFR superfamily, selected from CD28, CD137 (4lBB), CD134 (OX40), Dap10, CD27, CD2, CD5, ICAM1, LFA1(CD1 la/CD18), Lck, TNFRI, TNFRII, Fas, CD30, and CD40 or a combination thereof. Other co-stimulatory domains (*e.g.,* from other proteins) will be apparent to those of skill in the art and may be used in connection with alternate embodiments of the invention.

[0399] In some embodiments, the intracellular domain of the CAR comprises an ITAM containing domain and a costimulatory signaling domain that comprises a functional fragment or analog of a costimulatory molecule that is sufficient to produce an intracellular signal when an extracellular ADBD to which it is fused, binds cognate ligand. In some embodiments, the CAR comprises a costimulatory signaling domain corresponding to that found in a molecule selected from: CD137 (4lBB), OX40, LIGHT, TNFR2, TRANCE/RANKL, GITR, BAFFR, HVEM, B7H3, CDS, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, ITGA6, ITGAD, ITGAE, ITGAL, ITGAM, ITGAX, ITGB1, ITGB2, ITGB7, VLA1, VLA6, C49f, IA4,

LFA1, CD2, CD4, CD7, CD8 alpha, CD8 beta, CD11A, CD11B, CD11C, CD11D, CD18, CD19, CD27, CD28, CD29, CD30, CD40, CD49A, CD49D, CD69, CD84, CD96, CD100, CD103, CD150, CD160, CD162, CD226, CD229, CD278, ICAM1, CEACAM1, CRTAM, PSGL1, SLAMF1, SLAMF4, SLAMF6, SLAMF7, SLAMF8, LTBR, LAT, GADS, PAG/Cbp, SLP76, NKG2C, NKp30, NKp44, NKp46 and NKp80.

[0400] In some embodiments, the CAR comprises a costimulatory domain corresponding to that found in a molecule selected from the group consisting 41BB, CD28, CD27, ICOS, and OX40.

[0401] In some embodiments, the CAR comprises a plurality of costimulatory domains. In particular embodiments, the CAR comprises the following costimulatory signaling domains, from the extracellular to intracellular direction: 41BB-CD27, CD27-41BB, 41BB-CD28, CD28-41BB, OX40-CD28, CD28-OX40, CD28-41BB; or 41BB-CD28.

[0402] In some embodiments the costimulatory signaling domain of the CAR has at least 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99% identity with, or differs by no more than 30, 25, 20, 15, 10, 5, 4, 3, 2, or 1 amino acid residues from the corresponding residues of a naturally occurring costimulatory domain.

[0403] Polypeptide linkers may be positioned between adjacent elements of the CAR. For example linkers may be positioned between adjacent ADBDs or between an ADBD and the transmembrane domain or between the transmembrane domain and the cytoplasmic domain or between adjacent cytoplasmic domains. The cytoplasmic signaling sequences within the cytoplasmic signaling portion of the CAR may be linked to each other in a random or specified order. Optionally, a short linker, preferably between 2 and 10 amino acids in length may form the linkage. A glycine-serine doublet provides a particularly suitable linker.

VIe. Expression of CARs

[0404] CARs are intentionally cell associated and used in the context of the cell in which they are expressed. One particular embodiment relates to a strategy of adoptive cell transfer of T cells which have been transduced to express a CAR. Preferably, the cell can be genetically modified to stably express a CAR on its surface, conferring novel target specificity that is MHC independent.

[0405] A variety of viral-derived vectors can be used in applications in which viruses are used for transfection and integration into a mammalian cell genome. Viruses, which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, and lentiviruses. Lentiviral vectors are particularly suitable to achieving long-term gene transfer (*e.g.,* adoptive T cell immune therapy) since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers, (*e.g.,* Intl. Appl. Publ. Nos. WO 01/96584 and WO 01/29058; and U.S. Pat. No.

6,326,193). Several vector promoter sequences are available for expression of the transgenes. One example of a suitable promoter is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. Another example of a suitable promoter is EF- 1a. However, other constitutive promoter sequences can also be used, including, but not limited to the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV), human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the hemoglobin promoter, and the creatine kinase promoter. Inducible promoters include, but are not limited to a metallothionein promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

[0406] In order to assess the expression of a CAR polypeptide or portions thereof, the expression vector introduced into a cell can also contain either a selectable marker gene or a reporter gene or both to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. In other aspects, the selectable marker may be carried on a separate piece of DNA and used in a co- transfection procedure. Both selectable markers and reporter genes may be flanked with appropriate regulatory sequences to enable expression in the host cells. Useful selectable markers include, for example, antibiotic-resistance genes, such as neo and are otherwise known in the art.

[0407] Prior to expansion and genetic modification of the T cells of the invention, a source of T cells is obtained from a subject. T cells can be obtained from a number of sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors. In certain embodiments provided herein, any number of T cell lines available in the art, may be used.

[0408] A full discussion of T cell isolation, culturing, activation and expansion methods may be found in WO 2012079000, the contents of which is herein incorporated by reference in its entirety.

[0409] Additionally provided is a host cell comprising nucleic acids encoding a CAR described herein. Further provided is a composition comprising a nucleic acid sequence encoding the CAR.

VII. Chimeric antigen receptor cells

[0410] The disclosure provides compositions and methods to regulate the specificity and activity of cells modified to express one or more different CAR(s).

[0411] In some embodiments, cells are engineered to express one or more of the CARs described herein. Such CAR-containing cells, referred to as "CAR cells" have uses in monotherapy and in combination therapies that include other therapeutic agents, such as the Adapters described herein, for example, to kill a target cell.

[0412] In some embodiments, a CAR cell comprises a nucleic acid sequence encoding a CAR, wherein the CAR comprises an extracellular domain made up of, at least in part, an ADBD that binds a target of interest, a transmembrane domain, and a signaling domain. In several embodiments, the encoded CAR polypeptide binds specifically to a tumor antigen (and thus functions to deliver the cell expressing the CAR to the tumor). In several embodiments, the tumor antigen bound by the CAR is associated with a hematologic malignancy. In additional embodiments, tumor antigen bound by the CAR is associated with a solid tumor. In further embodiments the CAR is engineered to bind both solid and hematologic tumors. Depending on the embodiment, the cell expressing the CAR can be an immune effector cell (*e.g.,* a T cell or a natural killer (NK) cell) or another cell type. In several embodiments, the cell (whether T cell, NK cell or other cell type) exhibits an anti-tumor immunity when the antigen-binding domain of the CAR binds to its targeted tumor antigen(s).

[0413] In some embodiments, prior to expansion and genetic modification or other modification, a source of cells (*e.g.,* T cells or natural killer cells), can routinely be obtained from a subject using techniques known in the art. The term "subject" is intended to include living organisms in which an immune response can be elicited (*e.g.,* mammals). T cells can be obtained from sources, including but not limited to peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors.

[0414] In some embodiments, the CAR cell is capable of killing a target cell, *e.g.,* when the ADBD of the CAR interacts with an AD, which can be present on the surface of a target cell and/or in an Adapter. In some embodiments, the CAR cell is capable of degranulating, *e.g.,* when the ADBD of the CAR interacts with an AD, which can be present on the surface of a target cell and/or in an Adapter. In some embodiments, the CAR cell is capable of secreting a cytokine or cytokines, *e.g.,* when the ADBD of the CAR interacts with an AD, which can be present on the surface of a target cell and/or in an Adapter.

[0415] In some embodiments, the CAR-containing cell is an immune cell. In some embodiments, the CAR-containing cell is an immune effector cell. In further embodiments, the CAR-containing immune cell is a cytotoxic cell. In further embodiments, the cytotoxic cell is selected from a T cell, NK cell, or a cultured NK cell (*e.g.,* a NK92 cell).

[0416] In certain embodiments, an immune effector cell comprises a cell surface receptor for an immunoglobulin or other peptide binding molecule, such as a receptor for an immunoglobulin constant region and including the class of receptors commonly referred to as "Fc receptors" ("FcR"s). A number of FcRs have been structurally and/or functionally characterized and are known in the art, including FcR having specific abilities to interact with a restricted subset of immunoglobulin heavy chain isotypes, or that interact with Fc domains with varying affinities, and/or which may be expressed on restricted subsets of immune effector cells under certain conditions (*e.g.,* Kijimoto-Ochichai *et al.*, Cell Mol. Life. Sci. 59: 648 (2002); Davis *et al.*, Curr.

Top. Microbiol. Immunol. 266: 85 (2002); Pawankar, Curr. Opin. Allerg. Clin. Immunol. 1: 3 (2001); Radaev *et al.*, Mol. Immunol. 38: 1073 (2002); Wurzburg *et al.*, Mol. Immunol. 38: 1063 (2002); Sulica *et al.*, Int. Rev. Immunol. 20: 371 (2001); Underhill *et al.*, Ann. Rev. Immunol. 20: 825 (2002); Coggeshall, Curr. Dir. Autoimm. 5: 1 (2002); Mimura *et al.*, Adv. Exp. Med. Biol. 495: 49 (2001); Baumann *et al.*, Adv. Exp. Med. Biol. 495: 219 (2001); Santoso *et al.*, Ital. Heart J. 2: 811 (2001); Novak *et al.*, Curr. Opin. Immunol. 13: 721 (2001); Fossati *et al.*, Eur. J. Clin. Invest. 31: 821 (2001)), the contents of each of which is herein incorporated by reference in its entirety.

[0417] Cells that are capable of mediating ADCC are examples of immune effector cells. Other immune effector cells include Natural Killer cells, tumor-infiltrating T lymphocytes (TILs), cytotoxic T lymphocytes, and granulocytic cells such as cells that comprise allergic response mechanisms. Immune effector cells thus include, but are not limited to, cells of hematopoietic origin including cells at various stages of differentiation within myeloid and lymphoid lineages and which may (but need not) express one or more types of functional cell surface FcR, such as T lymphocytes, B lymphocytes, NK cells, monocytes, macrophages, dendritic cells, neutrophils, basophils, eosinophils, mast cells, platelets, erythrocytes, and precursors, progenitors (*e.g.,* hematopoietic stem cells), as well as quiescent, activated, and mature forms of such cells. Other immune effector cells may include cells of non-hematopoietic origin that are capable of mediating immune functions, for example, endothelial cells, keratinocytes, fibroblasts, osteoclasts, epithelial cells, and other cells. Immune effector cells can also include cells that mediate cytotoxic or cytostatic events, or endocytic, phagocytic, or pinocytotic events, or that effect induction of apoptosis, or that effect microbial immunity or neutralization of microbial infection, or cells that mediate allergic, inflammatory, hypersensitivity and/or autoimmune reactions.

[0418] In some embodiments, the CAR-containing cell is a T cell. In some embodiments, the CAR-containing cell is a NK cell. In additional embodiments, the CAR-containing cell is a B cell. Other immune cells, and/or combinations of different immune cell types can optionally be used. In some embodiments, combinations of cell types (*e.g.,* NK cells and T cells) are advantageous because they act synergistically to treat a disease or condition (*e.g.,* a hyperproliferative disease such as cancer). When combinations are used, the various cell types can target the same, different, or overlapping tumor antigenic determinants.

[0419] In some embodiments, the CAR-containing immune cell is a T cell, and the binding of the ADBD of the CAR to a cognate ligand (i.e., target of interest) stimulates the T cell to initiate intracellular signaling. In further embodiments, binding of the ADBD of the CAR to a cognate ligand stimulates the T cell to produce cytokines and degranulate, leading to the cytotoxic effects on the cell expressing the target of interest on its surface (*e.g.,* a cancer cell). In additional embodiments, the CAR-containing T cell proliferates in response to binding the target of interest. In some embodiments, the activity of the CAR-containing T cell does not result in the T cells exhibiting a phenotype associated with T cell exhaustion. In some embodiments where the CAR

cell is a T cell, the transmembrane domain of the CAR comprises 41BB or CD28, and the cytoplasmic domain comprises a T cell receptor alpha, beta, or zeta chain.

[0420] In some embodiments, the CAR-containing immune cell is a NK cell, the transmembrane domain comprises CD28, and the cytoplasmic domain comprises a zeta chain of a T cell receptor.

[0421] In some embodiments, the CAR-containing immune cell has been engineered to bind to a target of interest expressed by a cancer cell. In further embodiments the CAR-containing cell binds a tumor antigen selected from the group: CD137, PDL1, CD123, CTLA4, CD47, KIR, DR5, TIM3, PD1, EGFR, TCR, CD19, CD20, CD22, ROR1, mesothelin, CD33, lL3Ra, cMet, PSMA, Glycolipid F77, EGFRvIII, GD2, NY-ESO- 1, and MAGE A3. In further embodiments the CAR-containing cell binds 2, 3, 4, 5 or more of the above tumor antigens.

[0422] In some embodiments, the CAR of the CAR cell binds two or more targets of interest. In further embodiments, the CAR further comprises a second polypeptide comprising the amino acid of SEQ ID NO: 17-26, or 27, the polypeptide being able to specifically bind a second target of interest expressed by a cancer cell, and wherein the second polypeptide's specific binding the second target of interest is greater than binding of a polypeptide according to SEQ ID NO: 1 to the second target of interest.

[0423] In some embodiments, the CAR cell is engineered to express an Adapter disclosed herein (*e.g.,* as described in Section V).

[0424] In additional embodiments, the CAR cell is engineered to express a second CAR. In some embodiments, the second CAR comprises an extracellular domain comprising an ADBD, a transmembrane domain, and an intracellular signaling domain. In an additional embodiment the second CAR is comprised of an extracellular domain composed of one or more ADBDs (*e.g.,* as described in Section VI herein) with the same or different specificities. In some embodiments, the second CAR is able to transduce an effector function signal upon binding a target of interest. In further embodiments, the second CAR comprises an extracellular domain comprising an ADBD, and transmembrane or other cell-surface associating domain, but is unable to signal upon binding a target of interest.

[0425] In some embodiments the CAR cell is engineered such that the CAR coding sequence is site specifically introduced into a locus of a gene highly expressed in the corresponding host cell. In some embodiments the CAR coding sequence is introduced into a T cell receptor locus. In further embodiments, the CAR coding sequence is introduced into the T cell receptor α constant (*TRAC*) of the cell. Modified cells that lack expression of a functional TCR and/or HLA can routinely be obtained using any suitable means known in the art, including for example, siRNA, shRNA, CRISPR, TALEN, and/or ZFN.

[0426] In some embodiments, the immune effector cell can be an allogeneic immune effector cell, *e.g.,* T cell or NK cell.

VIIa. Genetic modifications of CAR cells

[0427] To avoid or reduce the possibility that CAR cells disclosed herein target an immune response (*e.g.*, kill) to themselves, a CAR cell can be genetically modified to reduce or eliminate the expression of one or more AD targeted by the CAR cell directly by a CAR provided herein or indirectly through an Adaptor provided herein. For example, a CAR cell provided herein with an ADBD that specifically binds to an AD of human CD45 or a CAR cell provided herein suited to be used in combination with an Adapter comprising an ADBD that specifically binds to an AD of human CD45 can be engineered to reduce or eliminate the expression of the human CD45 AD recognized by the ADBD. In some embodiments, the CAR cell is a human immune effector cell.

[0428] In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of one AD bound by a CAR or Adapter provided herein. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of more than one AD bound by a CAR or Adapter provided herein. In some embodiments, the CAR cell comprises more than one genetic modification that reduces or eliminates the expression of more than one AD bound by a CAR or Adapter provided herein. In some embodiments, the more then one AD is comprised by a single antigen. In some embodiments, the AD is a human CD45 AD. In some embodiments, the the AD is a human CD26, CD30, CD33, or CD38 AD. In some embodiments, the CAR cell is a human immune effector cell.

[0429] In some embodiments, the genetic modification reduces expression of the AD by about 50%, about 60%, about 70%, about 80%, about 90%, about 95% compared to a reference cell without the genetic modification. In some embodiments, the genetic modification eliminates expression of the AD.

[0430] In some embodiments, the genetic modification reduces expression of the polypeptide comprising the AD by about 50%, about 60%, about 70%, about 80%, about 90%, about 95% compared to a reference cell without the genetic modification. In some embodiments, the genetic modification eliminates expression of the polyeptide comprising the AD. In some embodiments, the AD is a human CD45 AD. In some embodiments, the AD is a human CD26, CD30, CD33, or CD38 AD.

[0431] In some embodiments, the genetic modification is a deletion, insertion, or substitution in a gene or fragment thereof encoding the AD. In some embodiments, the genetic modification is a deletion, insertion, or substitution in a gene or fragment thereof encoding the AD that eliminates expression of the AD. In some embodiments, the AD is a human CD45 AD. In some embodiments, the AD is a human CD26, CD30, CD33, or CD38 AD.

[0432] In some embodiments, the genetic modification is a substitution of a gene or fragment thereof encoding a polypeptide comprising the AD with a nucleotide sequence encoding a homologue, variant, or derivative of the polypeptide comprising the AD, wherein the encoded homologue, variant, or derivative does not comprise the AD. In some embodiments, the homologue is a non-human primate homologue. In some embodiments, the homologue is derived from rhesus macaque. In some embodiments, the homologue is

derived from cynomolgus monkey. In some embodiments, the variant is a naturally occurring variant. In some embodiments, the variant is a splice variant. In some embodiments, the variant ihas altered glycosylation pattern. In some embodiments, the variant or derivative is capable of signaling. In some embodiments, the AD is a human CD45 AD. In some embodiments, the AD is a human CD26, CD30, CD33, or CD38 AD.

[0433] The genetic modification can reduce or eliminate the expression of any AD for which it is desirable for a CAR or an Adapter to bind, *e.g.,* any of the ADs described in Section IIa.

[0434] The production of CAR cells comprising a genetic modification useful in practicing the provided methods may be carried out using a variety of standard techniques for recombinant DNA methodologies, genetic manipulation, and genome editing known in the art. Genetically modified CAR cells described herein that lack expression of an AD can routinely be obtained using any suitable means known in the art, including for example, siRNA, shRNA, CRISPR, TALEN, and/or ZFN. Methods for genetic manipulation of CAR cells is described, for example, in U.S. Patent Appl. Pub. 20170204372, which is encorporated herein by reference in its entirety.

[0435] In some embodiments the CAR cell is engineered to eliminate or reduce the expression of a functional T cell receptor (TCR) and/or human leukocyte antigen (HLA), *e.g.,* HLA class I and/or HLA class II. Modified cells that lack expression of a functional TCR and/or HLA can routinely be obtained using any suitable means known in the art, including for example, siRNA, shRNA, CRISPR, TALEN, and/or ZFN.

[0436] In some embodiments, the CAR cell is engineered to eliminate or reduce the expression of a molecule that may decrease the ability of a CAR cell to mount an immune effector response. In further embodiments, the CAR cell is engineered to eliminate or reduce the expression of a molecule selected from: PD1, PDL1, CTLA4, TIM3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGFR beta. In some embodiments, the CAR cell has been engineered to eliminate or reduce the expression of 2, 3, 4, 5 or more of the above molecules. Modified cells that lack expression of one or more of the above molecules can routinely be obtained using any suitable means known in the art, including for example, siRNA, shRNA, CRISPR, TALEN, and/or ZFN.

[0437] In further embodiments, the CAR cell is engineered to eliminate or reduce the expression of one or more of (a) a functional TCR and an HLA; and (b) a molecule selected from: PD1, PDL1, CTLA4, TIM3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGFR beta. In further embodiments, the CAR cell has been engineered to eliminate or reduce the expression of 2, 3, 4, 5, 6 or more of the above molecules.

VIII. Compositions

[0438] Described herein are compositions comprising a CAR cell (*e.g.,* as described in Section VII) and an Adapter (*e.g.,* as described in Section V).

[0439] For example, in one embodiment a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0440] In one embodiment, a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0441] In one embodiment, a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the binding of the Adapter cross-links the second AD on the target cell or complexes containing the second AD. In some embodiments, the Adapter contains an ADBD that is derived from a non-naturally occurring scaffold. In some embodiments, the Adapter contains an AD that is not expressed by the target cell. In some embodiments the Adapter contains an AD is on a secreted protein. In some embodiments the Adapter contains an alfafetoprotein AD. In some embodiments, the AD of the Adapter is not a nuclear protein. In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0442] In one embodiment, a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an alternative scaffold binding domain (ASBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in

Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0443] In one embodiment, a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD comprising an ASBD that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0444] In one embodiment a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; (b) an Adapter which comprises (i) said first AD and (ii) a D domain that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0445] In one embodiment, the composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described in Section V. In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0446] In one embodiment, a composition comprises (a) a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a first D domain that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) an Adapter which comprises (i) said first AD and (ii) a second D domain that binds to a second AD on a target cell. The CAR cell can be any CAR cell described herein (*e.g.,* as described in Section VII) and/or the Adapter can be any Adapter described herein (*e.g.,* as described in Section V). In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the first or second AD.

[0447] In certain embodiments, the CAR comprises a single-chain variable fragment (scFv) ADBD. In other embodiments, the CAR comprises an alternative scaffold binding domain (ASBD) ADBD. In further embodiments, the CAR comprises a D domain.

[0448] In some embodiments, the CAR comprises 2 ADBDs. In other embodiments, the CAR comprises an ASBD and a scFv. In further embodiments, the CAR comprises a D domain and a scFv. In some embodiments, the CAR comprises 2 ASBDs. In further embodiments, the CAR comprises 2 D domains.

[0449] In some embodiments, the CAR intracellular domain is a signaling domain. In further embodiments, the CAR intracellular domain comprises a primary signaling domain. In certain embodiments, the CAR intracellular domain comprises a CD3ζ primary signaling domain. In some embodiments, the CAR intracellular domain further comprises a costimulatory signaling domain. In further embodiments, the costimulatory signaling domain is selected from: CD28, 41BB, CD27, and CD134. In particular embodiments, the CAR intracellular signaling domain comprises a 41BB costimulatory signaling domain.

[0450] In some embodiments, the CAR binds to an antigen selected from: CD45, CD26, CD30, CD33, and CD38. In some embodiments, the CAR binds to CD26. In some embodiments, the CAR binds to CD30. In some embodiments, the CAR binds to CD33. In some embodiments, the CAR binds to CD38. In further embodiments, the CAR binds to CD45.

[0451] In some embodiments, the CAR binds to an antigen selected from: CD19, CD22, CD123, BCMA, CS1, HER2, TACI, BAFFR, and PDL1. In further embodiments, the CAR binds to BCMA. In further embodiments, the CAR binds to CS1. In other embodiments, the CAR binds to CD123. In other embodiments, the CAR binds to CD19. In other embodiments, the CAR binds to CD22. In other embodiments, the CAR binds to TACI. In other embodiments, the CAR binds to BAFFR. In other embodiments, the CAR binds to PDL1. In other embodiments, the CAR binds to HER2.

[0452] In some embodiments, the CAR comprises 2 ADBDs that bind to separate targets. In further embodiments, the CAR binds to BCMA and CS1. In further embodiments, the CAR binds to CD19 and CD123. In other embodiments, the CAR binds to CD22 and CD123. In other embodiments, the CAR binds to PDL1 and CD123. In some embodiments, the CAR binds to CD45 and a second target. In certain embodiments, the CAR comprises a first ASBD that binds to BCMA and a second ASBD that binds to CS1. In other embodiments, the CAR comprises a first D domain that binds to BCMA and a second D domain that binds to CS1. In other embodiments, the CAR comprises a D domain that binds to BCMA and a scFv that binds to CS1. In other embodiments, the CAR comprises a D domain that binds to CS1 and a scFv that binds to BCMA. In certain embodiments, the CAR comprises a first ASBD that binds to CD19 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD19 and a second D domain that binds to CD123. In some embodiments, the CAR comprises a first D domain that binds to a CD45 AD and a second D domain that binds to a second AD. In other embodiments, the CAR comprises a D domain that binds to CD19 and a scFv that binds to CD123. In other embodiments, the CAR comprises a first ASBD that binds to CD22 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD22 and a second D domain that binds to CD123. In other

embodiments, the CAR comprises a D domain that binds to CD22 and a scFv that binds to CD123. In some embodiments, the CAR comprises a first ASBD that binds to PDL1 and a second ASBD that binds to CD123. In some embodiments, the CAR comprises a first D domain that binds to PDL1 and a second D domain that binds to CD123. In some embodiments, the CAR comprises a D domain that binds to PDL1 and a scFv that binds to CD123. In some embodiments, the CAR comprises an ASBD that binds to CD19 and a scFv that binds to CD123.

[0453] In some embodiments, the Adapter comprises an AD of a tumor antigen. In further embodiments, the tumor antigen is selected from the group: BCMA, CD123, CD19, CD22, CS1, TACI, BAFFR, and PDL1. In further embodiments, the tumor antigen is HER2.

[0454] In some embodiments, the Adapter comprises an ADBD that is a scFv. In further embodiments, the Adapter comprises an ADBD that is an ASBD. In some embodiments, the Adapter comprises a D domain.

[0455] In some embodiments, the Adapter comprises two ADBDs. In further embodiments, the Adapter comprises two ADBDs that (a) are the same, (b) bind to the same antigenic determinant, (c) bind to different ADs of the same antigen, (d) bind to different antigens on the same cell, or (d) bind to different antigens on different cells. In further embodiments, the Adapter comprises two ASBDs. In certain embodiments, the Adapter comprises two D domains. In some embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is an ASBD. In other embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is a D domain.

[0456] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: CD45, CD26, CD30, CD33, and CD38. In certain embodiments, the Adapter comprises an ADBD binds to CD45. In other embodiments, the Adapter comprises an ADBD that binds to CD26. In some embodiments, the Adapter comprises an ADBD that binds to CD30. In other embodiments, the Adapter comprises an ADBD that binds to CD33. In other embodiments, the Adapter comprises an ADBD that binds to CD38. In some embodiments, the Adapter comprises an ADBD that binds to CD45.

[0457] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1. In certain embodiments, the Adapter comprises an ADBD binds to BCMA. In other embodiments, the Adapter comprises an ADBD that binds to CD123. In some embodiments, the Adapter comprises an ADBD that binds to CD19. In other embodiments, the Adapter comprises an ADBD that binds to CD22. In other embodiments, the Adapter comprises an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to HER2. In other embodiments, the Adapter comprises an ADBD that binds to TACI. In other embodiments, the Adapter comprises an ADBD that binds to BAFFR. In other embodiments, the Adapter comprises an ADBD that binds to PDL1.

[0458] In some embodiments, the Adapter is bispecific. In further embodiments, the Adapter comprises an ADBD that binds to CD19 and an ADBD that binds to CD123. In other embodiments, the Adapter comprises an ADBD that binds to BCMA and an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to CD22 and an ADBD that binds to CD123. In other embodiments, the Adapter comprises an ADBD that binds to PDL1 and an ADBD that binds to CD123. In some embodiments, the Adapter binds to a human CD45 AD and a second AD.

[0459] In some embodiments, the target cell is a tumor cell. In further embodiments, the tumor cell is selected from the group: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In further embodiments, the tumor cell is selected from the group: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cell is an AML tumor cell. In some embodiments, the tumor cell is an CLL tumor cell. In some embodiments, the tumor cell is an MM tumor cell.

[0460] In some embodiments, the target cell is a cancert cell. In further embodiments, the cancer cell is selected from the group: breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, colon cancer, and lung cancer. In further embodiments, the cancer cell is breast cancer. In some embodiments, the cancer cell is ovarian cancer.

[0461] In some embodiments, the composition comprises at least two target cells. In some embodiments, at least one target cell is a tumor cell. In further embodiments, the first and second target cells are tumor cells. In certain embodiments, the first and second tumor cells are of the same tumor type. In other embodiments, the first and second tumor cells are of a different tumor type. In some embodiments, the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In some embodiments, the tumor cells are selected from: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM).

[0462] In some embodiments, the cell expressing the CAR is an immune effector cell. In further embodiments, the immune effector cell is a T cell. In other embodiments, the immune effector cell is an NK cell. In some embodiments, the cell expressing the CAR kills the target cell. In some embodiments, binding of the Adapter to an AD blocks the activity of the antigen comprising the AD. In some embodiments, the cell expressing the CAR comprises a genetic modification that reduces or eliminates the expression of an AD described herein. In some embodiments, the cell expressing the CAR comprises a genetic modification that reduces or eliminates the expression of a human CD45 AD.

[0463] In one embodiment, the composition is within a patient, *e.g.,* a human patient.

[0464] In some embodiments, the CAR cell binds to an AD that is present on both a target cell and an Adapter. In other embodiments, the CAR cell binds to an AD that is present on an Adapter, but is not present on a target cell. In some embodiments, the AD is a naturally occurring protein/molecule. In some embodiments, the AD is a human protein/molecule.

IX. Methods that Comprise Contacting a Target Cell

[0465] Described herein are methods of use comprising contacting a target cell with a CAR cell (*e.g.,* as described above in Section VII) and an Adapter (*e.g.,* as described above in Section V) or a composition (*e.g.,* as described above in Section VIII).

[0466] For example, in one embodiment, a method of delivering an immune response to a target cell comprises contacting the target cell with any of the compositions described herein (*e.g.,* as described in Section VIII). In another embodiment, a method of killing a target cell comprises contacting the target cell with any of the compositions described herein (*e.g.,* as described in Section VIII). As used herein, "contacting" can refer to contacting a target cell in vitro (*e.g.,* in a cell culture) or contacting a target cell in vivo (*e.g.,* in a patient).

[0467] In one embodiment, a method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a CAR, wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0468] In one embodiment, a method of delivering an immune response to one or more target cells comprises contacting a composition comprising a first target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0469] In one embodiment, method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0470] In one embodiment, a method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell.

[0471] In one embodiment, a method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein (a) a first antigenic determinant (AD) is present on the target cell; (b) the composition comprising the first target cell further comprises an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on the target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0472] In one embodiment, a method of delivering an immune response to one or more target cells comprises contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein (a) a first AD is present on the first target cell; (b) the composition comprising the first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an antigenic determinant binding domain (ADBD) that binds to a second AD on a second target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0473] In one embodiment, a method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein (a) a first antigenic determinant (AD) is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0474] In one embodiment, a method of delivering an immune response to a target cell comprises contacting a composition comprising a target cell with a cell expressing a chimeric antigen receptor (CAR), wherein (a) a first antigenic determinant (AD) is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0475] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell

expressing a CAR, wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0476] In one embodiment, a method of killing one or more target cells comprising contacting a composition comprising a first target cell with an Adapter, wherein, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD on said first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell.

[0477] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell.

[0478] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with an Adapter, wherein (a) the composition comprising the target cell further comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first AD, (ii) a transmembrane domain, and (iii) an intracellular domain; and (b) the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD (*e.g.*, D domain) that binds to a second AD on said target cell.

[0479] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on the target cell and (c) the comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0480] In one embodiment, a method of killing one or more target cells comprises contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the first target cell, (b) the composition comprising a first target cell further comprises a second target cell and an Adapter comprising (i) said first AD and (ii) an ADBD that binds to a second AD on the second target cell; and (c) the CAR comprises (i) an ADBD that binds to said first AD on the first target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0481] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the

composition comprising the target cell further comprises an Adapter comprising (i) an ADBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0482] In one embodiment, a method of killing a target cell comprises contacting a composition comprising a target cell with a cell expressing a CAR, wherein (a) a first AD is present on the target cell; (b) the composition comprising the target cell further comprises an Adapter comprising (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to said first AD on said target cell and (ii) a second AD; and (c) the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain.

[0483] The contacting can occur *in vitro*, *ex vivo*, or *in vivo*. In one embodiment, the contacting occurs in a patient, *e.g.* a human patient, for example after administration of an Adapter to a patient who has received a cell expressing a CAR or after administration of a cell expressing a CAR to a patient who has received an Adapter.

[0484] In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of an AD recognized by a CAR described herein or by an Adapter described herein. In some embodiments, the AD is a human CD45 AD. In some embodiments, the CAR cell comprises a genetic modification that eliminates the expression of the AD recognized by the CAR or by an Adapter bound by the CAR. In some embodiments, the AD is a human CD45 AD.

[0485] In certain embodiments, the CAR comprises a single-chain variable fragment (scFv) ADBD. In other embodiments, the CAR comprises an alternative scaffold binding domain (ASBD) ADBD. In further embodiments, the CAR comprises a D domain.

[0486] In some embodiments, the CAR comprises 2 ADBDs. In other embodiments, the CAR comprises an ASBD and a scFv. In further embodiments, the CAR comprises a D domain and a scFv. In some embodiments, the CAR comprises 2 ASBDs. In further embodiments, the CAR comprises 2 D domains.

[0487] In some embodiments, the CAR intracellular domain is a signaling domain. In further embodiments, the CAR intracellular domain comprises a primary signaling domain. In certain embodiments, the CAR intracellular domain comprises a CD3 ζ primary signaling domain. In some embodiments, the CAR intracellular domain further comprises a costimulatory signaling domain. In further embodiments, the costimulatory signaling domain is selected from: CD28, 41BB, CD27, and CD134. In particular embodiments, the CAR intracellular signaling domain comprises a 41BB costimulatory signaling domain.

[0488] In some embodiments, the CAR binds to an antigen selected from: CD45, CD26, CD30, CD33, and CD38. In further embodiments, the CAR binds to CD26. In other embodiments, the CAR binds to CD30. In other embodiments, the CAR binds to CD33. In other embodiments, the CAR binds to CD38. In some embodiments, the CAR binds to CD45.

[0489] In some embodiments, the CAR binds to an antigen selected from: CD19, CD22, CD123, BCMA, CS1, HER2, TACI, BAFFR, and PDL1. In further embodiments, the CAR binds to BCMA. In other embodiments, the CAR binds to CS1. In other embodiments, the CAR binds to CD123. In other embodiments, the CAR binds to CD19. In other embodiments, the CAR binds to CD22. In other embodiments, the CAR binds to TACI. In other embodiments, the CAR binds to BAFFR. In other embodiments, the CAR binds to PDL1. In other embodiments, the CAR binds to HER2.

[0490] In some embodiments, the CAR comprises 2 ADBDs that bind to separate targets. In further embodiments, the CAR binds to CD19 and CD123. In other embodiments, the CAR binds to BCMA and CS1. In other embodiments, the CAR binds to CD22 and CD123. In other embodiments, the CAR binds to PDL1 and CD123. In some embodiments, the CAR binds to CD45 and second target. In certain embodiments, the CAR comprises a first ASBD that binds to CD19 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD19 and a second D domain that binds to CD123. In certain embodiments, the CAR comprises a first ASBD that binds to BCMA and a second ASBD that binds to CS1. In other embodiments, the CAR comprises a first D domain that binds to BCMA and a second D domain that binds to CS1. In other embodiments, the CAR comprises a D domain that binds to CS1 and a scFv that binds to BCMA. In some embodiments, the CAR comprises a first D domain that binds to a CD45 AD and a second D domain that binds to a second AD. In other embodiments, the CAR comprises a D domain that binds to CD19 and a scFv that binds to CD123. In other embodiments, the CAR comprises a first ASBD that binds to CD22 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD22 and a second D domain that binds to CD123. In other embodiments, the CAR comprises a D domain that binds to CD22 and a scFv that binds to CD123. In some embodiments, the CAR comprises a first ASBD that binds to PDL1 and a second ASBD that binds to CD123. In some embodiments, the CAR comprises a first D domain that binds to PDL1 and a second D domain that binds to CD123. In some embodiments, the CAR comprises a D domain that binds to PDL1 and a scFv that binds to CD123. In some embodiments, the CAR comprises an ASBD that binds to CD19 and a scFv that binds to CD123.

[0491] In some embodiments, the Adapter comprises an AD of a tumor antigen. In further embodiments, the tumor antigen is selected from the group: CD45, CD26, CD30, CD33, and CD38.

[0492] In some embodiments, the Adapter comprises an AD of a tumor antigen. In further embodiments, the tumor antigen is selected from the group: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1.

[0493] In some embodiments, the Adapter comprises an ADBD that is a scFv. In further embodiments, the Adapter comprises an ADBD that is an ASBD. In some embodiments, the Adapter comprises a D domain.

[0494] In some embodiments, the Adapter comprises two ADBDs. In further embodiments, the Adapter comprises two ADBDs that (a) are the same, (b) bind to the same antigenic determinant, (c) bind to different ADs of the same antigen, (d) bind to different antigens on the same cell, or (e) bind to different antigens on different cells. In some embodiments, the Adapter comprises two ASBDs. In certain embodiments, the Adapter comprises two D domains. In some embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is an ASBD. In other embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is a D domain.

[0495] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: CD45, CD26, CD30, CD33, and CD38. In certain embodiments, the Adapter comprises an ADBD binds to CD26. In other embodiments, the Adapter comprises an ADBD that binds to CD30. In some embodiments, the Adapter comprises an ADBD that binds to CD38. In other embodiments, the Adapter comprises an ADBD that binds to CD45.

[0496] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1. In certain embodiments, the Adapter comprises an ADBD binds to BCMA. In other embodiments, the Adapter comprises an ADBD that binds to CD123. In some embodiments, the Adapter comprises an ADBD that binds to CD19. In other embodiments, the Adapter comprises an ADBD that binds to CD22. In other embodiments, the Adapter comprises an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to HER2. In other embodiments, the Adapter comprises an ADBD that binds to TACI. In other embodiments, the Adapter comprises an ADBD that binds to BAFFR. In other embodiments, the Adapter comprises an ADBD that binds to PDL1.

[0497] In some embodiments, the Adapter is bispecific. In further embodiments, the Adapter comprises an ADBD that binds to CD19 and an ADBD that binds to CD123. In other embodiments, the Adapter comprises an ADBD that binds to BCMA and an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to CD22 and an ADBD that binds to CD123. In other embodiments, the Adapter comprises an ADBD that binds to PDL1 and an ADBD that binds to CD123. In some embodiments, the Adapter binds to a human CD45 AD and a second AD.

[0498] In some embodiments, the target cell is a tumor cell. In further embodiments, the tumor cell is selected from the group: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In further embodiments, the tumor cell is selected from the group: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cell is an AML tumor cell. In some embodiments, the tumor cell is an CLL tumor cell. In some embodiments, the tumor cell is an MM tumor cell.

[0499] In some embodiments, the composition comprises at least two target cells. In some embodiments, at least one target cell is a tumor cell. In further embodiments, the first and second target cells are tumor cells. In certain embodiments, the first and second tumor cells are of the same tumor type. In other embodiments, the first and second tumor cells are of a different tumor type. In some embodiments, the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In some embodiments, the tumor cells are selected from: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cells are multiple myeloma (MM). In the methods of killing a target cell provided herein, the target cell can be a cancer cell. Exemplary cancer cells the can be targeted according to the methods provided herein are discussed in Section X.

[0500] In some embodiments, the target cell is a tumor cell. In further embodiments, the tumor cell is selected from the group: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In some embodiments, the tumor cell is selected from: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cell is multiple myeloma (MM).

[0501] In some embodiments, the target cell is a cancer cell. In further embodiments, the cancer cell is selected from the group: breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, colon cancer, and lung cancer. In some embodiments, the cancer cell is breast cancer. In some embodiments, the cancer cell is ovarian cancer.

[0502] In some embodiments, the composition comprises at least two target cells. In some embodiments, at least one target cell is a tumor cell. In further embodiments, the first and second target cells are tumor cells. In certain embodiments, the first and second tumor cells are of the same tumor type. In other embodiments, the first and second tumor cells are of a different tumor type. In some embodiments, the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In some embodiments, the tumor cells are selected from: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cells are multiple myeloma (MM).

[0503] In the methods of killing a target cell provided herein, the target cell can be a cell of the immune system. In some embodiments, the target cell is a B cell. In some embodiments, the target cell is a T cell. In some embodiments, the target cell is a naïve T cell. In some embodiments, the target cell is a memory T cell.

[0504] In the methods of killing a target cell provided herein, the target cell can be a bacterial cell (*e.g.,* tuberculosis, smallpox, and anthrax), a cell of a parasite (*e.g.,* malaria or leishmaniosis) a fungal cell, a mold, a mycoplasma, or a cell infected with a virus (*e.g.,* HIV, hepatitis b, rabies, Nipah virus, west Nile virus, a meningitis virus, or CMV).

[0505] In some embodiments, the cell expressing the CAR is an immune effector cell. An immune effector cell is a cell that is involved in an immune response, *e.g.,* in the promotion of an immune effector response. Examples of immune effector cells include T cells (*e.g.,* alpha/beta T cells and gamma/delta T cells), B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloid-derived phagocytes. An immune effector function or immune effector response is a function or response of for example, an immune effector cell ***that*** enhances or promotes an immune attack of a target cell. In some embodiments, the immune effector function or response refers a property of a T or NK cell that promotes killing, or the inhibition of growth or proliferation, of a target cell. For example, primary stimulation and costimulation are examples of immune effector function or response of a T cell. In particular embodiments, an immune effector function or response is promoted by the action of the disclosed CAR, Adapter, and/or CAR and Adapter compositions. Such function or response results in, for example, a CAR cell that is more effective at proliferation, cytokine production, cytotoxicity or upregulation of cell surface markers such as CD25, CD69, and CD107a.

[0506] In some embodiments, the immune effector cell is a T cell. In other embodiments, the immune effector cell is an NK cell. In some embodiments, the cell expressing the CAR kills the target cell. In some embodiments, binding of the Adapter to an AD blocks the activity of the antigen comprising the AD.

[0507] In some embodiments, the CAR cell kills the target cell upon direct binding to the target cell. In some embodiments, the CAR cell kills the target cell upon binding to the Adapter, wherein the Adapter is bound to the target cell (*e.g.,* as depicted in FIGS. 3A-3C).

[0508] In some embodiments, binding of CAR to the target cell and/or to the Adapter results in intracellular signaling in the cell expressing the CAR.

[0509] In some embodiments, binding of the CAR to the target cell and/or to the Adapter results in degranulation. Degranulation can result in the release of, depending on the cell type, antimicrobial, cytotoxic or other molecules from secretory granules in the immune cell. Molecules like perforin (a pore forming cytotoxin) or granzymes (serine proteases that induce apoptosis in the target cell) aid T cells and NK cells in killing tumor cells (or other cell types).

[0510] In some embodiments, binding of the CAR to the target cell and/or to the Adapter results in cytokine secretion by the cell expressing the CAR. The cytokine can be, for example, interferon gamma (IFNγ).

[0511] In some embodiments, binding of the CAR to the target cell and/or to the Adapter results in proliferation of the cell expressing the CAR.

X. Therapeutic Uses

[0512] Described herein are methods of delivering an immune response to a target cell in a patient and/or killing a target cell in a patient comprising administering an Adapter (as described herein (*e.g.,* as described in Section V)) and/or a CAR cell described herein (*e.g.,* as described in Section VII) to the patient. Also described herein are methods of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprising administering an Adapter described herein (*e.g.,* as described in Section V) and/or a CAR cell described herein (*e.g.,* as described in Section VII) to the patient. In particular embodiments, provided herein are methods of treating hematological cancer or autoimmune disease comprising administering an Adapter described herein (*e.g.,* as described in Section V) and/or a CAR cell described herein (*e.g.,* as described in Section VII) to the patient.

[0513] In one embodiment,a method of delivering an immune response to a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment,a method of depleting lymphocytes in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating hematological cancer comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating an autoimmune disease or disorder comprises administering a cell expressing a CAR to the patient. In one embodiment, a first AD is present on the target cell, and the CAR comprises (i) an ADBD that binds to said first AD on the target cell, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; and the CAR comprises (i) an ADBD that is an ASBD that binds to said first AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR the cell expressing a CAR can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR.

[0514] In one embodiment, a method of delivering an immune response to a target cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting lymphocytes in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering an Adapter to the patient. In certain embodiments, a method of treating hematological cancer comprises administering an Adapter to the patient. In certain embodiments, a method of

treating an autoimmune disease or disorder comprises administering an Adapter to the patient. In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell. In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell. In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell. In the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can have been treated with any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In some embodiments of the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the patient has previously been treated with an Adapter (in addition to the cell expressing a CAR). In some embodiments, the Adapter that is administered to the patient and the Adapter that was previously administered to the patient bind to different ADs (*e.g.,* on the same or different target cells). In the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0515] In one embodiment, a method of delivering an immune response to a target cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting lymphocytes in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering an Adapter to the patient. In certain embodiments, a method of treating hematological cancer comprises administering an Adapter to the patient. In certain embodiments, a method of treating an autoimmune disease or disorder comprises administering an Adapter to the patient. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter

comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said target cell. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said target cell. In the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can comprise any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In some embodiments of the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the patient comprises an Adapter (in addition to the cell expressing a CAR). In some embodiments, the Adapter that is administered to the patient and the Adapter comprised by the patient bind to different ADs (*e.g.,* on the same or different target cells). In the methods of killing a target cell in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0516] In one embodiment, a method of redirecting an immune response to a target cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting target cell killing in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting lymphocyte depletion in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting treatment of a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection comprises administering an Adapter to the patient. In certain embodiments, a method of redirecting treatment of a hematological cancer comprises administering an Adapter to the patient. In certain embodiments, a method of redirecting treatment of an autoimmune disease or disorder comprises administering an Adapter to the patient. In one embodiment, the patient has been treated with a cell expressing a CAR, wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell. In the methods of redirecting target cell killing in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can have been treated with any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In one embodiment, the patient comprises a cell expressing a CAR, wherein the

CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on a first target cell, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on a second target cell. In the methods of redirecting target cell killing in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can comprise any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In the methods of redirecting target cell killing in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0517] In one embodiment, a method of delivering an immune response to a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of depleting lymphocytes in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating hematological cancer comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating an autoimmune disease or disorder comprises administering a cell expressing a CAR to the patient. In one embodiment, a first AD and a second AD are present on the target cell, the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to the second AD on said target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the patient has been treated with an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the patient has been treated with an Adapter comprising (i) an ADBD that binds to the first AD on said target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the patient has been treated with an Adapter comprising (i) an ADBD comprising an ASBD that binds to the first AD on the target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and/or the patient can have been treated with any of Adapters described herein (*e.g.,* as described in Section V). In the methods of killing a target cell in a patient

comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0518] In one embodiment, a method of delivering an immune response to a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of depleting lymphocytes in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating hematological cancer comprises administering a cell expressing a CAR to the patient. In certain embodiments, a method of treating an autoimmune disease or disorder comprises administering a cell expressing a CAR to the patient. In one embodiment, a first AD and a second AD are present on the target cell, the patient comprises an Adapter comprising (i) said first AD and (ii) an ADBD that binds to the second AD on said target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the patient comprises an Adapter comprising (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the patient comprises an Adapter comprising (i) an ADBD that binds to the first AD on said target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the patient comprises an Adapter comprising (i) an ADBD comprising an ASBD that binds to the first AD on the target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and/or the patient can comprise any of Adapters described herein (*e.g.,* as described in Section V). In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be in a pharmaceutically acceptable composition. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0519] In one embodiment, a method of delivering an immune response to a target cell in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of killing a target cell in a patient comprises administering a cell expressing a CAR and an Adapter to the

patient. In another embodiment, a method of depleting lymphocytes in in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of treating a proliferative disorder, cancer, autoimmune disease, infection, or allograft rejection in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In certain embodiments, a method of treating hematological cancer comprises administering a cell expressing a CAR and an Adapter to the patient. In certain embodiments, a method of treating an autoimmune disease or disorder comprises administering a cell expressing a CAR and an Adapter to the patient. In one embodiment, a first AD and a second AD are present on the target cell, the Adapter comprises (i) said first AD and (ii) an ADBD that binds to the second AD on said target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the target cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the Adapter comprises (i) a first AD and (ii) an ADBD that binds to a second AD on the target cell; and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the Adapter comprises (i) an ADBD that binds to the first AD on said target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the target cell; the Adapter comprises (i) an ADBD comprising an ASBD that binds to the first AD on the target cell and (ii) a second AD; and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR and an Adapter to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V). In the methods of killing a target cell in a patient comprising administering a cell expressing a CAR and an Adapter to a patient, the cell expressing a CAR and the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in a single pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in separate pharmaceutically acceptable compositions. In some embodiments, the CAR cell comprises a genetic modification that reduces or eliminates the expression of an AD bound by the CAR or the Adapter.

[0520] In certain embodiments, the CAR comprises a single-chain variable fragment (scFv) ADBD. In other embodiments, the CAR comprises an alternative scaffold binding domain (ASBD) ADBD. In further embodiments, the CAR comprises a D domain.

[0521] In some embodiments, the CAR comprises 2 ADBDs. In other embodiments, the CAR comprises an ASBD and a scFv. In further embodiments, the CAR comprises a D domain and a scFv. In some embodiments, the CAR comprises 2 ASBDs. In further embodiments, the CAR comprises 2 D domains.

[0522] In some embodiments, the CAR intracellular domain is a signaling domain. In further embodiments, the CAR intracellular domain comprises a primary signaling domain. In certain embodiments, the CAR intracellular domain comprises a CD3 ζ primary signaling domain. In some embodiments, the CAR intracellular domain further comprises a costimulatory signaling domain. In further embodiments, the costimulatory signaling domain is selected from: CD28, 41BB, CD27, and CD134. In particular embodiments, the CAR intracellular signaling domain comprises a 41BB costimulatory signaling domain.

[0523] In some embodiments, the CAR binds to an antigen selected from: CD45, CD26, CD30, CD33, and CD38. In further embodiments, the CAR binds to CD45. In other embodiments, the CAR binds to CD26. In other embodiments, the CAR binds to CD30 In other embodiments, the CAR binds to CD33. In other embodiments, the CAR binds to CD38. In some embodiments, the CAR binds to a CD45 AD.

[0524] In some embodiments, the CAR binds to an antigen selected from: CD19, CD22, CD123, BCMA, CS1, HER2, TACI, BAFFR, and PDL1. In further embodiments, the CAR binds to BCMA. In other embodiments, the CAR binds to CS1. In other embodiments, the CAR binds to CD123. In other embodiments, the CAR binds to CD19. In other embodiments, the CAR binds to CD22. In other embodiments, the CAR binds to TACI. In other embodiments, the CAR binds to BAFFR. In other embodiments, the CAR binds to PDL1. In other embodiments, the CAR binds to HER2.

[0525] In some embodiments, the CAR comprises 2 ADBDs that bind to separate targets. In further embodiments, the CAR binds to CD19 and CD123. In other embodiments, the CAR binds to BCMA and CS1. In other embodiments, the CAR binds to CD22 and CD123. In other embodiments, the CAR binds to PDL1 and CD123. In some embodiments, the CAR binds to CD45 and second target. In certain embodiments, the CAR comprises a first ASBD that binds to CD19 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD19 and a second D domain that binds to CD123. In other embodiments, the CAR comprises a D domain that binds to CD19 and a scFv that binds to CD123. In certain embodiments, the CAR comprises a first ASBD that binds to BCMA and a second ASBD that binds to CS1. In other embodiments, the CAR comprises a first D domain that binds to BCMA and a second D domain that binds to CS1. In other embodiments, the CAR comprises a D domain that binds to CS1 and a scFv that binds to BCMA. In other embodiments, the CAR comprises a first ASBD that binds to CD22 and a second ASBD that binds to CD123. In other embodiments, the CAR comprises a first D domain that binds to CD22 and a second D domain that binds to CD123. In some embodiments, the CAR comprises a first D domain that binds to a CD45 AD and a second D domain that binds to a second AD. In other embodiments, the CAR comprises a D domain that binds to CD22 and a scFv that binds to CD123. In some embodiments, the CAR comprises a first ASBD that binds to PDL1 and a second ASBD that binds to CD123. In some embodiments, the CAR comprises a first D domain that binds to PDL1 and a second D domain that binds to CD123. In some embodiments, the CAR comprises a D domain that binds to PDL1 and a scFv that binds to

CD123. In some embodiments, the CAR comprises an ASBD that binds to CD19 and a scFv that binds to CD123.

[0526] In some embodiments, the Adapter comprises an AD of a tumor antigen. In further embodiments, the tumor antigen is selected from the group: CD45, CD26, CD30, CD33, and CD38.

[0527] In some embodiments, the Adapter comprises an AD of a tumor antigen. In further embodiments, the tumor antigen is selected from the group: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1.

[0528] In some embodiments, the Adapter comprises an ADBD that is a scFv. In further embodiments, the Adapter comprises an ADBD that is an ASBD. In some embodiments, the Adapter comprises a D domain.

[0529] In some embodiments, the Adapter comprises two ADBDs. In further embodiments, the Adapter comprises two ADBDs that (a) are the same, (b) bind to the same antigenic determinant, (c) bind to different ADs of the same antigen, (d) bind to different antigens on the same cell, or (e) bind to different antigens on different cells. In some embodiments, the Adapter comprises two ASBDs. In certain embodiments, the Adapter comprises two D domains. In some embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is an ASBD. In other embodiments, the Adapter comprises an ADBD that is a scFv and an ADBD that is a D domain.

[0530] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: CD45, CD26, CD30, CD33, and CD38. In certain embodiments, the Adapter comprises an ADBD binds to CD26. In other embodiments, the Adapter comprises an ADBD that binds to CD30. In some embodiments, the Adapter comprises an ADBD that binds to CD33. In other embodiments, the Adapter comprises an ADBD that binds to CD38. In other embodiments, the Adapter comprises an ADBD that binds to CD45.

[0531] In some embodiments, the Adapter comprises an ADBD that binds to a member selected from: BCMA, CD123, CD19, CD22, CS1, HER2, TACI, BAFFR, and PDL1. In certain embodiments, the Adapter comprises an ADBD binds to BCMA. In other embodiments, the Adapter comprises an ADBD that binds to CD123. In some embodiments, the Adapter comprises an ADBD that binds to CD19. In other embodiments, the Adapter comprises an ADBD that binds to CD22. In other embodiments, the Adapter comprises an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to TACI. In other embodiments, the Adapter comprises an ADBD that binds to BAFFR. In other embodiments, the Adapter comprises an ADBD that binds to PDL1.

[0532] In some embodiments, the Adapter is bispecific. In further embodiments, the Adapter comprises an ADBD that binds to CD19 and an ADBD that binds to CD123. In other embodiments, the Adapter comprises an ADBD that binds to BCMA and an ADBD that binds to CS1. In other embodiments, the Adapter comprises an ADBD that binds to CD22 and an ADBD that binds to CD123. In other embodiments, the

Adapter comprises an ADBD that binds to PDL1 and an ADBD that binds to CD123. In some embodiments, the Adapter comprises an ADBD that binds to a CD45 AD and an ADBD that binds to a second AD.

[0533] In some embodiments, the target cell is a tumor cell. In further embodiments, the tumor cell is selected from the group: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In further embodiments, the tumor cell is selected from the group: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cell is an AML tumor cell. In some embodiments, the tumor cell is a CLL tumor cell. In some embodiments, the tumor cell is an MM tumor cell.

[0534] In some embodiments, the target cell is a cancer cell. In further embodiments, the cancer cell is selected from the group: breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, colon cancer, and lung cancer. In further embodiments, the cancer cell is breast cancer. In some embodiments, the cancer cell is ovarian cancer.

[0535] In some embodiments, the composition comprises at least two target cells. In some embodiments, at least one target cell is a tumor cell. In further embodiments, the first and second target cells are tumor cells. In certain embodiments, the first and second tumor cells are of the same tumor type. In other embodiments, the first and second tumor cells are of a different tumor type. In some embodiments, the tumor cells are selected from: acute leukemia, chronic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia, and myelodysplasia. In some embodiments, the tumor cells are selected from: acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the tumor cells are multiple myeloma (MM).

[0536] In some embodiments, the cell expressing the CAR is an immune effector cell. In further embodiments, the immune effector cell is a T cell. In other embodiments, the immune effector cell is an NK cell. In some embodiments, the cell expressing the CAR kills the target cell. In some embodiments, binding of the Adapter to an AD blocks the activity of the antigen comprising the AD.

[0537] In embodiments, a method of killing a target cell in a patient comprises administering an Adapter and a cell expressing a CAR to the patient. The Adapter and the cell expressing the CAR can be administered in the same pharmaceutical composition or in different pharmaceutical compositions. The Adapter and the cell expressing the CAR can be administered in different pharmaceutical compositions. The Adapter and the cell expressing the CAR can be administered simultaneously or consecutively.

[0538] In one embodiment of the methods of killing a target cell in a patient or the methods of redirecting target cell killing in a patient, the patient has been diagnosed with cancer and the target cell is a cancer cell. In one embodiment, the cancer cell is a prostate cancer cell, a breast cancer cell, a colorectal cancer cell, a lung

cancer cell, an osteosarcoma cell, or a glioblastoma cell. Thus, in some embodiments, the methods provided herein treat cancer.

[0539] Cancers that can be treated include tumors that are not vascularized, or not yet substantially vascularized, as well as vascularized tumors. The cancers can comprise non-solid tumors (such as hematological tumors, for example, leukemias and lymphomas) or can comprise solid tumors. Types of cancers to be treated include, but are not limited to, carcinoma, blastoma, and sarcoma, and certain leukemia or lymphoid malignancies, benign and malignant tumors, and malignancies *e.g.,* sarcomas, carcinomas, and melanomas. Adult tumors/cancers and pediatric tumors/cancers are also included.

[0540] Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, and other sarcomas, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, melanoma, and CNS tumors (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma, germinoma, medulloblastoma, Schwannoma craniopharyogioma, ependymoma, pineaioma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, neuroblastoma, retinoblastoma and brain metastases). In some embodiments, the solid tumor is breast cancer. In some embodiments, the solid tumr is ovarian cancer.

[0541] In another embodiment, the methods described herein are useful for treating a patient having a hematological cancer. Examples of hematological (or hematogenous) cancers include leukemias, including acute leukemias (such as acute lymphocytic leukemia, acute myelocytic leukemia, acute myelogenous leukemia and myeloblasts, promyeiocytic, myelomonocytic, monocytic and erythroleukemia), chronic leukemias (such as chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, and chronic lymphocytic leukemia), polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma (indolent and high grade forms), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia and myelodysplasia. Further examples of hematological (or hematogenous) cancers include acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the hematological (or hematogenous) cancer is AML. In some embodiments, the hematological (or hematogenous) cancer is CLL. In some embodiments, the hematological (or hematogenous) cancer is MM.

[0542] In some embodiments, the cancer is a relapsed of refractory cancer. In some embodiments, the cancer is a relapsed cancer. In some embodiments, the cancer has relapsed following chemotherapy. In some embodiments, the cancer has relapsed following treatment with a biological agent. In some embodiments, the biological agent is a therapeutic antibody or a CAR-T cell. In some embodiments, the cancer is a refractory cancer. In some embodiments, the cancer is refractory to chemotherapy. In some embodiments, the cancer is refractory to treatment with a biological agent. In some embodiments, the biological agent is a therapeutic antibody or a CAR-T cell.

[0543] In some embodiments, the cancer is a relapsed of refractory hematological cancer. In some embodiments, the cancer is a relapsed hematological cancer. In some embodiments, the cancer is a hematological cancer that has relapsed following chemotherapy. In some embodiments, the cancer is a hematological cancer that has relapsed following treatment with a biological agent. In some embodiments, the biological agent is a therapeutic antibody or a CAR-T cell. In some embodiments, the cancer is a hematological cancer that has relapsed following autologous bone marrow transplantation. In some embodiments, the cancer is a hematological cancer that has relapsed following allogeneic bone marrow transplantation. In some embodiments, the cancer is a hematological cancer that has relapsed following hematopoietic stem cell transplantation (HSCT). In some embodiments, the HSCT is autologous HSCT. In some embodiments, the cancer is a refractory hematological cancer. In some embodiments, the cancer is a hematological cancer that is refractory to chemotherapy. In some embodiments, the cancer is a hematological cancer that is refractory to treatment with a biological agent. In some embodiments, the biological agent is a therapeutic antibody or a CAR-T cell. In some embodiments, the hematological cancer is acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), or multiple myeloma (MM). In some embodiments, the hematological cancer is AML. In some embodiments, the hematological cancer is CLL. In some embodiments, the hematological cancer is MM. In some embodiments, the target cell cell is a B cell. In some embodiments, the target cell is a T cell. In some embodiments, the target cell is a naïve T cell. In some embodiments, the target cell is a memory T cell. In some embodiments, the target cell is a myeloma cell

[0544] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering an Adapter to the patient. In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said multiple myeloma cell (e.g., CS1 or BCMA), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii)

an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can have been treated with any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In some embodiments of the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the patient has previously been treated with an Adapter (in addition to the cell expressing a CAR). In some embodiments, the Adapter that is administered to the patient and the Adapter that was previously administered to the patient bind to different ADs (*e.g.,* on the same or different multiple myeloma cells). In some embodiments, the Adapter that is administered to the patient binds to CS1 and the Adapter that was previously administered to the patient binds to BCMA. In some embodiments, the Adapter that is administered to the patient binds to BCMA and the Adapter that was previously administered to the patient binds to CS1. In the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0545] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering an

Adapter to the patient. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said multiple myeloma cell (e.g., CS1 or BCMA), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can comprise any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In some embodiments of the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the patient comprises an Adapter (in addition to the cell expressing a CAR). In some embodiments, the Adapter that is administered to the patient and the Adapter comprised by the patient bind to different ADs (*e.g.,* on the same or different multiple myeloma cells). In some embodiments, the Adapter that is administered to the patient binds to CS1 and the Adapter comprised by the patient binds to BCMA. In some embodiments, the Adapter that is administered to the patient binds to BCMA and the Adapter comprised by the patient binds to CS1. In the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0546] In one embodiment, a method of redirecting an immune response to a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting

multiple myeloma cell killing in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting lymphocyte depletion in a patient comprises administering an Adapter to the patient. In another embodiment, a method of redirecting treatment of multiple myeloma comprises administering an Adapter to the patient. In certain embodiments, a method of redirecting treatment of an autoimmune disease or disorder comprises administering an Adapter to the patient. In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) on said multiple myeloma cell (e.g., CS1 or BCMA), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that is an ASBD that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In one embodiment, the patient has been treated with a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) an antigenic determinant binding domain (ADBD) that binds to a first antigenic determinant (AD) (e.g., AFP p26 or a variant thereof), (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) said first AD and (ii) an ADBD that is an ASBD that binds to a second AD on said multiple myeloma cell (e.g., CS1 or BCMA). In the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V) and/or the patient can have been treated with any of the cells expressing CARS described herein (*e.g.,* as described in Section VII). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In some embodiments of the methods of killing a multiple myeloma cell in a patient comprising administering an Adapter to a patient, the patient has previously been treated with an Adapter (in addition to the cell expressing a CAR). In some embodiments, the Adapter that is administered to the patient and the Adapter that was previously administered to the patient bind to different ADs (*e.g.,* on the same or different multiple myeloma cells). In some embodiments, the Adapter that is administered to the patient binds to CS1 and the Adapter that was previously administered to the patient binds to BCMA. In some embodiments, the Adapter that is administered to the patient binds to BCMA and the Adapter that was previously administered to the patient binds to CS1. In the methods of redirecting multiple myeloma cell killing in a patient comprising administering an Adapter to a patient, the Adapter can be in a pharmaceutically acceptable

composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0547] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering a cell expressing a CAR to the patient. In one embodiment, a first AD (e.g., BCMA) and a second AD (e.g., CS1) are present on the multiple myeloma cell, the patient has been treated with an Adapter comprising (i) said first AD and (ii) an ADBD that binds to the second AD on said multiple myeloma cell; and the CAR comprises (i) an ADBD that binds to said first AD on the multiple myeloma cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the patient has been treated with an Adapter comprising (i) a first AD (e.g., BCMA) and (ii) an ADBD that binds to a second AD on the multiple myeloma cell (e.g., CS1); and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the multiple myeloma cell (e.g., CS1); the patient has been treated with an Adapter comprising (i) an ADBD that binds to the first AD on said multiple myeloma cell and (ii) a second AD (e.g., BCMA); and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the multiple myeloma cell (e.g., CS1); the patient has been treated with an Adapter comprising (i) an ADBD comprising an ASBD that binds to the first AD on the multiple myeloma cell and (ii) a second AD (e.g., BCMA); and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and/or the patient can have been treated with any of Adapters described herein (*e.g.,* as described in Section V). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be in a pharmaceutically acceptable composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple

myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0548] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering a cell expressing a CAR to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering a cell expressing a CAR to the patient. In one embodiment, a first AD (e.g., BCMA) and a second AD (e.g., CS1) are present on the multiple myeloma cell, the patient comprises an Adapter comprising (i) said first AD and (ii) an ADBD that binds to the second AD on said multiple myeloma cell; and the CAR comprises (i) an ADBD that binds to said first AD on the multiple myeloma cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the patient comprises an Adapter comprising (i) a first AD (e.g., BCMA) and (ii) an ADBD that binds to a second AD (e.g., CS1) on the multiple myeloma cell; and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the multiple myeloma cell (e.g., CS1); the patient comprises an Adapter comprising (i) an ADBD that binds to the first AD on said multiple myeloma cell and (ii) a second AD (e.g., BCMA); and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the multiple myeloma cell (e.g., CS1); the patient comprises an Adapter comprising (i) an ADBD comprising an ASBD that binds to the first AD on the multiple myeloma cell and (ii) a second AD (e.g., BCMA or AFP p26 or a variant thereof); and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and/or the patient can comprise any of Adapters described herein (*e.g.,* as described in Section V). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR to a patient, the cell expressing a CAR can be in a pharmaceutically acceptable composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0549] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In one embodiment, a first AD (e.g., BCMA) and a second AD (e.g., CS1) are present on the multiple myeloma cell, the Adapter comprises (i) said first AD and (ii) an ADBD that binds to the second AD on said multiple myeloma cell; and the CAR comprises (i) an ADBD that binds to said first AD on the multiple myeloma cell or the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, the Adapter comprises (i) a first AD (e.g., BCMA) and (ii) an ADBD that binds to a second AD on the multiple myeloma cell (e.g., CS1); and the CAR comprises (i) an ADBD that binds to said first AD on the Adapter, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD (e.g., CS1) is present on the multiple myeloma cell; the Adapter comprises (i) an ADBD that binds to the first AD on said multiple myeloma cell and (ii) a second AD (e.g., BCMA); and the CAR comprises (i) an ADBD that is an ASBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In one embodiment, a first AD is present on the multiple myeloma cell (e.g., CS1); the Adapter comprises (i) an ADBD comprising an ASBD that binds to the first AD on the multiple myeloma cell and (ii) a second AD (e.g., BCMA or AFP p26 or a variant thereof); and the CAR comprises (i) an ADBD that binds to said second AD, (ii) a transmembrane domain, and (iii) an intracellular domain. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR and an Adapter to a patient, the cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII) and the Adapter can be any of the Adapters described herein (*e.g.,* as described in Section V). In some embodiments, the Adapter comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to CS1, BCMA, or CS1 and BCMA. In some embodiments, the CAR comprises an ADBD (e.g., D domain) that binds to AFP p26 or a variant thereof. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR and an Adapter to a patient, the cell expressing a CAR and the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in a single pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in separate pharmaceutically acceptable compositions. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic

agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0550] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering an Adapter to the patient. In one embodiment, the patient has been administered a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165. In one embodiment, the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the CAR comprises the amino acid sequence of SEQ ID NO: 1164. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg. In some embodiments, the Adapter is administered at about 0.07 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.4 mg, about 0.8 mg, about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, about 20 mg, about 24 mg, about 28 mg, about 40 mg, or about 80 mg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg to about 200 mg, about 0.5 mg to about 100 mg, about 1 mg to about 50 mg, about 2 mg to about 25 mg, or about 2 mg to about 12 mg. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter is administered daily. In some embodiments, the Adapter is administered twice a day, three times a day or four times a day. In some embodiments, the Adapter is administered every other day. In some embodiments, the Adapter is

administered every three days. In some embodiments, the Adapter is administered twice a week. In some embodiments, the Adapter is administered weekly. In some embodiments, the Adapter is administered for seven days. In some embodiments, the Adapter is administered for between about a week and about 2 months. In some embodiments, the Adapter is administered at the same frequency over the period of treatment. In some embodiments, the frequency of administration decreases over the period of treatment. In some embodiments, the Adapter is first administered daily for about a week followed by administration twice a week. In one embodiment, between about $50x10^6$ and about $300x10^6$ cells expressing the CAR has been administered to the patient. In one embodiment, about $100x10^6$ cells expressing the CAR has been administered to the patient. The cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In one embodiment, the cell expressing a CAR is a T cell or an NK cell. The Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, he patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0551] In one embodiment, a method of delivering an immune response to a multiple myeloma cell in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of killing a multiple myeloma cell in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of depleting multiple myeloma cells in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of treating multiple myeloma in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In one embodiment, the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165. In one embodiment, the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the CAR comprises the amino acid sequence of SEQ ID NO: 1164. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg. In some embodiments, the Adapter is administered at about 0.07 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In

some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg to about 200 mg, about 0.5 mg to about 100 mg, about 1 mg to about 50 mg, about 2 mg to about 25 mg, or about 2 mg to about 12 mg. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter is administered daily. In some embodiments, the Adapter is administered twice a day, three times a day or four times a day. In some embodiments, the Adapter is administered every other day. In some embodiments, the Adapter is administered every three days. In some embodiments, the Adapter is administered twice a week. In some embodiments, the Adapter is administered weekly. In some embodiments, the Adapter is administered for seven days. In some embodiments, the Adapter is administered for between about a week and about 2 months. In some embodiments, the Adapter is administered at the same frequency over the period of treatment. In some embodiments, the frequency of administration decreases over the period of treatment. In some embodiments, the Adapter is first administered daily for about a week followed by administration twice a week. In one embodiment, between about $50x10^6$ and about $300x10^6$ cells expressing the CAR are administered. In one embodiment, about $100x10^6$ cells expressing the CAR are administered. The cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In one embodiment, the cell expressing a CAR is a T cell or an NK cell. In the methods of killing a multiple myeloma cell in a patient comprising administering a cell expressing a CAR and an Adapter to a patient, the cell expressing a CAR and the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in a single pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in separate pharmaceutically acceptable compositions. In some embodiments, the patient has relapsed multiple myeloma. In some embodiments, the patient has multiple myeloma that relapsed following treatment with a biologic agent, for example, antibody or CAR-T cell. In some embodiments, the patient has multiple myeloma that relapsed following treatment with antibody or CAR-T cell that targeted CS1 or BCMA.

[0552] In one embodiment, a method of delivering an immune response to a B cell lymphoma or leukemia cell expressing BCMA in a patient comprises administering an Adapter to the patient. In another embodiment, a method of killing a B cell lymphoma or leukemia cell expressing BCMA in a patient comprises administering an Adapter to the patient. In another embodiment, a method of depleting B cell lymphoma or leukemia cells expressing BCMA in a patient comprises administering an Adapter to the patient. In another embodiment, a method of treating a B cell lymphoma or leukemia in a patient comprises administering an Adapter to the patient, wherein the B cell lymphoma or leukemia cells express BCMA. In one embodiment, the patient has been administered a cell expressing a chimeric antigen receptor (CAR), wherein the CAR

comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the patient comprises a cell expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165. In one embodiment, the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the CAR comprises the amino acid sequence of SEQ ID NO: 1164. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg. In some embodiments, the Adapter is administered at about 0.07 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg to about 200 mg, about 0.5 mg to about 100 mg, about 1 mg to about 50 mg, about 2 mg to about 25 mg, or about 2 mg to about 12 mg. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter is administered daily. In some embodiments, the Adapter is administered twice a day, three times a day or four times a day. In some embodiments, the Adapter is administered every other day. In some embodiments, the Adapter is administered every three days. In some embodiments, the Adapter is administered twice a week. In some embodiments, the Adapter is administered weekly. In some embodiments, the Adapter is administered for seven days. In some embodiments, the Adapter is administered for between about a week and about 2 months. In some embodiments, the Adapter is administered at the same frequency over the period of treatment. In some embodiments, the frequency of administration decreases over the period of treatment. In some embodiments, the Adapter is first administered daily for about a week followed by administration twice a week. In one embodiment, between about $50x10^6$ and about $300x10^6$ cells expressing the CAR has been administered to the patient. In one embodiment, about $100x10^6$ cells expressing the CAR has been administered to the patient. The cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In one embodiment, the cell expressing a CAR is a T cell or an NK cell. The Adapter can be in a pharmaceutically acceptable composition.

[0553] In one embodiment, a method of delivering an immune response to a B cell lymphoma or leukemia cell expressing BCMA in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of killing a B cell lymphoma or leukemia cell expressing BCMA in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of depleting B cell lymphoma or leukemia cells expressing BCMA in a patient comprises administering a cell expressing a CAR and an Adapter to the patient. In another embodiment, a method of treating B cell lymphoma or leukemia in a patient comprises administering a cell expressing a CAR and an Adapter to the patient, wherein the B cell lymphoma or leukemia cells express BCMA. In one embodiment, the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and the Adapter comprises (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA. In one embodiment, the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165. In one embodiment, the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201. In one embodiment, the CAR comprises the amino acid sequence of SEQ ID NO: 1164. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg. In some embodiments, the Adapter is administered at about 0.07 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg to about 200 mg, about 0.5 mg to about 100 mg, about 1 mg to about 50 mg, about 2 mg to about 25 mg, or about 2 mg to about 12 mg. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter is administered daily. In some embodiments, the Adapter is administered twice a day, three times a day or four times a day. In some embodiments, the Adapter is administered every other day. In some embodiments, the Adapter is administered every three days. In some embodiments, the Adapter is administered twice a week. In some embodiments, the Adapter is administered weekly. In some embodiments, the Adapter is administered for seven days. In some embodiments, the Adapter is administered for between about a week and about 2 months. In some embodiments, the Adapter is administered at the same frequency over the period of treatment. In some embodiments, the frequency of administration decreases over the period of treatment. In some embodiments, the Adapter is first administered daily for about a week followed by administration twice a week. In one embodiment, between about $50x10^6$

and about $300x10^6$ cells expressing the CAR are administered. In one embodiment, about $100x10^6$ cells expressing the CAR are administered. The cell expressing a CAR can be any of the cells expressing CARs described herein (*e.g.,* as described in Section VII). In one embodiment, the cell expressing a CAR is a T cell or an NK cell. The cell expressing a CAR and the Adapter can be in a pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in a single pharmaceutically acceptable composition. In some embodiments, the cell expressing a CAR and the Adapter are in separate pharmaceutically acceptable compositions.

[0554] In one embodiment, the methods described herein are useful for inhibiting tumor growth, reducing neovascularization, reducing angiogenesis, inducing differentiation, reducing tumor volume, and/or reducing the tumorigenicity of a tumor.

[0555] In one embodiment of the methods of killing a target cell in a patient or the methods of redirecting target cell killing in a patient, the patient has been diagnosed with a disease or disorder of the immune system and the target cell is a cell of the immune system. Thus in some embodiments, the methods provided herein treat a disease or disorder of the immune system.

[0556] In some embodiments, the disease or disorder of the immune system is an autoimmune disease or disorder. In some embodiments, the autoimmune disease or disorder is Type I diabetes, systemic sclerosis, multiple sclerosis, rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, or alopecia areata. In some embodiments, the autoimmune disease or disorder is Type I diabetes. In some embodiments, the autoimmune disease or disorder is systemic sclerosis. In some embodiments, the autoimmune disease or disorder is multiple sclerosis. In some embodiments, the autoimmune disease or disorder is rheumatoid arthritis. In some embodiments, the autoimmune disease or disorder is inflammatory bowel disease (IBD). In some embodiments, the autoimmune disease or disorder is Crohn's disease. In some embodiments, the autoimmune disease or disorder is ulcerative colitis.

[0557] In one embodiment of the methods of killing, a target cell in a patient or the methods of redirecting target cell killing in a patient, the target cell is a cell of the immune system. In some embodiments, the target cell is a B cell. In some embodiments, the target cell is a T cell. In some embodiments, the target cell is a naïve T cell. In some embodiments, the target cell is a memory T cell.

[0558] In one embodiment of the methods of killing, a target cell in a patient or the methods of redirecting target cell killing in a patient, the patient has been diagnosed with an autoimmune disease or disorder and the target cell is a cell of the immune system expressing a CD45 AD. In some embdoiments, the target cell is a B cell. In some embodiments, the target cel is a T cell. In some embdoments, the target cell is a mameory T cell. In some ebodiments, the target cell expresses CD45. In some embodiments, the target cell expresses CD45RO.

[0559] In one embodiment of the methods of killing a target cell in a patient or the methods of redirecting target cell killing in a patient, the patient has an infection, and the target cell is a bacterial cell (*e.g.,* tuberculosis, smallpox, and anthrax), a cell of a parasite (*e.g.,* malaria or leishmaniosis) a fungal cell, a mold, a mycoplasma, or a cell infected with a virus (*e.g.,* HIV, hepatitis b, rabies, Nipah virus, west Nile virus, a meningitis virus, or CMV). Thus in some embodiments, the methods provided herein treat an infection.

[0560] In one embodiment, the methods described herein are useful for preparing or conditioning a patient for bone marrow transplantation (BMT) or hematopoietic stem cell transplantation (HSCT). Thus in some embodiments, the methods of killing a target cell in a patient or the methods of redirecting target cell killing in a patient provided herein condition a subject for BMT or HSCT. In some embodiments, the methods provided herein condition a subject for HSCT. In some embodiments, the HSCT is autologous HSCT. In some embodiments, the methods for conditioning a patient disclosed herein does not comprise high dose chemotherapy or total body irradiation (TBI). In some embodiments, the methods for conditioning disclosed herein comprise reduced intensity chemotherapy. In some embodiments, the methods for conditioning disclosed herein comprise total body irradiation. In some embodiments, the patient is more than 65 years old. In some embodiments, the patient has cancer. In some embodiments, the patient has a hematologic cancer. In some embodiments, the patient has a relapsed hematologic cancer. In some embodiments, the hematologic cancer is acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), or multiple myeloma (MM). In some embodiments, the patient has an autoimmune disease or disorder. In some embodiments, the autoimmune disease or disorder is Type I diabetes, multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease (IBD), Crohn's disease, or ulcerative.

[0561] In several embodiments, the administration of the Adapter and/or chimeric antigen receptor cells is intravenous, though other routes, such as intra-arterial, intramuscular, local, or other acceptable route can be used for a given treatment scenario.

[0562] Also provided are therapeutic compositions useful for practicing therapeutic methods described herein. In one embodiment, therapeutic compositions provided herein contain a physiologically tolerable carrier together with at least one species of Adapter as described herein, dissolved or dispersed therein as an active ingredient. In another embodiment, therapeutic compositions provided herein contain a physiologically tolerable carrier together with at least one species of a CAR cell as described herein, dissolved or dispersed therein as an active ingredient. In a preferred embodiment, therapeutic composition is not immunogenic when administered to a human patient for therapeutic purposes.

[0563] The preparation of a pharmacological composition that contains active ingredients dissolved or dispersed therein is well understood in the art. Typically such compositions are prepared as sterile injectables either as liquid solutions or suspensions, aqueous or non-aqueous. However, solid forms suitable for solution, or suspensions, in liquid prior to use can also be prepared. The preparation can also be emulsified. Thus, an

Adapter-containing composition can take the form of solutions, suspensions, tablets, capsules, sustained release formulations or powders, or other compositional forms. In some embodiments, the Adapter compositions are formulated to ensure or optimize distribution in vivo, For example, the blood-brain barrier (BBB) excludes many highly hydrophilic compounds and if so desired, the compositions are prepared so as to increase transfer across the BBB, by for example, formulation in liposomes. For methods of manufacturing liposomes, *see*, *e.g.,* U.S. Pat. Nos. 4,522,811, 5,374,548, and 5,399,331. The liposomes can comprise one or more moieties that are selectively transported into specific cells or organs, thus enhance targeted drug delivery (*see*, *e.g.,* Ranade, Clin. Pharmacol. 29: 685 (1989)).

[0564] The Adapter (and/or CAR cell) can be mixed other active ingredients and/or excipients that are pharmaceutically acceptable and compatible with the active ingredient and in amounts suitable for use in therapeutic methods described herein. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol or the like and combinations thereof. In addition, if desired, the composition can contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents and other auxiliary substances known in the art, which enhance the effectiveness of the active ingredient.

[0565] Therapeutic Adapter formulations can include pharmaceutically acceptable salts of the components therein. Pharmaceutically acceptable salts include the acid addition salts (formed with the free amino groups of the polypeptide) that are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, tartaric, mandelic and other pharmaceutically acceptable salts known in the art. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium or ferric hydroxides, and such organic bases as isopropylamine, trimethylarnine, 2- ethylamino ethanol, histidine, procaine and other salts derived from inorganic bases known in the art.

[0566] Physiologically tolerable carriers are known in the art. Exemplary of liquid carriers are sterile aqueous solutions that contain no materials in addition to the active ingredients and water, or contain a buffer such as sodium phosphate at physiological pH value, physiological saline or both, such as phosphate-buffered saline. Still further, aqueous carriers can contain more than one buffer salt, as well as salts such as sodium and potassium chlorides, dextrose, propylene glycol, polyethylene glycol, and other solutes.

[0567] Liquid compositions can also contain liquid phases in addition to, and to the exclusion of water. Exemplary of such additional liquid phases are glycerin, vegetable oils such as cottonseed oil, organic esters such as ethyl oleate, and water-oil emulsions.

[0568] In one embodiment, a therapeutic composition contains an Adapter, typically in an amount of at least 0.1 weight percent of Adapter per weight of total therapeutic composition. A weight percent is a ratio by weight of Adapter per total composition. Thus, for example, 0.1 weight percent is 0.1 grams of Adapter per 100 grams of total composition.

[0569] Adapter-containing therapeutic compositions typically contains about 10 micrograms (µg) per milliliter (ml) to about 100 milligrams (mg) per ml of Adapter as active ingredient per volume of composition, and more preferably contains about 1 mg/ml to about 10 mg/ml (*i.e.*, about 0.1 to 1 weight percent).

[0570] The dosage ranges for the administration of the Adapter are those large enough to produce the desired effect in which the disease symptoms mediated by the target molecule are ameliorated. The dosage should not be so large as to cause adverse side effects, such as hyperviscosity syndromes, pulmonary edema, congestive heart failure, and other adverse side effects known in the art. Generally, the dosage will vary with the age, condition, sex and extent of the disease in the patient and can be determined by one of skill in the art. The dosage can be adjusted by the individual physician in the event of any complication.

[0571] The Adapter can be administered parenterally by injection or by gradual infusion over time. Although the target molecule can typically be accessed in the body by systemic administration and therefore most often treated by intravenous administration of therapeutic compositions, other tissues and delivery means are contemplated where there is a likelihood that the tissue targeted contains the target molecule. Thus, Adapter can be administered intravenously, intraperitoneally, intramuscularly, subcutaneously, intracavity, transdermally, and can be delivered by peristaltic means. Adapter can also be delivered by aerosol to airways and lungs.

[0572] Therapeutic compositions containing an Adapter can be conventionally administered intravenously, as by injection of a unit dose, for example. The term "unit dose" when used in reference to a therapeutic composition provided herein refers to physically discrete units suitable as unitary dosage for the subject, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required diluent; *e.g.,* carrier, or vehicle. In a specific embodiment, therapeutic compositions containing an Adapter are administered subcutaneously.

[0573] In some embodiments, the Adapter is administered in a manner compatible with the dosage formulation, and in a therapeutically effective amount. The quantity to be administered depends on the subject to be treated, capacity of the subject's system to utilize the active ingredient, and degree of therapeutic effect desired. Precise amounts of active ingredient required to be administered depend on the judgment of the practitioner and are peculiar to each individual. However, suitable dosage ranges for systemic application are disclosed herein and depend on the route of administration. Suitable regimes for administration are also variable, but are typified by an initial administration followed by repeated doses at one or more hour intervals by a subsequent injection or other administration. Alternatively, continuous intravenous infusion sufficient to maintain concentrations in the blood in the ranges specified for in vivo therapies are contemplated.

[0574] The Adapter compositions are formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the

particular mammal being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The dosage ranges for the administration of the Adapter are those large enough to produce the desired effect in which the disease symptoms mediated by the target molecule are ameliorated. The dosage should not be so large as to cause adverse side effects, such as, hyperviscosity syndromes, pulmonary edema, congestive heart failure, and other adverse side effects known in the art. Generally, the dosage will vary with the age, condition, sex and extent of the disease in the patient and can be determined by one of skill in the art. The dosage can be adjusted by the individual physician in the event of any complication.

[0575] The dosage schedule and amounts effective for therapeutic and prophylactic uses, *i.e.*, the "dosing regimen," will depend upon a variety of factors, including the cause, stage and severity of the disease or disorder, the health, physical status, age of the mammal being treated, and the site and mode of the delivery of the Adapter. Therapeutic efficacy and toxicity of the complex and formation can be determined by standard pharmaceutical, pharmacological, and toxicological procedures in cell cultures or experimental animals. Data obtained from these procedures can likewise be used in formulating a range of dosages for human use. Moreover, therapeutic index (*i.e.*, the dose therapeutically effective in 50 percent of the population divided by the dose lethal to 50 percent of the population (ED50/LD50)) can readily be determined using known procedures. The dosage is preferably within a range of concentrations that includes the ED50 with little or no toxicity, and may vary within this range depending on the dosage form employed, sensitivity of the patient, and the route of administration.

[0576] The dosage regimen also takes into consideration pharmacokinetics parameters known in the art, such as, drug absorption rate, bioavailability, metabolism and clearance (*see*, *e.g.,* Hidalgo-Aragones, J. Steroid Biochem. Mol. Biol. 58: 611-617 (1996); Groning *et al.*, Pharmazie 51: 337-341 (1996); Fotherby, Contraception 54: 59-69 (1996); and Johnson *et al.*, J. Pharm. Sci. 84: 1144-1146 (1995)). It is well within the state of the art for the clinician to determine the dosage regimen for each subject being treated. Moreover, single or multiple administrations of Adapter compositions can be administered depending on the dosage and frequency as required and tolerated by the subject. The duration of prophylactic and therapeutic treatment will vary depending on the particular disease or condition being treated. Some diseases are amenable to acute treatment whereas others require long-term, chronic therapy. Adapter can be administered serially, or simultaneously with the additional therapeutic agent.

[0577] In some embodiments, the Adapter is administered at about 1 mg/kg to about 50 mg/kg, about 1 mg/kg to about 25 mg/kg, about 1 mg/kg to about 20 mg/kg, about 1 mg/kg to about 15 mg/kg, about 1 mg/kg to about 10 mg/kg, or about 1 mg/kg to about 5 mg/kg.

[0578] In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 10 mg/kg, about 10 μg/kg to about 10 mg/kg, about 20 μg/kg to about 10 mg/kg, or about 50 μg/kg to about 10 mg/kg. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 1μg/kg to about 5 mg/kg, about 1 μg/kg to about 2 mg/kg, about 1 μg/kg to about 1 mg/kg, about 1 μg/kg to about 5 mg/kg, or about 1 μg/kg to about 2 mg/kg. In some embodiments, the Adapter is administered at about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg. In some embodiments, the Adapter is administered at about 0.07 mg/kg. In some embodiments, the Adapter is administered at about 0.01 mg/kg. In some embodiments, the Adapter is administered at about 0.1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg/kg. In some embodiments, the Adapter is administered at about 0.3 mg/kg. In some embodiments, the Adapter is administered at about 0.4 mg/kg. In some embodiments, the Adapter is administered at about 0.5 mg/kg. In some embodiments, the Adapter is administered at about 0.6 mg/kg. In some embodiments, the Adapter is administered at about 0.7 mg/kg. In some embodiments, the Adapter is administered at about 0.8 mg/kg. In some embodiments, the Adapter is administered at about 0.9 mg/kg. In some embodiments, the Adapter is administered at about 1 mg/kg. In some embodiments, the Adapter is administered at about 0.2 mg to about 200 mg, about 0.5 mg to about 100 mg, about 1 mg to about 50 mg, about 2 mg to about 25 mg, or about 2 mg to about 12 mg. In some embodiments, the Adapter is administered at about 0.4 mg, about 0.8 mg, about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, about 20 mg, about 24 mg, about 28 mg, about 40 mg, or about 80 mg. In some embodiments, the Adapter is administered at about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg. In some embodiments, the Adapter is administered intravenously. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter comprises a D domain that specifically binds to BCMA. In some embodiments, the Adapter comprises a D domain comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

[0579] In some embodiments, more than one dose of the the Adapter is administered. In some embodiments, the more than one dose of the the Adapter is a constant dose. In some embodiments, the Adapter is administered at different doses. In some embodiments, the amount of Adapter administered is increased over time. In some embodiments, the amount of Adapter administered is decreased over time. In some embodiments, the Adapter is first administered at a low dose of between about 0.1 mg/kg and about 5 mg/kg, followed by administration at a high dose between about 0.01 mg/kg and about 0.5 mg/kg. In some

embodiments, the Adapter is administered intravenously. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter comprises a D domain that specifically binds to BCMA. In some embodiments, the Adapter comprises a D domain comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

[0580] In some embodiments, the Adapter is administered daily. In some embodiments, the Adapter is administered twice a day. In some embodiments, the Adapter is administered three times a day. In some embodiments, the Adapter is administered four times a day. In some embodiments, the Adapter is administered every 12 hours. In some embodiments, the Adapter is administered every 8 hours. In some embodiments, the Adapter is administered every 6 hours. In some embodiments, the Adapter is administered every 4 hours. In some embodiments, the Adapter is administered every other day. In some embodiments, the Adapter is administered every three days. In some embodiments, the Adapter is administered twice a week. In some embodiments, the Adapter is administered weekly. In some embodiments, the Adapter is administered intravenously. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter comprises a D domain that specifically binds to BCMA. In some embodiments, the Adapter comprises a D domain comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

[0581] In some embodiments, the Adapter is administered for seven days. In some embodiments, the Adapter is administered for 2 weeks. In some embodiments, the Adapter is administered for 3 weeks. In some embodiments, the Adapter is administered for 4 weeks. In some embodiments, the Adapter is administered for 1 month. In some embodiments, the Adapter is administered for 2 months. In some embodiments, the Adapter is administered for 3 months. In some embodiments, the Adapter is administered intravenously. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter comprises a D domain that specifically binds to BCMA. In some embodiments, the Adapter comprises a D domain comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

[0582] In some embodiments, the Adapter is administered at the same frequency over the period of treatment. In some embodiments, the frequency of administration decreases over the period of treatment. In some embodiments, the Adapter is first administered daily for about a week followed by administration twice a week. In some embodiments, the Adapter is first administered between one and three times a day for about a week followed by daily administration. In some embodiments, the Adapter is first administered between one and three times a day for about a week followed by twice weekly or weekly administration. In some embodiments, the Adapter is administered intravenously. In some embodiments, the Adapter is administered subcutaneously. In some embodiments, the Adapter comprises a D domain that specifically binds to BCMA.

In some embodiments, the Adapter comprises a D domain comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

[0583] In another embodiment, an Adapter is administered in combination with more one or more additional therapeutics.

[0584] A therapeutically effective amount of an Adapter, such as an Adapter fusion protein, can be an amount such that when administered in a physiologically tolerable composition is sufficient to achieve a plasma concentration of from about 0.1 microgram (μg) per milliliter (ml) to about 100 μg/ml, preferably from about 1 μg/ml to about 5 μg/ml, and usually about 5 μg/ml. Stated differently, the dosage can vary from about 0.1 mg/kg to about 300 mg/kg, preferably from about 0.2 mg/kg to about 200 mg/kg, most preferably from about 0.5 mg/kg to about 20 mg/kg, in one or more dose administrations daily, for one or several days.

[0585] In one embodiment the disease or disorder is a disease or disorder of the immune system, such as inflammation or an autoimmune disease.

[0586] The cells expressing a CAR provided herein can be administered either alone, or as a pharmaceutical composition in combination with diluents and/or with other components such as chemotherapeutics, antibodies, cytokines or cell populations. Compositions provided herein are preferably formulated for intravenous administration that can be administered one or more times.

[0587] The CAR-modified T cells can also serve as a type of vaccine for ex vivo immunization and/or in vivo therapy in a mammal. Preferably, the mammal is a human.

[0588] Cancers that can be treated with the Adapter or CAR cells include tumors that are not vascularized, or not yet substantially vascularized, as well as vascularized tumors. The cancers can comprise non-solid tumors (such as hematological tumors, for example, leukemias and lymphomas) or can comprise solid tumors. Types of cancers to be treated with the Adapter include, but are not limited to, carcinoma, blastoma, and sarcoma, and certain leukemia or lymphoid malignancies, benign and malignant tumors, and malignancies *e.g.,* sarcomas, carcinomas, and melanomas. Adult tumors/cancers and pediatric tumors/cancers are also included.

[0589] Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, and other sarcomas, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, melanoma, and CNS tumors (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma, germinoma, medulloblastoma, Schwannoma

craniopharyogioma, ependymoma, pineaioma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, neuroblastoma, retinoblastoma and brain metastases). In some embodiments, the solid tumor is breast cancer. In some embodiments, the solid tumr is ovarian cancer.

[0590] In another embodiment, the Adapters and/or CAR cells described herein are useful for treating a patient having hematological cancers. Examples of hematological (or hematogenous) cancers include leukemias, including acute leukemias (such as acute lymphocytic leukemia, acute myelocytic leukemia, acute myelogenous leukemia and myeloblasts, promyeiocytic, myelomonocytic, monocytic and erythroleukemia), chronic leukemias (such as chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, and chronic lymphocytic leukemia), polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma (indolent and high grade forms), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia and myelodysplasia. Further examples of hematological (or hematogenous) cancers include acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the hematological (or hematogenous) cancer is AML. In some embodiments, the hematological (or hematogenous) cancer is CLL. In some embodiments, the hematological (or hematogenous) cancer is MM.

[0591] In one embodiment, the antigenic determinant binding domain portion of the Adapter and/or CAR is designed to treat a particular cancer. Cancers that can be treated include tumors that are not vascularized, or not yet substantially vascularized, as well as vascularized tumors. The cancers can comprise non-solid tumors (such as hematological tumors, for example, leukemias and lymphomas) or can comprise solid tumors. Types of cancers to be treated with the CARs include, but are not limited to, carcinoma, blastoma, and sarcoma, and certain leukemia or lymphoid malignancies, benign and malignant tumors, and malignancies *e.g.,* sarcomas, carcinomas, and melanomas. Adult tumors/cancers and pediatric tumors/cancers are also included.

[0592] Examples of hematological (or hematogenous) cancers include leukemias, including acute leukemias (such as acute lymphocytic leukemia, acute myelocytic leukemia, acute myelogenous leukemia and myeloblasts, promyelocytic, myelomonocytic, monocytic and erythroleukemia), chronic leukemias (such as chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, and chronic lymphocytic leukemia), polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma (indolent and high grade forms), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia and myelodysplasia. Further examples of hematological (or hematogenous) cancers include acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). In some embodiments, the hematological (or hematogenous) cancer is AML. In some embodiments, the hematological (or hematogenous) cancer is CLL. In some embodiments, the hematological (or hematogenous) cancer is MM.

[0593] Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, and other sarcomas, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, melanoma, and CNS tumors (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma, germinoma, medulloblastoma, Schwannoma craniopharyogioma, ependymoma, pineaioma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, neuroblastoma, retinoblastoma and brain metastases).

[0594] In one embodiment, cancers and disorders can be treated using the Adapters or CAR cells that target CD19, CD20, CD22, and ROR1. In one specific embodiment, the CAR, Adapter and/or CAR/Adapter combination targets CD22 and is used to treat B-cell lymphoma. In another embodiment the CAR, Adapter and/or CAR/Adapter combination targets CD19 and is used to treat cancers and disorders including but are not limited to pre-B ALL (pediatric indication), adult ALL, mantle cell lymphoma, diffuse large B- cell lymphoma, and salvage post allogenic bone marrow transplantation. In another embodiment the CAR, Adapter and/or CAR/Adapter combination targets CS1 and is used to treat multiple myeloma. In another embodiment the CAR, Adapter and/or CAR/Adapter combination targets BCMA and is used to treat multiple myeloma. In another embodiment the CAR, Adapter and/or CAR/Adapter combination targets CS1 and BCMA, and is used to treat multiple myeloma.

[0595] "B-cell associated diseases" as used herein include B-cell immunodeficiencies, autoimmune diseases and/or excessive/uncontrolled cell proliferation associated with B-cells (including lymphomas and/or leukemias). Examples of such diseases, wherein the CARs, Adapters and/or CAR/Adapter combinations provided herein may be used for therapeutic approaches include but are not limited to: systemic lupus erythematosus (SLE), diabetes, rheumatoid arthritis (RA), reactive arthritis, multiple sclerosis (MS), pemphigus vulgaris, celiac disease, Crohn's disease, inflammatory bowel disease, ulcerative colitis, autoimmune thyroid disease, X-linked agammaglobulinaemis, pre-B acute lymphoblastic leukemia, systemic lupus erythematosus, common variable immunodeficiency, chronic lymphocytic leukemia, diseases associated with selective IgA deficiency and/or IgG subclass deficiency, B lineage lymphomas (Hodgkin's lymphoma and/or non-Hodgkin's lymphoma), immunodeficiency with thymoma, transient hypogammaglobulinemia and/or hyper IgM syndrome, as well as virally-mediated B-cell diseases such as

EBV mediated lymphoproliferative disease, and chronic infections in which B-cells participate in the pathophysiology.

[0596] In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target mesothelin to treat mesothelioma, pancreatic cancer, ovarian cancer, and other mesothelin-expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target CD33/IL3Ra to treat acute myelogenous leukemia and other CD33/IL3Ra-expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target c-Met to treat triple negative breast cancer, non-small cell lung cancer, and other c-Met expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target PSMA to treat prostate cancer and other PSMA-expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target Glycolipid F77 to treat prostate cancer and other Glycolipid F77-expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target EGFRvIII to treat gliobastoma and other EGFRvIII-expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target GD2 to treat neuroblastoma, melanoma, and other GD2 expressing cancers known in the art. In one embodiment, the CAR, Adapter and/or CAR/Adapter combination is designed to target NY-ESO-1 to treat myeloma, sarcoma, melanoma, and other NY-ESO-1-expressing cancers known in the art. In one embodiment, CAR, Adapter and/or CAR/Adapter combination is can be designed to target MAGEA3 to treat myeloma, sarcoma, melanoma, and other MAGEA3-expressing cancers known in the art. However, the invention should not be construed to be limited to solely to the antigen targets and diseases disclosed herein. Rather, the invention should be construed to include any antigenic target that is associated with a disease where a CAR, Adapter and/or CAR/Adapter combination can be used to treat the disease.

[0597] In a preferred embodiment, the CAR is expressed in a T cell and provides a method for treating or preventing cancer, comprising the administration of host cells expressing CAR to a cancer patient in which the cancer cell expresses a tumor antigen on its surface, and wherein the Adapter specifically binds the target antigen. Exemplary target antigenic determinants that the Adapter and CAR bind include, but are not limited to, BCMA, CS1, CD19, CD123, TSLPR, and CD267. In some embodiments, the CAR is expressed in a T cell and provides a method for treating multiple myeloma, comprising the administration of host cells expressing CAR to a multiple myeloma patient in which the tumor cell expresses BCMA and/or CS1 on its surface, and wherein the Adapter specifically binds BCMA, CS1, or BCMA and CS1.

[0598] Articles of manufacture, including kits containing the Adapter, CAR cell, and/or CAR cell/Adapter compositions, are provided herein. The article of manufacture may comprise a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials or syringes. The containers may be formed from a variety of materials such as glass or plastic. The container

holds one or more Adapter, CAR cell, nucleic acids encoding Adapter, and/or vectors or host cells of the present disclosure. The label or package insert may include directions for administering the Adapter, CAR cell, and/or CAR cell/Adapter compositions to a patient. Such kits have uses including, but not limited to, therapeutic applications of the Adapter, CAR cell, and/or CAR/Adapter compositions.

[0599] Various embodiments of the invention will now be illustrated through the description of experiments in accordance therewith. The examples that follow are provided to facilitate the practice of the disclosed embodiments, and are not to be construed as limiting in any way the remainder of the disclosure. In the examples, reference is made to the appended figures.

Examples

Example 1. Exemplary D domains and ADs

Table 3. Exemplary D-domains

SEQ ID NO:	D-Domain Sequence	Target	ELISA_avg
44	MGSWYEFSWRLQAIHQRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRAYAAGIRGALQAYRHN	BCMA	9.4868
45	MGSWHEFTWRLIAIQQRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRAYAAGIRHHLQAYRHN	BCMA	17.125
46	MGSWREFAWRLVAINSRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHYAASIRDGLQAYRHN	BCMA	9.66
47	MGSWHEFAWRLQAINQRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHYAAHIRNGLQAYRHN	BCMA	13.14
48	MGSWNEFAWRLTAIEQRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHYAAGIRDNLQAYRHN	BCMA	18.28
49	MGSWTEFAWRLQAIHQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVYAAKIRISLQAYRHN	BCMA	18.71
50	MGSWIEFAWRLQAIHQRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREYAANIRDSLQAYRHN	BCMA	18.97
51	MGSWHEFTWRLVAIQQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRKFAAKIRYELQAYRHN	BCMA	19.51
52	MGSWHEFTWRLIAIRERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREYAASIRNMLQAYRHN	BCMA	12.99
53	MGSWIEFSWRLEAIRQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRSYAARIRQELQAYRHN	BCMA	9.92
54	MGSWVEFSWRLEAIRQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRSYAARIRQELQAYRHN	BCMA	19.14
55	MGSWVEFSWRLEAIRQRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRKYAARIRGELQAYRHN	BCMA	21.3
56	MGSWVEFAWRLTAIDQRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRFYAAKIRSHLQAYRHN	BCMA	8.43
57	MGSWVEFAWRLEAIKQRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRLYAAKIRRVLQAYRHN	BCMA	8.9
58	MGSWVEFAWRLTAIHTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRKYAAKIRKQLQAYRHN	BCMA	6.08
59	MGSWTEFAWRLEAINQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGKP EVEALRAYAAKIRTRLQAYRHN	BCMA	15.148

60	MGSWSEFAWRLEAIHQRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRLFAAQIRENLQAYRHN	BCMA	18.04
61	MGSWNEFAWRLIAINQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRHFAANIRNDLQAYRHN	BCMA	11.53
62	MGSWTEFAWRLIAIDQRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRELAAEIRFHLQAYRHN	BCMA	8.55
63	MGSWSEFMNRLDAITYRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRHYAAQIRDSLQAYRHN	BCMA	12.9
64	MGSWTEFMERLDAISYRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDYAAIIRNSLQAYRHN	BCMA	9.87
65	MGSWAEFMDRLDAITYRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRGYAAIIRSELQAYRHN	BCMA	10.83
66	MGSWIEFQERLDAIFYRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDAAATIRRQLQAYRHN	BCMA	18.58
67	MGSWIEFQQRLDAIFYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDMAAIIRKQLQAYRHN	BCMA	20.02
68	MGSWYEFQSRLDAIFYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREAAASIRTQLQAYRHN	BCMA	14.08
69	MGSWSEFIDRLDAITYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRWYAGVIREQLQAYRHN	BCMA	10.18
70	MGSWSEFYDRLYAINQRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAAFIRAQLQAYRHN	BCMA	5.98
71	MGSWYEFYDRLDAIVHRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRWYAAMIRVRLQAYRHN	BCMA	14.68
72	MGSWVEFQDRLEAITDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAAMIRVILQAYRHN	BCMA	8.8783
73	MGSWVEFQERLMAISDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWQAAMIRYTLQAYRHN	BCMA	6.7
74	MGSWFEFQHRLEAISMRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWQAAYIRVVLQAYRHN	BCMA	4.05
75	MGSWVEFQSRLEAIATRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWQAAWIRMMLQAYRHN	BCMA	18.008
76	MGSWEEFQYRLGAIAARLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWQAAMIRFMLQAYRHN	BCMA	3.11
77	MGSWYEFQVRLQAISWRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNH EVEELRIQAALIRVMLQAYRHN	BCMA	14.23
78	MGSWVEFRSRLEAISNRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRTTAALIRVYLQAYRHN	BCMA	3.04
79	MGSWVEFKARLEAISSRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRVYLQAYRHN	BCMA	8.7071
80	MGSWSEFYTRLEAINNRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYTAALIRIYLQAYRHN	BCMA	3.66
81	MGSWAEFYHRLDAISSRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYTAALIRIYLQAYRHN	BCMA	4.31
82	MGSWTEFASRLVAIRQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAAIIRVMLQAYRHN	BCMA	7.99
83	MGSWSEFDQRLAAIYQRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRVMLQAYRHN	BCMA	7.72
84	MGSWVEFHNRLSAISDRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRVMLQAYRHN	BCMA	7.36
85	MGSWNEFEDRLSAISARLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRVMLQAYRHN	BCMA	4.09
86	MGSWVEFEYRLVAIFDRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYQAALIRVMLQAYRHN	BCMA	7.63
87	MGSWVEFQGRLGAIHERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRVFLQAYRHN	BCMA	3.8343

88	MGSWYEFSMRLSAIWERLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYQAALIRFYLQAYRHN	BCMA	7.12
89	MGSWTEFSQRLGAISERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRFMLQAYRHN	BCMA	4.15
90	MGSWTEFHDRLEAITHRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALLRVFLQAYRHN	BCMA	5.79
91	MGSWTEFEHRLEAIAGRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAALIRFWLQAYRHN	BCMA	6.34
92	MGSWTEFANRLEAINARLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFSAALIRVYLQAYRHN	BCMA	6.42
93	MGSWEEFDRRLYAIARRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYQAALIRVWLQAYRHN	BCMA	8.85
94	MGSWIEFHQRLEAIVTRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYQAALIRVFLQAYRHN	BCMA	8
95	MGSWSEFYDRLKAIADRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRTEAAIIRVYLQAYRHN	BCMA	8.215
96	MGSWWEFEDRLSAIMERLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYRAAIIRVYLQAYRHN	BCMA	10.39
97	MGSWVEFEERLAAIATRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWRAAIIRVYLQAYRHN	BCMA	16.29
98	MGSWSEFRGRLQAIHSRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYSAAIIRIYLQAYRHN	BCMA	7.585
99	MGSWTEFRDRLGAIYHRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYQAAIIRVYLQAYRHN	BCMA	6.7
100	MGSWVEFYHRLEAIRYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYVAAVIRYRLQAYRHN	BCMA	7.8
101	MGSWVEFYDRLEAIRYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYIAAVIRYRLQAYRHN	BCMA	5.636
102	MGSWVEFYDRLAAIRKRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFRAALIRIWLQAYRHN	BCMA	9.76
103	MGSWEEFSERLEAISIRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVSAAIIRVWLQAYRHN	BCMA	11.26
104	MGSWSEFSDRLHAISDRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRIQAAIIRVWLQAYRHN	BCMA	6.3725
105	MGSWIEFSHRLEAIVDRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRNTAAIIRVYLQAYRHN	BCMA	18.67
106	MGSWEEFSDRLEAILRRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRFAAAIIRVQLQAYRHN	BCMA	9.08
107	MGSWMEFSHRLDAIHERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRFAAAIIRVQLQAYRHN	BCMA	6.3
108	MGSWSEFQQRLHAIRTRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFEAAIIRVMLQAYRHN	BCMA	11.615
109	MGSWYEFQNRLGAINRRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFEAAIIRVMLQAYRHN	BCMA	4.68
110	MGSWQEFTGRLHAIRHRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFEAAYIRVWLQAYRHN	BCMA	3.315
111	MGSWTEFDHRLGAIWERLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFHAAIIRIFLQAYRHN	BCMA	9.54
112	MGSWTEFHVRLSAIWDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFHAAIIRIVLQAYRHN	BCMA	23.62
113	MGSWNEFDNRLQAIWDRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFHAAMIRITLQAYRHN	BCMA	9.87
114	MGSWTEFHERLQAIWFRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFRAAIIRLYLQAYRHN	BCMA	12.066
115	MGSWNEFSGRLTAIKDRLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRFRAAVIRLWLQAYRHN	BCMA	3.39

116	MGSWVEFDERLVAIWFRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRARAAYIRIWLQAYRHN	BCMA	8.96
117	MGSWSEFGQRLSAIWERLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRADAAFIRIWLQAYRHN	BCMA	14.01
118	MGSWYEFEDRLVAIWIRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYNAAFIRGALQAYRHN	BCMA	4.93
119	MGSWYEFGDRLSAIWERLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRTHAAEIRTILQAYRHN	BCMA	8.895
120	MGSWHEFYYRLEAIEQRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRFDAALIRIYLQAYRHN	BCMA	3.73
121	MGSWSEFEERLAAIGSRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRFDAALIRIYLQAYRHN	BCMA	4.85
122	MGSWLEFHYRLHAIQFRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRHIAALIRNQLQAYRHN	BCMA	12.749
123	MGSWQEFYNRLEAIHMRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRSDAAPIRDVLQAYRHN	BCMA	6.47
124	MGSWNEFHHRLWAIFDRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRKMAAGIRGGLQAYRHN	BCMA	3.88
125	MGSWYEFHYRLKAINDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRYSAAMIRHKLQAYRHN	BCMA	6.04
126	MGSWTEFHQRLGAIHARLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFSAAFIRLKLQAYRHN	BCMA	8.87
127	MGSWFEFQYRLEAIFYRLLALGGSEAELAAFEKEIAAFESELQAYKGKGKP EVEELRVRAALIRHLLQAYRHN	BCMA	17.31
128	MGSWVEFHARLDAIYTRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRVLAAHIRISLQAYRHN	BCMA	3.8
129	MGSWVEFGTRLSAIYNRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRFEAAIIRIMLQAYRHN	BCMA	15.425
130	MGSWVEFTHRLDAIYIRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHEAAVIREELQAYRHN	BCMA	13.917
131	MGSWVEFHGRLAAIYVRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRYHAAMIRRNLQAYRHN	BCMA	4
132	MGSWVEFDRRLVAIYIRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRDDAALIRLLLQAYRHN	BCMA	8.93
133	MGSWVEFDRRLVAIYIRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYDAATIRETLQAYRHN	BCMA	8
134	MGSWLEFDRRLTAIYLRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALREDAAMIRDMLQAYRHN	BCMA	9.82
135	MGSWIEFDRRLLAIHVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRADAAKIRMELQAYRHN	BCMA	13.72
136	MGSWIEFDRRLIAIWIRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRSDAADIRQKLQAYRHN	BCMA	9.45
137	MGSWVEFDRRLIAIWVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRSDAAMIREHLQAYRHN	BCMA	5.77
138	MGSWYEFHTRLIAIYVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRGDAAKIRGYLQAYRHN	BCMA	4.06
139	MGSWSEFSTRLSAIYVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRNKAASIRKTLQAYRHN	BCMA	5.35
140	MGSWVEFRYRLGAIYHRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDRAATIRRLLQAYRHN	BCMA	10.81
141	MGSWNEFRNRLGAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRAHAAIIRSVLQAYRHN	BCMA	4.6967
142	MGSWHEFRNRLGAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRARAAMIRSVLQAYRHN	BCMA	3.4936
143	MGSWTEFYQRLEAINFRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDKAALIRLMLQAYRHN	BCMA	6.955

144	MGSWNEFYNRLHAINLRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREHAAIIRQALQAYRHN	BCMA	3.004
145	MGSWEEFYGRLSAIQDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRMHAAVIRRALQAYRHN	BCMA	3.28
146	MGSWGEFNLRLVAIHVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRSQAANIRAQLQAYRHN	BCMA	12.81
147	MGSWGEFSDRLEAINERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRWQAAFIRANLQAYRHN	BCMA	4.26
148	MGSWMEFQGRLPAILARLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDKAAYIRWMLQAYRHN	BCMA	8.32
149	MGSWMEFEGRLPAILARLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDKAAYIRWMLQAYRHN	BCMA	3.93
150	MGSWFEFQNRLQAILFRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDKAAYIRLMLQAYRHN	BCMA	5.3933
151	MGSWVEFDMRLQAILERLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDSAAYIRLMLQAYRHN	BCMA	23.525
152	MGSWVEFNARLDAILFRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDQAAYIRLMLQAYRHN	BCMA	13.52
153	MGSWMEFNVRLRAILDRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDKAAYIRFMLQAYRHN	BCMA	15.59
154	MGSWIEFDTRLAAIVHRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDKAAYIRYMLQAYRHN	BCMA	13.948
155	MGSWIEFDYRLKAILHRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRDKAAYIRFLLQAYRHN	BCMA	11.877
156	MGSWYEFEDRLLAIKVRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRDQAAYIRFMLQAYRHN	BCMA	17.613
157	MGSWYEFQDRLSAITTRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDKAAYIRFMLQAYRHN	BCMA	10.085
158	MGSWEEFDDRLNAIVYRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRDQAAYIRLMLQAYRHN	BCMA	18.64
159	MGSWVEFEQRLHAIVVRLRALGGSEAELAAFEKEIAAFESELQAYKGGGNP EVENLRDQAAYIRFMLQAYRHN	BCMA	17.747
160	MGSWVEFEWRLEAIVVRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDKAAYIRYMLQAYRHN	BCMA	14.95
161	MGSWYEFEHRLKAIVSRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDKAAYIRYMLQAYRHN	BCMA	4.55
162	MGSWMEFKHRLAAITFRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDKAAYIRLLLQAYRHN	BCMA	6.06
163	MGSWMEFEGRLHAIKRRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDQAAYIRLLLQAYRHN	BCMA	7.335
164	MGSWSEFVFRLDTIKSRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRDQAAYIRLMLQAYRHN	BCMA	19.86
165	MGSWYEFDERLSAIKLRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRAQAAYIRAILQAYRHN	BCMA	16.94
166	MGSWMEFDERLWAIKKRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRHQAAYIRMLLQAYRHN	BCMA	9.526
167	MGSWHEFDGRLSAIKRRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDQAAYIRYMLQAYRHN	BCMA	5.4
168	MGSWYEFDGRLQAIIARLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRFRAAYIRWILQAYRHN	BCMA	3.29
169	MGSWFEFDKRLYAIIHRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYKAAIIRLYLQAYRHN	BCMA	11.82
170	MGSWVEFDNRLYAIVDRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRQKAAYIRLILQAYRHN	BCMA	11.717
171	MGSWIEFHQRLNAIFNRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRHHAAYIREMLQAYRHN	BCMA	7.3417

172	MGSWNEFRLRLWAITERLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVECLRAEAAWIRTMLQAYRHN	BCMA	3.8718
173	MGSWYEFWLRLSAISYRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRKEAAEIRSWLQAYRHN	BCMA	14.465
174	MGSWYEFQLRLWAIHWRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRMRAAEIRNELQAYRHN	BCMA	20.59
175	MGSWYEFAHRLEAIEWRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRQYAAAIRNYLQAYRHN	BCMA	9.48
176	MGSWYEFDTRLGAIRNRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRFQAAYIRFLLQAYRHN	BCMA	13.934
177	MGSWYEFWVRLTAIRWRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREQAASIRWVLQAYRHN	BCMA	5.72
178	MGSWFEFDRRLKAIDRRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRMQAAIIRNYLQAYRHN	BCMA	6.1625
179	MGSWVEFWERLDAIDNRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRWHAAYIRGYLQAYRHN	BCMA	11.42
180	MGSWAEFWDRLDAIDSRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREWAAYIRGYLQAYRHN	BCMA	18.22
181	MGSWAEFDLRLRAIAKRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRLDAAYIRGVLQAYRHN	BCMA	4.09
182	MGSWSEFWDRLYAIRIRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRSVAARIRNWLQAYRHN	BCMA	12.52
183	MGSWSEFWFRLGAIRNRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRDVAAHIRHWLQAYRHN	BCMA	14.93
184	MGSWSEFNDRLDAIRWRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQVAATIRYRLQAYRHN	BCMA	13.59
185	MGSWVEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAAAIRHYLQAYRHN	BCMA	5.22
186	MGSWAEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAAAIRHYLQAYRHN	BCMA	
187	MGSWTEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAAAIRHYLQAYRHN	BCMA	
188	MGSWVEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLKYTAAAIRHYLQAYRHN	BCMA	
189	MGSWVEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLQYTAAAIRHYLQAYRHN	BCMA	
190	MGSWVEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAAAIKHYLQAYRHN	BCMA	
191	MGSWAEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLQYTAAAIKHYLQAYRHN	BCMA	
192	MGSWTEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLQYTAAAIKHYLQAYRHN	BCMA	
193	MGSWVEFWDRLGAIRERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYVAAVIRHRLQAYRHN	BCMA	4.18
194	MGSWVEFWDRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRASAAAIRIALQAYRHN	BCMA	3.07
195	MGSWVEFWDRLGAIRDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRNTAAYIRTFLQAYRHN	BCMA	16.034
196	MGSWSEFWVRLGAIRDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRVTAAQIRHYLQAYRHN	BCMA	23.5
197	MGSWSEFWVRLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAATIRRFLQAYRHN	BCMA	7.5567
198	MGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAATIRRFLQAYRHN	BCMA	
199	MGSWSEFWVRLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAGTIRRFLQAYRHN	BCMA	

200	MGSWSEFWVRLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAATIKRFLQAYRHN	BCMA	
201	MGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAGTIKRFLQAYRHN	BCMA	
202	MGSWSEFWDRLTAIRVRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRYTAAHIRKFLQAYRHN	BCMA	16.14
203	MGSWTEFWTRLNAIYERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRFTAASIRMYLQAYRHN	BCMA	8.43
204	MGSWFEFWDRLAAIRDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYVAAKIRVRLQAYRHN	BCMA	12.78
205	MGSWTEFWVRLNAIRDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRHTAAIIRNYLQAYRHN	BCMA	12.53
206	MGSWVEFWHRLGAIYDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRRTAALIRQTLQAYRHN	BCMA	19.904
207	MGSWVEFWNRLGAIYDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRHTAAVIRLYLQAYRHN	BCMA	14.55
208	MGSWSEFWERLEAIYDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRRTAATIRSFLQAYRHN	BCMA	18.78
209	MGSWEEFDNRLEAIFDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREFAATIRITLQAYRHN	BCMA	3.93
210	MGSWMEFWDRLYAIEFRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRRVAATIRNELQAYRHN	BCMA	11.693
211	MGSWTEFWERLYAIEYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRSVAATIRYELQAYRHN	BCMA	12.7
212	MGSWNEFWERLYAIELRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRMTAAYIRNELQAYRHN	BCMA	9.945
213	MGSWYEFWKRLYAIEYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKVAAKIREQLQAYRHN	BCMA	14.785
214	MGSWTEFWARLYAIEMRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRRVAALIREQLQAYRHN	BCMA	12.46
215	MGSWHEFWDRLYAIEFRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRQVAAKIRWHLQAYRHN	BCMA	7.3
216	MGSWDEFEFRLGALRWRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFGAAHIRHILQAYRHN	BCMA	9.2
217	MGSWTEFYHRLYAIRERLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFGAAHIRHLLQAYRHN	BCMA	9.6275
218	MGSWVEFETRLDAIRMRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFGAAHIRALLQAYRHN	BCMA	14.072
219	MGSWGEFDVRLFAIRERLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRGYAAQIRSFLQAYRHN	BCMA	7.3533
220	MGSWVEFDERLSAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRLYAAQIRVFLQAYRHN	BCMA	5.61
221	MGSWSEFDGRLGAIWDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRDRAAQIREFLQAYRHN	BCMA	10.031
222	MGSWGEFEGRLHAIRSRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRGYAAWIRALLQAYRHN	BCMA	6.17
223	MGSWGEFNGRLGAIRERLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRAYAASIRAVLQAYRHN	BCMA	4.9533
224	MGSWWEFTFRLAAIEFRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRAIAAEIRKSLQAYRHN	BCMA	5.75
225	MGSWDEFQFRLAAIGFRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRRQAARIRHLLQAYRHN	BCMA	6.155
226	MGSWYEFVTRLHAIDHRLKALGGSEADLAAFEKEIAAFESELQAYKGKGNP EVEWLRFYAAGIRMNLQAYRHN	BCMA	4.12
227	MGSWSIEFWRLEAIKFRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRVEAAAIRRVLQAYRHN	BCMA	8.43

228	MGSWGEFEHRLDPSTCVWLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRRGAAVIRHWLQAYRHN	BCMA	4.05
229	MGSWIEFAMRLEAIENRLTALGGSEAELAIFESMIAHFEELLQNYKGKGNP EVEALIHEAFAIHKELWAYRHN	BCMA	10.73
230	MGSWNEFYQRLEAIENRLQALGGSEAELAMFEVRIALFEDMLQGYKGKGNP EVEALKQEAIAILRELIAYRHN	BCMA	6.01
231	MGSWNEFYDRLRAIKKRLYALGGSEAELADFEEDIAQFEVDLQDYKGKGNP EVEALHREAHAITHELWAYRHN	BCMA	12.36
232	MGSWGEFKHRLALIKWYLEALGGSEAELAHFEDWIAVFEVQLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	17.09
233	MGSWYEFKHRLAIIKWYLEALGGSEAELAKFEAWIAEFEMILQRYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	5.505
234	MGSWYEFKHRLAIIKWYLEALGGSEAELAHFEQYIADFEGTLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.833
235	MGSWYNFKHRLAIIKWYLEALGGSEAELARFENFIANFETQLQLYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.7615
236	MGSWFQFKHRLAIIKWQLEALGGSEAELAWFEQWIADFEHQLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.39
237	MGSWYNFKHRLAIIKWFLEALGGSEAELAVFEVWIADFEHQLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	16.38
238	MGSWDAFKHRLALIKWYLEALGGSEAELAHFEEYIAEFESNLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.98
239	MGSWDGFKHRLALIKWYLEALGGSEAELANFENWIAEFEQRLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	23.62
240	MGSWNGFKHRLAIIKWYLEALGGSEAELASFESYIAEFESGLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	16.53
241	MGSWNSFKHRLALIKWYLEALGGSEAELATFEWYIASFESELQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.34
242	MGSWSDFKYRLAVIKFYLEALGGSEAELASFESFIAHFEDDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.04
243	MGSWSGFKYRLAVIKFYLEALGGSEAELASFELFIAKFEIDLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.066
244	MGSWYGFKYRLAVIKWYLEALGGSEAELASFEKYIAHFEHDLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.05
245	MGSWYGFKYRLAVIKWYLEALGGSEAELASFEKYIAQFEHDLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.6333
246	MGSWYGFKYRLALIKWYLEALGGSEAELASFETYIADFEDLLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.03
247	MGSWSTFKYHLAVIKWYLEALGGSEAELASFEDYIAQFETDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.65
248	MGSWHEFKYRLALIKWYLEALGGSEAELATFEHHIAQFEWDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	16.19
249	MGSWNMFKYRLAHIKWYLEALGGSEAELATFEAYIADFEVDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	16.33
250	MGSWHGFKYRLAIIKWWLEALGGSEAELAFFEEWIASFERDLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.025
251	MGSWHGFKYRLAVIKWYLEALGGSEAELAMFEGWIAQFEITLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	5.99
252	MGSWQGFKYRLAVIKWMLEALGGSEAELAFFENWIAEFETKLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.75
253	MGSWSGFKYRLAVIKWYLEALGGSEAELATFEEWIAEFETELQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.975
254	MGSWGYFKYRLAMIKWYLEALGGSEAELASFESWIAEFEGSLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.018
255	MGSWHAFKYKLAMIKWYLEALGGSEAELAHFEEWIAEFEALLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.63

256	MGSWQHFKYRLAIIKWYLEALGGSEAELAFFESFIAKFEHDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	8.91
257	MGSWNDFKYRLAIIKYYLEALGGSEAELAHFESYIASFEHDLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.123
258	MGSWGAFKYRLAIIKFYLEALGGSEAELARFEEFIANFEHDLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.88
259	MGSWYNFKYRLAIIKFYLEALGGSEAELAQFEIWIAEFEHDLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	19.91
260	MGSWEQFKYRLAIIKYMLEALGGSEAELAWFESWIANFESDLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.01
261	MGSWQQFKYRLAIIKYYLEALGGSEAELAGFETYIAKFEEVLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.12
262	MGSWAGFKYRLAVIKYYLEALGGSEAELAHFEQWIAHFEGMLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.68
263	MGSWTAFKYRLAIIKFYLEALGGSEAELAHFESYIAHFEDMLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.43
264	MGSWAHFKYRLAIIKFWLEALGGSEAELANFEEYIAEFESTLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.12
265	MGSWANFKYRLALIKWHLEALGGSEAELASFEIWIADFEESLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.288
266	MGSWATFKYRLALIKWHLEALGGSEAELADFEEYIAGFEEGLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.07
267	MGSWTHFKYRLALIKWWLEALGGSEAELAGFEVHIADFEAQLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.3669
268	MGSWNTFKYHLAVIKFMLEALGGSEAELAFFEQWIAEFEVTLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.601
269	MGSWTQFKYHLAVIKWYLEALGGSEAELAGFEQWIAEFEKTLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	21.118
270	MGSWNQFKYRLAVIKFYLEALGGSEAELAHFETWIAAFEEQLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.85
271	MGSWNEFKYHLAVIKFYLEALGGSEAELAHFETWIAEFEYELQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.68
272	MGSWVQFKYHLAVIKFYLEALGGSEAELAHFETWIAEFEVALQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.696
273	MGSWVDFKYHLAVIKFWLEALGGSEAELANFETWIANFEQELQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.22
274	MGSWVDFKYHLAVIKWYLEALGGSEAELADFENWIAHFESILQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.43
275	MGSWVEFKYHLAVIKFTLEALGGSEAELADFEEEIARFEMILQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.92
276	MGSWSHFKYHLALIKWYLEALGGSEAELAKFEFWIAEFEHNLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.93
277	MGSWYHFKYHLALIKWYLEALGGSEAELAHFEHWIAEFEWTLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	8.85
278	MGSWQGFKYHLALIKFYLEALGGSEAELAHFEHWLAEFEHDLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	21.2
279	MGSWLSFKHHLALIKWYLEALGGSEAELASFEAWIALFEHQLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.305
280	MGSWSEFKYKLALIKWYLEALGGSEAELAHFEGWIANFETTLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.288
281	MGSWIEFKYKLAIIKFYLEALGGSEAELAHFEHWIADFEFVLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.88
282	MGSWQNFKYHLAMIKWYLEALGGSEAELANFEEFIAQFEINLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.55
283	MGSWYNFKYHLAIIKWWLEALGGSEAELADFEHYIADFERNLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	8.6264

284	MGSWYQFKYHLAIIKWYLEALGGSEAELAGFENYIATFEQELQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.41
285	MGSWSHFKYHLAIIKFYLEALGGSEAELAGFEIWIAKFEDELQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.34
286	MGSWVGFKAHLAIIKWYLEALGGSEAELAGFEIFIADFEALLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.71
287	MGSWVNFKYKLAIIKYMLEALGGSEAELAFFEDWIAEFERTLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.3895
288	MGSWSNFKYRLAVIKYMLEALGGSEAELAFFEDWIADFELHLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.34
289	MGSWTNFKYKLAVIKFMLEALGGSEAELAFFEDWIAGFEIDLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.408
290	MGSWTGFKYRLAIIKFMLEALGGSEAELAFFEQWIADFENELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.89
291	MGSWHNFKYRLAIIKFMLEALGGSEAELAWFENWIADFEDSLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.59
292	MGSWFAFKHRLAVIKYMLEALGGSEAELAFFEHWIAQFEHDLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	11.985
293	MGSWYEFKHRLAVIKYMLEALGGSEAELAFFENWIAQFEHELQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	3.71
294	MGSWYKFKHKLAVIKYMLEALGGSEAELAWFEEWIAEFEVTLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	4.54
295	MGSWFYFKQKLAFIKWYLEALGGSEAELANFEIYIAEFEVMLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.23
296	MGSWFSFKHHLAVIKWNLEALGGSEAELASFEEQIAEFESVLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.45
297	MGSWGNFKYRLAIIKFHLEALGSSEAELATFEAWIANFESMLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	22.7
298	MGSWSYFKYGLAIIKIRLEALGGSEAELADFERWIAAFEHDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.33
299	MGSWSYFKFGLAHIKLRLEALGGSEAELADFEQWIASFEEQLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.354
300	MGSWSYFKWGLAHIKLRLEALGGSEAELADFEFWIAEFEGLLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	17.64
301	MGSWIYFKYGLAHIKTRLEALGGSEAELADFEQWIAEFEKMLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	21.12
302	MGSWGYFKYGLATIKHRLEALGGSEAELADFELWIAKFEEQLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.01
303	MGSWEYFKYGLATIKMHLEALGGSEAELADFEHWIAHFEHQLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.403
304	MGSWSYFKYGLATIKEKLEALGGSEAELADFETWIAMFEKQLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.15
305	MGSWHYFKNGLAIIKEKLEALGGSEAELADFEIWIAMFEMELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	19.85
306	MGSWQYFKYGLAIIKIKLEALGGSEAELADFEAWIATFEKQLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.28
307	MGSWVYFKHGLAVIKMRLEALGGSEAELADFETWIAQFEMTLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	21.45
308	MGSWVYFKYGLAVIKEKLEALGGSEAELADFETWIAEFEFGLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	17.58
309	MGSWYYFKYGLAVIKGKLEALGGSEAELADFETWIAKFENHLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	3.84
310	MGSWTYFKYGLALIKYRLEALGGSEAELADFEEWIAQFEVSLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.21
311	MGSWDYFKYGLALIKIKLEALGGSEAELADFEVWIAQFEMALQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.76

312	MGSWTYFKFGLAHIKDSLEALGGSEAELADFEQWIAMFEQDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	17.01
313	MGSWGYFKHGLAHIKSSLEALGGSEAELADFEVWIAAFENELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.505
314	MGSWGYFKTGLAIIKAQLEALGGSEAELADFELWIAQFEETLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.75
315	MGSWAYFKYGLAVIKLHLEALGGSEAELADFERYIAEFEYELQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.44
316	MGSWLDFKEGLADIKRSLEALGGSEAELADFEGVIALFEWKLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	3.03
317	MGSWEVFKHELAVIKDYLEALGGSEAELAHFEWGIAWFEGFLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.33
318	MGSWIVFKQSLAWIKEHLEALGGSEAELAEFEFYIANFEHTLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.57
319	MGSWIYFKDSLAYIKKYLEALGGSEAELATFEYYIANFEHELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	3.2
320	MGSWDHFKYNLAWIKKYLEALGGSEAELATFEWYIANFEKRLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.81
321	MGSWFTFKQNLAWIKLHLEALGGSEAELARFEYYIADFENKLQLYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.204
322	MGSWREFKYGLAHIKRVLEALGGSEAELAVFEYYIAKFEQELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	14.7
323	MGSWIQFKYGLAHIKRTLEALGGSEAELAVFEWYIADFEQQLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	8.3567
324	MGSWVEFKHNLAWIKVTLEALGGSEAELAVFEYYIAQFEEQLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	15.83
325	MGSWISFKDNLAMIKEFLEALGGSEAELAVFEWYIATFEVELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.16
326	MGSWHIFKDNLATIKAFLEALGGSEAELAVFEWYIAKFEEELQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	3.47
327	MGSWTSFKHGLAGIKRVLEALGGSEAELATFEWYIAQFERHLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	9.765
328	MGSWQSFKHALADIKINLEALGGSEAELAQFEYAIAVFEYRLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	13.719
329	MGSWHTFKEALAQIKGELEALGGSEAELASFEYAIAVFEYRLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.76
330	MGSWTDFKTSLADIKAELEALGGSEAELAKFEYYIAIFEYRLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	18.76
331	MGSWTNFKEGLAEIKRDLEALGGSEAELARFEYVIAVFEFRLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	12.327
332	MGSWHTFKDGLAEIKSELEALGGSEAELAMFEYVIAIFEYRLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.65
333	MGSWQFFKEHLASIKFWLEALGGSEAELAFFEDAIADFEYHLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.58
334	MGSWTYFKEHLASIKFWLEALGGSEAELAFFEDAIAEFEKDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	6.5951
335	MGSWIIFKGYLAHIKHHLEALGGSEAELADFEFYIAIFEMELQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	5.18
336	MGSWYLFQSHLAHIKHHLEALGGSEAELAWFEFTIAGFEQELQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	7.69
337	MGSWYSFKWTLARIKLELEALGGSEAELAYFENVIAHFEMELQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	4.05
338	MGSWTTLKWRLAHIKQHLEALGGSEAELALFEYDIAHFEELLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	17.82
339	MGSWYGFKWYLATIKKHLEALGGSEAELALFETEIATFELWLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	BCMA	10.65

340	MGSWIEFNMRVLAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRYEACLDPWSSAAYRHN	CD123	3.2
341	MGSWIEFHERLWAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREMAASIRHGLQAYRHN	CD123	3.4
342	MGSWFEFYERLWAIDDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAASIRSSLQAYRHN	CD123	6
343	MGSWFEFWDRLEAIDDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRYNAAEIRKELQAYRHN	CD123	4.9
344	MGSWHEFWSRLDAIDDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRGAAADIRAELQAYRHN	CD123	3.8
345	MGSWYEFWIRLEAIDDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVDILRDFAADIRTELQAYRHN	CD123	10.4
346	MGSWHEFWDRLEAIDDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAYIRELLQAYRHN	CD123	10.6
347	MGSWEEFWDRLFAIDDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRNEAAEIRMALQAYRHN	CD123	3.1
348	MGSWWEFDDRLFAIDTRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREWAATIRMELQAYRHN	CD123	3.5
349	MGSWTEFHDRLEAIDDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREEAAQIRWELQAYRHN	CD123	5.8
350	MGSWAEFEDRLWAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREEAAAIRFELQAYRHN	CD123	6.2
351	MGSWVEFWFRLEAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAAAIREDLQAYRHN	CD123	3.2
352	MGSWVEFWQRLEAIESRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAEIRWELQAYRHN	CD123	7.7
353	MGSWSEFWQRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRENAAMIRDELQAYRHN	CD123	4.7
354	MGSWSEFITRLEAIDDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILREEAAEIRQHLQAYRHN	CD123	3.3
355	MGSWYEFETRLEAIYDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRVEAAEIREDLQAYRHN	CD123	3.2
356	MGSWTEFYYRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRVEAANIRDMLQAYRHN	CD123	7.5
357	MGSWYEFVIRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRWYAADIRHELQAYRHN	CD123	6.4
358	MGSWTEFSIRLEAIYDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRTYAANIRHELQAYRHN	CD123	11.9
359	MGSWTEFSIRLEAIYDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRTYAAFIRHELQAYRHN	CD123	10.2
360	MGSWTEFVWRLEAIWDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREDAAVIRHFLQAYRHN	CD123	3.6
361	MGSWVEFHERLEAIEDRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREDAAFIRQLLQAYRHN	CD123	3.7
362	MGSWVEFHDRLEAIEDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAYIRSILQAYRHN	CD123	4.6
363	MGSWIEFYDRLEAIYDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAFIRSWLQAYRHN	CD123	7.5
364	MGSWVEFDQRLEAIYDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAQIRKWLQAYRHN	CD123	5.1
365	MGSWVEFHDRLEAIEDRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREYAAGIRWFLQAYRHN	CD123	3.3
366	MGSWEEFAQRLYAIEWRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRYVAAQIRYHLQAYRHN	CD123	16.9
367	MGSWDEFAWRLDVIFARLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRKNAAQIRDGLQAYRHN	CD123	4.6

368	MGSWDEFYYRLEAIEMRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHYAAQIRHMLQAYRHN	CD123	7.2
369	MGSWEEFYDRLEAIYNRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREYAADIREMLQAYRHN	CD123	18.6
370	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKEAAVIRENLQAYRHN	CD123	
371	MGSWDEFGRRLYAIEWQLYALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKEAAVIRENLQAYRHN	CD123	
372	MGSWDEFGRRLYAIETQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
373	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
374	MGSWDEFGRRLYAIKWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
375	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRKIAAVIRENLQAYRHN	CD123	
376	MGSWDEFGRRLYAIEWQLYALGGGEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
377	MGSWDEFGRRLYAIEWQLYALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
378	MGSWDEFGRRLYAIEWQLYALGGGEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
379	MGSWDEFGRRLYAIEWQLYALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
380	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
381	MGSWDEFGRRLAAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
382	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEALREIAAVIRENLQAYRHN	CD123	
383	MGSWDEFGRRLYAIEWQLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREEAAVIRENLQAYRHN	CD123	
384	MGSWDEFGRRLYAIEWRLYALGGSEAELAAFEKEIAAFESELQAYKGKGSP EVEKLREIAAVIRSNLQAYRHN	CD123	
385	MGSWDEFGRRLYAIEWRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	5.8
386	MGSWDEFGRRLYAIEWRLYALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
387	MGSWDEFGRRLYAIEWQLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
388	MGSWDEFSRRLYAIEWRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRSNLQAYRHN	CD123	
389	MGSWDEFGRRLYAIEWRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
390	MGSWDEFGRRLAAIKTQLAALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
391	MGSWDEFGRRLAAIKTQLAALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREIAAVIRENLQAYRHN	CD123	
392	MGSWDEFGRRLAAIKTQLAALGGEEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKEAAVIRENLQAYRHN	CD123	
393	MGSWDEFGRRLAAIKTQLAALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKEAAVIRENLQAYRHN	CD123	
394	MGSWDEFEQRLIAIEERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAAVIRKYLQAYRHN	CD123	5.9
395	MGSWVEFDQRLGAIWDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRQGAAVIRDDLQAYRHN	CD123	5.3

396	MGSWVEFDMRLSAIWERLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAEIREFLQAYRHN	CD123	3.3
397	MGSWVEFDQRLDAIYERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAEIREHLQAYRHN	CD123	10.5
398	MGSWHEFDQRLWAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRLYAALIRHDLQAYRHN	CD123	3.3
399	MGSWVEFWDRLDAIEGRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWLAAEIRADLQAYRHN	CD123	3.5
400	MGSWVEFYSRLDAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRIAAASIREDLQAYRHN	CD123	9.4
401	MGSWYEFYERLDAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDWAAWIREDLQAYRHN	CD123	8.4
402	MGSWFEFDDRLWAIENRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRDNAAWIREILQAYRHN	CD123	4.2
403	MGSWYEFWDRLDALEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRDSAAFIREELQAYRHN	CD123	9.7
404	MGSWMEFVDRLDAIESRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRIEAAFIREELQAYRHN	CD123	5.8
405	MGSWDEFVDRLWAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRIQAAIIREALQAYRHN	CD123	6
406	MGSWFEFNYRLGAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRQIAAEIREFLQAYRHN	CD123	6.9
407	MGSWEEFFTRLDAINERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRYEAAEIRHMLQAYRHN	CD123	3.9
408	MGSWYEFSNRLDAIGERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRHQAAEIRWFLQAYRHN	CD123	3.9
409	MGSWYEFWGRLDAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGRGNP EVEMLREDAAEIRGQLQAYRHN	CD123	5.4
410	MGSWVEFWDRLWAIDYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRDEAAWIREELQAYRHN	CD123	3.6
411	MGSWVEFVDRLWAIDERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRTWAAWIREDLQAYRHN	CD123	3.2
412	MGSWFEFWDRLEAIWERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRREAAIIREDLQAYRHN	CD123	10.3
413	MGSWFEFEDRLEAIYQRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAWIRSDLQAYRHN	CD123	5.5
414	MGSWFEFHDRLWAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILREEAADIRLDLQAYRHN	CD123	3.5
415	MGSWYEFEDRLWAIDNRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVHAADIRDDLQAYRHN	CD123	4.9
416	MGSWFEFQDRLWAIDNRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRDHAAMIRWELQAYRHN	CD123	3.2
417	MGSWDEFEERLFAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRYLAADIREELQAYRHN	CD123	5
418	MGSWEEFWERLDAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRNDAADIREPLQAYRHN	CD123	6.8
419	MGSWMEFWERLEAIDMRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRDDAAVIRDDLQAYRHN	CD123	4.2
420	MGSWLEFMWRLDAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLREMAAAIRDDLQAYRHN	CD123	5.1
421	MGSWTEFYNRLDAIDQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLREYAADIRTDLQAYRHN	CD123	3.3
422	MGSWWEFIWRLEAIEQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRSRAADIRTDLQAYRHN	CD123	4
423	MGSWSEFYDRLWAIEERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRYYAAEIREELQAYRHN	CD123	17

424	MGSWSEFEDRLWAIDQRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRAYAADIRWELQAYRHN	CD123	4.2
425	MGSWTEFWERLNAIDERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRLYAAEIRSELQAYRHN	CD123	4
426	MGSWWEFEERLWAIDYRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRSWAAEIRALLQAYRHN	CD123	4.1
427	MGSWWEFENRLWAIEERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRNYAAEIRWELQAYRHN	CD123	5.6
428	MGSWVEFEERLWAIDERLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDWAADIRWWLQAYRHN	CD123	4.1
429	MGSWVEFEERLEAIEERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDDAANIRHWLQAYRHN	CD123	3.8
430	MGSWMEFEERLWAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRSEAAWIRMELQAYRHN	CD123	3.2
431	MGSWSEFEHRLEAIESRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRSEAAWIREQLQAYRHN	CD123	7.6
432	MGSWFEFWERLDAIEWRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRSTAADIRRYLQAYRHN	CD123	3.4
433	MGSWFEFWGRLEAIESRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREHAAWIRAYLQAYRHN	CD123	4.9
434	MGSWQEFTMRLDAIYNRLETLGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQSAANIRSELQAYRHN	CD123	13.7
435	MGSWSEFNMRLDAIYERLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRHSAARIRLELQAYRHN	CD123	13.7
436	MGSWSEFNMRLDAIYERLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRHSAALIRLELQAYRHN	CD123	11.4
437	MGSWIEFNMRLDAIYERLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRKVAANIRLELQAYRHN	CD123	11.4
438	MGSWYEFHHRLDAIYERLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRSSAANIRKELQAYRHN	CD123	11.9
439	MGSWYEFAKRLDAIYERLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRSSAANIREELQAYRHN	CD123	15.3
440	MGSWTEFYVRLDAIYERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRMVAANIRTELQAYRHN	CD123	16
441	MGSWVEFYTRLDAIYGRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQVAANIRMELQAYRHN	CD123	14.4
442	MGSWVEFHMRLDAIYERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRTAAANIRVELQAYRHN	CD123	9.1
443	MGSWYEFAIRLDAIYERLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRVWAANIRTELQAYRHN	CD123	25.5
444	MGSWNEFVIRLDAIYERLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRMAAANIRMELQAYRHN	CD123	16.6
445	MGSWSEFYVRVDAIYARLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRVWAANIRHELQAYRHN	CD123	14.7
446	MGSWSEFHVRLDAIYARLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLREWAANIRRELQAYRHN	CD123	14.4
447	MGSWVEFHLRLDAIYGRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVWAANIRNELQAYRHN	CD123	17.5
448	MGSWVEFEMRLDAIVGRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRRWAANIRSELQAYRHN	CD123	25.3
449	MGSWVEFNIRLDAIYERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRHWAASIRRELQAYRHN	CD123	13.4
450	MGSWHEFGVRLDAIYDRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRQAAANIRSELQAYRHN	CD123	15.6
451	MGSWTEFNLRLDAIYDRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRASAAAIRVELQAYRHN	CD123	14.4

452	MGSWTEFNLRLDAIYGRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRAAAANIRVELQAYRHN	CD123	19.3
453	MGSWVEFNWRLDAIYDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRVSAAKIRGELQAYRHN	CD123	9.3
454	MGSWNEFAWRLDAIYSRLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRVAAANIRYELQAYRHN	CD123	17.7
455	MGSWTEFAWRLDAIYDRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRHVAANIRRELQAYRHN	CD123	16.1
456	MGSWVEFSIRLDAIYTRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRKGAANIRKELQAYRHN	CD123	15.1
457	MGSWVEFYIRLDAIYVRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRSYAANIRQELQAYRHN	CD123	16.1
458	MGSWYEFSMRLDAIYDRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEQLRGYAANIRNELQAYRHN	CD123	13
459	MGSWVEFIYRLDAIYDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRRYAANIRNELQAYRHN	CD123	17
460	MGSWIEFEVRLDAIYNRLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLRRYAANIRHELQAYRHN	CD123	20.8
461	MGSWFEFYDRLDAIYMRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRRYAANIRAELQAYRHN	CD123	13.6
462	MGSWFEFYMRLDAIYDRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLRTFAANIRKELQAYRHN	CD123	13.1
463	MGSWYEFDYRLDAIYDRLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLRKWAANIREELQAYRHN	CD123	24.9
464	MGSWSEFYLRLDAIYDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRKTAANIREELQAYRHN	CD123	15.7
465	MGSWFEFYERLDAINWRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRGEAAAIREDLQAYRHN	CD123	3
466	MGSWNEFEDRLDAIWWRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRVEAAFIRTMLQAYRHN	CD123	5.1
467	MGSWFYFKDDLADINYMLEALGGSEAELAMFEDDIAGFELTLLKYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.7
468	MGSWHFFKDDLAWIKNELEALGGSEAELAMFEDDIAMFETMLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.2
469	MGSWHWFKTDLADIKEELEALGGSEAELAMFEDDIAEFEEFLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.5
470	MGSWWLFKDDLAEIKYWLEALGGSEAELAFFEDDIAEFERGLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
471	MGSWYEFKDDLAEIKEWLEALGGSEAELAFFELDIADFEWLLQLYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
472	MGSWQWFKDDLAYIKETLEALGGSEAELALFEDMIADFEFELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.3
473	MGSWILFKDDLAWIKETLEALGGSEAELAFFEDNIADFEEQLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6
474	MGSWIVFKDDLADIKRWLEALGGSEAELAMFEDEIADFEWQLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.9
475	MGSWGHFKQDLAWIKDTLEALGGSEAELAFFEDDIAMFEMELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.9
476	MGSWGYFKDDLAWIKGELEALGGSEAELAEFEWFIAVFEEDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.5
477	MGSWYWFKDDLAEIKGLLEALGGSEAELAEFEDEIAVFEQELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	10.4
478	MGSWMFFKEDLADIKWALEALGGSEAELAFFEEEIALFEQHLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.2
479	MGSWTFFKEDLAGIKWELEALGGSEAELAWFEDEIALFEEELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	7

480	MGSWVFFKDDLADIKDELEALGGSEAELAFFEIAIALFEWELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	8.8
481	MGSWTFFKNDLAEIKDWLEALGGSEAELADFEWDIAEFEYSLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.9
482	MGSWTYFKDDLADIKQWLEALGGSEAELAFFEIEIAEFEEELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.6
483	MGSWTVFKYDLADIKWWLEALGGSEAELADFEEEIAEFEEELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.9
484	MGSWYWFKQDLAHIKSMLEALGGSEAELAWFEEDIADFESELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
485	MGSWTFFKWDLADIKANLEALGGSEAELAWFEEDLAGFEAELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.8
486	MGSWSFFKEELANIQVYLEALGGSEAELAWFEEDIADFEEDLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
487	MGSWEFFKYELADIKDELEALGGSEAELAWFEEDIATFEEWLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.4
488	MGSWQTFKDELAHIKWELEALGGSEAELAWFEWDIANFEEELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.5
489	MGSWYWFKEELAFIKWELEALGGSEAELALFEEDIAYFEEMLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	9.4
490	MGSWNSFKDELAEIKAELEALGGSEAELAFFEEDIAWFEEHLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
491	MGSWDLFKWELAEIKLGLEALGGSEAELAEFEYDIAWFEEDLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.4
492	MGSWIFFKQDLAEIKLNLEALGGSEAELAWFEDDIAWFESHLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
493	MGSWHLFKWTLAEIKYELEALGGSEAELAWFEDDIATFEEELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4
494	MGSWVTFKDELADIKDFLEALGGSEAELAFFEVDIAEFEAELQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	7.6
495	MGSWVYFKDELADIKDFLEALGGSEAELAEFEEDIATFEYDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.6
496	MGSWETFKYELAEIKDYLEALGGSEAELAWFEDDIAEFEFELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.4
497	MGSWNTFKYELAEIKHFLEALGGSEAELAMFEDDIAMFEWELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5
498	MGSWYVFKDELAEIKQFLEALGGSEAELAWFEDDIAEFETQLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	9.9
499	MGSWIFFKEQLAIIKWELEALGGSEAELAWFEDDIAAFEDDLQFYKGQGNP EVEALRKEAAAIRDELQAYRHN	CD123	15
500	MGSWEFFKEVLAEIKYDLEALGGSEAELAWFETDIAGFEIDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	8.2
501	MGSWVFFKEDLATIKNDLEALGGSEAELAWFEMMIADFEADLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.1
502	MGSWEEFKEDLAEIKVWLEALGGSEAELAWFEMGIADFEDGLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.3
503	MGSWHWFKEDLANIKDWLEALGGSEAELAWFEDNIADFEGDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
504	MGSWFWFKEDLAFIKEDLEALGGSEAELAWFEDGIAFFEWDLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	13.7
505	MGSWQWFKEDLAEIKHDLEALGGSEAELAWFEDFIAQFEFDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
506	MGSWHWFKEDLAIIKQDLEALGGSEAELATFEQWIAEFEWDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.5
507	MGSWNWFKEDLAIIKMDLEALGGSEAELAWFEHNIAGFEFELQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.1

508	MGSWSWFKEDLAEIKMELEALGGSEAELAYFEWYIAEFEFQLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.8
509	MGSWSWFKQDLADIKIQLEALGGSEAELAWFEWDIAEFEFELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4
510	MGSWSWFKEDLADIKFELEALGGSEAELAWFELDIADFEQALQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.8
511	MGSWSWFKEDLASIKAVLEALGGSEAELAFFESDIAEFEQELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.9
512	MGSWWEFKEDLAEIKWFLEALGGSEAELAWFEHDIAKFEFELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.1
513	MGSWEWFKSDLASIKWELEALGGSEAELAWFEHDIAEFEEDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.7
514	MGSWNEFKDDLAMIKMTLEALGGSEAELAWFEHDIAEFEDDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.5
515	MGSWTFFKDDLAEIKWMLEALGGSEAELAWFESDIAYFEDELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
516	MGSWSDFKDDLAEIKMILEALGGSEAELAYFENDIAWFEDDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.7
517	MGSWSMFKDDLAEIKASLEALGGSEAELAWFEDDIAWFEDDLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.2
518	MGSWQYFKDDLAEIKMVLEALGGSEAELAWFEADIAMFEDDLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.6
519	MGSWSFFKDDLAEIKYFLEALGGSEAELAMFEQTIAEFEYDLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	10.1
520	MGSWMEFKEELAEIKYILEALGGSEAELAWFEQSIADFEYDLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5
521	MGSWAWFKEDLAEIKVFLEALGGSEAELAEFEVSIADFEYELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.5
522	MGSWYEFKFDLAEIKEQLEALGGSEAELALFEDDIAFFEYDLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.6
523	MGSWYDFKYDLAEIKMDLEALGGSEAELAQFEFDIAFFEEELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.2
524	MGSWYIFKEDLAEIKEELEALGGSEAELAYFEEEIALFEMELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	11.1
525	MGSWVLFKEELAYIKFELEALGGSEAELALFENVIAIFESNLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.5
526	MGSWQDFKEDLAWIKYELEALGGSEAELAFFEYDIAIFENNLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.2
527	MGSWDHFKNDLAWIKKHLEALGGSEAELAEFEAVIAYFELYLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
528	MGSWYDFKEDLADIKWMLEALGGSEAELAEFENVIAYFENDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	8
529	MGSWYMFKEELADIKWYLEALGGSEAELAWFEDDIAGFEWDLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	7
530	MGSWYYFKDELADIKWDLEALGGSEAELAWFEMLIAQFELDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4
531	MGSWMYFKDTLADIKWYLEALGGSEAELAFFEDWIAEFEDDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.1
532	MGSWYQFKHDLADIKYGLEALGGSEAELAWFEDDIADFELDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.7
533	MGSWYVFKDDLADIKYMLEALGGSEAELAWFEWEIANFEFDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
534	MGSWNFFKYDLADIMAYLEALGGSEAELAFFEDEIANFEHDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.4
535	MGSWHWFKIVLADIKDGLEALGGSEAELAYFETTIADFEMDLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.3

536	MGSWHWFKIVLADIKDGLEALGGSEAELAYFETTIADFEMDLHHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.5
537	MGSWFMFKEELADIKDWLEALGGSEAELASFESYIAWFEQDLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.7
538	MGSWFMFKQELAWIKEDLEALGGSEAELADFEWDIAEFEWDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	7.2
539	MGSWQIFKGELAYIKQYLEALGGSEAELAFFEFDIAEFEEDLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.7
540	MGSWDFFKEELAEIKHYLEALGGSEAELAFFEFWIADFEQDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.7
541	MGSWFNFKEELAVIKFQLEALGGSEAELAFFEWVIADFEDDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.1
542	MGSWYQFKTELAWIKDDLEALGGSEAELAWFEWVIADFEDDLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.6
543	MGSWFEFKDYLADIKWDLEALGGSEAELAIFEHDIAYFEHNLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
544	MGSWVRFKDFLADIKMDLEALGGSEAELADFEYHIAEFEHNLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.8
545	MGSWWLFKEQLALIKYNLEALGGSEAELADFESWIAEFEHQLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.1
546	MGSWHVFKTELADIKFYLEALGGSEAELAMFELWIAEFEHELQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.4
547	MGSWIWFKDWLADIKDLLEALGGSEAELAEFEYDIALFEDQLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	7.3
548	MGSWGWFKHELAFIKADLEALGGSEAELAWFEEEIAEFEYELQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
549	MGSWTWFKDNLAWIKEDLEALGGSEAELAWFELEIASFETALQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.9
550	MGSWTYFKNDLAGIKEDLEALGGSEAELAQFEFEIAEFEWLLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.6
551	MGSWTWFKWDLADIKGDLEALGGSEAELAFFEEEIAEFEWRLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.9
552	MGSWLYFKEYLADIKSDLEALGGSEAELAWFEYEIADFEEQLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.7
553	MGSWHWFKEELAEIKEDLVALGGSEAELAWFEYDIAMFELSLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.1
554	MGSWNDFKEELAWIKFDLEALGGSEAELAWFEEDIAMFEQQLQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.8
555	MGSWWDFKDWLAEIKHDLEALGGSEAELALFESEIADFEFGLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.2
556	MGSWDEFKEDLAHIKTDLEALGGSEAELALFEDEIADFEMYLQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	6.3
557	MGSWDFFKYDLANINEWLEALGGSEAELADFEYGIADFELWLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.5
558	MGSWYQFKDDLAHIKHLLEALGGSEAELAVFEYIIADFESFLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4
559	MGSWAEFKHDLADIKRELEALGGSEAELAWFELSIAFFEDELQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.3
560	MGSWVVFKQDLADINHQLEALGGSEAELAWFEWEIADFEWELQHYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.6
561	MGSWFQFKEFLAMITHNLEALGGSEAELAEFEHDIALFESELQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	3.1
562	MGSWHWFKEDLAMITDVLEALGGSEAELAAFESEIAVFEADLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	5.2
563	MGSWSWFQWDLAGIKDHLEALGGSEAELAEFESEIAYFEDELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	12.9

564	MGSWTEFKGELAEIKWILEALGGSEAELAFFEDEIAAFEWDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	8.2
565	MGSWFEFKWTLALIKQELEALGGSEAELADFEQEIAEFEWWLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD123	4.9
566	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFMDEIMAFEWELWAYKGKGNP EVEALMNEAFAIDVELYAYRHN	CD123	3.4
567	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEWEIVAFFSELFAYKGKGNP EVEALRDEAIAIETELVAYRHN	CD123	3.6
568	MGSWWEFDHRLTAIDTRLQALGGSEAELAEFESSIAEFEWWLQDYKGKGNP EVEALFAEAEAIYVELDAYRHN	CD123	4.3
569	MGSWWEFQFRLYAIDQRLLALGGSEAELAEFEQDIADFEWMLQDYKGKGNP EVEALMLEADAIEAELKAYRHN	CD123	3.1
570	MGSWYEFDHRLDAIYQRLWALGGSEAELAEFEYGIAEFEEYLQDYKGKGNP EVEALISEAWAIEWELSAYRHN	CD123	4.6
571	MGSWYEFDMRLDAIWERLTALGGSEAELADFEQYIAEFERQLQDYKGKGNP EVEALFDEAWAIEDELYAYRHN	CD123	13.7
572	MGSWSEFDSRLDAIAYRLFALGGSEAELAQFEWIIADFEEDLQMYKGKGNP EVEALFSEAYAIEIELNAYRHN	CD123	4.3
573	MGSWYEFDDRLDAIAYRLNALGGSEAELAWFEWEIAEFELDLQWYKGKGNP EVEALVWEADAIEWELEAYRHN	CD123	4.6
574	MGSWFEFDERLDAIGSRLTALGGSEAELASFEFYIADFEEWLQQYKGKGNP EVEALEWEAFAIDEELGAYRHN	CD123	3.8
575	MGSWEEFDQRLDAIDVRLYALGGSEAELAEFEFDIAAFEEWLQLYKGKGNP EVEALNMEAFAITDELCAYRHN	CD123	3.6
576	MGSWEEFDVRLDAIFNRLWALGGSEAELAEFEFDIAWFEMDLQEYKGKGNP EVEALFDEAEAITNELVAYRHN	CD123	4.7
577	MGSWEEFDKRLDAITRRLMALGGSEAELAEFESTIAWFEWDLQEYKGKGNP EVEALDWEAYAIDYELGAYRHN	CD123	4.5
578	MGSWYEFDHRLEAIYDRLWALGGSEAELAFFEFDIADFEWDLQSYKGKGNP EVEALFDEAAAIGHELLAYRHN	CD123	4.5
579	MGSWNEFDDRLLAIWGRLDALGGSEAELAFFEEQIAGFEDELQWYKGKGNP EVEALDQEAEAIEKELWAYRHN	CD123	4.1
580	MGSWVEFDDRLDAIWERLDALGGSEAELAWFEEQIAVFEHQLQDYKGKGNP EVEALNQEAEAIDLELKAYRHN	CD123	5
581	MGSWTEFDDRLFAIYWRLDALGGSEAELAWFEEVIAEFENDLQVYKGKGNP EVEALDDEAHAISIELEAYRHN	CD123	6.4
582	MGSWSEFDQRLEAIWNRLDALGGSEAELADFEREIAYFENQLQWYKGKGNP EVEALNNEAFAIVDELGAYRHN	CD123	3.4
583	MGSWYEFDERLWAIWERLDALGGSEAELAHFEWVIADFENDLQWYKGKGNP EVEALEFEAEAIVTELHAYRHN	CD123	3.6
584	MGSWMEFDYRLEAIWMRLIALGGSEAELADFESSIADFEHHLQSYKGKGNP EVEALEWEAFAIGVELDAYRHN	CD123	3.1
585	MGSWYEFESRLEAIWWRLEALGGSEAELAQFEQYIADFEQHLQWYKGKGNP EVEALDWEADAIWLELQAYRHN	CD123	4.4
586	MGSWEEFYMRLVAIHMRLRALGGSEAELAVFENYIAEFEEYLQYYKGKGNP EVEALTIEADAIGTELGAYRHN	CD123	4.4
587	MGSWDEFYYRLVAITHRLHALGGSEAELAWFEDDIAGFEWDLQTYKGKGNP EVEALYKEAGAIGMELTAYRHN	CD123	5.4
588	MGSWEEFDTRLLAIFGRLGALGGSEAELALFEMLIAKFEDDLQNYKGKGNP EVEALSEEAFAIDHELGAYRHN	CD123	6.7
589	MGSWREFDQRLWAIDWRLEALGGSEAELAMFEWMIATFEDDLQWYKGKGNP EVEALYREAFAIDWELDAYRHN	CD123	3.4
590	MGSWEEFHERLDAIDERLEALGGSEAELAFFEDDIASFEDWLQWYKGKGNP EVEALSREADAINFELEAYRHN	CD123	4.3
591	MGSWNEFYERLEAIDRRLFALGGSEAELALFEWMIADFEDDLQMYKGKGNP EVEALINEAGAIGFELEAYRHN	CD123	5.2

592	MGSWTEFTQRLEAIVDRLFALGGSEAELAEFENSIADFEWDLQWYKGKGNP EVEALNREAVAIDNELWAYRHN	CD123	3.9
593	MGSWVEFIMRLDAIYERLDALGGSEAELAEFEWHIADFEDHLQWYKGKGNP EVEALFEEADAIWEELWAYRHN	CD123	6.4
594	MGSWNEFLLRLDAIEHRLFALGGSEAELAEFEWEIADFEDDLQWYKGKGNP EVEALVEEAEAIDVELVAYRHN	CD123	3.2
595	MGSWYEFNMRLGAIDDRLQALGGSEAELAWFEDMIAIFEDDLQIYKGKGNP EVEALEQEAAAIHQELWAYRHN	CD123	3.8
596	MGSWEEFHWRLGAIDARLEALGGSEAELAWFEDGIADFEAILQDYKGKGNP EVEALDSEAVAIHHELWAYRHN	CD123	3.3
597	MGSWYEFYERLWAIDDRLWALGGSEAELAEFEDSIATFEPSLQMYKGKGNP EVEALVAEAWAIFDELAAYRHN	CD123	3.6
598	MGSWFEFDQRLDAITFRLWALGGSEAELAEFEDVIALFEYHLQDYKGKGNP EVEALEVEAWAIFHELGAYRHN	CD123	3.2
599	MGSWSEFWFRLDAIEDRLWALGGSEAELAEFEDNIALFEYSLQHYKGKGNP EVEALVKEANAIDDELGAYRHN	CD123	4.5
600	MGSWYEFWDRLTAIEHRLWALGGSEAELAYFEDSIAHFEGSLQVYKGKGNP EVEALYKEAEAIEWELEAYRHN	CD123	4.4
601	MGSWYEFDDRLWAIFDRLFALGGSEAELAFFEDSIAEFEEELQHYKGKGNP EVEALYLEAWAIENELGAYRHN	CD123	4.7
602	MGSWNEFVERLSAIDHRLWALGGSEAELADFEQQIAEFEIHLQEYKGKGNP EVEALDFEADAIFDELLAYRHN	CD123	3.2
603	MGSWSEFVDRLDAIFDRLWALGGSEAELAWFEDTIAHFEWNLQEYKGKGNP EVEALNGEADAITDELHAYRHN	CD123	5.3
604	MGSWAEFDSRLDAIAQRLFALGGSEAELAHFEDFIAQFEYSLQEYKGKGNP EVEALSNEADAIFNELKAYRHN	CD123	3.6
605	MGSWAEFDSRLIAIFDRLWALGGSEAELAWFEDDIAQFEQHLQAYKGKGNP EVEALRQEADAITFELKAYRHN	CD123	3.6
606	MGSWTEFEERLEAIWDRLYALGGSEAELAAFEWDIAYFEDGLQEYKGKGNP EVEALFMEAEAIIRELKAYRHN	CD123	5.9
607	MGSWYEFEDRLAAIWDRLNALGGSEAELAIFEWDIAWFEEGLQEYKGKGNP EVEALKHEASAIQTELFAYRHN	CD123	6.4
608	MGSWLEFESRLWAIWDRLDALGGSEAELAHFEQDIADFEMSLQEYKGKGNP EVEALIREAEAIETELYAYRHN	CD123	3.4
609	MGSWMEFEDRLIAIWARLDALGGSEAELAWFEADIADFEESLQEYKGKGNP EVEALIFEAIAINKELMAYRHN	CD123	3.7
610	MGSWFEFTIRLEAIQDRLDALGGSEAELAWFEWDIAEFEEGLQFYKGKGNP EVEALHTEADAIMNELVAYRHN	CD123	3.5
611	MGSWYEFVSRLDAIEYRLWALGGSEAELAWFEWDIADFEQGLQFYKGKGNP EVEALAQEANAIGSELTAYRHN	CD123	3.2
612	MGSWEEFDYRLYAIQDRLYALGGSEAELAFFEWEIADFEHMLQMYKGKGNP EVEALFQEADAIDAELHAYRHN	CD123	4.4
613	MGSWIEFFHRLDAIQDRLDALGGSEAELAYFEWAIADFEHMLQLYKGKGNP EVEALQFEAFAIEGELYAYRHN	CD123	3.5
614	MGSWYEFSSRLNAIDDRLWALGGSEAELAYFETDIADFESLLQWYKGKGNP EVEALLNEADAIDYELYAYRHN	CD123	3.8
615	MGSWFEFEYRLDAIIDRLFALGGSEAELAEFESMIANFEYSLQEYKGKGNP EVEALYFEADAIVDELTAYRHN	CD123	4
616	MGSWLEFEYRLDAIYDRLFALGGSEAELAAFEQDIADFEKYLQYYKGKGNP EVEALWEEADAIMWELFAYRHN	CD123	3.1
617	MGSWHEFEERLMAIEDRLWALGGSEAELAEFEQWIALFEYDLQEYKGKGNP EVEALGMEAFAINNELSAYRHN	CD123	5.8
618	MGSWYEFEERLDAIEDRLIALGGSEAELAIFEDIIAFFEQDLQYYKGKGNP EVEALEMEAEAISIELDAYRHN	CD123	4.1
619	MGSWHEFEKRLYAIEDRLIALGGSEAELAWFEDSIAWFEWDLQMYKGKGNP EVEALNEEADAIYQELDAYRHN	CD123	3.6

620	MGSWIEFEDRLDAITDRLWALGGSEAELAEFEHQIAFFEEDLQWYKGKGNP EVEALHMEAEAIMEELGAYRHN	CD123	9.5
621	MGSWMEFEDRLMAIVDRLWALGGSEAELADFEWNIAMFEEELQWYKGKGNP EVEALGDEAEAIEWELYAYRHN	CD123	6.8
622	MGSWEEFEDRLFAIDSRLWALGGSEAELAEFENIIASFEEVLQEYKGKGNP EVEALSVEAFAIDRELGAYRHN	CD123	3.7
623	MGSWEEFLFRLEAIQDRLWALGGSEAELAWFEYEIASFEDVLQSYKGKGNP EVEALSTEAKAIDYELFAYRHN	CD123	8.2
624	MGSWVEFDNRLFAIDERLWALGGSEAELAWFEEEIASFEDNLQKYKGKGNP EVEALQLEAFAIMEELDAYRHN	CD123	3.3
625	MGSWFEFDDRLEAIFDRLWALGGSEAELAMFEFAIAEFEDALQEYKGKGNP EVEALYEEAVAIDEELYAYRHN	CD123	4.1
626	MGSWFEFDARLMAINDRLWALGGSEAELAAFEYHIALFEDQLQMYKGKGNP EVEALTLEAVAINEELWAYRHN	CD123	4
627	MGSWVEFDSRLAAIDYRLEALGGSEAELAWFEYTIANFEHTLQMYKGKGNP EVEALVYEAHAIATELQAYRHN	CD123	3.4
628	MGSWTEFDERLDAIDWRLEALGGSEAELAWFEGDIALFEQYLQVYKGKGNP EVEALMEEADAIKAELDAYRHN	CD123	4.5
629	MGSWIEFDERLDAIDFRLWALGGSEAELAWFEGWIAEFESDLQLYKGKGNP EVEALNEEANAIFHELSAYRHN	CD123	7
630	MGSWWEFDSRLDAIDFRLWALGGSEAELAWFEVEIADFEDWLQLYKGKGNP EVEALWHEADAIVTELYAYRHN	CD123	3.2
631	MGSWYEFDERLDAIFDRLWALGGSEAELAYFEQVIATFEKTLQRYKGKGNP EVEALDTEAKAISWELDAYRHN	CD123	3
632	MGSWYEFQERLDAIDSRLWALGGSEAELAWFEYTIAEFEKELQMYKGKGNP EVEALGTEAVAISEELMAYRHN	CD123	5.5
633	MGSWEEFEDRLWAIDGRLYALGGSEAELAWFEQWIATFEEDLQDYKGKGNP EVEALEYEASAIFEELEAYRHN	CD123	9.4
634	MGSWFEFGDRLEAIDERLYALGGSEAELAQFEWWIAEFEHHLQDYKGKGNP EVEALEYEADAIWGELHAYRHN	CD123	4.5
635	MGSWFEFNDRLDAISERLSALGGSEAELAYFEWQIAVFEKTLQNYKGKGNP EVEALTLEANAIFEELEAYRHN	CD123	3.9
636	MGSWVEFMDRLEAIEERLSALGGSEAELAFFEWEIAEFEEHLQVYKGKGNP EVEALEWEALAITEELAAYRHN	CD123	4
637	MGSWIEFMDRLWAIDQRLWALGGSEAELAWFEEEIAWFEEELQVYKGKGNP EVEALEWEATAISEELWAYRHN	CD123	6.5
638	MGSWEEFNWRLRAIDERLFALGGSEAELAWFEYDIAEFEEQLQVYKGKGNP EVEALRVEAAAIAEELYAYRHN	CD123	5.4
639	MGSWWEFEIRLDAIDERLWALGGSEAELAWFEQSIAFFENDLQVYKGKGNP EVEALRWEANAIIEELFAYRHN	CD123	3.2
640	MGSWYEFEWRLDAIDRRLWALGGSEAELADFEEEIADFEWMLQNYKGKGNP EVEALVDEASAIQTELWAYRHN	CD123	10
641	MGSWYEFVYRLRAIDERLDALGGSEAELAMFEFEIAFFEDQLQRYKGKGNP EVEALVDEAQAIDFELFAYRHN	CD123	4.5
642	MGSWWEFEDRLYAIDDRLWALGGSEAELAQFEREIAQFEIWLQEYKGKGNP EVEALDDEATAINSELFAYRHN	CD123	5.5
643	MGSWDEFEFRLEAIDSRLWALGGSEAELAVFEYEIAQFEFMLQEYKGKGNP EVEALGMEAWAIENELFAYRHN	CD123	3.6
644	MGSWEEFEWRLDAIDERLWALGGSEAELATFEYEIAIFENELQQYKGKGNP EVEALDSEAYAIERELGAYRHN	CD123	4.3
645	MGSWYEFFDRLDAIDERLWALGGSEAELAWFEAEIAEFEMELQGYKGKGNP EVEALDVEAHAIEMELFAYRHN	CD123	3.7
646	MGSWYEFMGRLEAIDERLQALGGSEAELAWFEHEIAEFEWSLQWYKGKGNP EVEALRFEAGAIPWELWAYRHN	CD123	3.5
647	MGSWVEFSNRLDAIWERLQALGGSEAELAYFEWEIAEFEWELQSYKGKGNP EVEALNAEADAIEWELEAYRHN	CD123	5.1

648	MGSWEEFHMRLIAIDERLWALGGSEAELAGFEESIAYFESQLQDYKGKGNP EVEALDYEAHAIWRELYAYRHN	CD123	3.9
649	MGSWWEFKYRLDAICFRLAALGGSEAELASFEDEIAYFEEDLQGYKGKGNP EVEALDYEALAIWDELAAYRHN	CD123	3.1
650	MGSWDEFAMRLEAIQARLFALGGSEAELAIFEDEIAFFETMLQDYKGKGNP EVEALEYEAAAIEAELGAYRHN	CD123	3.7
651	MGSWWEFNARLDAIEDRLMALGGSEAELAYFEDIIASFENILQQYKGKGNP EVEALWYEAYAIEKELNAYRHN	CD123	3.4
652	MGSWIEFWNRLEAIEERLYALGGSEAELAYFEDEIAEFEIYLQQYKGKGNP EVEALKHEAEAINKELMAYRHN	CD123	5.2
653	MGSWNEFVIRLFAIDDRLYALGGSEAELAWFEDEIATFEYELQRYKGKGNP EVEALEYEAEAIVSELFAYRHN	CD123	3.5
654	MGSWYEFLARLYAIDERLWALGGSEAELATFEHWIADFEEQLQSYKGKGNP EVEALTDEAVAIGEELSAYRHN	CD123	4.5
655	MGSWLEFETRLHAIDERLWALGGSEAELAEFEEHIAWFEEDLQFYKGKGNP EVEALDFEADAIGWELWAYRHN	CD123	4.6
656	MGSWFEFETRLEAIDLRLWALGGSEAELATFEDVIAFFEDWLQFYKGKGNP EVEALKMEAWAIGEELHAYRHN	CD123	6.6
657	MGSWHEFWQRLEAIEGRLWALGGSEAELADFESLIADFEEQLQEYKGKGNP EVEALMAEAEAIDNELRAYRHN	CD123	7
658	MGSWYEFEQRLEAIEWRLGALGGSEAELATFEEDIADFEEWLQEYKGKGNP EVEALQYEAYAIAEELHAYRHN	CD123	4.4
659	MGSWYEFENRLFAIEERLWALGGSEAELAWFEYEIANFEWGLQSYKGKGNP EVEALDNEAEAIDIELAAYRHN	CD123	3.3
660	MGSWYEFEQRLGAIEERLWALGGSEAELAAFEDIIAYFEYQLQSYKGKGNP EVEALDEEAWAIDDELWAYRHN	CD123	10.6
661	MGSWWEFEQRLDAIETRLWALGGSEAELAYFEHIIADFEDELQIYKGKGNP EVEALGWEAFAIDGELTAYRHN	CD123	4.7
662	MGSWFEFPYRLEAIEERLYALGGSEAELAQFEQFIAWFEMDLQDYKGKGNP EVEALWFEANAIVEELDAYRHN	CD123	3.1
663	MGSWVEFYDRLEAIEIRLWALGGSEAELADFESFIAHFEDDLQAYKGKGNP EVEALMDEANAIVFELDAYRHN	CD123	4
664	MGSWVEFWDRLDAIEERLWALGGSEAELAEFEFMIAMFEQHLQEYKGKGNP EVEALIPEAGAIDKELTAYRHN	CD123	10
665	MGSWDEFDARLWAIEERLWALGGSEAELAEFEFMIAAFEDVLQEYKGKGNP EVEALMGEANAIVMELDAYRHN	CD123	4.3
666	MGSWYEFWRRLDAIEERLWALGGSEAELAMFETDIAGFEWMLQLYKGKGNP EVEALEHEAWAINSELDAYRHN	CD123	3.6
667	MGSWHEFIWRLDAIEERLWALGGSEAELAWFETEIATFEAQLQDYKGKGNP EVEALEWEAIAIAWELDAYRHN	CD123	3.3
668	MGSWYEFYWRLEAIEERLWALGGSEAELAEFEKAIATFEDQLQTYKGKGNP EVEALETEALAIHAELEAYRHN	CD123	3.7
669	MGSWFEFQWRLEAIEDRLWALGGSEAELAEFETIIAGFEEQLQVYKGKGNP EVEALEEEAMAIQTELHAYRHN	CD123	3.4
670	MGSWWEFEDRLWAIEQRLDALGGSEAELAVFENSIAKFEDMLQVYKGKGNP EVEALHEEADAIIWELYAYRHN	CD123	4.4
671	MGSWWEFEDRLWAIDRRLMALGGSEAELAVFEQMIAHFEQILQVYKGKGNP EVEALHFEAHAIGMELAAYRHN	CD123	4.6
672	MGSWWEFLDRLEAIEYRLQALGGSEAELAVFEWEIAMFEDHLQGYKGKGNP EVEALHSEAHAIISELSAYRHN	CD123	3.1
673	MGSWAEFEDRLAAIERRLEALGGSEAELADFESSIAWFEPDLQYYKGKGNP EVEALMYEAEAIFSELYAYRHN	CD123	4.2
674	MGSWWEFYDRLTAIEARLWALGGSEAELADFEEGIADFEYDLQDYKGKGNP EVEALFWEAWAIQSELTAYRHN	CD123	3.2
675	MGSWYEFEDRLAAIEARLWALGGSEAELADFEEEIAYFEHGLQWYKGKGNP EVEALESEAMAIIDELHAYRHN	CD123	3.8

676	MGSWWEFSWRLEAIETRLDALGGSEAELAFFEMDIAWFEQDLQLYKGKGNP EVEALEEEAYAIYEELEAYRHN	CD123	3.3
677	MGSWEEFFFRLEAIDDRLYALGGSEAELALFEEVIAYFEQDLQWYKGKGNP EVEALYVEAYAIQEELYAYRHN	CD123	3.2
678	MGSWFEFEERLNAISWRLHALGGSEAELAYFEEDIAWFEDDLQFYKGKGNP EVEALENEAYAIWEELDAYRHN	CD123	13
679	MGSWFEFEERLEAIIYRLWALGGSEAELAMFEESIAWFESDLQQYKGKGNP EVEALEYEAMAISKELKAYRHN	CD123	3.7
680	MGSWAEFDDRLEAIEYRLHALGGSEAELAWFEEGIAGFEHALQSYKGKGNP EVEALETEAGAINEELWAYRHN	CD123	5.8
681	MGSWDEFEERLQAIEYRLWALGGSEAELAWFEEVIAQFEYDLQKYKGKGNP EVEALSTEAQAIQDELWAYRHN	CD123	3.8
682	MGSWWEFTDRLDAIFDRLWALGGSEAELAAFEESIAIFEQDLQYYKGKGNP EVEALEYEANAIQYELEAYRHN	CD123	7.5
683	MGSWWEFTDRLEAIEDRLWALGGSEAELAHFEDSIAQFEQELQWYKGKGNP EVEALADEADAIESELHAYRHN	CD123	16.6
684	MGSWVEFFWRLDAIEDRLWALGGSEAELANFEFEIADFEAWLQKYKGKGNP EVEALHSEADAIQLELRAYRHN	CD123	4
685	MGSWVEFYNRLDAIENRLWALGGSEAELAFFEELIAQFEFALQDYKGKGNP EVEALEDEADAIWEELMAYRHN	CD123	6.9
686	MGSWEEFYYRLHAIDNRLWALGGSEAELAYFEWHIADFELELQDYKGKGNP EVEALSEEATAIFEELWAYRHN	CD123	3
687	MGSWREFHDRLFAIDGRLWALGGSEAELANFEWDIADFEFELQDYKGKGNP EVEALSWEADAIMQELGAYRHN	CD123	5.6
688	MGSWEEFDERLWAISDRLWALGGSEAELAYFEGEIAYFEQNLQTYKGKGNP EVEALQTEALAIDTELWAYRHN	CD123	6.5
689	MGSWEEFEQRLWAIDDRLWALGGSEAELAFFEYEIAEFEMDLQWYKGKGNP EVEALFYEAHAINEELWAYRHN	CD123	5.7
690	MGSWDEFHQRLAAIGDRLWALGGSEAELAYFEWEIATFEWDLQVYKGKGNP EVEALYFEATAIDEELMAYRHN	CD123	3.7
691	MGSWVEFEYRLDAISDRLWALGGSEAELAFFENEIASFESDLQFYKGKGNP EVEALMFEAEAIDDELHAYRHN	CD123	6.5
692	MGSWDEFDTRLDAIFSRLYALGGSEAELAMFEGEIAEFEGSLQHYKGKGNP EVEALDFEAHAIDEELWAYRHN	CD123	4
693	MGSWHEFDDRLDAIMSRLDALGGSEAELATFEAEIATFEFVLQLYKGKGNP EVEALLAEAYAIDWELEAYRHN	CD123	7.7
694	MGSWYEFFDRLDAIYDRLYALGGSEAELASFEAQIAEFEVELQSYKGKGNP EVEALEWEAWAIDEELYAYRHN	CD123	4.7
695	MGSWFEFLYRLDAIEDRLWALGGSEAELAEFEQEIAKFESELQSYKGKGNP EVEALEWEAHAIDMELEAYRHN	CD123	6.6
696	MGSWLEFEDRLVAIDHRLFALGGSEAELAEFEEEIALFESYLQDYKGKGNP EVEALNWEADAIHAELYAYRHN	CD123	3.9
697	MGSWYEFESRLDAIVDRLWALGGSEAELAEFEYEIAKFEWELQDYKGKGNP EVEALNWEAGAIEFELYAYRHN	CD123	5.1
698	MGSWYEFEDRLDAILYRLLALGGSEAELAWFERDIAFFESELQWYKGKGNP EVEALEWEAMAIDDELFAYRHN	CD123	4.3
699	MGSWGEFMDRLEAIDYRLWALGGSEAELAWFESDIAEFEQELQMYKGKGNP EVEALWDEAMAIRDELFAYRHN	CD123	4.6
700	MGSWEEFDDRLDAIEHRLWALGGSEAELADFEGSIAAFESWLQVYKGKGNP EVEALEAEAEAIADELWAYRHN	CD123	4
701	MGSWYEFADRLDAIMDRLVALGGSEAELAYFEWEIAAFEEFLQMYKGKGNP EVEALDEEAEAIKDELMAYRHN	CD123	3.3
702	MGSWNEFWERLDAIEWRLFALGGSEAELAFFELDIAWFEEELQWYKGKGNP EVEALIFEAHAITLELDAYRHN	CD123	3
703	MGSWYEFDARLDAIEERLYALGGSEAELAAFEFEIAGFEEALQWYKGKGNP EVEALLKEAEAITDELYAYRHN	CD123	8.9

704	MGSWDEFSERLDAIWGRLEALGGSEAELATFEFHIAEFEHELQYYKGKGNP EVEALQGEAAAIINELYAYRHN	CD123	3.2
705	MGSWDEFWDRLDAIEDRLFALGGSEAELADFERVIAWFENDLQEYKGKGNP EVEALDNEADAIRIELHAYRHN	CD123	3.9
706	MGSWDEFDDRLEAIVDRLFALGGSEAELAMFEFEIAQFEHQLQYYKGKGNP EVEALRDEADAIWIELDAYRHN	CD123	5.6
707	MGSWEEFTIRLGAIYWRLFALGGSEAELANFEWFIAEFEYELQPYKGKGNP EVEALVIEANAIDGELQAYRHN	CD123	3.3
708	MGSWFEFEWRLDAIENRLNALGGSEAELAWFEYHIAAFEDSLQHYKGKGNP EVEALEWEAHAIQSELQAYRHN	CD123	3.3
709	MGSWYEFDDRLEAIWDRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRETAADIRAELQAYRHN	CD123	3.3
710	MGSWGEFWARLEAIWIRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAADIRRSLQAYRHN	CD123	15
711	MGSWIEFEVRLDAIWDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRDEAADIRQSLQAYRHN	CD123	4.2
712	MGSWTEFDRRLDAIWDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAADIRDYLQAYRHN	CD123	9.2
713	MGSWTEFDMRLDAIWDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREEAATIRGVLQAYRHN	CD123	3.1
714	MGSWEEFHDRLMAIETRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRYEAADIRDYLQAYRHN	CD123	4.3
715	MGSWVEFRDRLDAIETRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRYEAAEIRMVLQAYRHN	CD123	4.2
716	MGSWMEFIDRLDAIEHRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAEIRMYLQAYRHN	CD123	4.3
717	MGSWTEFVWRLDAIEWRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAEIRDWLQAYRHN	CD123	4.2
718	MGSWVEFYDRLYAIEVRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRQEAAEIRDWLQAYRHN	CD123	5.8
719	MGSWYEFYDRLDAIEWRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAQIRDFLQAYRHN	CD123	6.2
720	MGSWVEFYDRLDAIEHRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAFIRDMLQAYRHN	CD123	3.4
721	MGSWFEFVDRLTAIQVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREEAALIRYSLQAYRHN	CD123	5.1
722	MGSWFEFLDRLDAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAAVIRDSLQAYRHN	CD123	12.2
723	MGSWYEFMVRLDAIEERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAASIRYHLQAYRHN	CD123	4.1
724	MGSWYEFEDRLDAIQWRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRESAANIRQHLQAYRHN	CD123	6.3
725	MGSWSEFEYRLFAIENRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAMIRQLLQAYRHN	CD123	3.2
726	MGSWVEFEYRLDAITERLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILREEAAFIRQWLQAYRHN	CD123	3.9
727	MGSWWEFLDRLDAIEMRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREEAALIRNMLQAYRHN	CD123	9
728	MGSWWEFEDRLDAIEYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREEAAFIRIFLQAYRHN	CD123	4.9
729	MGSWWEFESRLDAIFMRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREDAAFIREFLQAYRHN	CD123	3.7
730	MGSWVEFWHRLDAIKARLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAADFRLILQAYRHN	CD123	3.5
731	MGSWYEFYNRLSAIYARLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAADIRYMLQAYRHN	CD123	10.6

732	MGSWYEFYDRLSAIYARLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAADIRYMLQAYRHN	CD123	5.3
733	MGSWNEFYDRLSAIYFRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRWYAADIRMILQAYRHN	CD123	10.6
734	MGSWNEFYDRLSAIYFRLQALGGFEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRWYAADIRMILQAYRHN	CD123	9
735	MGSWEEFYDRLGAIFARLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAADIRMILQAYRHN	CD123	3.9
736	MGSWVEFYDRLHAIYFRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRWYAADIRLVLQAYRHN	CD123	4.8
737	MGSWKEFDNRLYAIEDRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRWYAADIRMILQAYRHN	CD123	3.9
738	MGSWVEFWDRLWAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRHYAADIRVWLQAYRHN	CD123	4.5
739	MGSWYEFADRLWAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRYYAADIRWVLQAYRHN	CD123	4
740	MGSWYEFEERLYAIEDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRQEAADIRLMLQAYRHN	CD123	11.5
741	MGSWTEFEWRLYAIEDRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRDEAADIRQYLQAYRHN	CD123	4.2
742	MGSWIEFESRLWAIEDRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRLEAADIREDLQAYRHN	CD123	8.7
743	MGSWFEFEDRLDAIWDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRMDAAMIRYILQAYRHN	CD123	5.1
744	MGSWEEFEDRLWAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRYDAAYIREILQAYRHN	CD123	4.1
745	MGSWIEFEDRLYAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRYEAAEIRYWLQAYRHN	CD123	4
746	MGSWYEFWDRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRYSAAEIRYQLQAYRHN	CD123	4.2
747	MGSWVEFESRLAAIEHRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREYAAEIRDWLQAYRHN	CD123	3.7
748	MGSWWEFEHRLFAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRDYAAEIRDYLQAYRHN	CD123	7.6
749	MGSWYEFDSRLMAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRQEAAEIRMILQAYRHN	CD123	3.2
750	MGSWYEFEWRLMAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRHEAAEIRDVLQAYRHN	CD123	3.4
751	MGSWYEFYNRLDAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRQEAADIRGQLQAYRHN	CD123	11.3
752	MGSWWEFHDRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRIEAADIRRQLQAYRHN	CD123	6.4
753	MGSWYEFWDRLEAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRLEAADIRRILQAYRHN	CD123	4.6
754	MGSWYEFEERLWAIEERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRYEAAWIRDFLQAYRHN	CD123	5.4
755	MGSWYEFENRLEAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLREEAAFIRDWLQAYRHN	CD123	6.1
756	MGSWYEFEYRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREEAAWIRVWLQAYRHN	CD123	6.2
757	MGSWYEFENRLGAIGDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAYIRAVLQAYRHN	CD123	4.8
758	MGSWYEFEHRLDAIYDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREEAAWIRLWLQAYRHN	CD123	6.3
759	MGSWYEFEWRLDAIYDRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAEIRALLQAYRHN	CD123	6

760	MGSWVEFENRLEAIENRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAAQIRMMLQAYRHN	CD123	6.2
761	MGSWYEFEERLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREQAAFIRTMLQAYRHN	CD123	6
762	MGSWFEFEWRLEAIFDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRAEAAEIRLRLQAYRHN	CD123	6.9
763	MGSWWEFEDRLMAIYDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRAEAALIRETLQAYRHN	CD123	15.3
764	MGSWFEFEDRLYAIEDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRWGAATIRDELQAYRHN	CD123	4.7
765	MGSWIEFWDRLEAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRDEAAWIRDSLQAYRHN	CD123	4.5
766	MGSWFEFWDRLDAIEDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRDEAAWIRGTLQAYRHN	CD123	4.9
767	MGSWEEFTDRLWAIEDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAFIRKSLQAYRHN	CD123	8.9
768	MGSWVEFVDRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRDQAAYIRFMLQAYRHN	CD123	4.9
769	MGSWFEFVDRLEAIEMRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRWRAAMIRYDLQAYRHN	CD123	7.1
770	MGSWWEFEMRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRWEAAFIRDILQAYRHN	CD123	4
771	MGSWFEFEIRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRDEAAEIRQVLQAYRHN	CD123	3
772	MGSWYEFYQRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRDEAAEIRVVLQAYRHN	CD123	3
773	MGSWIEFEDRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQEAAEIRLMLQAYRHN	CD123	21.8
841	MGSWVEFYERLDAIDRRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVHAASIRAWLQAYRHN	P26	
842	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRAHAAAIREWLQAYRHN	P26	
843	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVHAAAIREWLQAYRHN	P26	
844	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRAHAAAIREWLQAYRHN	P26	
845	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLKAHAAAIREWLQAYRHN	P26	
846	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLQAHAAAIREWLQAYRHN	P26	
847	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRAHAAGIREWLQAYRHN	P26	
848	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAHIREWLQAYRHN	P26	
849	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAAIREWLQAYRHN	P26	
850	MGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAAIREWLQAYRHN	P26	
851	MGSWHEFYDRLDAIYFRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRLLAAEIRKELQAYRHN	P26	9.6
852	MGSWHEFITRLEAIDQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFWAAEIRFILQAYRHN	P26	16.91
853	MGSWMEFFDRLVAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRMWAAEIRFLLQAYRHN	P26	18.62
854	MGSWVEFSGRLIAIDNRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRMWAAEIRYILQAYRHN	P26	5.28

855	MGSWVEFHHRLFAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRMVAAEIRYILQAYRHN	P26	21.39
856	MGSWHEFMERLIAIDGRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFVAAFIRDVLQAYRHN	P26	17.85
857	MGSWKEFIQRLDAIHYRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFVAAFIRFELQAYRHN	P26	18.41
858	MGSWSEFIFRLDAIHSRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFIAAEIRLKLQAYRHN	P26	28.3
859	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAAIREWLQAYRHN	P26	5.92
860	MGSWLEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAAIREWLQAYRHN	P26	
861	MGSWFEFYHRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAAIREWLQAYRHN	P26	
862	MGSWFEFYDRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAAIREWLQAYRHN	P26	
863	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVHAAAIREWLQAYRHN	P26	
864	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDHAAAIREWLQAYRHN	P26	
865	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLREHAAAIREWLQAYRHN	P26	
866	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAHIREWLQAYRHN	P26	
867	MGSWLEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRVHAAAIREWLQAYRHN	P26	
868	MGSWLEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAHIREWLQAYRHN	P26	19.23
869	MGSWFEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAHIREWLQAYRHN	P26	
870	MGSWLEFYDRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAHIREWLQAYRHN	P26	
871	MGSWLEFYHRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAHIREWLQAYRHN	P26	
872	MGSWLEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDHAAHIREWLQAYRHN	P26	
873	MGSWLEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVHAAHIREWLQAYRHN	P26	
874	MGSWLEFYHRLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAAIREWLQAYRHN	P26	
875	MGSWFEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDHAAHIREWLQAYRHN	P26	
876	MGSWFEFYERLNAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRAHAASIRTWLQAYRHN	P26	27.1
877	MGSWIEFYWRLEAIDQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRVHAAAIRWWLQAYRHN	P26	9.4
878	MGSWSEFVKRLDAIDQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVHAAAIRAWLQAYRHN	P26	27
879	MGSWEEFYYRLEAIDARLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVHAAHIRDWLQAYRHN	P26	30.3
880	MGSWVEFHYRLQAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVHAAHIRKWLQAYRHN	P26	14.8
881	MGSWVEFVGRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHHAAEIRNWLQAYRHN	P26	26
882	MGSWNEFMDRLNAIDNRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRKQAASIRLWLQAYRHN	P26	10

883	MGSWNEFFQRLNAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRQHAANIRWWLQAYRHN	P26	28.7
884	MGSWYEFVVRLFAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAHIRSWLQAYRHN	P26	18.25
885	MGSWYEFYLRLDAIDHRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLREHAAHIRKWLQAYRHN	P26	16
886	MGSWYEFRARLLAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLREHAAHIRNFLQAYRHN	P26	20.9
887	MGSWTEFWHRLEAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAHIRVWLQAYRHN	P26	13.19
888	MGSWTEFQNRLNAIDHRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAKIRVWLQAYRHN	P26	30.5
889	MGSWSEFFKRLEAIDRRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREHAAHIRVWLQAYRHN	P26	30.2
890	MGSWYEFQQRLEAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREHAAHIRHWLQAYRHN	P26	27.3
891	MGSWTEFEKRLHAIDYRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREHAAAIRHWLQAYRHN	P26	17.1
892	MGSWTEFHQRLDAIDERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREHAAKIRMWLQAYRHN	P26	24.4
893	MGSWLEFSQRLTAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLREHAAKIRNWLQAYRHN	P26	30.4
894	MGSWTEFVNRLYAIDSRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRTHAAKIRHWLQAYRHN	P26	16.7
895	MGSWMEFVDRLSAIDRRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREHAANIRQWLQAYRHN	P26	32.1
896	MGSWVEFVSRLYAIDFRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALREHAAQIRDWLQAYRHN	P26	29
897	MGSWSEFHTRLDAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRRHAAAIRFWLQAYRHN	P26	23.5
898	MGSWLEFHSRLDAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLREHAAAIRHYLQAYRHN	P26	30.8
899	MGSWTEFYQRLDAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRQQAAQIRAWLQAYRHN	P26	29.7
900	MGSWAEFSDRLNAIDQRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILREHAAEIRKFLQAYRHN	P26	25.3
901	MGSWMEFNHRLQAIDGRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLREHAAAIRAFLQAYRHN	P26	33.4
902	MGSWYEFYKRLEAIDNRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREHAAAIRHWLQAYRHN	P26	30.8
903	MGSWYEFYYRLEAIDNRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREHAAKIREWLQAYRHN	P26	29.6
904	MGSWYEFVSRLEAIDDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEMLRQHAAAIRHWLQAYRHN	P26	33.1
905	MGSWYEFSHRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEPLREHAAYIRHWLQAYRHN	P26	26
906	MGSWFEFFERLAAIEDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVHAAAIRAFLQAYRHN	P26	20.3
907	MGSWIEFKYRLDAIEWRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRIHAAAIRTWLQAYRHN	P26	18.3
908	MGSWYEFMYRLDAIEYRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRIHAAMIREWLQAYRHN	P26	19.4
909	MGSWVEFVTRLEAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRAHAAHIRHWLQAYRHN	P26	11.7
910	MGSWYEFVIRLDAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRVHAAHIRVWLQAYRHN	P26	30.1

911	MGSWVEFVERLDAIEFRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRNHAAHIRSWLQAYRHN	P26	23.8
912	MGSWSEFVHRLDAIEVRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRYHAAKIRSWLQAYRHN	P26	16.9
913	MGSWSEFYYRLAAIESRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLREHAAHIRRWLQAYRHN	P26	30.8
914	MGSWYEFYLRLSAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVQAAHIRTWLQAYRHN	P26	27.4
915	MGSWYEFYDRLDAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRDQAAYIRTWLQAYRHN	P26	31.9
916	MGSWHEFWVRLEAIESRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRVQAAHIRSWLQAYRHN	P26	26.9
917	MGSWVEFYHRLEAIEQRLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREQAAAIRSWLQAYRHN	P26	28.5
918	MGSWVEFYERLNAIEYRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLREHAAYIRQWLQAYRHN	P26	28.7
919	MGSWVEFYHRLDAIFDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRANAAGIRSWLQAYRHN	P26	20
920	MGSWSEFTDRLFAIEDRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRMHAASIRLWLQAYRHN	P26	25.4
921	MGSWHEFYDRLYAIWDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRNAAAVIRIFLQAYRHN	P26	22.91
922	MGSWFEFSNRLYAIWHRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRTQAAFIRILLQAYRHN	P26	15.25
923	MGSWFEFSDRLYAIWERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRFQAAFIRYQLQAYRHN	P26	18.99
924	MGSWFEFEDRLFAIWTRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRQSAASIRWLLQAYRHN	P26	10.89
925	MGSWHEFSERLFAIWTRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRQSAAFIRVMLQAYRHN	P26	8.21
926	MGSWGEFTVRLYAIDRRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRRFAAIIRAFLQAYRHN	P26	8.54
927	MGSWYEFDHRLMAISFRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRRRAANIRHLLQAYRHN	P26	20.1
928	MGSWSIFKYHLADIKLLLEALGGSEAELAYFEFLIADFEFTLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	20.21
929	MGSWHHFKYFLADIKSILEALGGSEAELAIFEVQIAYFEDLLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	8
930	MGSWLYFKYNLAVIKHWLEALGGSEAELAIFEMSIADFEYELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	13.3
931	MGSWFYFKYELAWIKHWLEALGGSEAELASFETHIAFFEHQLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	13.7
932	MGSWADFKWTLAYIKHRLEALGGSEAELAFFEMEIAYFEQSLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	31.5
933	MGSWAYFKGQLAYIKSGLEALGGSEAELAYFELRIAYFEHWLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	11.4
934	MGSWENFKDTLAWIKEYLEALGGSEAELAGFEHRIAIFEHYLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	19.2
935	MGSWVLFKDYLADIKHYLEALGGSEAELANFEHLIANFEGDLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	13.8
936	MGSWSLFKHRLANIKVYLEALGGSEAELADFETFIAYFEKDLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	19.6
937	MGSWEHFKVELAGIKAYLEALGGSEAELALFEWAIADFESILQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	18.1
938	MGSWIYFKDELAGIKKYLEALGGSEAELAMFEVAIADFEAILQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	15.9

939	MGSWVLFKQELAWIKWLLEALGGSEAELAAFEEQIARFEHDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	29.5
940	MGSWVLFKQELAWIKWYLEALGGSEAELAAFEWEIAAFEQRLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	22.5
941	MGSWFLFKSELAWIKWRLEALGGSEAELAYFEYQIAEFEFWLQSYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	25.8
942	MGSWLLFKSELAWIKWYLEALGGSEAELAEFEWNIAEFEKNLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	25.7
943	MGSWLLFKSDLAWIKWRLEALGGSEAELAEFEESIAMFEHWLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	33.3
944	MGSWLYFKSDLAWIKWRLEALGGSEAELADFEEAIAEFEQALQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	21.2
945	MGSWKLFKYELAWIKWRLEALGGSEAELADFEASIAQFEKYLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	23.4
946	MGSWYLFKNELAWIKWRLEALGGSEAELADFEMVIAMFEDHLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	31.1
947	MGSWVYFKAHLAFIKWELEALGGSEAELANFESTIAEFEKYLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	20.8
948	MGSWMYFKSHLAWIKWELEALGGSEAELAFFEDNIAQFEYWLQLYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	19.8
949	MGSWTLFKWDLAFIKWQLEALGGSEAELAWFEYEIAAFEDSLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	12.1
950	MGSWILFKEDLAFIKWQLEALGGSEAELAWFETTIANFESDLQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	23.3
951	MGSWYFFKSRLAYIKVYLEALGGSEAELAGFEWEIAHFEEWLQRYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	30.1
952	MGSWYIFKSELAWIKWYLEALGGSEAELANFEVEIATFETWLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	29.6
953	MGSWYIFKQELASIKLSLEALGGSEAELAHFEAEIAWFEWWLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	19.4
954	MGSWVRFKTELAYIKESLEALGGSEAELAMFESEIAIFEHSLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	20.5
955	MGSWYLFKTELAAIKYRLEALGGSEAELASFEYEIAWFEHILQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	20.1
956	MGSWYWFKYELAEIKWHLEALGGSEAELAHFEHSIAVFESQLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	21.5
957	MGSWWVFKKTLAEIKWTLEALGGSEAELAYFEAEIAFFEFILQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	18.6
958	MGSWVYFKDHLAEIKSQLEALGGSEAELALFEYDIAWFEFILQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	22.1
959	MGSWVYFKHRLAEIKDQLEALGGSEAELAEFETDIAWFEWMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	11.1
960	MGSWIIFKTDLARIKNYLEALGGSEAELATFERDIAWFEFMLQIYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	16.7
961	MGSWMHFKQDLAEIKGYLEALGGSEAELAIFEMDIAWFEYMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	18.9
962	MGSWQIFKQDLAAIKDYLEALGGSEAELAIFEFDIAWFEHMLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	17.4
963	MGSWLAFKEDLAHIKSILEALGGSEAELAEFEHDIAWFEYMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	18.6
964	MGSWFVFKEDLAGIKFILEALGGSEAELAMFETDIAWFEYMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	14.2
965	MGSWTHFKEDLAHIKDRLEALGGSEAELAAFELDIAWFEFMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	30.4
966	MGSWYYFKERLAAIKDRLEALGGSEAELAIFEADIAWFEFMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	31.5

967	MGSWYTFKGSLAEIKNRLEALGGSEAELAMFESDIAWFEFMLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	32.3
968	MGSWFTFKDDLAQIKNRLEALGGSEAELANFEMSIAWFEFMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	30.8
969	MGSWVLFKQDLAMIKQRLEALGGSEAELAMFEYDIAWFEHMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	29.7
970	MGSWVEFKRDLANIKQRLEALGGSEAELAQFEMQIAWFEHTLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	30.4
971	MGSWSYFKEDLANIKSSLEALGGSEAELAWFESSIAWFEHTLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	11.6
972	MGSWSIFKQDLADIKDSLEALGGSEAELAMFEMDIAWFEHTLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	16.6
973	MGSWEIFKDDLASIKKVLEALGGSEAELALFESDIAWFELMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	27.9
974	MGSWSIFKDDLAVIKERLEALGGSEAELAHFEQDIAWFEHLLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	25.6
975	MGSWSVFKDDLAQIKDRLEALGGSEAELAQFELDIAWFEYVLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	30.3
976	MGSWAVFKDSLAHIKDVLEALGGSEAELALFEMDIAWFEYVLQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	24.1
977	MGSWIAFKDHLAIIKQRLEALGGSEAELARFEFEIAWFEWMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	29.9
978	MGSWIHFKNDLAVIKDELEALGGSEAELARFEIMIAWFEDALQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	17.9
979	MGSWMVFKQDLAEIKANLEALGGSEAELADFEFAIAWFEYELQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	17.8
980	MGSWKNFKLELALIKSKLEALGGSEAELAQFEADIAFFEWSLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	20.6
981	MGSWHSFKQDLAYIKYLLEALGGSEAELAQFEELIAFFEYYLQTYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	25.6
982	MGSWVVFKSSLAQIKILLEALGGSEAELAIFEVKIAHFEQELQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	8.6
983	MGSWDQFKNSLASIKRVLEALGGSEAELAIFEVKIAHFEHFLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	15.6
984	MGSWNNFKSSLASIKQVLEALGGSEAELAVFELQIAHFERELQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	P26	24.1
985	MGSWVEFGHRLWAIDQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRQRAAFIRFRLQAYRHN	CD137	
986	MGSWVEFANRLWAIDQRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRDQAAFIRHKLQAYRHN	CD137	
987	MGSWYEFRHRLWAIDQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLREAAAFIRAKLQAYRHN	CD137	
988	MGSWYEFSMRLWAIDQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRAKAAYIRWKLQAYRHN	CD137	
989	MGSWYEFGHRLWAIDQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRETAAHIRTRLQAYRHN	CD137	
990	MGSWYEFHYRLHAIDQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRIKAAFIRDRLQAYRHN	CD137	
991	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFLGEIWAFEMELAAYKGKGNP EVEALGREAAAIRMELQAYRHN	CD137	
992	MGSWYEFDLRLHAIYDRLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRDNAAYIRQMLQAYRHN	CD47	
993	MGSWTEFTYRLSAIEWRLWALGGSEAELAWFEQKIAFFEDFLQYYKGKGNP EVEALKHEAGAILNELMAYRHN	CD47	
994	MGSWAEFDHRLHAIRERLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRGNAAYIRALLQAYRHN	CD47	

995	MGSWTEFVGRLAAIEFRLWALGGSEAELAWFEAHIAFFEDYLQWYKGKGNP EVEALREEAGAIMEELKAYRHN	CD47	
996	MGSWTEFYSRLEAIWVRLQALGGSEAELAMFEDRIAHFEWFLQQYKGKGNP EVEALHEEAIAIRKELAAYRHN	CD47	
997	MGSWHEFHDRLQAIHERLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRIAAAHIRQVLQAYRHN	CTLA4	
998	MGSWNYFKDHLAWIKNSLEALGGSEAELAHFETAIASFERQLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
999	MGSWLYFKEHLAHIKAWLEALGGSEAELAHFELAIADFEYHLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1000	MGSWVYFKEHLAWIKTELEALGGSEAELAHFEHSIADFEMSLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1001	MGSWFYFKQHLAWIKSYLEALGGSEAELAHFERAIAAFEQHLQMYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1002	MGSWHYFKDHLAEIKGLLEALGGSEAELAHFEMAIADFEHNLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1003	MGSWHYFKGHLAEIKNHLEALGGSEAELAHFERAIAAFERSLQWYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1004	MGSWIYFKEHLAYIKKELEALGGSEAELAHFESAIAVFESTLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1005	MGSWTYFKEHLAEIKYMLEALGGSEAELAHFEVAIADFEKMLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1006	MGSWWLFKDHLAEIKTALEALGGSEAELAHFEMAIAAFEKQLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1007	MGSWSEFYNRLDAIESRLLALGGSEAELALFEIQIARFEKVLQAYKGKGNP EVEALRGEARAIFAELYAYRHN	KIR	
1008	MGSWYEFYNRLYAIEIRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVERLRVRAAKIRVILQAYRHN	KIR	
1009	MGSWLWFKIFLAEIKYFLEALGGSEAELAAFDFEIHAFHVELFAYKGKGNP EVEVLREVAAEIRWDLQAYRHN	KIR	
1010	MGSWTEFQSRLDAIHSRLRALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDDAAFIRHFLQAYRHN	PDL1	
1011	MGSWQEFDDRLNAIKARLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDDAAFIRRFLQAYRHN	PDL1	
1012	MGSWYEFQNRLHAIHERLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLRDDAAFIRHFLQAYRHN	PDL1	
1013	MGSWFEFQDRLTAINERLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRSDAAFIRRFLQAYRHN	PDL1	
1014	MGSWYEFESRLDAIHERLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRGDAAFIRHFLQAYRHN	PDL1	
1015	MGSWYEFNHRLDAISKRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRGDAAFIRHFLQAYRHN	PDL1	
1016	MGSWFEFENRLHAIVHRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRADAAFIRHYLQAYRHN	PDL1	
1017	MGSWVVFKVDLATIKYILEALGGSEAELAEFEGEIAGFEYSLQFYKGKGNP EVEALRKEAAAIRDELQAYRHN	TIM3	
1018	MGSWTIFKEWLAFIKTDLEALGGSEAELAFFEGWIASFEMELQKYKGKGNP EVEALRKEAAAIRDELQAYRHN	PD1	
1019	MGSWVMFKWLLADIKSHLEALGGSEAELAFFEGFIAAFETHLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	PD1	
1020	MGSWYAFKDYLADIKGWLEALGGSEAELAFFEIFIARFELELQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	PD1	
1021	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRKEAAAIRDELQAYRHN	None known	
1030	MGSWEEFELRLNAIEERLYALGGSEAELAYFEYVIADFEGNLQRYKGKGNP EVEALYFEADAIFEELVAYRHN	CD19	

1031	MGSWFEFNHRLWAIFERLMALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRAMAAVIRYHLQAYRHN	CD19	
1032	MGSWEEFDGRLFAIEQRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRWFAAGIRDFLQAYRHN	CD19	
1033	MGSWAEFYHRLYAIETRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRHWAAWIRTYLQAYRHN	CD19	
1034	MGSWVEFSDRLYAIEERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRELAAIIRHSLQAYRHN	CD19	
1035	MGSWWEFEGRLYAIEERLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLREWAAWIRQMLQAYRHN	CD19	
1036	MGSWWEFEHRLYAIEERLVALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRNWAAYIRMALQAYRHN	CD19	
1037	MGSWWEFEARLYAIEFRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRSWAAYIRTSLQAYRHN	CD19	
1038	MGSWWEFEARLWAIESRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRHWAAYIRVILQAYRHN	CD19	
1039	MGSWWEFEARLYAIEFRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRSWAAYIRTSLQAYRHN	CD19	
1040	MGSWEEFYHRLDAIELRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRWYAAEIREILQAYRHN	CD19	
1041	MGSWYEFYERLDAIDTRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLREYAAEIRHFLQAYRHN	CD19	
1042	MGSWNEFFDRLDAILYRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRFVAADIRSWLQAYRHN	CD19	
1043	MGSWIEFDDRLLAIMDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDVAADIRHYLQAYRHN	CD19	
1044	MGSWYEFWERLDAITFRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRTWAADIRAILQAYRHN	CD19	
1045	MGSWEEFYIRLDAIMERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYAAADIRHFLQAYRHN	CD19	
1046	MGSWIEFEERLYAIETRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRVVAADIREWLQAYRHN	CD19	
1047	MGSWIEFEHRLSAINDRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREWAADIRSLLQAYRHN	CD19	
1048	MGSWFEFEMRLDAIMARLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYAAADIRDYLQAYRHN	CD19	
1049	MGSWYEFVYRLDAIYDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYAAADIRDFLQAYRHN	CD19	
1050	MGSWVEFEDRLDAILERLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRELAADIRDFLQAYRHN	CD19	
1051	MGSWFEFEERLIAIEERLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRWIAADIRDVLQAYRHN	CD19	
1052	MGSWIEFADRLDAILDRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREIAADIRAYLQAYRHN	CD19	
1053	MGSWLEFEYRLDAILDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLREVAADIRMLLQAYRHN	CD19	
1054	MGSWYEFHDRLDAITNRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDWAADIRVWLQAYRHN	CD19	
1055	MGSWQEFEQRLDAINWRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELREWAADIRIFLQAYRHN	CD19	
1056	MGSWYEFYSRLDAIDSRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRDYAAEIRRYLQAYRHN	CD19	
1057	MGSWEEFHDRLEAISDRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDWAADIRFYLQAYRHN	CD19	
1058	MGSWWEFDERLYAIEDRLFALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRIVAADIREILQAYRHN	CD19	

1059	MGSWEEFEYRLMAIEVRLWALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLREIAADIRQILQAYRHN	CD19	
1060	MGSWVVFKQRLAYIKDLLEALGGSEAELAYFEMSIAFFEEDLQVYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD22	
1061	MGSWYEFKNDLAWIKVHLEALGGSEAELAYFEFRIAHFENALQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	CD22	
1062	MGSWVEFYNRLWAIDHRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRYHAASIRVTLQAYRHN	CD22	
1063	MGSWSEFYDRLHAIHHRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRDTAAFIRTRLQAYRHN	CD22	
1064	MGSWKEFHFRLHAIEHRLIALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEFLRAKAANIRTHLQAYRHN	CD22	
1065	MGSWFEFHGRLHAIYGRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRAHAAHIRDHLQAYRHN	CD22	
1066	MGSWYEFADRLHAIHQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRMTAAFIRSRLQAYRHN	CD22	
1067	MGSWNEFYNRLHAIHQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRQTAAYIRDRLQAYRHN	CD22	
1068	MGSWNEFADRLHAIHQRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRMTAAFIRSRLQAYRHN	CD22	
1069	MGSWTEFSYRLGAIQSRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRYNAAKIRHFLQAYRHN	CD22	
1070	MGSWQEFTTRLEAIYHRLRALGGSEAELANFEGFIAEFEGNLQMYKGKGNP EVEALVHEAYAIMEELHAYRHN	DR5	
1071	MGSWVEFFDRLKAIHDRLEALGGSEAELAHFEKLIAHFEHRLQNYKGKGNP EVEALEKEADAILYELAAYRHN	DR5	
1072	MGSWYYFKHHLAWIKMELEALGGSEAELAHFESSIASFERDLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	DR5	
1073	MGSWVEFHIRLHAIQYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRHWAAFIRLQLQAYRHN	DR5	
1074	MGSWNEFHDRLNAIHARLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDDAAFIRRFLQAYRHN	PDL1	
1075	MGSWYEFTVRLEAIHERLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRDDAAFIRRFLQAYRHN	PDL1	
1076	MGSWKEFDDRLNAIKARLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDDAAFIRRFLQAYRHN	PDL1	
1077	MGSWYEFDDRLNAIHDRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRDDAAFIRRFLQAYRHN	PDL1	
1078	MGSWNEFKNRLDAIHKRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRDDAAFIRHFLQAYRHN	PDL1	
1079	MGSWTEFEQRLEAIHNRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRNDAAFIRHFLQAYRHN	PDL1	
780	MGSWVEFEARLSAIYERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRRHAAGIRSNLQAYRHN	CS1	
781	MGSWVEFFVRLDAIWERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRFHAAGIRQKLQAYRHN	CS1	
782	MGSWTEFNLRLDAIYERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRWHAAGIRQQLQAYRHN	CS1	
783	MGSWMEFYDRLDAIWVRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRFHAAGIREQLQAYRHN	CS1	
784	MGSWHEFNGRLWAIYARLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRRHAAGIRGILQAYRHN	CS1	
785	MGSWYEFVQRLHAINDRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRRHAAGIRYTLQAYRHN	CS1	
786	MGSWAEFYQRLNAIWNRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEVLRRHAAGIRGQLQAYRHN	CS1	

787	MGSWVEFNERLHAIYLRLDALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRRHAAGIRWQLQAYRHN	CS1	
788	MGSWNEFKLELAFIKDWLEALGGSEAELANFEEAIAEFEAGLQGYKGKGNP EVEALRKEAAAIRDELQAYRHN	CS1	
789	MGSWMEFEARLEAIWDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVESLRFHAAGIRQHLQAYRHN	CS1	
790	MGSWVEFEDRLNAIWWRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRRHAAGIRTQLQAYRHN	CS1	
791	MGSWHHFKMHLAGIKLQLEALGGSEAELAEFEEWIADFEGALQDYKGKGNP EVEALRKEAAAIRDELQAYRHN	CS1	
792	MGSWAEFFARLDAIWERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRFHAAGIRQKLQAYRHN	CS1	
793	MGSWAEFFARLDAIWDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRFHAAGIRQKLQAYRHN	CS1	
794	MGSWAEFFARLDAIWERLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLKFHAAGIRQKLQAYRHN	CS1	
795	MGSWAEFFARLDAIWDRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLKFHAAGIRQKLQAYRHN	CS1	
800	MGSWHEFRWRLFAIWQRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRLDAALIRVMLQAYRHN	HER2	10.02
801	MGSWAEFRWRLHAIWLKLGELGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAEQIKYILQAYRHN	HER2	
802	MGSWAEFRWALHAIWLKLGELGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLREDAEQIKYILQAYRHN	HER2	
803	MGSWAEFRWRLHAIWLKLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
804	MGSWAEFRWRLHAIWLQLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
805	MGSWAEFRWRLHAIWLRLGALGGTEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
806	MGSWAEFRWRLHAIWLRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
807	MGSWAEFRWKLEAIWLRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
808	MGSWAEFRWKLGAIWLRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIKYILQAYRHN	HER2	
809	MGSWYEFRWRLHAIWLRLGALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEWLRQDAAQIRYILQAYRHN	HER2	7.18
810	MGSWHEFLRRLLAIEMRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEHLRVRAASIRQMLQAYRHN	HER2	8.15
811	MGSWWGFKVNLAWIKWKLEALGGSEAELAYFELWIANFEHSLQEYKGKGNP EVEALRKEAAAIRDELQAYRHN	HER2	8.69
812	MGSWVNFKTHLARIKVHLEALGGSEAELALFEHDIANFEQVLQQYKGKGNP EVEALRKEAAAIRDELQAYRHN	HER2	7.91
813	MGSWLVFKDELAGIKNYLEALGGSEAELATFEQDIAWFEQWLQNYKGKGNP EVEALRKEAAAIRDELQAYRHN	HER2	3.28
814	MGSWKTFKIELAGIKLELEALGGSEAELAGFENAIAQFESSLQYYKGKGNP EVEALRKEAAAIRDELQAYRHN	HER2	4.95
815	MGSWWEFKVRLSAIQYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALREQAALIRTILQAYRHN	HER2	5.17
816	MGSWWEFHIRLHAINYRLAALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRELAAKIRGDLQAYRHN	HER2	11.90
817	MGSWWEFQVRLRAIQYRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRGLAAQIRFDLQAYRHN	HER2	14.39
818	MGSWWEFKIRLYAIEYRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRAKAAQIRYNLQAYRHN	HER2	4.49

819	MGSWFEFNIRLHAIEYRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRNYAASIRKLLQAYRHN	HER2	7.86
820	MGSWFEFEIRLRAIEYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRELAAEIRYALQAYRHN	HER2	7.75
821	MGSWFEFKIRLYAIQYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRNLAAEIRHSLQAYRHN	HER2	13.08
822	MGSWWEFKVRLRAIEYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRVLAASIRIHLQAYRHN	HER2	10.09
823	MGSWSEFWFRLHAILYRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVETLRDAAAEIRVALQAYRHN	HER2	14.79
824	MGSWIEFWVRLNAILYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEALRDSAAEIRRWLQAYRHN	HER2	3.91
825	MGSWVEFWIRLNAIKYRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEKLRQDAADIRELLQAYRHN	HER2	10.62
826	MGSWTEFWWRLSAIVYRLNALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRDMAADIRSLLQAYRHN	HER2	5.76
827	MGSWWEFYLRLRAISYRLQALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEGLRQDAAEIRKLLQAYRHN	HER2	5.10
828	MGSWWEFHVRLRAIEYRLEALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEQLRLIAANIRHLLQAYRHN	HER2	5.48
829	MGSWWEFHVRLKAIEYRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYIAANIRQLLQAYRHN	HER2	4.56
830	MGSWWEFKVRLKAIEYRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRYIAANIRQLLQAYRHN	HER2	
831	MGSWWEFQVRLAAIEYRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVENLRQLAAHIRSVLQAYRHN	HER2	6.33
832	MGSWWEFQVRLSAIEYRLTALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEELRQKAARIRSLLQAYRHN	HER2	9.61
833	MGSWWEFNIRLHAIDYRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVELLREKAAQIRAQLQAYRHN	HER2	9.75
834	MGSWWEFRVRLEAIDYRLKALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRMKAATIRAILQAYRHN	HER2	6.82
835	MGSWYEFDIRLEAIKYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEYLRKKAAVIRSMLQAYRHN	HER2	5.35
836	MGSWWEFRIRLEAIWYRLHALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRIFAANIRSKLQAYRHN	HER2	8.04
837	MGSWWEFNVRLQAIKYRLSALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRKTAAHIRWQLQAYRHN	HER2	5.23
838	MGSWWEFNVRLSAIRYRLLALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRASAAQIRAMLQAYRHN	HER2	6.73
839	MGSWWEFNMRLSAIKYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEILRRLAADIRERLQAYRHN	HER2	3.08
840	MGSWWEFHIRLRAIKYRLYALGGSEAELAAFEKEIAAFESELQAYKGKGNP EVEDLRILAAEIRAQLQAYRHN	HER2	14.79

Table 4. Exemplary Antigenic Determinant Sequences

SEQ ID	Antigen	Sequence
2	CD19	MPPPRLLFFLLFLTPMEVRPEEPLVVKVEEGDNAVLQCLKGTSDGPTQQLTWSRESPLKPFL KLSLGLPGLGIHMRPLAIWLFIFNVSQQMGGFYLCQPGPPSEKAWQPGWTVNVEGSGELFRW NVSDLGGLGCGLKNRSSEGPSSPSGKLMSPKLYVWAKDRPEIWEGEPPCLPPRDSLNQSLSQ DLTMAPGSTLWLSCGVPPDSVSRGPLSWTHVHPKGPKSLLSLELKDDRPARDMWVMETGLLL PRATAQDAGKYYCHRGNLTMSFHLEITARPVLWHWLLRTGGWK

3	CD19 – Signal	PEEPLVVKVEEGDNAVLQCLKGTSDGPTQQLTWSRESPLKPFLKLSLGLPGLGIHMRPLAIW LFIFNVSQQMGGFYLCQPGPPSEKAWQPGWTVNVEGSGELFRWNVSDLGGLGCGLKNRSSEG PSSPSGKLMSPKLYVWAKDRPEIWEGEPPCLPPRDSLNQSLSQDLTMAPGSTLWLSCGVPPD SVSRGPLSWTHVHPKGPKSLLSLELKDDRPARDMWVMETGLLLPRATAQDAGKYYCHRGNLT MSFHLEITARPVLWHWLLRTGGWK
4	BCMA	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGL SLIISLAVFVLMFLLRKINSEPLKDEFKNTGSGLLGMANIDLEKSRTGDEIILPRGLEYTVE ECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKSLPAALSATEIEKSISAR
5	BCMA_ECD	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNA
6	CD20	AGIYAPI
7	CD20	FLKMESLNFIRAHTP
8	CD20	EPANPSEK
9	CD20	KISHFLKMESLNFIRAHTPYINIYNCEPANPSEKNSPSTQYCYSIQS
10	CD20	PICVTV
11	CD123 – Signal	TKEDPNPPITNLRMKAKAQQLTWDLNRNVTDIECVKDADYSMPAVNNSYCQFGAISLCEVTN YTVRVANPPFSTWILFPENSGKPWAGAENLTCWIHDVDFLSCSWAVGPGAPADVQYDLYLNV ANRRQQYECLHYKTDAQGTRIGCRFDDISRLSSGSQSSHILVRGRSAAFGIPCTDKFVVFSQ IEILTPPNMTAKCNKTHSFMHWKMRSHFNRKFRYELQIQKRMQPVITEQVRDRTSFQLLNPG TYTVQIRARERVYEFLSAWSTPQRFECDQEEGANTRAWR
12	CD37	DKTSFVSFVGLAFVPLQIWSK
13	CD37	RAQLERSLRDVVEKTIQKYGTNPEETAAEESWDYVQFQLRCCGWHYPQDWFQVLILRGNGSE AHRVPCSCYNLSATNDSTILDKVILPQLSRLGHLARSRHSADICAVPAESHIYREGCAQGLQ KWLHNN
14	AFP	MKWVESIFLIFLLNFTESRTLHRNEYGIASILDSYQCTAEISLADLATIFFAQFVQEATYKE VSKMVKDALTAIEKPTGDEQSSGCLENQLPAFLEELCHEKEILEKYGHSDCCSQSEEGRHNC FLAHKKPTPASIPLFQVPEPVTSCEAYEEDRETFMNKFIYEIARRHPFLYAPTILLWAARYD KIIPSCCKAENAVECFQTKAATVTKELRESSLLNQHACAVMKNFGTRTFQAITVTKLSQKFT KVNFTEIQKLVLDVAHVHEHCCRGDVLDCLQDGEKIMSYICSQQDTLSNKITECCKLTTLER GQCIIHAENDEKPEGLSPNLNRFLGDRDFNQFSSGEKNIFLASFVHEYSRRHPQLAVSVILR VAKGYQELLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVA YTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPG VGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV
15	AFP – Signal	RTLHRNEYGIASILDSYQCTAEISLADLATIFFAQFVQEATYKEVSKMVKDALTAIEKPTGD EQSSGCLENQLPAFLEELCHEKEILEKYGHSDCCSQSEEGRHNCFLAHKKPTPASIPLFQVP EPVTSCEAYEEDRETFMNKFIYEIARRHPFLYAPTILLWAARYDKIIPSCCKAENAVECFQT KAATVTKELRESSLLNQHACAVMKNFGTRTFQAITVTKLSQKFTKVNFTEIQKLVLDVAHVH EHCCRGDVLDCLQDGEKIMSYICSQQDTLSNKITECCKLTTLERGQCIIHAENDEKPEGLSP NLNRFLGDRDFNQFSSGEKNIFLASFVHEYSRRHPQLAVSVILRVAKGYQELLEKCFQTENP LECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITR KMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFS GLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV
16	P26	LEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQL TSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEE QLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV
1117	P26Q217P	LEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQL TSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEE QLEAVIADFSGLLEKCCQGQEQEVCFAEEGPKLISKTRAALGV

1118	P26(Q26-V229)	QESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDD KFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVC FAEEGQKLISKTRAALGV
1119	P26(Q26-V229) Q217P	QESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDD KFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVC FAEEGPKLISKTRAALGV
1120	p26(K23-V229)	KYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQL SEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAF SDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQ EVCFAEEGQKLISKTRAALGV
1121	p26(K23-V229) Q217P	KYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQL SEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAF SDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQ EVCFAEEGPKLISKTRAALGV
1122	p26(G17-V229)	GEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATA ATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDET YVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKC CQGQEQEVCFAEEGQKLISKTRAALGV
1123	p26(G17-V229) Q217P	GEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATA ATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDET YVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGLLEKC CQGQEQEVCFAEEGPKLISKTRAALGV
41	CD22 mature ECD	DSSKWVFEHPETLYAWEGACVWIPCTYRALDGDLESFILFHNPEYNKNTSKFDGTRLYESTKDGKVPSE QKRVQFLGDKNKNCTLSIHPVHLNDSGQLGLRMESKTEKWMERIHLNVSERPFPPHIQLPPEIQESQEV TLTCLLNFSCYGYPIQLQWLLEGVPMRQAAVTSTSLTIKSVFTRSELKFSPQWSHHGKIVTCQLQDADG KFLSNDTVQLNVKHTPKLEIKVTPSDAIVREGDSVTMTCEVSSSNPEYTTVSWLKDGTSLKKQNTFTLN LREVTKDQSGKYCCQVSNDVGPGRSEEVFLQVQYAPEPSTVQILHSPAVEGSQVEFLCMSLANPLPTNY TWYHNGKEMQGRTEEKVHIPKILPWHAGTYSCVAENILGTGQRGPGAELDVQYPPKKVTTVIQNPMPIR EGDTVTLSCNYNSSNPSVTRYEWKPHGAWEEPSLGVLKIQNVGWDNTTIACAACNSWCSWASPVALNVQ YAPRDVRVRKIKPLSEIHSGNSVSLQCDFSSSHPKEVQFFWEKNGRLLGKESQLNFDSISPEDAGSYSC WVNNSIGQTASKAWTLEVLYAPRRLRVSMSPGDQVMEGKSATLTCESDANPPVSHYTWFDWNNQSLPYH SQKLRLEPVKVQHSGAYWCQGTNSVGKGRSPLSTLTVYYSPETIGRR
1081	CD137 mature ECD	LQDPCSNCPAGTFCDNNRNQICSPCPPNSFSSAGGQRTCDICRQCKGVFRTRKECSSTSNAECDCTPGF HCLGAGCSMCEQDCKQGQELTKKGCKDCCFGTFNDQKRGICRPWTNCSLDGKSVLVNGTKERDVVCGPS PADLSPGASSVTPPAPAREPGHSPQ
1102	Human CD45RABC	MTMYLWLKLLAFGFAFLDTEVFVTGQSPTPSPTGLTTAKMPSVPLSSDPLPTHTTAFSPASTFERENDF SETTTSLSPDNTSTQVSPDSLDNASAFNTTGVSSVQTPHLPTHADSQTPSAGTDTQTFSGSAANAKLNP TPGSNAISDVPGERSTASTFPTDPVSPLTTTLSLAHHSSAALPARTSNTTITANTSDAYLNASETTTLS PSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTEC KNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCG NMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNP PQRSFHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSA PPSQVWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTF KAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYDLHKKRSCNLDEQQELVER DDEKQLMNVEPIHADILLETYKRKIADEGRLFLAEFQSIPRVFSKFPIKEARKPFNQNKNRYVDILPYD YNRVELSEINGDAGSNYINASYIDGFKEPRKYIAAQGPRDETVDDFWRMIWEQKATVIVMVTRCEEGNR NKCAEYWPSMEEGTRAFGDVVVKINQHKRCPDYIIQKLNIVNKKEKATGREVTHIQFTSWPDHGVPEDP HLLLKLRRRVNAFSNFFSGPIVVHCSAGVGRTGTYIGIDAMLEGLEAENKVDVYGYVVKLRRQRCLMVQ VEAQYILIHQALVEYNQFGETEVNLSELHPYLHNMKKRDPPSEPSPLEAEFQRLPSYRSWRTQHIGNQE ENKSKNRNSNVIPYDYNRVPLKHELEMSKESEHDSDESSDDDSDSEEPSKYINASFIMSYWKPEVMIAA QGPLKETIGDFWQMIFQRKVKVIVMLTELKHGDQEICAQYWGEGKQTYGDIEVDLKDTDKSSTYTLRVF ELRHSKRKDSRTVYQYQYTNWSVEQLPAEPKELISMIQVVKQKLPQKNSSEGNKHHKSTPLLIHCRDGS QQTGIFCALLNLLESAETEEVVDIFQVVKALRKARPGMVSTFEQYQFLYDVIASTYPAQNGQVKKNNHQ EDKIEFDNEVDKVKQDANCVNPLGAPEKLPEAKEQAEGSEPTSGTEGPEHSVNGPASPALNQGS

1103	Human CD45RO	MTMYLWLKLLAFGFAFLDTEVFVTGQSPTPSPTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDE KYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDV PPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGNMIFDNKEIKLENLEPEHEYKCD SEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNL DKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCR PPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYN SKALIAFLAFLIIVTSIALLVVLYKIYDLHKKRSCNLDEQQELVERDDEKQLMNVEPIHADILLETYKR KIADEGRLFLAEFQSIPRVFSKFPIKEARKPFNQNKNRYVDILPYDYNRVELSEINGDAGSNYINASYI DGFKEPRKYIAAQGPRDETVDDFWRMIWEQKATVIVMVTRCEEGNRNKCAEYWPSMEEGTRAFGDVVVK INQHKRCPDYIIQKLNIVNKKEKATGREVTHIQFTSWPDHGVPEDPHLLLKLRRRVNAFSNFFSGPIVV HCSAGVGRTGTYIGIDAMLEGLEAENKVDVYGYVVKLRRQRCLMVQVEAQYILIHQALVEYNQFGETEV NLSELHPYLHNMKKRDPPSEPSPLEAEFQRLPSYRSWRTQHIGNQEENKSKNRNSNVIPYDYNRVPLKH ELEMSKESEHDSDESSDDDSDSEEPSKYINASFIMSYWKPEVMIAAQGPLKETIGDFWQMIFQRKVKVI VMLTELKHGDQEICAQYWGEGKQTYGDIEVDLKDTDKSSTYTLRVFELRHSKRKDSRTVYQYQYTNWSV EQLPAEPKELISMIQVVKQKLPQKNSSEGNKHHKSTPLLIHCRDGSQQTGIFCALLNLLESAETEEVVD IFQVVKALRKARPGMVSTFEQYQFLYDVIASTYPAQNGQVKKNNHQEDKIEFDNEVDKVKQDANCVNPL GAPEKLPEAKEQAEGSEPTSGTEGPEHSVNGPASPALNQGS
1104	Rhesus CD45RABC	MTMCLWLKLLAFVFAFLDTEVFVTGQGSTLSPTGRRTTKMPSVPLSSDPLPTHTTAFSPASISERENDF SETTPSLSSDNTSTHVSPDSLDNASAFNTTGVSSALTPHLPTHADSQTPSTGTDTQTPSGSAANTTLSP TPRSNDISDVPGERSTASTFPTDPISPLATTLIPARNSSAALPARTSNTTITANTSVSYLNASETTTPS PSGSTVISTPTIATTTSKPTCAEKYATIPVDYLYNNKTKLFTAKLNVNENVECTNNNHTHNICTNNEVL NLPECKEMNVFVSHNSCTDRHKELKLDVPPEVEKFQLDDCTPDVEANTTICLKWKIIETFACDKSKITY RFQCGNKTYNKEGIYLENLEPEYEYKCDSEILYNNHKYINITKLIKTDFGIPGQPQNVVCRHEDAHQGV ITWNPPQRSFHNFTLCYVSKTAKKCLSLDKHLTTYHLQNLKPYTNYSLSLHAYIIAKVQRNGTAATCNF TTESAPPSQVQNMIVSTSDNSMRVKCEGPRDVNGPTGLYHLEVEAGNTLVRNLSQSKCDFSVNNLQYST YYNLKAYYHNGKYSGEPVILRESTSYNSKALIAFLAFLIIVTSIALLVVLYKIYDLHKKRSCNLDEQQE LVERDDEKQLMNVEPIHADILLETYKRKIADEGRLFLAEFQSIPRVFSKFPIKEARKPFNQNKNRYVDI LPYDYNRVELSEINGDAGSNYINASYIDGFKEPRKYIAAQGPRDETVDDFWRMIWEQKATVIVMVTRCE EGNRNKCAEYWPSMEEGTRAFGDVVVKINQHKRCPDYIIQKLNIVNKKEKATGREVTHIQFTSWPDHGV PEDPHLLLKLRRRVNAFSNFFSGPIVVHCSAGVGRTGTYIGIDAMLEGLEAENKVDVYGYVVKLRRQRC LMVQVEAQYILIHQALVEYNQFGETEVNLSELHPYLHNMKKRDPPSEPSPLEAEFQRLPSYRSWRTQHI GNQEENKNKNRNSNVIPYDYNRVPLKHELEMSKESDHDSDESSDDDSDSEEPSKYINASFIMSYWKPEV MIAAQGPLKETIGDFWQMIFQRKVKVIVMLTELKHGDQEICAQYWGEGKQTYGDIEVDMKDTNKSSTYT LRVFELRHSKRKDSRTVYQYQYTNWSVEQLPAEPKELVSLIQVLKEKLPQKNSSEGNKHHKSTPLLIHC RDGSQQTGIFCALLNLLESAETEEVVDIFQVVKALRKARPGMVSTFEQYQFLYDIIASTYPAQNGQVKK NNHQEDKIEFDNEVDKVKQDANCVNPLGATEKLPEAKEQATGSEPTSGTEGPEHSVNGPASPALNQGS
1105	cynomolgus CD45RABC	MTMCLWLKLLAFVFAFLDTEVFVTGQGSTLSPTGRRTTKMPSVPLSSDPLPTHTTAFSPASISERENDF SETTPSLSSDNTSTQVSPDSLDNASAFNTTGVSSALTPHLPTHADSQTPSTGTDTQTPSGSAANTTLSP TPRSNDISDVPGERSTASTFPTDPISPLATTLIPARNSSAALPARTSNTTITANTSVSYLNASETTTPS PSGSTVISTPTIATTTSKPTCAEKYATIPVDYLYNNKTKLFTAKLNVNENVECTNNNHTHNICTNNEVL NLPECKEMNVFVSHNSCTDRHKELKLDVPPEVEKFQLDDCTPDVEANTTICLKWKIIETFACDKSKITY RFQCGNKTYNKEGIYLENLEPEYEYKCDSEILYNNHKYINITKLIKTDFGIPGQPQNVVCRHEDAHQGV ITWNPPQRSFHNFTLCYVNKPAKKCLILDKHLTTYHLQNLKPYTNYSLSLHAYIIAKVQRNGTAATCNF TTESAPPSQVQNMIVSTSDNSMHVKCEVPRDVNGPTGLYHLEVEAGNTLVRNLSQSKCDFSVNNLQYST YYNLKAYYHNGKYSGEPVILRESTSYNSKALIAFLAFLIIVTSIALLVVLYKIYDLHKKRSCNLDEQQE LVERDDEKQLMNVEPIHADILLETYKRKIADEGRLFLAEFQSIPRVFSKFPIKEARKPFNQNKNRYVDI LPYDYNRVELSEINGDAGSNYINASYIDGFKEPRKYIAAQGPRDETVDDFWRMIWEQKATVIVMVTRCE EGNRNKCAEYWPSMEEGTRAFGDIVVKINQHKRCPDYIIQKLNIVNKKEKATGREVTHIQFTSWPDHGV PEDPHLLLKLRRRVNAFSNFFSGPIVVHCSAGVGRTGTYIGIDAMLEGLEAENKVDVYGYVVKLRRQRC LMVQVEAQYILIHQALVEYNQFGETEVNLSELHPYLHNMKKRDPPSEPSPLEAEFQRLPSYRSWRTQHI GNQEENKNKNRNSNVIPYDYNRVPLKHELEMSKESDHDSDESSDDDSDSEEPSKYINASFIMSYWKPEV MIAAQGPLKETIGDFWQMIFQRKVKVIVMLTELKHGDQEICAQYWGEGKQTYGDIEVDMKDTNKSSTYT LRVFELRHSKRKDSRTVYQYQYTNWSVEQLPAEPKELVSLIQVLKEKLPQKNFSEGNKHHKSTPLLIHC RDGSQQTGIFCALLNLLESAETEEVVDIFQVVKALRKARPGMVSTFEQYQFLYDIIASTYPAQNGQVKK NNHQEDKIEFDNEVDKVKQDANCVNPLGATEKLPEAKEQATGSEPTSGTEGPEHSVNGPASPALNQGS
1106	Human CD45RABC ECD	QSPTPSPTGLTTAKMPSVPLSSDPLPTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDNAS AFNTTGVSSVQTPHLPTHADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDVPGERSTASTFPTDPV SPLTTTLSLAHHSSAALPARTSNTTITANTSDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKY ANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPP GVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSE

		ILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDK NLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPP RDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSK
1107	Human CD45RO ECD	QSPTPSPTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVN ENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLK WKNIETFTCDTQNITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPG EPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAY IIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRN ESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSK
1108	Human CD45RA ECD	QSPTPSPTGLTTAKMPSVPLSSDPLPTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDNAS AFNTTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVNENV ECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKN IETFTCDTQNITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQ IIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAYIIA KVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESH KNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSK
1109	Human CD45RB	QSPTPSPTGVSSVQTPHLPTHADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNASETTTLSP SGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECK NASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGN MIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPP QRSFHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAP PSQVWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFK AYFHNGDYPGEPFILHHSTSYNSK
1110	Human CD45RAB ECD	QSPTPSPTGLTTAKMPSVPLSSDPLPTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDNAS AFNTTGVSSVQTPHLPTHADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNASETTTLSPSGS AVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECKNAS VSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGNMIF DNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRS FHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQ VWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYF HNGDYPGEPFILHHSTSYNSK
1111	Human CD45RAC ECD	QSPTPSPTGLTTAKMPSVPLSSDPLPTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDNAS AFNTTDVPGERSTASTFPTDPVSPLTTTLSLAHHSSAALPARTSNTTITANTSDAYLNASETTTLSPSG SAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECKNA SVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGNMI FDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQR SFHNFTLCYIKETEKDCLNLDKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPS QVWNMTVSMTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAY FHNGDYPGEPFILHHSTSYNSK
1112	Human CD45RBC ECD	QSPTPSPTGVSSVQTPHLPTHADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDVPGERSTASTFPT DPVSPLTTTLSLAHHSSAALPARTSNTTITANTSDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCD EKYANITVDYLYNKETKLFTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILD VPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNITYRFQCGNMIFDNKEIKLENLEPEHEYKC DSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKC RPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSY NSK
1113	Human CD26	MKTPWKVLLGLLGAAALVTIITVPVVLLNKGTDDATADSRKTYTLTDYLKNTYRLKLYSLRWISDHEYL YKQENNILVFNAEYGNSSVFLENSTFDEFGHSINDYSISPDGQFILLEYNYVKQWRHSYTASYDIYDLN KRQLITEERIPNNTQWVTWSPVGHKLAYVWNNDIYVKIEPNLPSYRITWTGKEDIIYNGITDWVYEEEV FSAYSALWWSPNGTFLAYAQFNDTEVPLIEYSFYSDESLQYPKTVRVPYPKAGAVNPTVKFFVVNTDSL SSVTNATSIQITAPASMLIGDHYLCDVTWATQERISLQWLRRIQNYSVMDICDYDESSGRWNCLVARQH IEMSTTGWVGRFRPSEPHFTLDGNSFYKIISNEEGYRHICYFQIDKKDCTFITKGTWEVIGIEALTSDY LYYISNEYKGMPGGRNLYKIQLSDYTKVTCLSCELNPERCQYYSVSFSKEAKYYQLRCSGPGLPLYTLH SSVNDKGLRVLEDNSALDKMLQNVQMPSKKLDFIILNETKFWYQMILPPHFDKSKKYPLLLDVYAGPCS QKADTVFRLNWATYLASTENIIVASFDGRGSGYQGDKIMHAINRRLGTFEVEDQIEAARQFSKMGFVDN KRIAIWGWSYGGYVTSMVLGSGSGVFKCGIAVAPVSRWEYYDSVYTERYMGLPTPEDNLDHYRNSTVMS RAENFKQVEYLLIHGTADDNVHFQQSAQISKALVDVGVDFQAMWYTDEDHGIASSTAHQHIYTHMSHFI KQCFSLP

1114	Human CD30	MRVLLAALGLLFLGALRAFPQDRPFEDTCHGNPSHYYDKAVRRCCYRCPMGLFPTQQCPQRPTDCRKQC EPDYYLDEADRCTACVTCSRDDLVEKTPCAWNSSRVCECRPGMFCSTSAVNSCARCFFHSVCPAGMIVK FPGTAQKNTVCEPASPGVSPACASPENCKEPSSGTIPQAKPTPVSPATSSASTMPVRGGTRLAQEAASK LTRAPDSPSSVGRPSSDPGLSPTQPCPEGSGDCRKQCEPDYYLDEAGRCTACVSCSRDDLVEKTPCAWN SSRTCECRPGMICATSATNSCARCVPYPICAAETVTKPQDMAEKDTTFEAPPLGTQPDCNPTPENGEAP ASTSPTQSLLVDSQASKTLPIPTSAPVALSSTGKPVLDAGPVLFWVILVLVVVVGSSAFLLCHRRACRK RIRQKLHLCYPVQTSQPKLELVDSRPRRSSTQLRSGASVTEPVAEERGLMSQPLMETCHSVGAAYLESL PLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEKIYIMKADTVIVGTVKAELPEGRGLAGPAEPELEEEL EADHTPHYPEQETEPPLGSCSDVMLSVEEEGKEDPLPTAASGK
1115	Human CD33	MPLLLLLPLLWAGALAMDPNFWLQVQESVTVQEGLCVLVPCTFFHPIPYYDKNSPVHGYWFREGAIISR DSPVATNKLDQEVQEETQGRFRLLGDPSRNNCSLSIVDARRRDNGSYFFRMERGSTKYSYKSPQLSVHV TDLTHRPKILIPGTLEPGHSKNLTCSVSWACEQGTPPIFSWLSAAPTSLGPRTTHSSVLIITPRPQDHG TNLTCQVKFAGAGVTTERTIQLNVTYVPQNPTTGIFPGDGSGKQETRAGVVHGAIGGAGVTALLALCLC LIFFIVKTHRRKAARTAVGRNDTHPTTGSASPKHQKKSKLHGPTETSSCSGAAPTVEMDEELHYASLNF HGMNPSKDTSTEYSEVRTQ
1116	Human CD38	MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVLILVVVLAVVVPRWRQQWSGPGTTKRFPETVLARCVK YTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPCNKILLWSRIKDLAHQFTQV QRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDCSNNPVSVFWKTVSRRFAEAACDVVHVM LNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEAWVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCK NIYRPDKFLQCVKNPEDSSCTSEI
1138	CS1 mature ECD	SGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVTIQPEGGTIIVTQNRNRERVDFPDGGYSLK LSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHVYEHLSKPKVTMGLQSNKNGTCVTNLTCCMEHGEEDV IYTWKALGQAANESHNGSILPISWRWGESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSM
1139	CS1	MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVTIQPEGGT IIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHVYEHLSKPKVTMGLQ SNKNGTCVTNLTCCMEHGEEDVIYTWKALGQAANESHNGSILPISWRWGESDMTFICVARNPVSRNFSS PILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLWFLKRERQEEYIEEKKRVDICRETPNICP HSGENTEYDTIPHTNRTILKEDPANTVYSTVEIPKKMENPHSLLTMPDTPRLFAYENVI
42	HER2 mature ECD	TQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNLELTYLPTNASLSFLQDIQEVQGYVLIAHNQV RQVPLQRLRIVRGTQLFEDNYALAVLDNGDPLNNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQ LCYQDTILWKDIFHKNNQLALTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKG PLPTDCCHEQCAAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTA CPYNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSANIQEFAGC KKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLPDLSVFQNLQVIRGRIL HNGAYSLTLQGLGISWLGLRSLRELGSGLALIHHNTHLCFVHTVPWDQLFRNPHQALLHTANRPEDECV GEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQECVEECRVLQGLPREYVNARHCLPCHPECQPQNGSV TCFGPEADQCVACAHYKDPPFCVARCPSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVDLDDKGCP AEQRASPLT

TABLE: 5 Exemplary Adapters

SEQ ID NO:	Adapter Design	Adapter Sequence
1082	**CD123(cg06)-BCMS-HIS tag**	DEMGSWDEFGRRLYAIEWRLYALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLREIAAVIRSNLQAYRHNGGGGSGGGGSGGG GSGMLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYC NASVTNSVKGTNAGGGGSGGGGSGGGGSHHHHHHHHHH
1083	**none(α3D)-BCMA-HIS tag**	DEGGGGSMGSWAEFKQRLAAIKTRLQALGGSEAELAAFEKEIAA FESELQAYKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGG GSGGGGSGMLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLT CQRYCNASVTNSVKGTNAGGGGSGGGGSGGGGSHHHHHHHHHH
1084	**HIS tag-CD123(cg06)-p26**	DEHHHHHHHHHHKLENLYFQGGGGGSMGSWDEFGRRLYAIEWRL YALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKLREIAAV IRSNLQAYRHNGGGGSGGGGSGGGGSLEKCFQTENPLECQDKGE EELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQL TSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCI RHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDK FIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIAD FSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV

1085	HIS tag-BCMA(bc40)-p26	DEHHHHHHHHHHKLENLYFQGGGGGSMGSWSEFWVRLGAIRERL DALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKLRYTAAT IRRFLQAYRHNGGGGSGGGGSGGGGSLEKCFQTENPLECQDKGE EELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQL TSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCI RHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDK FIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIAD FSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV
1086	HIS tag- none(α3D-Q19E)-p26	DEHHHHHHHHHHKLENLYFQGGGGGSMGSWAEFKQRLAAIKTRL EALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEALRKEAAA IRDELQAYRHNGGGGSGGGGSGGGGSLEKCFQTENPLECQDKGE EELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQL TSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCI RHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDK FIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIAD FSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV
1087	CD123(cg06-210)-p26-CD123(cg06-210)-HIS tag	DEGGGGSMGSWDEFGRRLYAIEWQLYALGGTEAELAAFEKEIAA FESELQAYKGKGNPEVEKLREIAAVIRENLQAYRHNGGGGSGGG GSGGGGSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSC GLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAAT CCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTM KQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCF AEEGQKLISKTRAALGVGGGGSGGGGSGGGGSMGSWDEFGRRLY AIEWQLYALGGTEAELAAFEKEIAAFESELQAYKGKGNPEVEKL REIAAVIRENLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1088	BCMA(bc40)-p26- BCMA(bc40)-HIS tag	DEGGGGSMGSWSEFWVRLGAIRERLDALGGSEAELAAFEKEIAA FESELQAYKGKGNPEVEKLRYTAATIRRFLQAYRHNGGGGSGGG GSGGGGSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSC GLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAAT CCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTM KQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCF AEEGQKLISKTRAALGVGGGGSGGGGSGGGGSMGSWSEFWVRLG AIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKL RYTAATIRRFLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1124	BCMA(bc98)-p26 JPE-HIS tag	DEGGGGSMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAA FESELQAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGG GSGGGGSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSC GLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAAT CCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTM KQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCF AEEGQKLISKTRAALGVGGGGSGGGGSGGGGSHHHHHHHHHH
1125	BCMA(bc98)-p26-HIS tag	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQK LGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLS EDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRR PCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFL INLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQ KLISKTRAALGVGGGGSGGGGSGGGGSHHHHHHHHHH
1126	BCMA(bc98)-p26 (Q26-V229)-HIS tag	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSE LMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEM TPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFH KDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGL LEKCCQGQEQEVCFAEEGQKLISKTRAALGVGGGGSGGGGSGGG GSHHHHHHHHHH
1127	BCMA(bc98)-p26 (K23-V229)-HIS tag	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLT

		SSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIR HEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKF IFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADF SGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGVGGGGSGGGGS GGGGSHHHHHHHHH
1128	**BCMA(bc98)-p26 (G17-V229)-HIS tag**	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGGEEELQKYIQESQALAKRSCGLFQKLGEYYLQNAFLVAYTK KAPQLTSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIII GHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPA FSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLE AVIADFSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGVGGGG SGGGGSGGGGSHHHHHHHHH
1129	**BCMA(bc98)-p26-BCMA(bc98)-HIS tag**	DEGGGGSMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAA FESELQAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGG GSGGGGSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSC GLFQKLGEYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAAT CCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSS YANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTM KQEFLINLVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCF AEEGQKLISKTRAALGVGGGGSGGGGSGGGGSMGSWSEFWARLG AIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKL RYTAGTIKRFLQAYRHNGGGGDGGGGSGGGGSHHHHHHHHH
1130	**BCMA(bc98)-p26(Q26-V229; Q217P)-BCMA(bc98)-HIS tag**	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSE LMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEM TPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFH KDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGL LEKCCQGQEQEVCFAEEGPKLISKTRAALGVGGGGSGGGGSGGG GSMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGSGGGGSGGG GSHHHHHHHHH
1131	**BCMA(bc98)-p26(Q26-V229; Q217P)-HIS tag**	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSE LMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEM TPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFH KDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGL LEKCCQGQEQEVCFAEEGPKLISKTRAALGVGGGGSGGGGSGGG GSHHHHHHHHH
1132	**BCMA(bc98)-p26(Q26-V229)-BCMA(bc98)-HIS tag**	DEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGGG GSGQESQALAKRSCGLFQKLGEYYLQNAFLVAYTKKAPQLTSSE LMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEM TPVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFH KDLCQAQGVALQTMKQEFLINLVKQKPQITEEQLEAVIADFSGL LEKCCQGQEQEVCFAEEGQKLISKTRAALGVGGGGSGGGGSGGG GSMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESEL QAYKGKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGSGGGGSGGG GSHHHHHHHHH
1141	**Anti-CD45 scFv(VH-VL)-p26**	QVQLVESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKG LEWIGEINPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRS EDTALYYCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSAG GGSDIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQ QKPGQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEE DAATYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK

		QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGV
1142	**Anti-CD45 scFv(VH-VL)-p26**	DIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKP GQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEEDAA TYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSAGGGSQVQLVE SGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGE INPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALY YCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGV
1143	**p26-Anti-CD45 scFv(VH-VL)**	LEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGE YYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDK LLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCF SSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINL VKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLI SKTRAALGVGGGGSGGGGSGGGGSGQVQLVESGGGLVQPGGSLK LSCAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPS LKDKVFISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDA MDYWGQGTSVTVSGGGGSGGGGSAGGGSDIVLTQSPASLAVSLG QRATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLES GVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGS GTKLEIK
1144	**p26-Anti-CD45 scFv(VH-VL)**	LEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGE YYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDK LLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCF SSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINL VKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLI SKTRAALGVGGGGSGGGGSGGGGSGDIVLTQSPASLAVSLGQRA TISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLESGVP ARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGTK LEIKGGGGSGGGGSAGGGSQVQLVESGGGLVQPGGSLKLSCAAS GFDFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPSLKDKVF ISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMDYWGQ GTSVTVS
1145	**Anti-CD45 scFv(VH-VL)-p26-Anti-CD45 scFv(VH-VL)**	DIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKP GQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEEDAA TYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSAGGGSQVQLVE SGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGE INPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALY YCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGVGGGGSGGGGSGGGGSGDIVLTQSPASLAVSLGQRATI SCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLESGVPAR FSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGTKLE IKGGGGSGGGGSAGGGSQVQLVESGGGLVQPGGSLKLSCAASGF DFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPSLKDKVFIS RDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMDYWGQGT SVTVS
1146	**Anti-CD45 scFv(VH-VL)-p26-Anti-CD45 scFv(VH-VL)**	QVQLVESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKG LEWIGEINPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRS EDTALYYCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSAG GGSDIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQ QKPGQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEE DAATYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY

		LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGVGGGGSGGGGSGGGGSGQVQLVESGGGLVQPGGSLKLS CAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPSLK DKVFISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMD YWGQGTSVTVSGGGGSGGGGSAGGGSDIVLTQSPASLAVSLGQR ATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLESGV PARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGT KLEIK
1147	**Anti-CD45 scFv(VH-VL)-p26-Anti-CD45 scFv(VH-VL)**	DIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKP GQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEEDAA TYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSAGGGSQVQLVE SGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGE INPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALY YCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGVGGGGSGGGGSGGGGSGQVQLVESGGGLVQPGGSLKLS CAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPSLK DKVFISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMD YWGQGTSVTVSGGGGSGGGGSAGGGSDIVLTQSPASLAVSLGQR ATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLESGV PARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGT KLEIK
1148	**Anti-CD45 scFv(VH-VL)-p26-Anti-CD45 scFv(VH-VL)**	QVQLVESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKG LEWIGEINPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRS EDTALYYCARGNYYRYGDAMDYWGQGTSVTVSGGGGSGGGGSAG GGSDIVLTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQ QKPGQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEE DAATYYCQHSRELPFTFGSGTKLEIKGGGGSGGGGSGGGGSGLE KCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLL ACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPCFSS LVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISK TRAALGVGGGGSGGGGSGGGGSGDIVLTQSPASLAVSLGQRATI SCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLESGVPAR FSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGTKLE IKGGGGSGGGGSAGGGSQVQLVESGGGLVQPGGSLKLSCAASGF DFSRYWMSWVRQAPGKGLEWIGEINPTSSTINFTPSLKDKVFIS RDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMDYWGQGT SVTVS
1150	α3D Q19E-p26-cc08.HIS **none(α3D Q19E)-p26-CS1(cc08)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWVEFNERLHAIYLRL DALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVETLRRHAAG IRWQLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1151	α3D Q19E-p26-cc01.HIS **none(α3D Q19E)-p26-CS1(cc01)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN

		LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWVEFEARLSAIYERL EALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKLRRHAAG IRSNLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1152	α3D Q19E-p26-cc02.HIS **none(α3D Q19E)-p26-CS1(cc02)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWVEFFVRLDAIWERL EALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVETLRFHAAG IRQKLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1153	α3D Q19E-p26-cc09.HIS **none(α3D Q19E)-p26-CS1(cc09)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWNEFKLELAFIKDWL EALGGSEAELANFEEAIAEFEAGLQGYKGKGNPEVEALRKEAAA IRDELQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1154	α3D Q19E-p26-cc10.HIS **none(α3D Q19E)-p26-CS1(cc10)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWMEFEARLEAIWDRL EALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVESLRFHAAG IRQHLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1155	α3D Q19E-p26-cc12.HIS **none(α3D Q19E)-p26-CS1(cc12)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWHHFKMHLAGIKLQL EALGGSEAELAEFEEWIADFEGALQDYKGKGNPEVEALRKEAAA IRDELQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1156	α3D(Q19E).3xGS.p26.3xGS.α3D(Q19E) .HIS **none(α3D Q19E)-p26-none(α3D Q19E)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWAEFKQRLAAIKTRL EALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEALRKEAAA IRDELQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1157	α3D(Q19E).3xGS.p26.3xGS.eb03.HIS **none(α3D Q19E)-p26-HER2(eb03)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWAEFRWRLHAIWLQL

		GALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEWLRQDAAQ IKYILQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1158	α3D(Q19E).3xGS.p26.3xGS.eb04.HIS **none(α3D Q19E)-p26-HER2(eb04)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWKTFKIELAGIKLEL EALGGSEAELAGFENAIAQFESSLQYYKGKGNPEVEALRKEAAA IRDELQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1159	α3D(Q19E).3xGS.p26.3xGS.eb05.HIS **none(α3D Q19E)-p26-HER2(eb05)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWHEFLRRLLAIEMRL YALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEHLRVRAAS IRQMLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1160	α3D(Q19E).3xGS.p26.3xGS.eb06.HIS **none(α3D Q19E)-p26-HER2(eb06)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWWEFRVRLEAIDYRL KALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEYLRMKAAT IRAILQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1161	α3D(Q19E).3xGS.p26.3xGS.eb08.HIS **none(α3D Q19E)-p26-HER2(eb08)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWYEFRWRLHAIWLRL GALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEWLRQDAAQ IRYILQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1162	α3D(Q19E).3xGS.p26.3xGS.eb09.HIS **none(α3D Q19E)-p26-HER2(eb09)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWWEFNIRLHAIDYRL KALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVELLREKAAQ IRAQLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH
1163	α3D(Q19E).3xGS.p26.3xGS.eb10.HIS **none(α3D Q19E)-p26-HER2(eb10)-HIS tag**	MGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQA YKGKGNPEVEALRKEAAAIRDELQAYRHNGGGGSGGGGSGGGGS GLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLG EYYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSED KLLACGEGAADIIIGHLCIRHEMTPVNPGVGQCCTSSYANRRPC FSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLIN LVKQKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKL ISKTRAALGVGGGGSGGGGSGGGGSGMGSWWEFNMRLSAIKYRL YALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEILRRLAAD IRERLQAYRHNGGGGSGGGGSGGGGSHHHHHHHHHH

TABLE: 6 Exemplary ADBD CAR Sequences

SEQ ID NO:	CAR Design	CAR Sequence
1089	CTsp-Flag-GSlinker-α3D(Q19E)-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWAEFKQRLAAIKTRLEALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVEALRKEAAAIRDELQAYRHNGQAGSGTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQN QLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1090	CTsp-Flag-GSlinker-cg06-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWDEFGRRLYAIEWRLYALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVEKLREIAAVIRSNLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1091	CTsp-Flag-GSlinker-bc40-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWSEFWVRLGAIRERLDALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVEKLRYTAATIRRFLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1092	CTsp-Flag-GSlinker-af03-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWFEFYDRLNAIDARLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVENLRVHAAAIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASMGSWAEFKQRLAAIKTRLEALGGSEAELAAFEKEIAAFESELQAYK GKGNPEVEALRKEAAAIRDELQAYRHNQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAP LAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELR VKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNEL QKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1093	CTsp-Flag-GSlinker-af05-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWLEFYHRLNAIDSRLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVESLRDHAAHIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1133	CTsp-Flag-GSlinker-af59-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWFEFYDRLNAIDARLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVESLRVHAAAIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1134	CTsp-Flag-GSlinker-af83-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWSEFYDRLNAIDARLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVESLRVHAAAIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1135	CTsp-Flag-GSlinker-af99-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWFEFYDRLNAIDARLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVESLREHAAAIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
1136	CTsp-Flag-GSlinker-af101-GSlinker-CD8H-TM-41BB-CD3ζ	MAFLWLLSCWALLGTTFGDYKDDDDKGGGGSGGGGSMGSWSEFYDRLNAIDARLWALGGSE AELAAFEKEIAAFESELQAYKGKGNPEVESLREHAAAIREWLQAYRHNGGGGSGGGGSGTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

Example 2. D-domain CAR T cells kill tumor cells expressing the D domain target

[0600] The cytolytic activity of ADBD CAR expressing T cells was assessed on a panel of tumors using effector cell to target cell ratios ranging from 1: 4 to 1: 64. The cytolytic activity of a CD123-binding CAR (cg06, SEQ ID NO: 1090); a BCMA binding CAR (bc40, SEQ ID NO: 1091) were compared to a CAR with no known target-specificity (α3D-Q19E, SEQ ID NO: 1089).

[0601] 10,000 T cells expressing the indicated CARs were incubated with increasing numbers of a $CD123^+/BCMA^-$ tumor target (MOLM13)(**FIG. 1A**); a $CD123^-/BCMA^+$ tumor target (H929)(**FIG. 1B**); a $CD123^-$ tumor target (RAJI)(**FIG. 1C**); or a $CD123^+/BCMA^-$ tumor target (MOLM13)(**FIG. 1D**). After 16 hours, cells were washed and luciferase activity was assessed.

Example 3. Adapter binding associates with Adapter and CAR binding specificity

[0602] Jurkat NFAT-Luciferase reporter cells were transduced with a negative control CAR (α3D-Q19E, SEQ ID NO: 1089), an p26-binding CAR (af03, SEQ ID NO: 1092), or a BCMA-binding CAR (bc40, SEQ ID NO: 1091). In **FIG. 2A**, CAR transduced Jurkat cells were incubated with 0.5μg of Adapter protein (SEQ ID NO: 1082-1085) at 4°C for 20 minutes, washed, and then stained with anti-HIS PE (clone J095G46, 4°C for 20 minutes). CAR expression based on FLAG staining (clone L5) versus mock transduced Jurkat cells was also evaluated (**FIG. 2B**).

Example 4. Adapter binding of matching CAR: Adapter and Target: Adapter specificity drives lysis of target cells

[0603] 40,000 $CD123^+BCMA^-$ MOLM13-GFP/Luciferase cells were incubated with various Adapters (SEQ ID NO: 1082-1084) in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D14-053017, Day 7) transduced with BCMA-binding CAR (bc40, SEQ ID NO: 1091) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/ Luciferase cultured in the absence of T cells or Adapter protein (*see*, **FIG. 3A**). A control of CD123-specific CAR T cells (cg06, SEQ ID NO: 1090) cultured at the same ratio was used as a positive control for lysis.

[0604] In **FIG. 3B,** 40,000 $CD123^+BCMA^-$ MOLM13-GFP/Luciferase cells were incubated with Adapter (cg06-p26, SEQ ID NO: 1084) in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D16-061317, Day 7) transduced with p26-binding CARs (Af03, SEQ ID NO: 1092) or Af05, SEQ ID NO: 1093) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/Luciferase cultured in the absence of T cells or Adapter protein. A control of CD123-binding CAR T cells (cg06, SEQ ID NO: 1090) cultured at the same ratio was used as a positive control for lysis

[0605] In **FIG. 3C**, 40,000 $BCMA^+$ NCI H929-GFP/Luciferase cells were incubated with Adapter (bc40-p26, SEQ ID NO: 1085 in the presence or absence of 10,000 T cells (E: T ratio of 1: 4, donor D15-062017,

Day 8) mock transduced, or transduced with p26-binding CARs (Af03, SEQ ID NO: 1092 or Af05, SEQ ID NO: 1093) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of NCI-H929-GFP/Luciferase cultured in the absence of T cells or Adapter protein.

Example 5. Adapter binding of matching CAR: Adapter and Target: Adapter specificity drives cytokine production by CAR T-cells

[0606] Donor D14-053017 T cells transduced with BCMA-binding CAR (bc40, SEQ ID NO: 1091) were cultured overnight with various Adapters (cg06-BCMA, SEQ ID NO: 1082; α3D-BCMA, SEQ ID NO: 1083; or cg06-p26, SEQ ID NO: 1084) in the presence or absence of $CD123^{+}BCMA^{-}$ MOLM13 cells (25,000 T cells and target cells). Cultured supernatants were collected and assessed for the production of IL-2 (**FIG. 4A**) and IFN-γ (**FIG. 4B**). In **FIGS. 4C** and **4D**, donor D15-062017 T cells transduced with p26-binding CARs (Af03, SEQ ID NO: 1092 or Af05, SEQ ID NO: 1093) were cultured overnight with CD123 binding Adapter (cg06p26, SEQ ID NO: 1084) Adapter in the presence or absence of $CD123^{+}BCMA^{-}$ MOLM13 cells (25,000 T cells and target cells). Cultured supernatants were collected and assessed for the production of IL-2 (**FIG. 4C**) and IFN-γ (**FIG. 4D**).

Example 6. CAR T cells proliferate following exposure to an Adapter that is bound by the CAR and bound to a tumor expressing the AD recognized by the Adapter

[0607] In **FIG. 5**, Donor D16-062717 cells transduced with AFP-binding CAR (Af03, SEQ ID NO: 1092) were CFSE labeled (10 minutes at 0.5μM), then cultured (25,000) in the presence of CD123-binding Adapter (cg06-p26, SEQ ID NO: 1084) or BCMA-binding Adapter (bc40-p26, SEQ ID NO: 1085) in the presence or absence of mitomycin-C treated $CD123^{-}BCMA^{+}$ NCI-H929 cells (25,000) for 72 hours. At 72 hours, cells were stained for CD3, then analyzed for absolute numbers of $CD3^{+}$ cells via flow cytometry.

Example 7. Adapter binding of matching CAR: Adapter and Target: Adapter specificity signaling by CAR T cells

[0608] 50,000 reporter cells previously transduced with a BCMA-binding CAR (bc40, SEQ ID NO: 1091) were cultured for 5 hours in the presence of various Adapters (cg06-BCMA, SEQ ID NO: 1082; α3D-BCMA, SEQ ID NO: 1083; or cg06-p26, SEQ ID NO: 1084) in the presence or absence of 50,000 $CD123^{+}BCMA^{-}$ MOLM14 cells, then assessed for luciferase activity (**FIG. 6A**).

[0609] 50,000 reporter cells previously transduced with an p26-binding CAR (af03, SEQ ID NO: 1092) were cultured for 5 hours in the presence of Adapters (α3DQ19E-BCMA, SEQ ID: 1086; bc40-p26, SEQ ID NO: 1085) in the presence or absence of 50,000 $BCMA^{+}$ NCI-H929 cells, then assessed for luciferase activity (**FIG. 6B**).

[0610] **FIGS. 6A** and **6B** show that Adapter binding of matching CAR: Adapter and Target: Adapter drives signaling by CAR-expressing Jurkat NFAT-Luciferase reporter cells.

Example 8. Adapters containing D domains or ScFvs drive CAR cell: Adapter mediated lysis of target cells

[0611] A CD123-binding Adapter with a BCMA AD (SEQ ID NO: 1082) was evaluated for its ability to function with a control CAR (α3DQ19E, SEQ ID NO: 1089), a BCMA-binding CAR (bc40, SEQ ID NO: 1091) or a BCMA-specific scFv CAR (c11D5-3) obtained from WO 2010/104949 A2.

[0612] 40,000 $CD123^{+}BCMA^{-}$ MOLM13-GFP/Luciferase cells were incubated with the Cg06-BCMA Adapter (SEQ ID NO: 1082) in the presence or absence of 20,000 T cells (E: T ratio of 1: 2, donor D14-062717, Day 9) transduced with a control CAR (SEQ ID NO: 1089), the BCMA-binding CAR (SEQ ID NO: 1091), or the BCMA-binding scFv CAR (c11D5-3) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of MOLM13-GFP/Luciferase cultured in the absence of T cells or Adapter protein. Solid lines indicate calculated 3-parameter non-linear curves, while the dashed line for c11D5-3 is present for illustrative purposes only (**FIG. 7A**).

$CD123^{+}BCMA^{-}$ MOLM13-GFP/Luciferase cells were cultured in the same experiment as in **FIG. 7A** with transduced T cells in the absence of Adapter protein (**FIG. 7B**).

[0613] **FIGS. 7A and 7B** show that the CD123-specific Adapter with a BCMA antigenic determinant can function with either a BCMA-specific D domain CAR (bc40) or a BCMA-specific scFv CAR (c11D5-3).

Example 9. Use of multiple Adapters target a CAR cell to multiple antigen targets

[0614] 10^5 Jurkat NFAT-Luciferase transduced with a p26-binding CAR (af03, SEQ ID NO: 1092) were incubated with a total of 0.5μg of Adapters (SEQ ID NO: 1084, SEQ ID NO: 1085) at the indicated ratiosat4°C for 20 minutes, washed, and then incubated with CD123-Fc and biotinylated BCMA (0.5μg of each/(4°C for 20 minutes), washed, then binding detected with Anti-Fc A488 and Streptavidin-PE. **FIG. 8A** presents a flow cytometric analysis of CD123-binding and BCMA-binding to their respective target proteins, **FIG. 8B** provides a comparison of mean fluorescence intensity (MFI) of A488 MFI (CD123-binding, left axis) and PE MFI (BCMA-binding, right axis) flow cytometric data presented in **FIG. 8A**.

[0615] **FIGS. 8A and 8B** show that AFP-specific CARs can simultaneously have CD123 and BCMA-binding capacity via incubation with multiple Adapter proteins.

Example 10. Use of dual binding domain Adapters to enhance CAR signaling

[0616] 50,000 reporter cells previously transduced with an p26-binding CAR (af03, SEQ ID NO: 1092) were cultured for 5 hours in the presence of the CD123-binding Adaptor (cg06-p26, SEQ ID NO: 1084) or the bivalent Adaptor (cg06-p26-cg06, SEQ ID NO: 1087) in the presence of 50,000 $CD123^{+}$ MOLM13 or CD123-deficient MOLM13 cells, then assessed for luciferase activity. CD123 deficient cells were generated

using CRISPR/Cas9 genetic engineering technology (**FIG. 9A**). 50,000 reporter cells previously transduced with an p26-binding CAR (af03, SEQ ID NO: 1092) were cultured for 5 hours in the presence of the BCMA-binding Adaptor (bc40-p26, SEQ ID NO: 1085) or the bivalent Adapter ((bc40-p26-bc40, SEQ ID NO: 1088) in the presence or absence of 50,000 $BCMA^+$ U266 cells, then assessed for luciferase activity (**FIG. 9B**).

[0617] **FIGS. 9A and 9B** show that dual-binding domain adaptor proteins drive enhanced signaling by CAR-expressing Jurkat cells over single-binding domain adaptor proteins.

Example 11. CD45 specific D-domain CAR T cells kill CD45 expressing target cells

[0618] T-cells will be transduced with a CAR comprising a CD45 specific D domain. CD45- CAR T-cells expressing a CAR comprising a human CD45 specific D domain will be generated using CRISPR/Cas9 genetic engineering technology. CD45 specific gRNA and crRNA and Cas9 will be obtained from commercial sources. The self-lysing activity of the CD45- CAR T cells will be assessed using assays for cell proliferation, viability and/or cytotoxicity, for example 7-AAD staining and chromium release assay. Self-lysing of CD45- CAR T-cells will be compared to CD45+ control CAR T-cells expressing the same CAR comprising the CD45 specific D domain.

[0619] The cytolytic activity of CD45- T cells expressing a CAR comprising a human CD45 specific D domain will be assessed on a panel of CD45+ target cells using effector cell to target cell ratios ranging from 1: 4 to 1: 64. The cytolytic activity of the CD45- CAR T cells will be compared to a CAR with no known target-specificity.

Example 12. CD45 specific Adapter directed lysis of target cells

[0620] CD45- CAR T-cells will be generated using CRISPR/Cas9 genetic engineering technology. CD45 specific gRNA and crRNA and Cas9 will be obtained from commercial sources. The self-lysing activity of the CD45- CAR T cells will be assessed using assays for cell proliferation, viability and/or cytotoxicity, for example 7-AAD staining and chromium release assay. Self-lysing of CD45- CAR T-cells will be compared to CD45+ control CAR T-cells.

[0621] The cytolytic activity of CD45- T cells expressing a CAR comprising a human CD45 specific D domain will be assessed on a panel of CD45+ target cells using effector cell to target cell ratios ranging from 1: 4 to 1: 64. The cytolytic activity of the CD45- CAR T cells will be compared to a CAR with no known target-specificity.

[0622] CD45+ target cells will be incubated with various Adapters comprising a CD45 specific D domain and p26 in the presence or absence of CD45- T cells transduced with a p26-binding CAR for 16 hours. After 16 hours, cells will be washed and luciferase activity will be assessed. Percent lysis will be assessed based on wells of target cells cultured in the absence of T cells or Adapter protein. A control of CD45-specific CAR T cells cultured at the same ratio will be used as a positive control for lysis.

Example 13. Adapter comprising truncated p26 have improved bioactivity in cytotoxicity assay

[0623] Analysis of p26 structure revealed an N-terminal stretch of residues that were predicted to increase the potential for aggregation and/or proteolysis. This N-terminal sequence also contains a predicted disulfide bond pair, which could potentially destabilize the protein if the cysteines are un-paired, or reinforce a suboptimal protein conformation if the disulfide bond is formed. To eliminate these potential developmental liabilities, N-terminal truncated variants of p26 were prepared. In p26(G17-V229) (SEQ ID NO: 1118) the first 16 residues of p26 were removed to eliminate the disulfide pair of cysteines (C4 - C13). In p26(K23-V229) (SEQ ID NO: 1120) the first 22 residues of p26 were removed to additionally eliminate the beginning of a predicted albumin 3 domain. In p26(Q26-V229) the first 25 residues were removed to eliminate two hydrophobic residues (YI) beyond the K23 truncation and thus make the N-terminus flush with the predicted globular region of p26. The binding of full length and truncated p26 to FcRn was assessed using ELISA. Adapters comprising full-length p26 or the truncated p26(Q26-V229) variant bind to FcRn in a pH dependent manner, with higher binding affinity observed at pH 6.0 than at pH 7.4.

[0624] The bioactivity of Adapters comprising full length p26 or the truncated p26(G17-V229), p26(K23-V229) or p26(Q26-V229) variants were tested in various Luciferase-based Cytotoxicity Assays. Surprisingly, Adapters comprising truncated p26 had higher bioactivity than Adapters comprising full-length p26.

[0625] 40,000 $BCMA^+$ NALM6/Luciferase cells were incubated with Adapters BCMA(bc98)-p26 JPE (SEQ ID NO: 1124), BCMA(bc98)-p26 (SEQ ID NO: 1125), BCMA(bc98)-p26(Q26-V229) (SEQ ID NO: 1126), BCMA(bc98)-p26(K23-V229) (SEQ ID NO: 1127), or BCMA(bc98)-p26(G17-V229) (SEQ ID NO: 1128), in the presence of 10,000 T cells (E: T ratio of 1: 4) transduced with a p26-binding CAR (Af59, SEQ ID NO: 1133) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of NALM6/Luciferase cultured in the absence of T cells or Adapter protein. Adapters comprising the truncated p26 variants had higher bioactivity than the Adapters comprising the full-length p26. The EC50 values measured for the Adaptors were as follows:

Adapter	**EC50**
BCMA(bc98)-p26 JPE	1.135
BCMA(bc98)-p26	1.962
BCMA(bc98)-p26(Q26-V229)	0.1294
BCMA(bc98)-p26(K23-V229)	0.2232
BCMA(bc98)-p26(G17-V229)	0.367

[0626] 40,000 $BCMA^+$ NCI H929/Luciferase cells were incubated with Adapters BCMA(bc98)-p26 JPE (SEQ ID NO: 1124), BCMA(bc98)-p26 (SEQ ID NO: 1125), BCMA(bc98)-p26(Q26-V229) (SEQ ID NO: 1126), BCMA(bc98)-p26(K23-V229) (SEQ ID NO: 1127), or BCMA(bc98)-p26(G17-V229) (SEQ ID NO: 1128), in the presence of 10,000 T cells (E: T ratio of 1: 4) transduced with a p26-binding CAR (Af59, SEQ ID NO: 1133) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent

lysis was assessed based on wells of NCI-H929/Luciferase cultured in the absence of T cells or Adapter protein. Adapters comprising the truncated p26 variants had higher bioactivity than the Adapters comprising the full-length p26. The EC50 values measured for the Adaptors were as follows:

Adapter	**EC50**
BCMA(bc98)-p26 JPE	0.367
BCMA(bc98)-p26	0.3869
BCMA(bc98)-p26(Q26-V229)	0.04357
BCMA(bc98)-p26(K23-V229)	0.06069
BCMA(bc98)-p26(G17-V229)	0.1318

[0627] The presence of the Q127P substitution in the truncated p26 did not alter the Adapter's bioactivity. 40,000 $BCMA^+$ NCI H929/Luciferase cells were incubated with Adapters BCMA(bc98)-p26 (SEQ ID NO: 1124), BCMA(bc98)-p26(Q26-V229) (SEQ ID NO: 1126), or BCMA(bc98)-p26(Q26-V229)Q217P (SEQ ID NO: 1131), in the presence of 10,000 T cells (E: T ratio of 1: 4) transduced with a p26-binding CAR (Af59, SEQ ID NO: 1133) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of NCI-H929/Luciferase cultured in the absence of T cells or Adapter protein. Adapters comprising the truncated p26 variants had higher bioactivity than the Adapters comprising the full-length p26. Adapters comprising the truncated p26 variants with or without the Q217P substitution had substantially the same bioactivity. The EC50 values measured were as follows:

Adapter	**EC50**
BCMA(bc98)-p26	0.5243
BCMA(bc98)-p26(Q26-V229)	0.1142
BCMA(bc98)-p26(Q26-V229)Q217P	0.143

[0628] Bivalent Adapters comprising a truncated p26 variant also performed better than a corresponding Adapter comprising full-length p26. 40,000 $BCMA^+$ NCI H929 /Luciferase cells were incubated with Adapters BCMA(bc98)-p26-BCMA(bc98) (SEQ ID NO: 1129), BCMA(bc98)-p26(Q26-V229)-BCMA(bc98) (SEQ ID NO: 1132), or BCMA(bc98)-p26(Q26-V229)Q217P-BCMA(bc98) (SEQ ID NO: 1130), in the presence of 10,000 T cells (E: T ratio of 1: 4) transduced with a p26-binding CAR (Af59, SEQ ID NO: 1133) for 16 hours. After 16 hours, cells were washed and luciferase activity was assessed. Percent lysis was assessed based on wells of NCI-H929/Luciferase cultured in the absence of T cells or Adapter protein. Adapters comprising the truncated p26 variants had higher bioactivity than the Adapters comprising the full-length p26. Adapters comprising the truncated p26 variants with or without the Q217P substitution had substantially the same bioactivity. The EC50 values measured for the Adaptors were as follows:

Adapter	**EC50**
BCMA(bc98)-p26-BCMA(bc98)	0.008227
BCMA(bc98)-p26(Q26-V229)-BCMA(bc98)	0.00256

BCMA(bc98)-p26(Q26-V229)Q217P-BCMA(bc98)	0.001812

Example 14. Binding of truncated and full length p26 to human FcRn is pH dependent

[0629] The binding of full length and truncated p26 to FcRn was assessed using an ELISA format in which wells of 96-well plate were coated with adapter (bc40-p26 (SEQ ID NO:1085), bc98-p26(Q26-V229)-bc98 (SEQ ID NO:1132), HSA, bc40 (SEQ ID NO:197 with HIS-tag) or uncoated) overnight at 4°C. Wells were then blocked with PBS + 1% fish gelatin for 1 hour at 22°C. Parallel wells were then washed with PBS + 0.1% Tween at pH 6.0 or 7.4. Biotinylated human FcRn in PBS + 1% fish gelatin (either pH 6.0 or 7.4) was serially diluted and added to wells and incubated for 1 hour at 22°C. After washing with PBS + 0.1% Tween at pH 6.0 or 7.4, streptavidin-HRP (in PBS + 1% fish gelatin at pH 6.0 or 7.4) was added. After a final wash, signal was developed using TMB reagent and quantified by reading absorbance at A450. As shown in Figure 10, adapters comprising full-length p26 or the truncated p26(Q26-V229) variant bind to FcRn in a pH dependent manner, with higher binding affinity observed at pH 6.0 than at pH 7.4.

Example 15. Adapters comprising CS1 (SLAMF7, CRACC, CD319) specific ADBD modulate intracellular signaling and killing of CS1 positive tumors

[0630] CS1 binding domains (ADBD) were isolated by panning ADBD phage libraries on the extracellular domain of human CS1 protein. Representative CS1 binding ADBD were fused to p26 in a bispecific format with non-binding α3DQ19E (SEQ ID NO: 1021) to generate adapter proteins for functional testing in combination with af59-CAR (SEQ ID NO:1133) expressing JNL10 cells or human T cells expressing af59-CAR.

CS1 (SLAMF7, CRACC, CD319) Adapter Constructs	**Adapter SEQ ID NO:**	**CS1 ADBD SEQ ID NO:**	**CS1 ADBD clone ID**
□3D Q19E-p26-cc08.HIS	1500	787	cc08
□3D Q19E-p26-cc01.HIS	1501	780	cc01
□3D Q19E-p26-cc02.HIS	1502	781	cc02
□3D Q19E-p26-cc09.HIS	1503	788	cc09
□3D Q19E-p26-cc10.HIS	1504	789	cc10
□3D Q19E-p26-cc12.HIS	1505	791	cc12

[0631] Among the adapters tested in, the cc02 and cc08 ADBD displayed the most potent NFAT signaling when cultured in the presence of af59-CAR expressing JNL10 cells and the CS1 positive tumor cell line, MM.1S (Figure 11A).

[0632] The cc02 CS1 ADBD (SEQ ID NO: 781) was fused to p26 and either the non-binding α3DQ19E DD (SEQ ID NO: 1021) or the BCMA-binding bc98 DD (SEQ ID NO: 201). The ability of the resulting adapters to induce signaling in af59-CAR expressing JNL10 cells in the presence of the BCMA positive and CS1

positive cell line, MM.1S was assessed. As shown in Figure 11B, the bispecific bc98-p26-cc02 adapter capable of binding both CS1 and BCMA was more potent in its ability to signal than were the monospecific BCMA-binding bc98-p26-α3DQ19E adapter and the monospecific CS1-binding α3DQ19E-p26-cc02 adapter.

[0633] The af59-CAR (SEQ ID NO: 1133) was transduced into normal human T cells and the ability of those cells to kill H929 (BCMA++, CS1+) and MM.1S (BCMA++, CS1++) tumors using the indicated adapters was assessed. The data shown in Figures 11C and D indicate the bispecific bc98-p26-cc02 is an effective adapter in killing HT929 (high expression of both BCMA and CS1) and MM.1S (high BCMA, low CS1).

Example 16. Adapters comprising HER2 binding ADBD induce signaling in Af59-CAR expressing JNL10-cells cultured with HER2-positive SKBR3 tumor cells α3D(Q19E)-p26-Eb(08), or Affibody/Darpin-Based adaptors

[0634] HER2 (ERBB2, CD340) binding domains (ADBD) were isolated by panning ADBD phage libraries on the extracellular domain of human HER2 protein. Representative HER2 binding ADBD were fused to p26 in a bispecific format with non-binding α3DQ19E (SEQ ID NO: 1021) to generate adapter proteins for functional testing in combination with af59-CAR (SEQ ID NO:1133) expressing JNL10 cells or human T cells expressing af59-CAR.

HER2 (erbB2) Adapter Constructs	**Adapter Construct SEQ ID NO:**	**HER2 ADBD SEQ ID NO:**	**ADBD clone ID**
α3D(Q19E).3xGS.p26.3xGS. α3D(Q19E).HIS	**1506**	N/A	N/A
α3D(Q19E).3xGS.p26.3xGS.eb03.HIS	**1507**	804	eb03
α3D(Q19E).3xGS.p26.3xGS.eb04.HIS	**1508**	814	eb04
α3D(Q19E).3xGS.p26.3xGS.eb05.HIS	**1509**	810	eb05
α3D(Q19E).3xGS.p26.3xGS.eb06.HIS	**1510**	834	eb06
α3D(Q19E).3xGS.p26.3xGS.eb08.HIS	**1511**	809	eb08
α3D(Q19E).3xGS.p26.3xGS.eb09.HIS	**1512**	833	eb09
α3D(Q19E).3xGS.p26.3xGS.eb10.HIS	**1513**	839	eb10

[0635] The adapters demonstrated a range of activities in their ability to induce JNL10 NFAT signaling when cultured in the presence of af59-CAR expressing JNL10 cells and HER2 positive SKBR3 tumor cells. As shown in Figure 12A, the adapter comprising eb08 was the most potent stimulator in this assay.

[0636] The adapter comprising eb08 was then compared to other adapters containing a HER2 binding domains derived from affibodies (zHER2(4) and zHER2(342)) or DARPins (9.29 and G3). As shown in Figure 12B, the NFAT signaling in JNL10 cells mediated by the adapter comprising eb08 is greater than that of mediated by the adapter comprising zHERs:4, comparable to that of mediated by the adapter comprising 9.29, and less than that of G3 and zHER2:342.

[0637] The ability of adapters comprising the HER2-binding eb08 and eb04 domain to induce tumor (SKBR3) kill was compared with adapters containing other HER2 binding domains derived from affibodies (zHER2(4) and zHER2(342)) or DARPins (9.29 and G3). Each adapter was incubated with normal human T cells transduced with af59-CAR that binds p26 found in each adapter. SKBR3 lysis was quantitated in a 16-hour luciferase-based assay at an effector to target ratio of 1:5. The results of the assay shown in Figure 12C demonstrate that adapters comprising eb08 or eb04 modulate tumor lysis in a dose-dependent manner.

Example 17. Administration of T cells transduced with a p26-binding CAR in combination with a BCMA specific Adapter eliminate MM.1S tumor cells in vivo.

[0638] NSG mice (NOD-scid IL2Rg^{null}) were engrafted with 2×10^6 MM.1S cells expressing GFP and Luciferase. 14 days later (Day 0), mice received 5×10^6 T cells transduced with a CAR comprising a BCMA specific D domain (bc98-CAR, SEQ ID NO: 1166) ("ddBCMA-CAR") (group 1) or 5×10^6 T cells transduced with a p26-binding CAR (Af101, SEQ ID NO: 1164) ("ARC-T cells") (groups 2-5). Mice that received ARC-T cells were dosed daily with a BCMA specific Adapter (bc98-p26-bc98, SEQ ID NO: 1165) ("sparX-BCMA") or a control Adapter ("SPRX-α3D") intraperitoneally at 3 mg/kg, 1 mg/kg or 0.3 mg/kg dose levels for 21 days. Animals were subsequently imaged by IVIS throughout the to assess tumor burden. Figure 13 shows the total flux measured. Administration of T cells transduced with the p26-binding CAR in combination with the BCMA specific Adapter eliminated MM.1S tumor cells in vivo comparably to the tumor cell elimination by the T cells transduced with a CAR comprising a BCMA specific D domain. Adapter doses of 0.3 mg/kg daily were able to eliminate measurable tumor burden as early as 7 days post dosing that lasted for the duration of the study.

[0639] SEQ ID NO: 1164:

MAFLWLLSCWALLGTTFGDEMGSWSEFYDRLNAIDARLWALGGSEAELAAFEKEIAAFESELQAYK
GKGNPEVESLREHAAAIREWLQAYRHNGGGGDGGGGSGTTTPAPRPPTPAPTIASQPLSLRPEACRP
AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDG
CSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRR
KNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (

[0640] SEQ ID NO: 1165:

MGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKLRYTAGTIKRFL
QAYRHNGGGGDGGGGSGGGGSGLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGE
YYLQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMT
PVNPGVGQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVK
QKPQITEEQLEAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGVGGGGSGGGGSGGGGSM
GSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYKGKGNPEVEKLRYTAGTIKRFLQ
AYRHN

[0641] SEQ ID NO: 1166:

MAFLWLLSCWALLGTTFGDEMGSWSEFWARLGAIRERLDALGGSEAELAAFEKEIAAFESELQAYK
GKGNPEVEKLRYTAGTIKRFLQAYRHNGGGGDGGGGSGTTTPAPRPPTPAPTIASQPLSLRPEACRPA
AGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGC
SCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRK
NPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

Example 18. T cells transduced with a p26-binding CAR exhibit comparable activity in vivo with intermittent dosing of a BCMA specific Adapter in a disseminated model of BCMA+ B-cell leukemia.

[0642] NSG mice (NOD-scid IL2Rg^{null}) were engrafted with 1×10^6 NALM6-BCMA cells expressing GFP and Luciferase. 10 days later (Day 0), mice were engrafted with 5×10^6 T cells transduced with a p26-binding CAR (Af101, SEQ ID NO: 1164) ("ARC-T cells") and were dosed with 3 mg/kg of a BCMA specific Adapter (bc98-p26-bc98, SEQ ID NO: 1165) ("SPRX-BCMA") daily, every other day, twice per week, or weekly for 21 days. Control mice were dosed with 3 mg/kg of the negative control Adapter ("SPRX-α3D") daily for 21 days. Animals were subsequently imaged by IVIS throughout to assess tumor burden. Figure 14 shows the total flux measured. Adapter doses of 3 mg/kg twice a week were able to eliminate measurable tumor burden as early as 7 days post dosing that lasted for the duration of the study.

[0643] The in vivo residence time the BCMA specific Adapter (bc98-p26-bc98, SEQ ID NO: 1165) ("SPRX-BCMA") on NALM6-BCMA tumor cells was assessed in mice following I.V. Adapter administration. Femurs were collected at various timepoints post-injection, flushed, samples fixed, and Adapter-binding was detected on tumor cells via an anti-tag antibody. Binding is presented as percent positive in Figure 15, left. Representative histograms for each time point are also presented (Figure 15, right).

[0644] Throughout this application, various publications are referenced by author name and date, or by Patent No. or Patent Publication No. The disclosure of these publications are hereby incorporated in their entireties by reference into this application in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed herein. However, the citation of a reference herein should not be construed as an acknowledgement that such reference is prior art to the present invention.

WHAT IS CLAIMED IS:

1. A method of treating a lymphoma or leukemia comprising administering to a subject in need thereof

   a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

   b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA.

2. The method of claim 1, wherein the lymphoma or leukemia comprises cells expressing BCMA.

3. The method of claim 1 or claim 2, wherein the lymphoma or leukemia is a B cell lymphoma or leukemia.

4. The method of claim 1 or claim 2, wherein the lymphoma or leukemia is multiple myeloma.

5. A method of delivering an immune response to a multiple myeloma cell comprising administering to a subject in need thereof

   a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

   b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA.

6. A method a method of killing a multiple myeloma cell comprising administering to a subject in need thereof

   a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

   b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA.

7. A method of depleting multiple myeloma cells comprising administering to a subject in need thereof

   a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA.

8. The method of any one of claims 1 to 7, wherein the cells are immune effector cells.

9. The method of any one of claims 1 to 8, wherein the cells are T cells or NK cells.

10. The method of any one of claims 1 to 9, wherein the D domain that binds to AFP p26 comprises the amino acid sequence of SEQ ID NO: 201.

11. The method of any one of claims 1 to 10, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 1164.

12. The method of any one of claims 1 to 11, wherein the D domain that binds to BCMA comprises the amino acid sequence of SEQ ID NO: 201.

13. The method of any one of claims 1 to 12, wherein the Adapter comprises the amino acid sequence of SEQ ID NO: 1165.

14. The method of any one of claims 1 to 13, wherein the Adapter is formulated for intravenous administration.

15. The method of any one of claims 1 to 13, wherein the Adapter is formulated for subcutaneous administration.

16. The method of any one of claims 1 to 15, wherein the cells and the Adapter are administered simultaneously.

17. The method of any one of claims 1 to 15, wherein the cells and the Adapter are administered consecutively.

18. The method of any one of claims 1 to 15, wherein the cells are administered before the Adapter.

19. The method of any one of claims 1 to 18, wherein the cells and the Adapter are administered on the same day.

20. The method of any one of claims 1 to 18, wherein the cells and the Adapter are administered on different days.

21. The method of claim 20, wherein the cells and the Adapter are administered on consecutive days.

22. The method of claim 20, wherein the cells and the Adapter are administered 1, 2, 3, 4, 5, 6, or 7 days apart.

23. The method of any one of claims 1 to 22, wherein the cells and the Adapter are administered on

different days.

24. The method of any one of claims 1 to 23, comprising administering between about $20x10^6$ and about $500x10^6$ or between about $50x10^6$ and about $200x10^6$ cells expressing the CAR.

25. The method of any one of claims 1 to 23, comprising administering about $100x10^6$ cells expressing the CAR.

26. The method of any one of claims 1 to 24, comprising administering one or more doses of about 1 μg/kg to about 10 mg/kg, about 5 μg/kg to about 5 mg/kg, about 10 μg/kg to about 2 mg/kg, about 20 μg/kg to about 1 mg/kg, or about 50 μg/kg to about 0.5 mg/kg of the Adapter.

27. The method of any one of claims 1 to 24, comprising administering one or more doses of about 20 μg/kg to about 1 mg/kg of the Adapter.

28. The method of any one of claims 1 to 24, comprising administering one or more doses of about 0.01 mg/kg, about 0.02 mg/kg, about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 1 mg/kg, or about 2 mg/kg of the Adapter.

29. The method of any one of claims 1 to 24, comprising administering one or more doses of about 0.04 mg/kg, about 0.07 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, or about 0.3 mg/kg of the Adapter.

30. The method of any one of claims 1 to 24, comprising administering one or more doses of about 0.4 mg, about 0.8 mg, about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, about 20 mg, about 24 mg, about 28 mg, about 40 mg, or about 80 mg of the Adapter.

31. The method of any one of claims 1 to 24, comprising administering one or more doses of about 1.6 mg, about 2.8 mg, about 3 mg, about 4 mg, about 8 mg, about 12 mg, about 16 mg, or about 20 mg of the Adapter.

32. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered 3 times a day, twice a day, daily, every two days, twice a week, or weekly.

33. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily.

34. The method of any one of claims 1 to 31, comprising administering more than one doses of the

Adapter, wherein the more than one doses are administered every two days.

35. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for between about 1 to about 4 weeks, followed by administration every other day, twice a week, or weekly.

36. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by every other day administration.

37. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by twice weekly administration.

38. The method of any one of claims 1 to 31, comprising administering more than one doses of the Adapter, wherein the more than one doses are administered daily for about 1 week, followed by weekly administration.

39. The method of any one of claims 1 to 38, comprising administering the Adapter at different doses.

40. The method of any claim 36, comprising administering one or more loading doses of about 0.1 mg/kg to about 10 mg/kg of the Adapter, followed by the administration of one or more maintenance doses of about 0.01mg/kg to about 0.1 mg/kg.

41. The method of any claim 39, comprising administering one or more loading doses of about 4 mg to about 200 mg of the Adapter, followed by the administration of one or more maintenance doses of about 0.4 mg to about 10 mg.

42. The method of any claim 40 or 41, wherein the one or more loading doses are administered for about 1 day to about 3 weeks.

43. The method of any claim 40 or 41, wherein the one or more loading doses are administered for about 1 day to about 1 week.

44. The method of any claim 40 or 41, wherein the one or more loading doses are administered for 1 day, 2 days, 3 days, 4 days or about 1 week.

45. A method of treating a lymphoma or leukemia comprising administering to a subject in need thereof

a. a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain; and

b. one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA.

46. The method of claim 45, wherein the lymphoma or leukemia comprises cells expressing BCMA.

47. The method of claim 45 or claim 46, wherein the lymphoma or leukemia is a B cell lymphoma or leukemia.

48. The method of claim 45 or claim 46, wherein the lymphoma or leukemia is multiple myeloma.

49. A method of delivering an immune response to a multiple myeloma cell comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain.

50. A method a method of killing a multiple myeloma cell comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain.

51. A method of depleting multiple myeloma cells comprising administering to a subject in need thereof one or more therapeutically effective dose of an Adapter comprising (i) AFP p26 or a variant thereof and (ii) a D domain that binds to BCMA, wherein the subject has been administered a therapeutically effective dose of cells expressing a chimeric antigen receptor (CAR), wherein the CAR comprises (i) a D domain that binds to AFP p26 or a variant thereof, (ii) a transmembrane domain, and (iii) an intracellular domain.

FIG. 1A

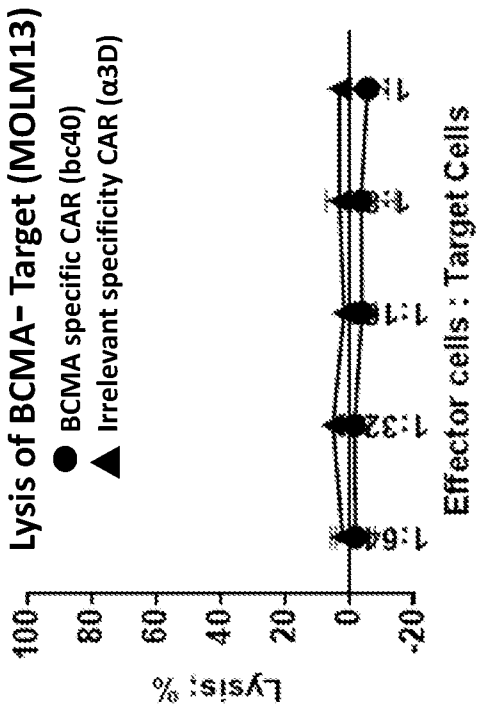


FIG. 1B

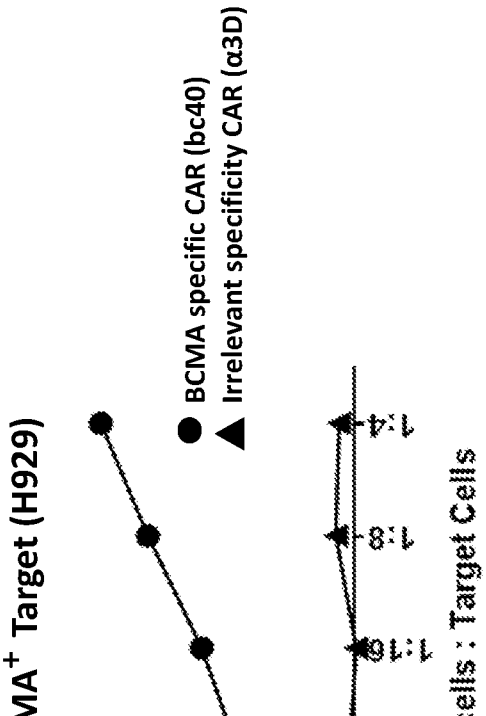
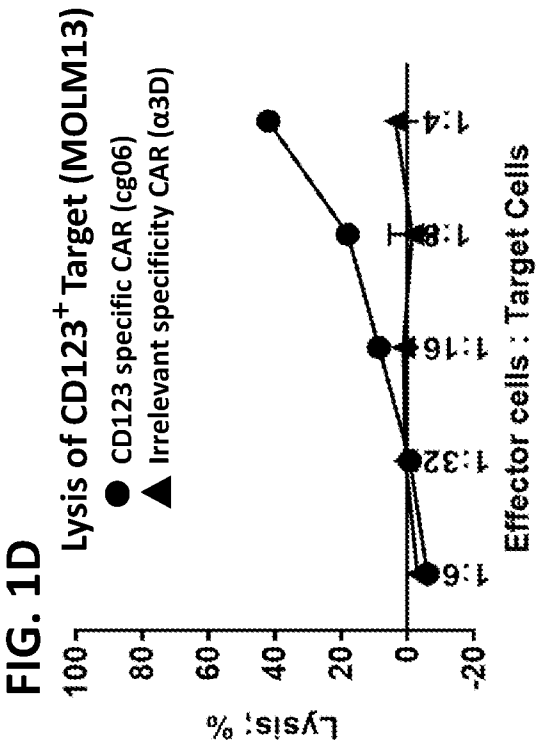


FIG. 1C

FIG. 1D



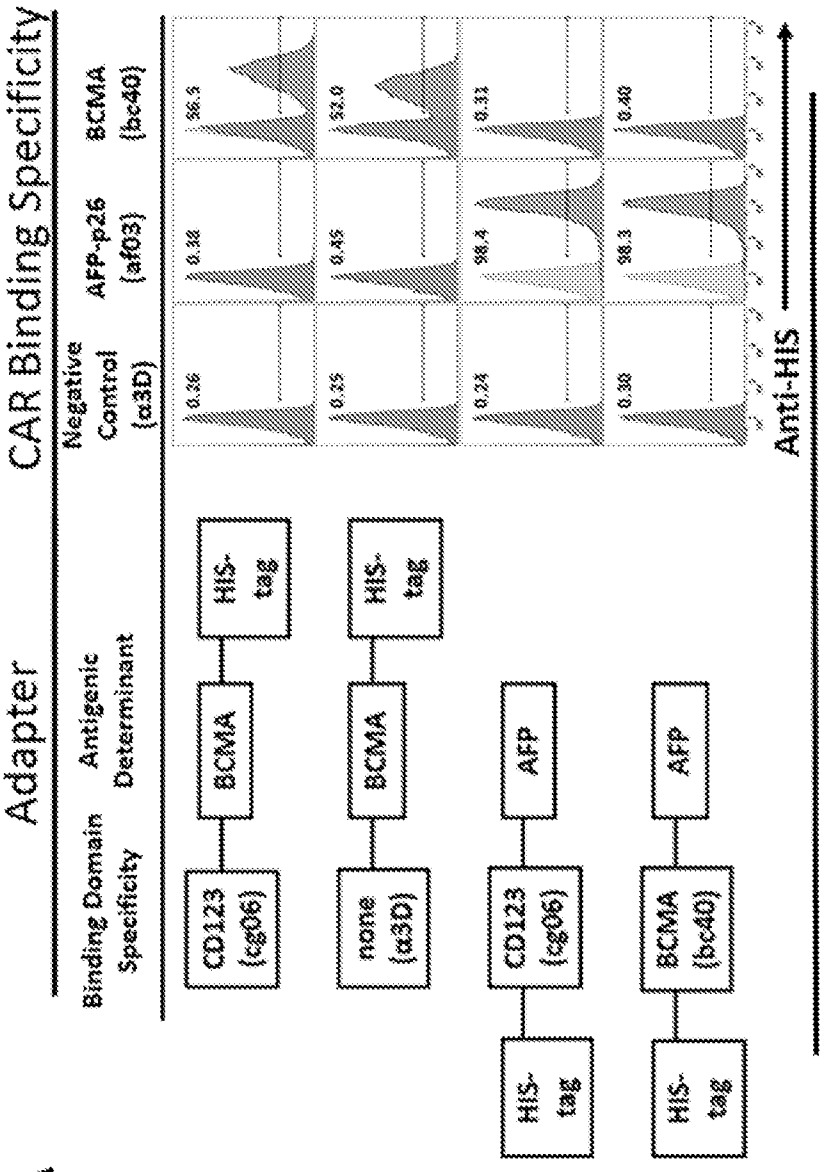

Adapter
CAR Binding Specificity
Binding Domain Specificity
Antigenic Determinant
Negative Control (α3D)
AFP-p26 (af03)
BCMA (bc40)
CD123 (cg06)
BCMA
HIS-tag
none (α3D)
BCMA
HIS-tag
CD123 (cg06)
AFP
HIS-tag
BCMA (bc40)
AFP
HIS-tag
0.36
0.38
56.5
0.35
0.45
52.0
0.24
98.4
0.33
0.38
98.3
0.40
Anti-HIS
Anti-FLAG

FIG. 2A

FIG. 2B

FIG. 3A

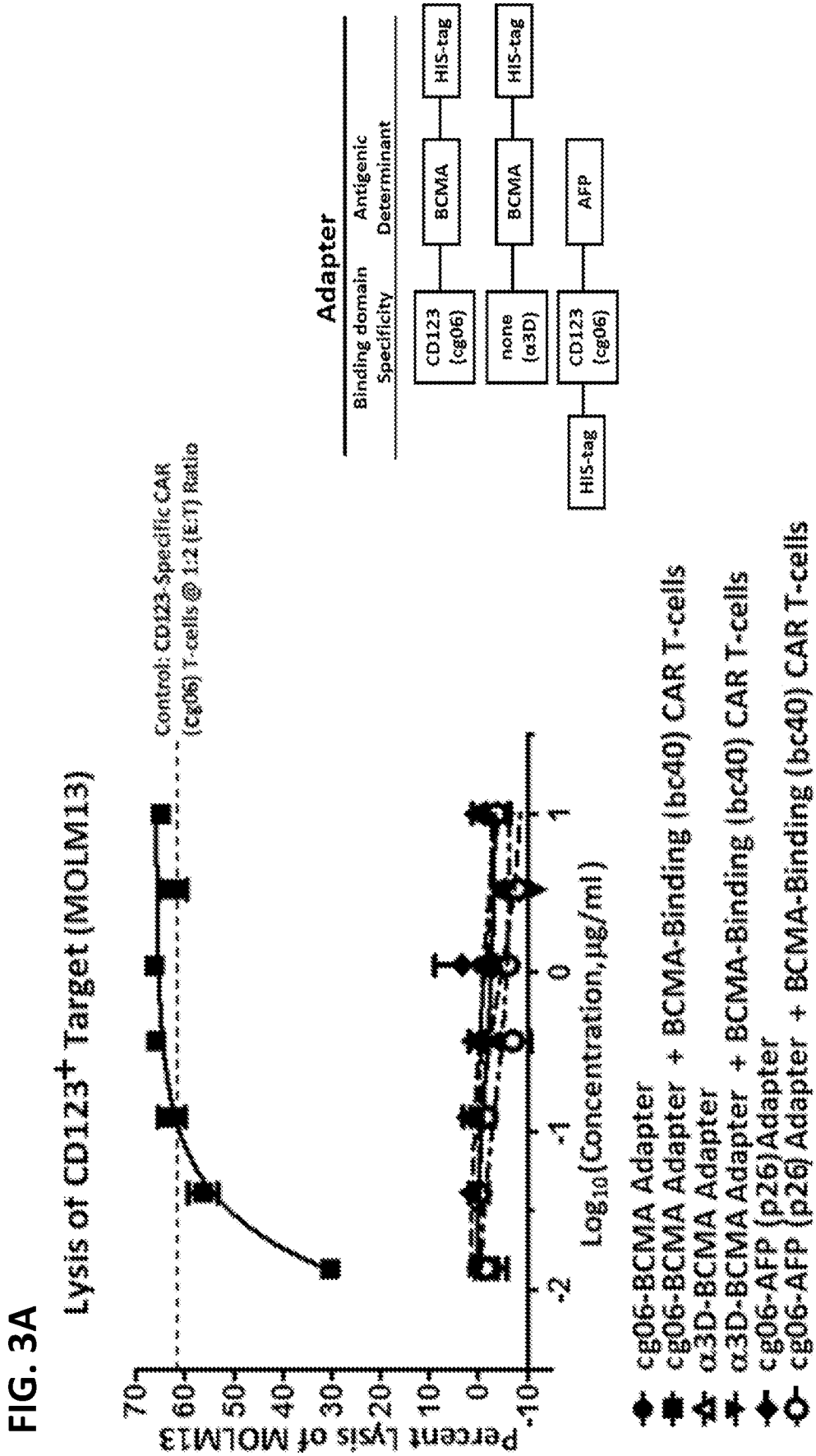

Lysis of CD123+ Target (MOLM13)
Control: CD123-Specific CAR (cg06) T-cells @ 1:2 (E:T) Ratio
Percent Lysis of MOLM13
70
60
50
40
30
20
10
0
-10
-2
-1
0
1
Log10(Concentration,µg/ml)
Adapter
Binding domain Specificity
Antigenic Determinant
CD123 (cg06)
BCMA
HIS-tag
none (α3D)
BCMA
HIS-tag
CD123 (cg06)
AFP
HIS-tag
cg06-BCMA Adapter
cg06-BCMA Adapter + BCMA-Binding (bc40) CAR T-cells
α3D-BCMA Adapter
α3D-BCMA Adapter + BCMA-Binding (bc40) CAR T-cells
cg06-AFP (p26)Adapter
cg06-AFP (p26) Adapter + BCMA-Binding (bc40) CAR T-cells

FIG. 3B

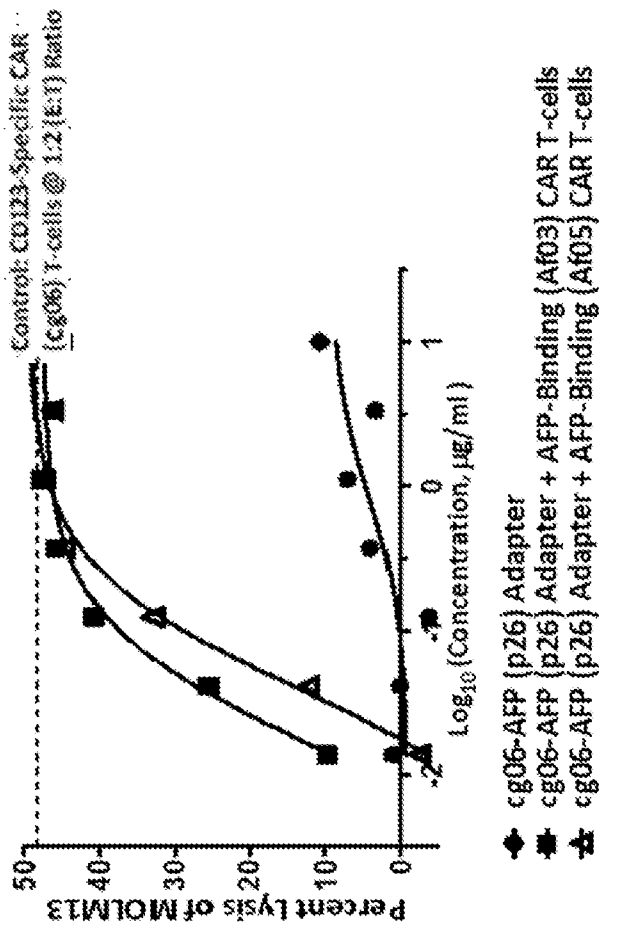
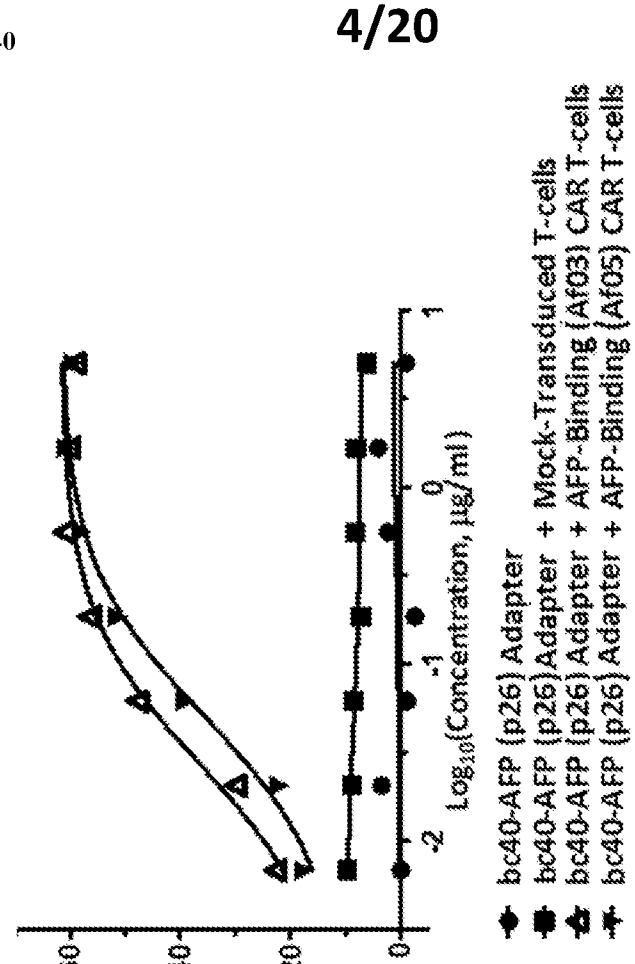

Lysis of CD123+ Target (MOLM13)
Control: CD123-Specific CAR (cg06) T-cells @ 1:2 (E:T) Ratio
Percent Lysis of MOLM13
Log10 (Concentration, µg/ml)
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + AFP-Binding (Af03) CAR T-cells
cg06-AFP (p26) Adapter + AFP-Binding (Af05) CAR T-cells

FIG. 3C


Lysis of BCMA+ Target (H929)
Percent Lysis of H929
Log10 (Concentration, µg/ml)
bc40-AFP (p26) Adapter
bc40-AFP (p26) Adapter + Mock-Transduced T-cells
bc40-AFP (p26) Adapter + AFP-Binding (Af03) CAR T-cells
bc40-AFP (p26) Adapter + AFP-Binding (Af05) CAR T-cells

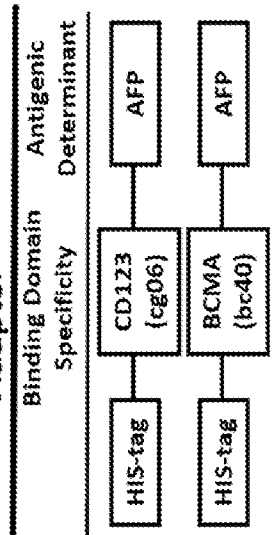

Adapter
Binding Domain Specificity
Antigenic Determinant
HIS-tag
CD123 (cg06)
AFP
HIS-tag
BCMA (bc40)
AFP

FIG. 4A

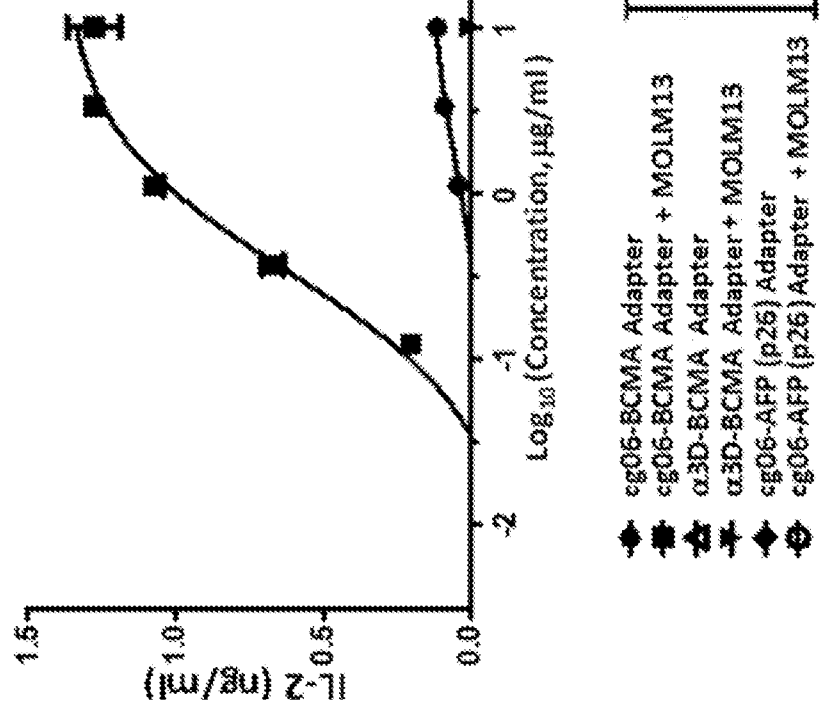

IL-2 (ng/ml)
1.5
1.0
0.5
0.0
-2
-1
0
1
Log10(Concentration, µg/ml)
cg06-BCMA Adapter
cg06-BCMA Adapter + MOLM13
α3D-BCMA Adapter
α3D-BCMA Adapter+ MOLM13
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + MOLM13
BCMA-Specific (bc40) CAR T-cells

FIG. 4B

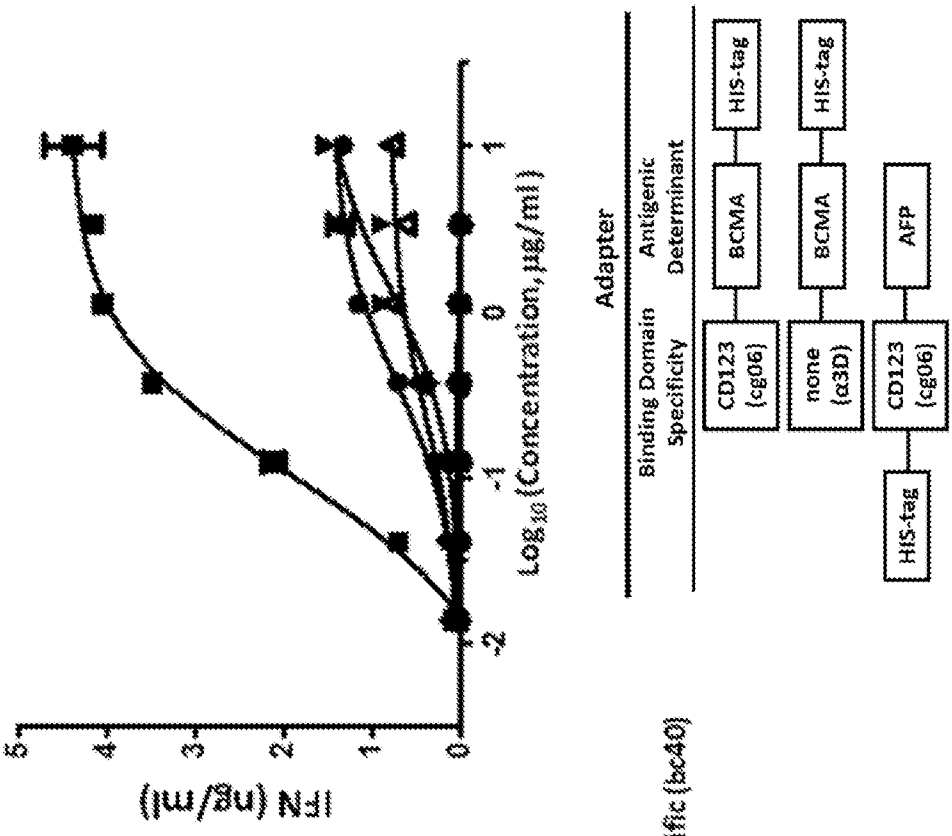

IFN (ng/ml)
5
4
3
2
1
0
-2
-1
0
1
Log10(Concentration, µg/ml)
Adapter
Binding Domain Specificity
Antigenic Determinant
CD123 (cg06)
BCMA
HIS-tag
none (α3D)
BCMA
HIS-tag
CD123 (cg06)
AFP
HIS-tag

FIG. 4C

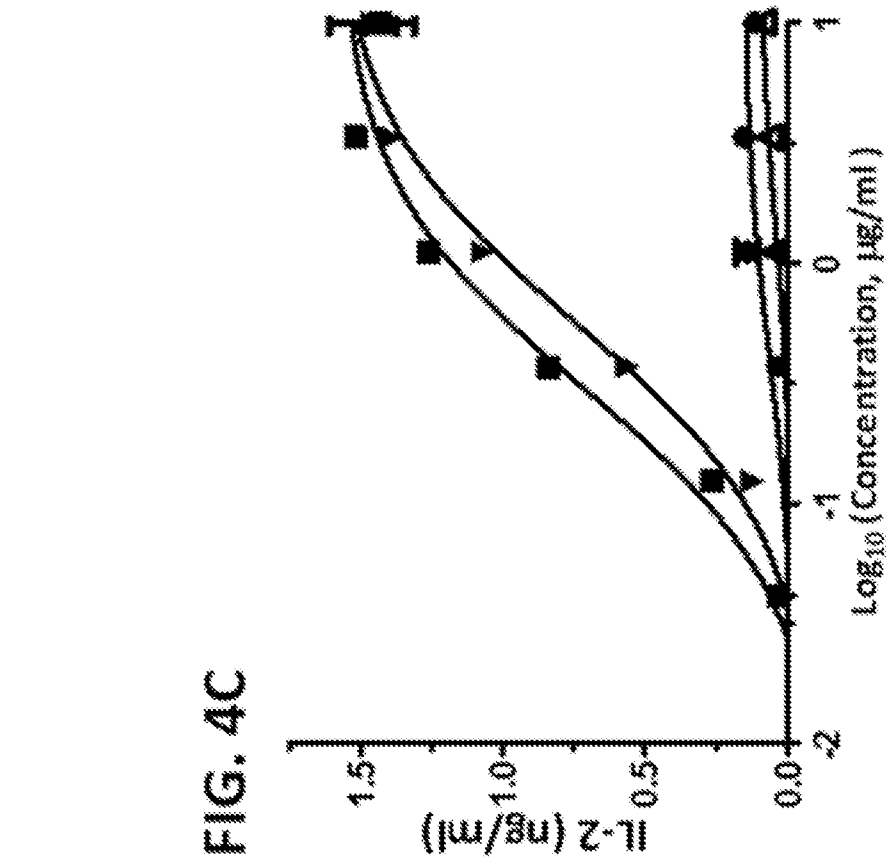
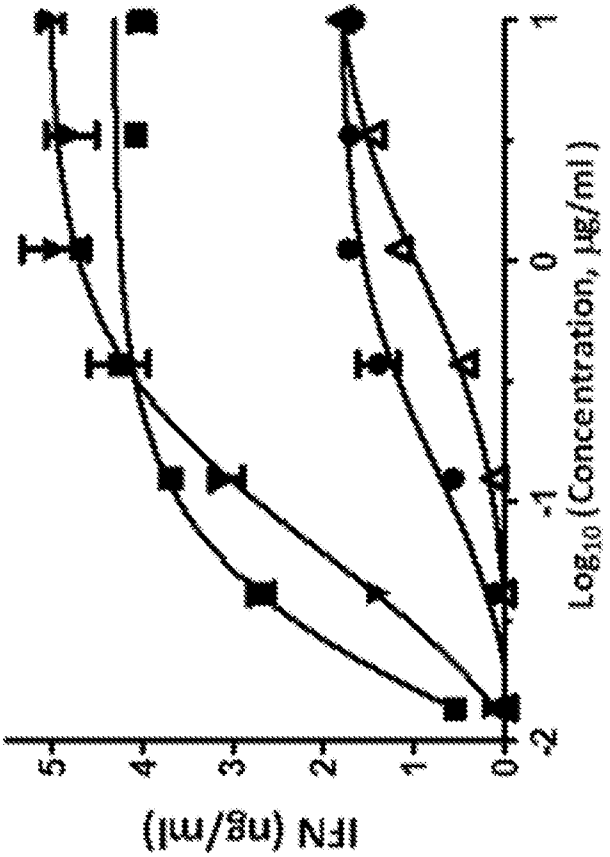

IL-2 (ng/ml)
1.5
1.0
0.5
0.0
-2
-1
0
1
Log10 (Concentration, µg/ml)
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + MOLM13
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + MOLM13
AFP-p26 specific (Af03) CAR T-cells
AFP-p26 specific (Af05) CAR T-cells

FIG. 4D


IFN (ng/ml)
5
4
3
2
1
0
-2
-1
0
1
Log10 (Concentration, µg/ml)

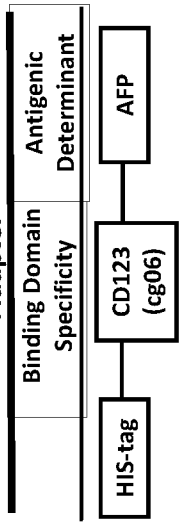

Adapter
Binding Domain Specificity
Antigenic Determinant
HIS-tag
CD123 (cg06)
AFP

FIG. 5

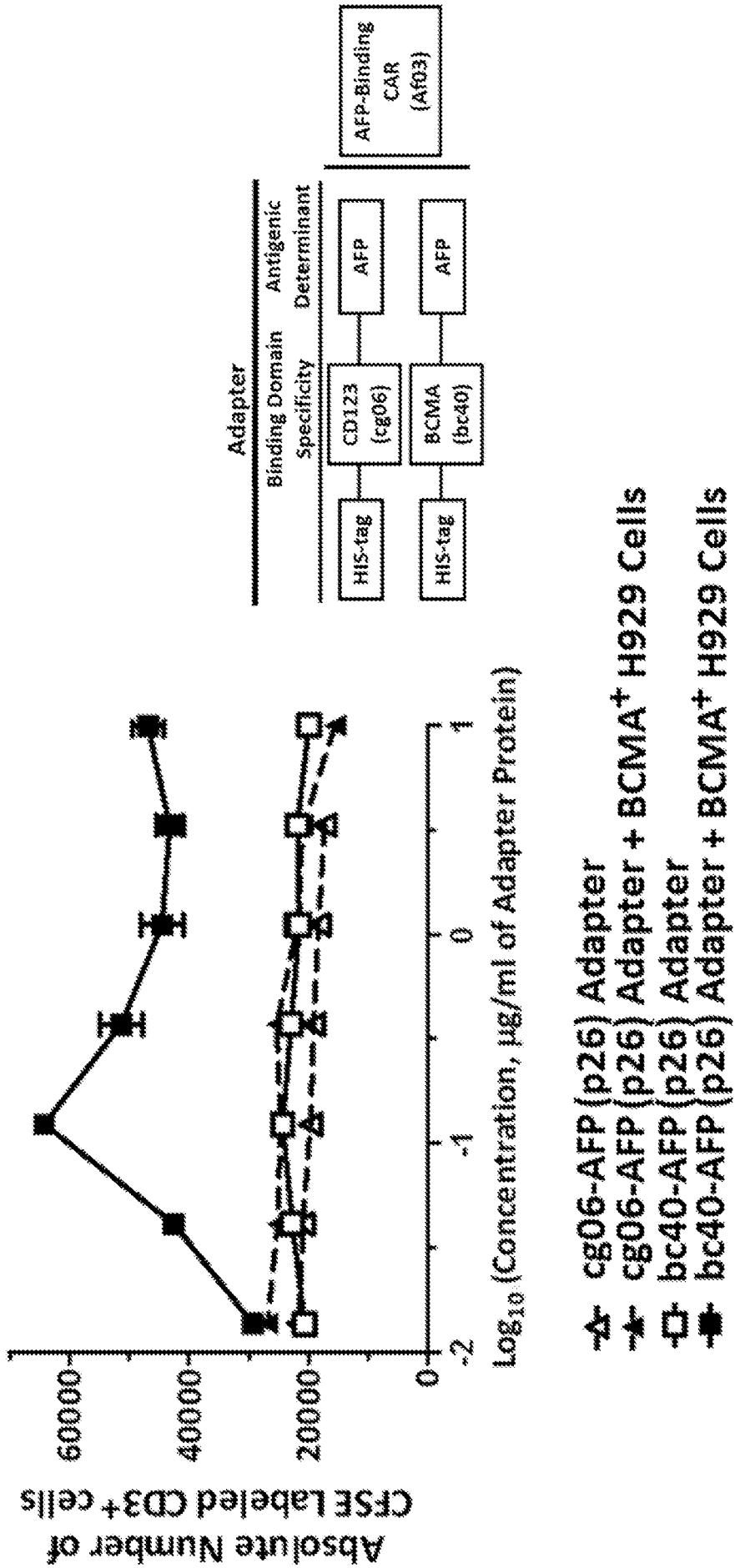

Proliferation Assay with Adapter Proteins at 72 Hours
Absolute Number of CFSE Labeled CD3+ cells
60000
40000
20000
0
-2
-1
0
1
Log10 (Concentration, µg/ml of Adapter Protein)
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + BCMA+ H929 Cells
bc40-AFP (p26) Adapter
bc40-AFP (p26) Adapter + BCMA+ H929 Cells
Adapter
Binding Domain Specificity
Antigenic Determinant
HIS-tag
CD123 (cg06)
AFP
HIS-tag
BCMA (bc40)
AFP
AFP-Binding CAR (Af03)

FIG. 6A

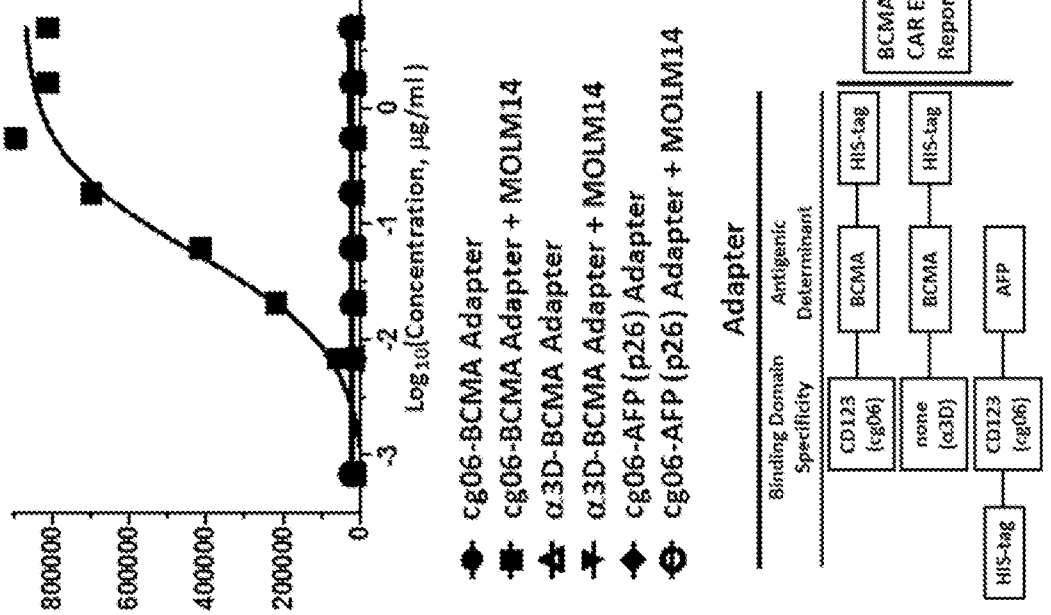

luciferase Signal
800000
600000
400000
200000
0
-3
-2
-1
0
1
Log10(Concentration, µg/ml)
cg06-BCMA Adapter
cg06-BCMA Adapter + MOLM14
α3D-BCMA Adapter
α3D-BCMA Adapter + MOLM14
cg06-AFP (p26) Adapter
cg06-AFP (p26) Adapter + MOLM14
Adapter
Binding Domain Specificity
Antigenic Determinant
CD123 (cg06)
BCMA
HIS-tag
none (α3D)
BCMA
HIS-tag
CD123 (cg06)
AFP
HIS-tag
BCMA-Specific (bc40) CAR Expressing Jurkat Reporter Cells

FIG. 6B

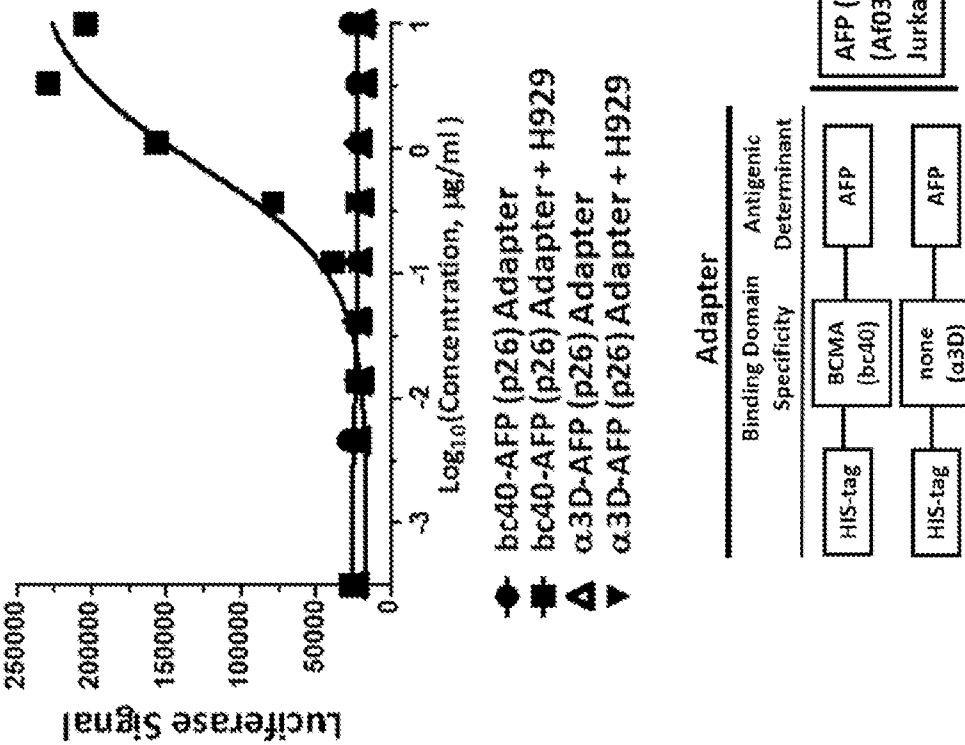

luciferase Signal
250000
200000
150000
100000
50000
0
-3
-2
-1
0
1
Log10(Concentration, µg/ml)
bc40-AFP (p26) Adapter
bc40-AFP (p26) Adapter + H929
α3D-AFP (p26) Adapter
α3D-AFP (p26) Adapter + H929
Adapter
Binding Domain Specificity
Antigenic Determinant
BCMA (bc40)
AFP
HIS-tag
none (α3D)
AFP
HIS-tag
AFP (p26)-Specific (Af03) CAR Expressing Jurkat Reporter Cells

FIG. 7A

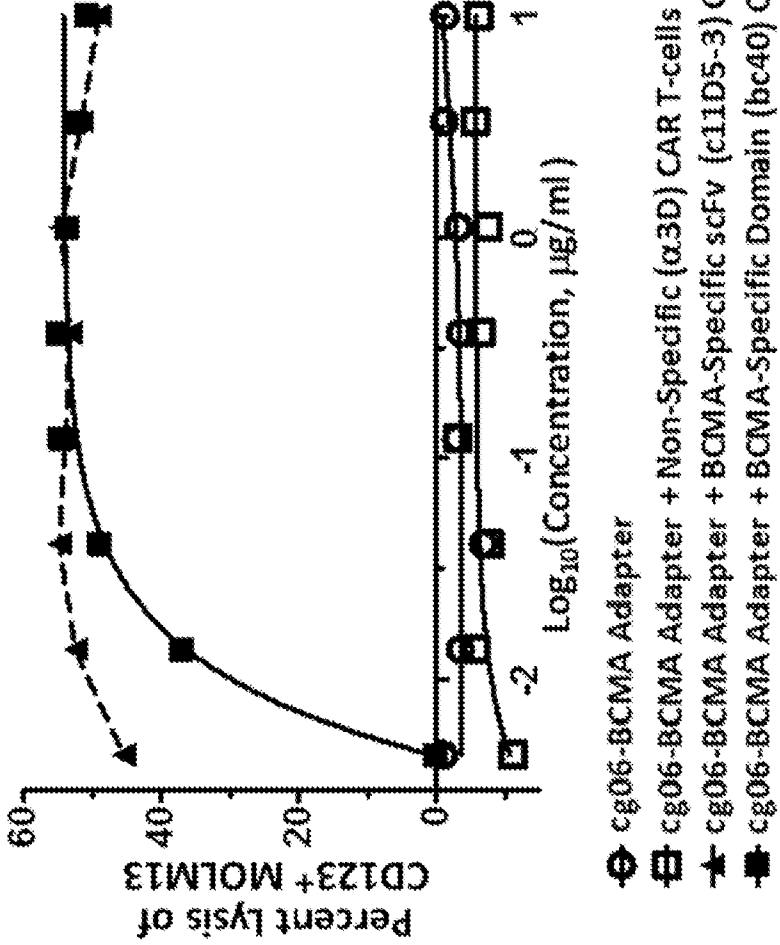

Lysis of CD123+ Target (MOLM13)
Percent Lysis of CD123+ MOLM13
60
40
20
0
-2
-1
0
1
Log10(Concentration, µg/ml)
cg06-BCMA Adapter
cg06-BCMA Adapter + Non-Specific (α3D) CAR T-cells
cg06-BCMA Adapter + BCMA-Specific scFv (c11D5-3) CAR T-cells
cg06-BCMA Adapter + BCMA-Specific Domain (bc40) CAR T-cells

FIG. 7B

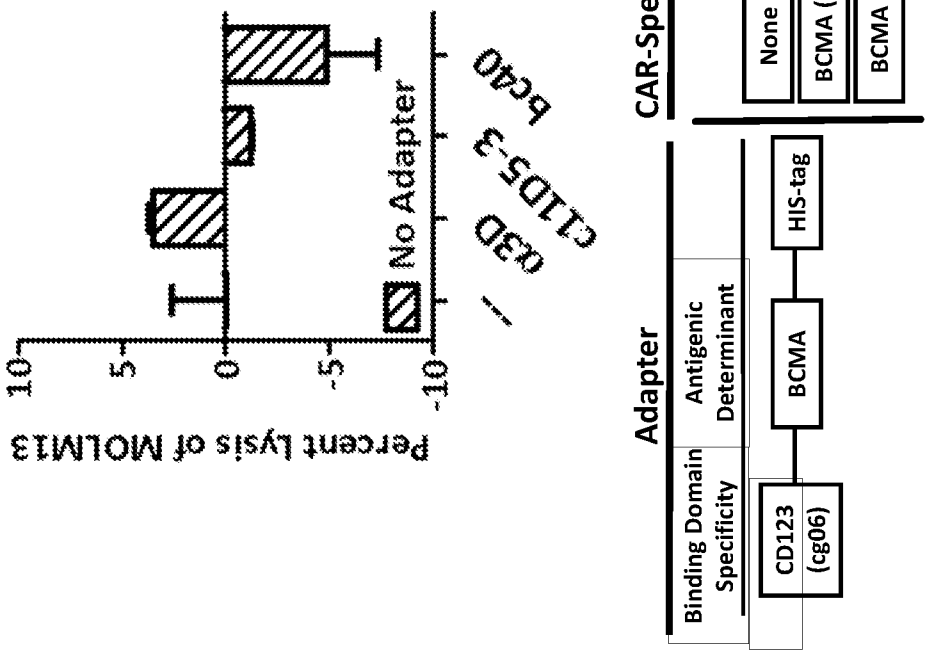

Percent Lysis of MOLM13
10
5
0
-5
-10
No Adapter
α3D
c11D5-3
bc40
Adapter
Binding Domain Specificity
Antigenic Determinant
CD123 (cg06)
BCMA
HIS-tag
CAR-Specificity
None (α3D)
BCMA (c11D5-3)
BCMA (bc40)

FIG. 8A

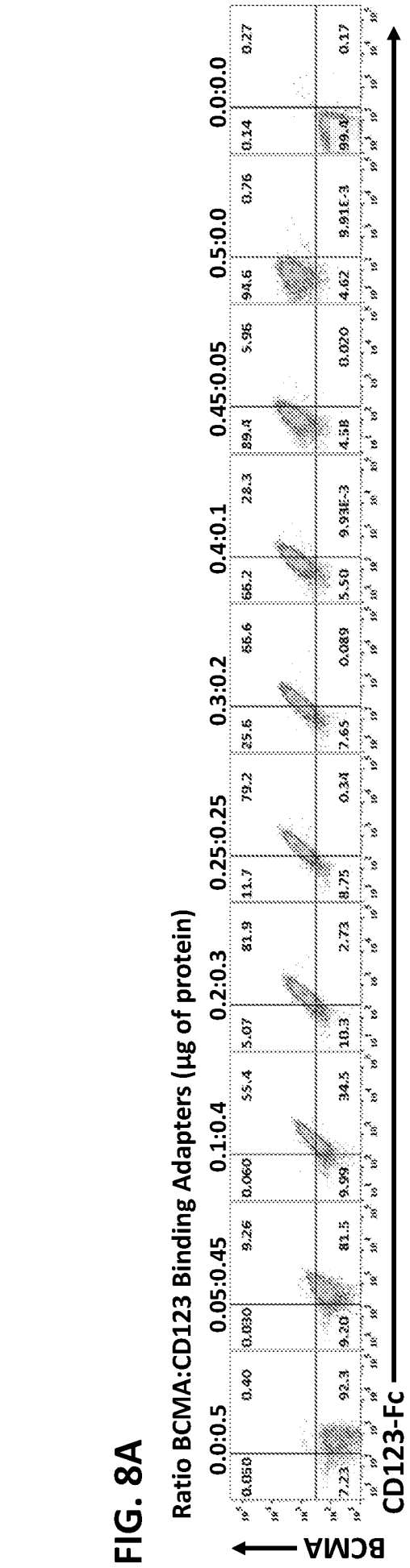

Ratio BCMA:CD123 Binding Adapters (µg of protein)
0.0:0.5
0.05:0.45
0.1:0.4
0.2:0.3
0.25:0.25
0.3:0.2
0.4:0.1
0.45:0.05
0.5:0.0
0.0:0.0
BCMA
CD123-Fc

FIG. 8B

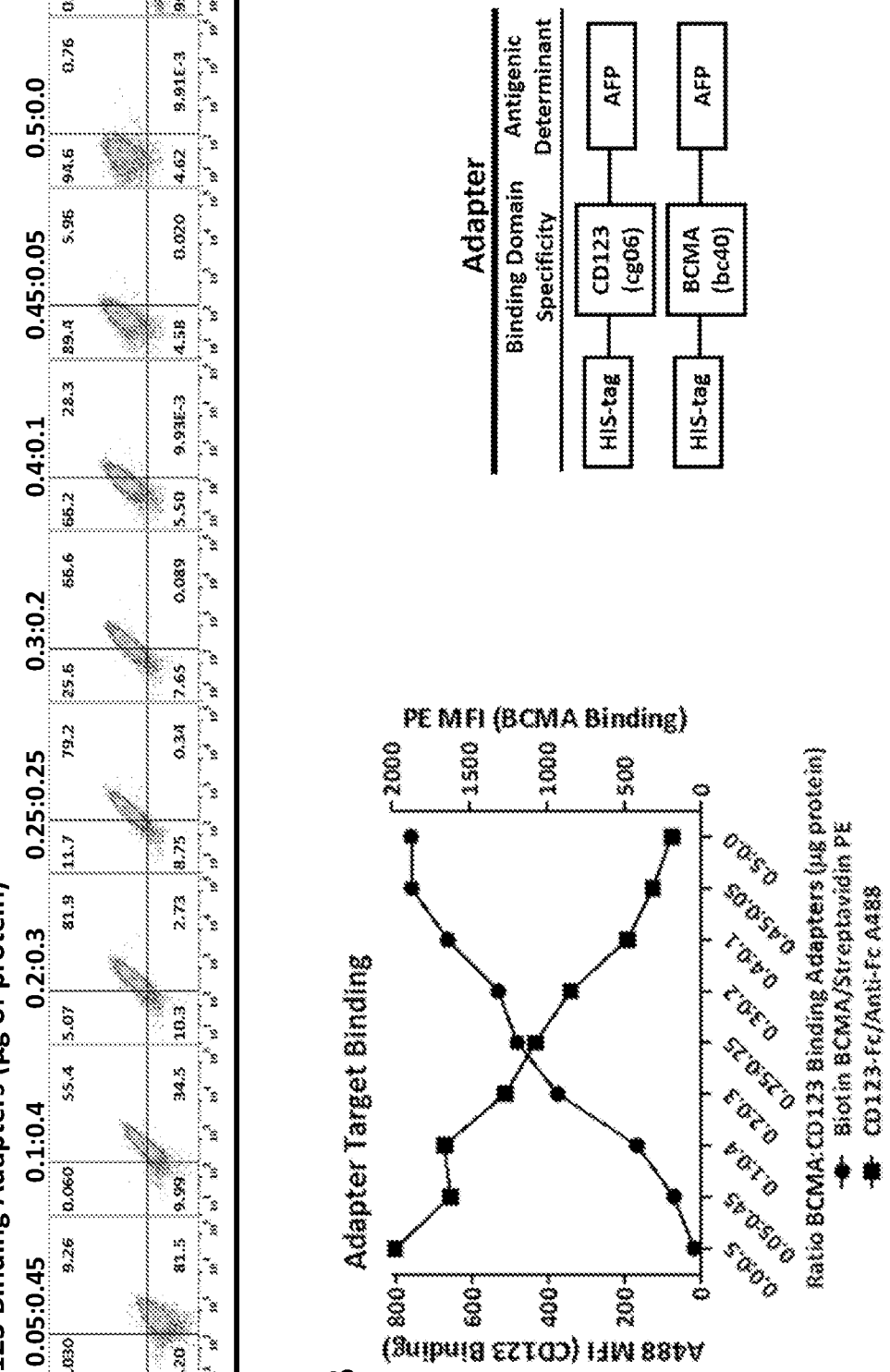

Adapter
Binding Domain Specificity
Antigenic Determinant
HIS-tag
CD123 (cg06)
AFP
HIS-tag
BCMA (bc40)
AFP
Adapter Target Binding
A488 MFI (CD123 Binding)
PE MFI (BCMA Binding)
Ratio BCMA:CD123 Binding Adapters (µg protein)
Biotin BCMA/Streptavidin PE
CD123-Fc/Anti-Fc A488

FIG. 9A

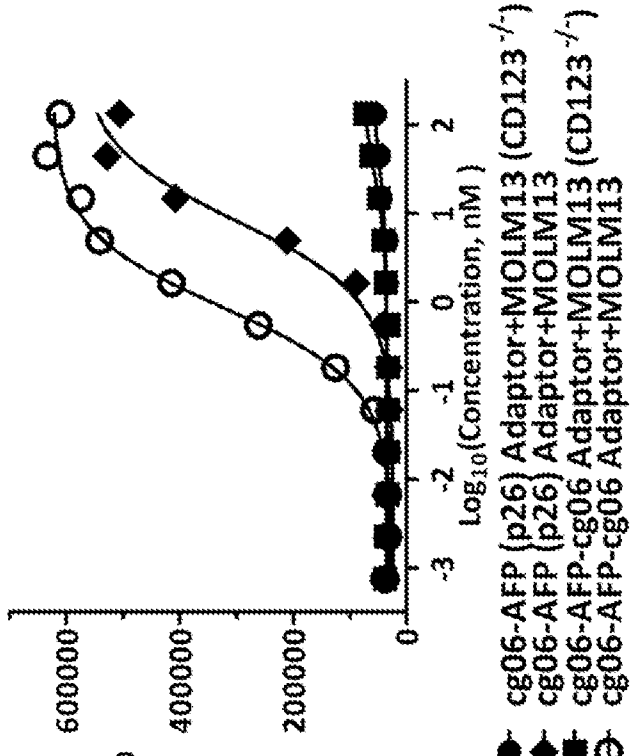

Luciferase Signal
600000
400000
200000
0
-3
-2
-1
0
1
2
Log10(Concentration, nM)
cg06-AFP (p26) Adaptor+MOLM13 (CD123 -/-)
cg06-AFP (p26) Adaptor+MOLM13
cg06-AFP-cg06 Adaptor+MOLM13 (CD123 -/-)
cg06-AFP-cg06 Adaptor+MOLM13
Adapter
Binding Domain Specificity
Antigenic Determinant
Binding Domain Specificity
HIS-tag
CD123 (cg06)
AFP
CD123 (cg06)
HIS-tag
CD123 (cg06)
AFP
CD123 (cg06)

FIG. 9B

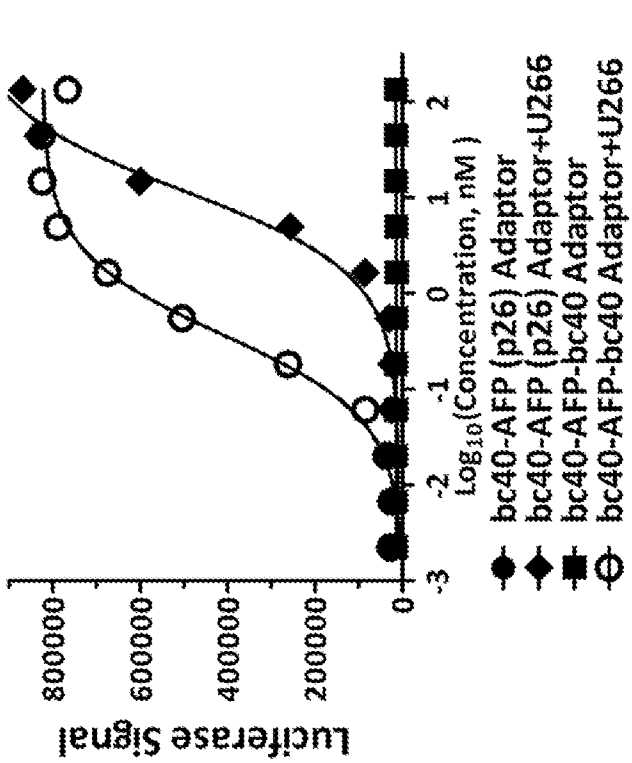

Luciferase Signal
800000
600000
400000
200000
0
-3
-2
-1
0
1
2
Log10(Concentration, nM)
bc40-AFP (p26) Adaptor
bc40-AFP (p26) Adaptor+U266
bc40-AFP-bc40 Adaptor
bc40-AFP-bc40 Adaptor+U266
Adapter
Binding Domain Specificity
Antigenic Determinant
Binding Domain Specificity
HIS-tag
BCMA (bc40)
AFP
BCMA (bc40)
HIS-tag
BCMA (bc40)
AFP
BCMA (bc40)

FIG. 10

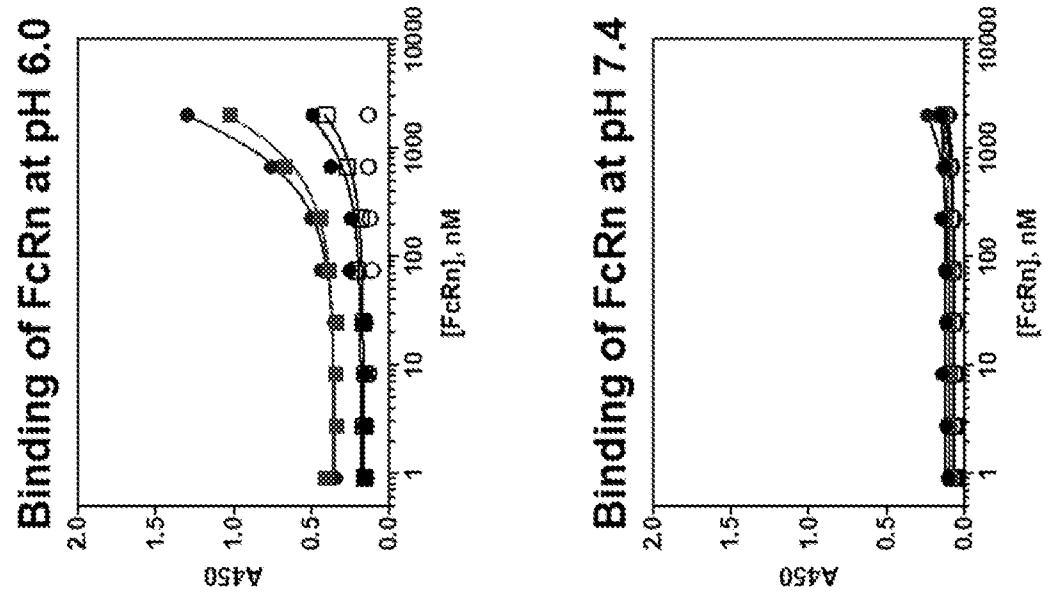

Binding of FcRn at pH 6.0
Well Coating
BC40-P26 SEQ ID NO: 1085
BC98-P26(Q26-V229)-BC98 SEQ ID NO: 2032
HSA
BC40 SEQ ID NO: 197 with his-tag
No Coating
A450
[FcRn], nM
Binding of FcRn at pH 7.4
Well Coating
BC40-P26 SEQ ID NO: 1085
BC98-P26(Q26-V229)-BC98 SEQ ID NO: 2032
HSA,
BC40 SEQ ID NO: 197 with his-tag
No Coating
A450
[FcRn], nM

FIG. 11A

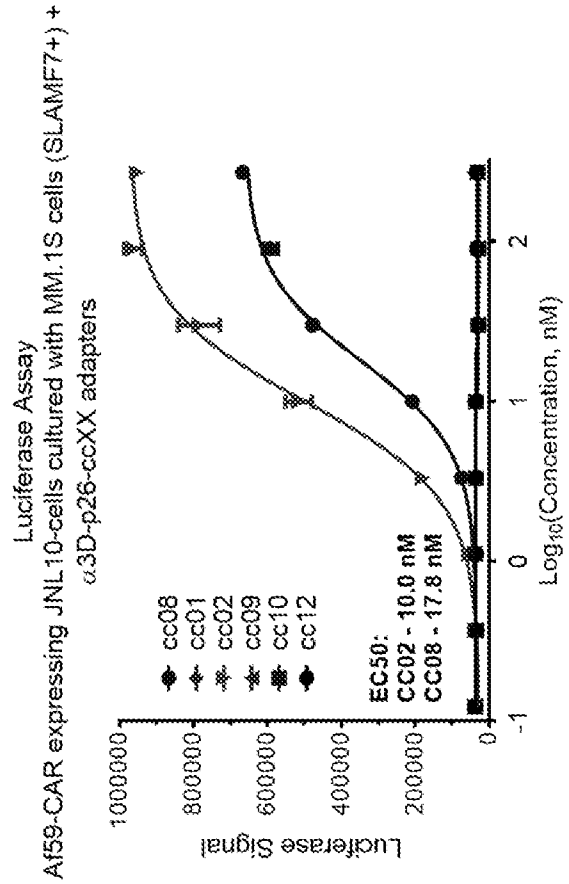


FIG. 11B

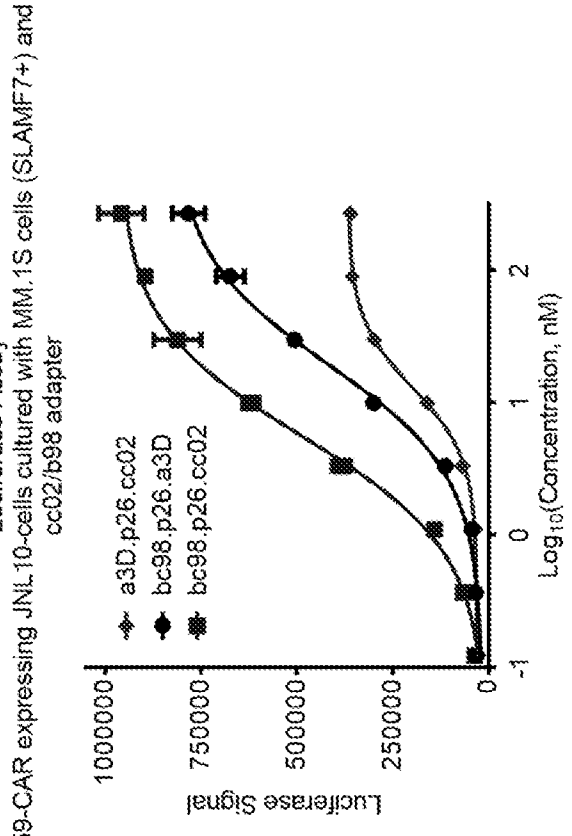


FIG. 11C

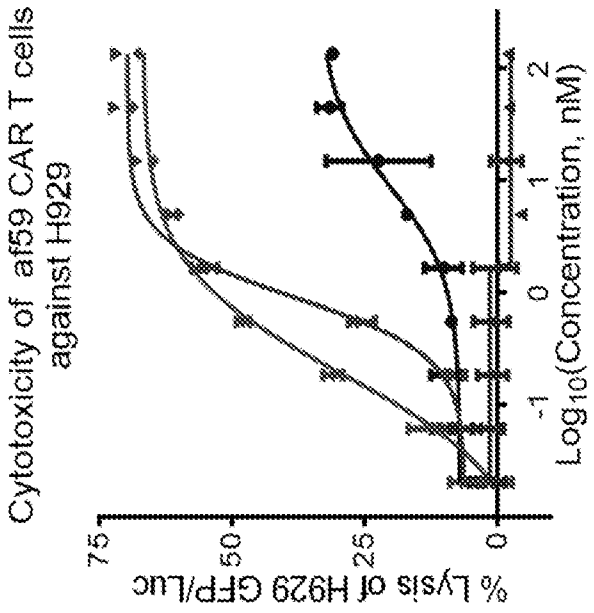


FIG. 11D

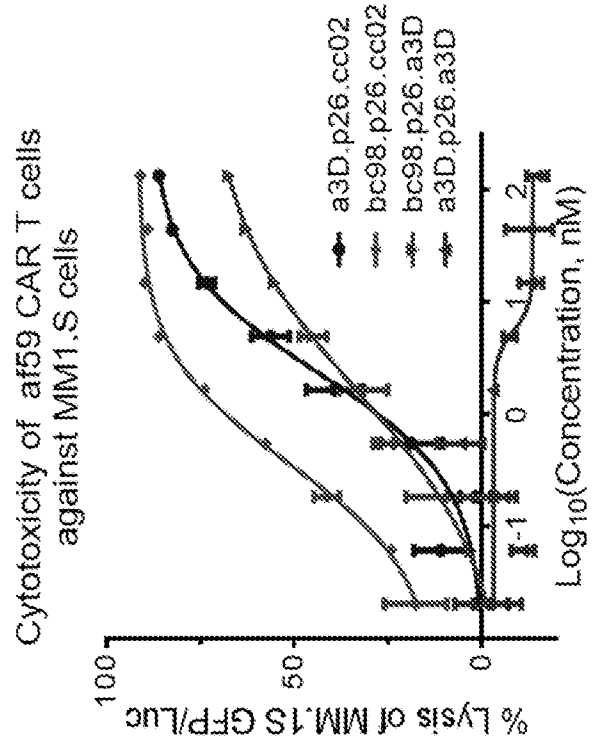
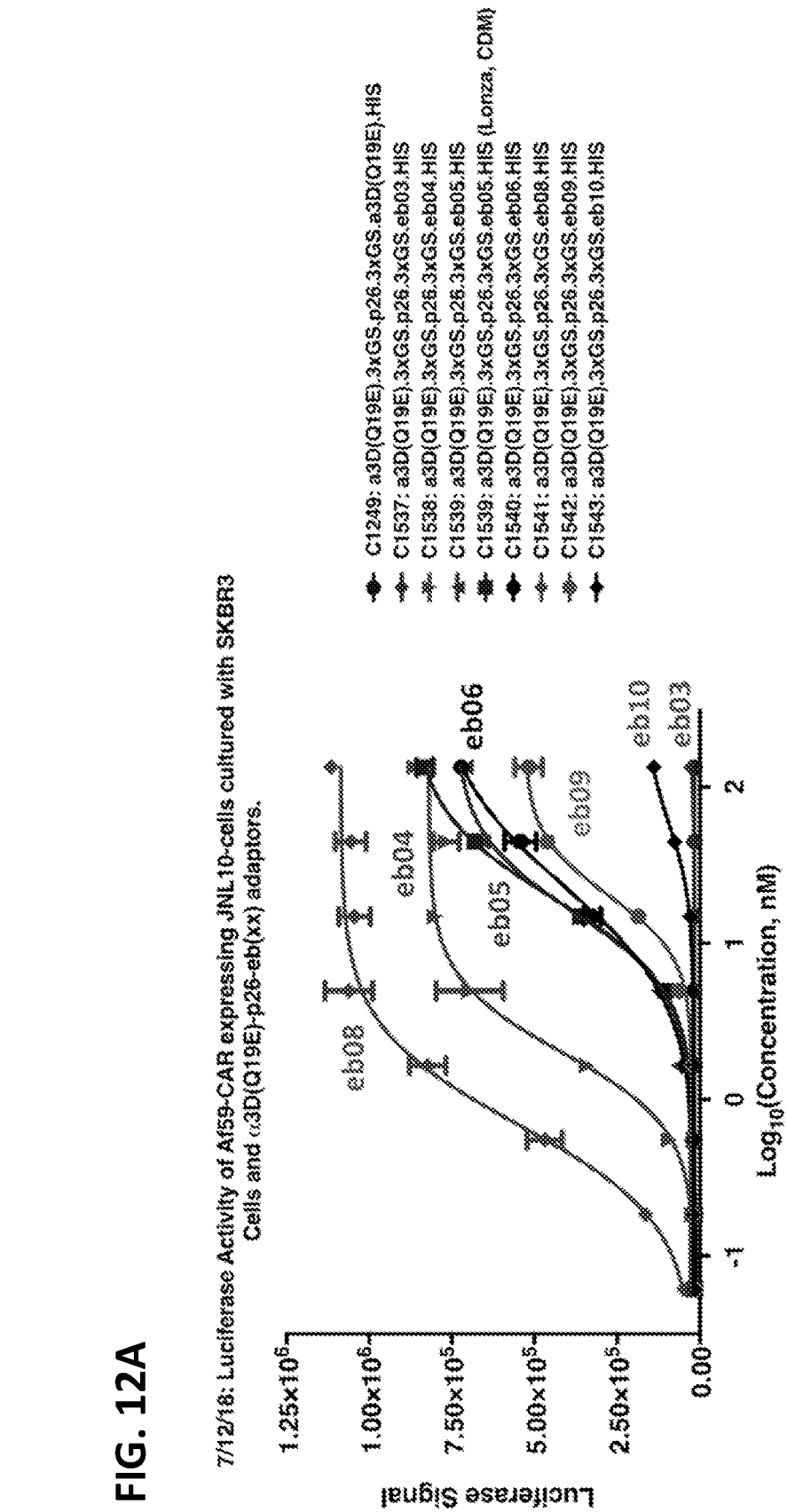


FIG. 12A


7/12/18: Luciferase Activity of A459-CAR expressing JNL10-cells cultured with SKBR3 Cells and α3D(Q19E)-p26-eb(xx) adaptors.
C1249: a3D(Q19E).3xGS.p26.3xGS.a3D(Q19E).HIS
C1537: a3D(Q19E).3xGS.p26.3xGS.eb03.HIS
C1538: a3D(Q19E).3xGS.p26.3xGS.eb04.HIS
C1539: a3D(Q19E).3xGS.p26.3xGS.eb05.HIS
C1539: a3D(Q19E).3xGS.p26.3xGS.eb05.HIS (Lonza, CDM)
C1540: a3D(Q19E).3xGS.p26.3xGS.eb06.HIS
C1541: a3D(Q19E).3xGS.p26.3xGS.eb08.HIS
C1542: a3D(Q19E).3xGS.p26.3xGS.eb09.HIS
C1543: a3D(Q19E).3xGS.p26.3xGS.eb10.HIS
Luciferase Signal
1.25x10^6
1.00x10^6
7.50x10^5
5.00x10^5
2.50x10^5
0.00
eb08
eb04
eb06
eb05
eb09
eb10
eb03
-1
0
1
2
Log10(Concentration, nM)

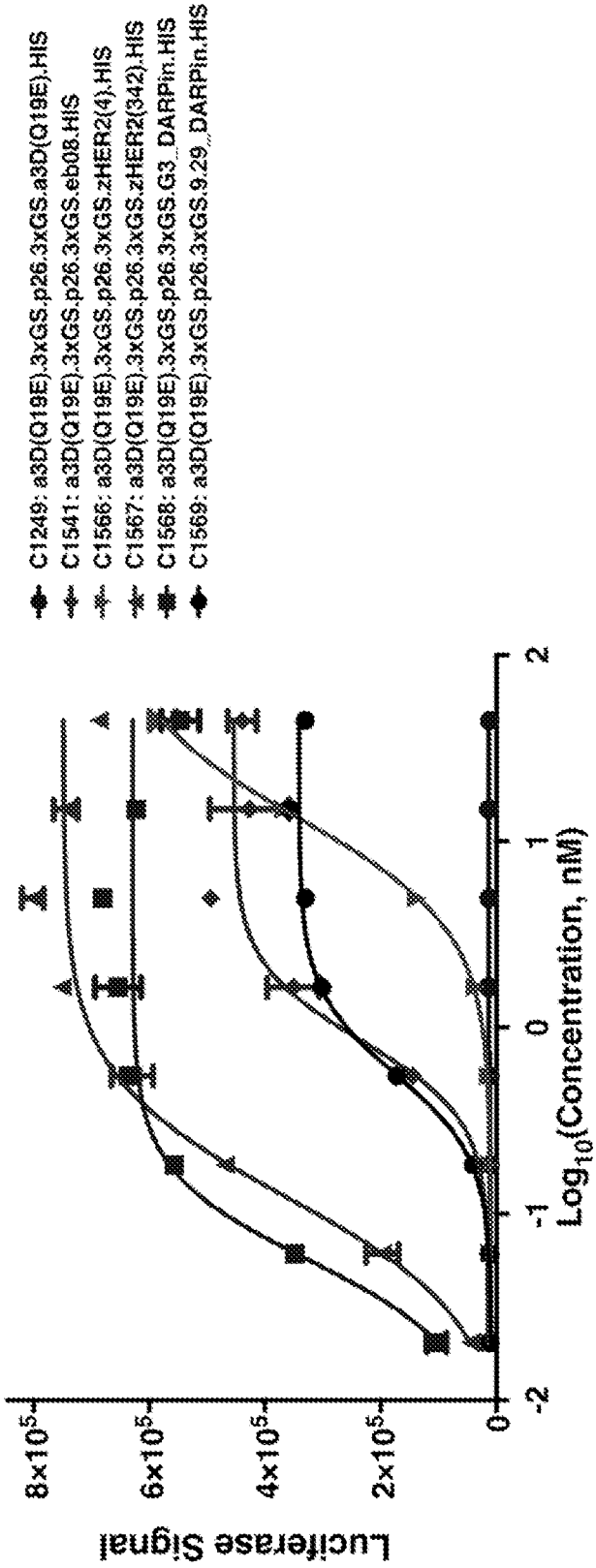
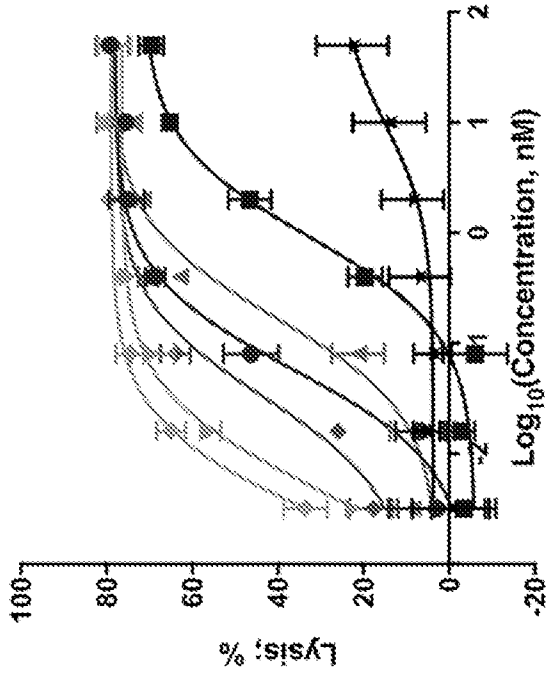

C1249: a3D(Q19E).3xGS.p26.3xGS.a3D(Q19E).HIS
C1541: a3D(Q19E).3xGS.p26.3xGS.eb08.HIS
C1566: a3D(Q19E).3xGS.p26.3xGS.zHER2(4).HIS
C1567: a3D(Q19E).3xGS.p26.3xGS.zHER2(342).HIS
C1568: a3D(Q19E).3xGS.p26.3xGS.G3_DARPin.HIS
C1569: a3D(Q19E).3xGS.p26.3xGS.9.29_DARPin.HIS
Luciferase Signal
8x10^5
6x10^5
4x10^5
2x10^5
0
-2
-1
0
1
2
Log10(Concentration, nM)

FIG. 12B

FIG. 12C


C1249: a3D(Q19E).3xGS.p26.3xGS.a3D(Q19E).HIS
C1541: a3D(Q19E).3xGS.p26.3xGS.eb08.HIS
C1566: a3D(Q19E).3xGS.p26.3xGS.zHER2(4).HIS
C1567: a3D(Q19E).3xGS.p26.3xGS.zHER2(342).HIS
C1568: a3D(Q19E).3xGS.p26.3xGS.G3_DARPin.HIS
C1569: a3D(Q19E).3xGS.p26.3xGS.9.29 DARPin.HIS
C1538: a3D(Q19E).3xGS.p26.3xGS.eb04.HIS
Lysis; %
100
80
60
40
20
0
-20
-2
-1
0
1
2
Log10(Concentration, nM)

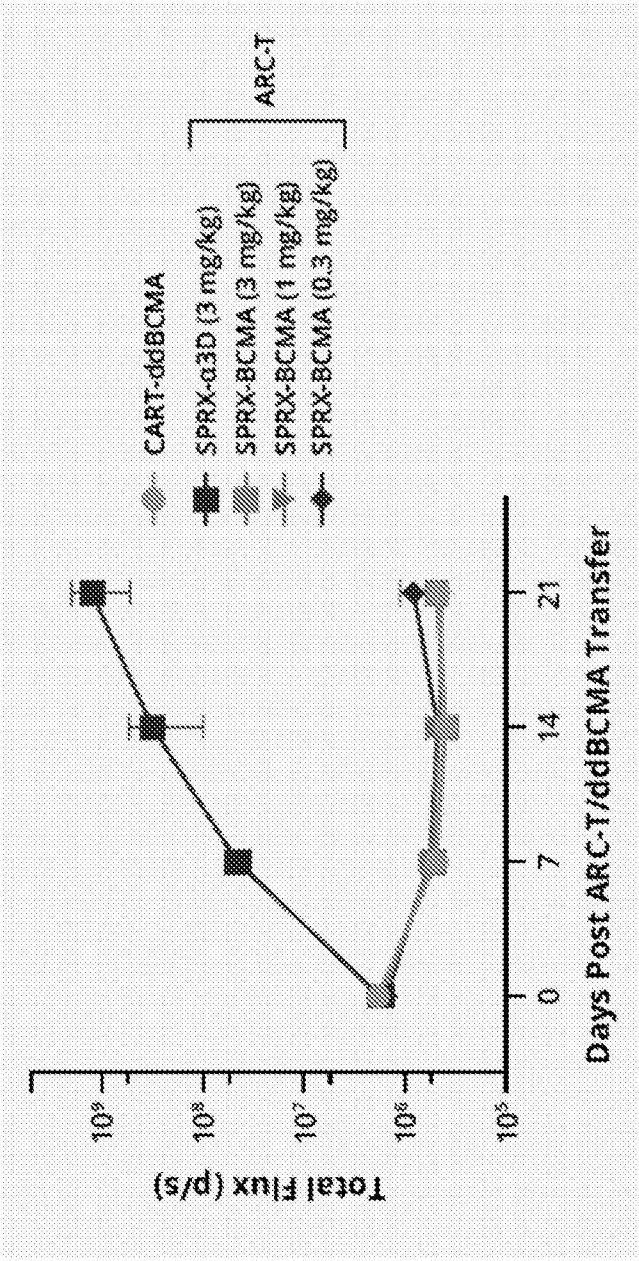

CART-ddBCMA
SPRX-a3D (3 mg/kg)
SPRX-BCMA (3 mg/kg)
SPRX-BCMA (1 mg/kg)
SPRX-BCMA (0.3 mg/kg)
ARC-T
Total Flux (p/s)
10^9
10^8
10^7
10^6
10^5
0
7
14
21
Days Post ARC-T/ddBCMA Transfer

FIG. 13

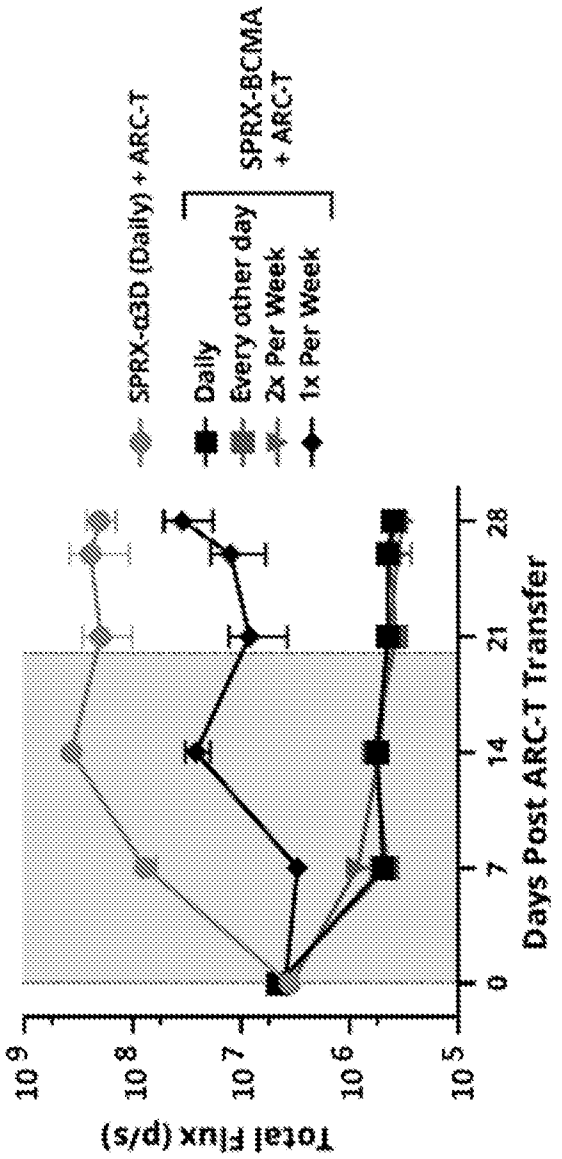
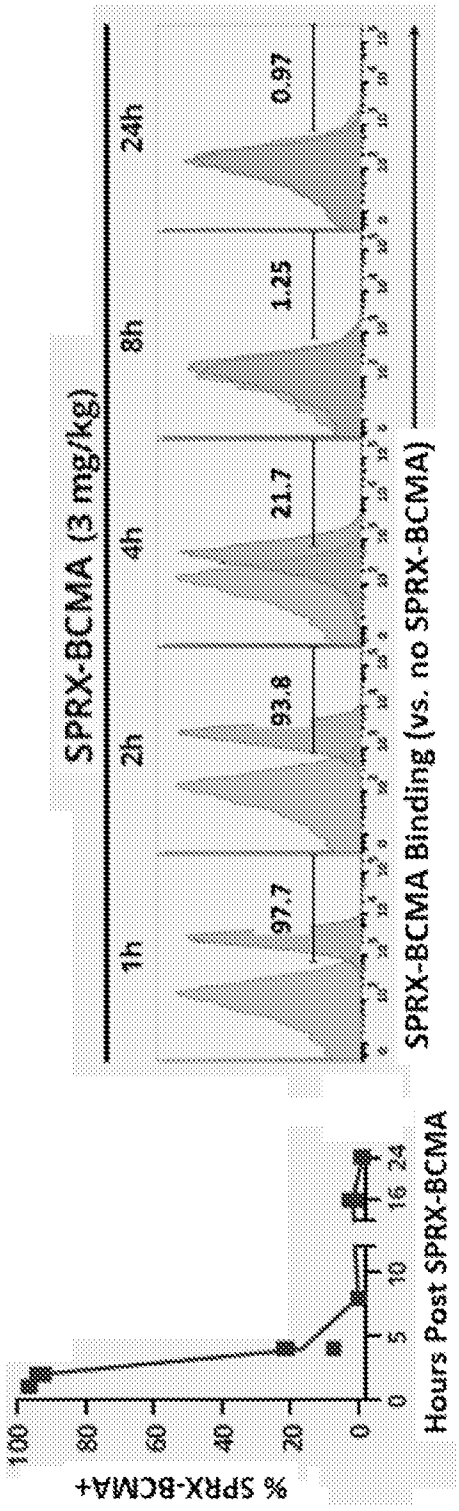

SPRX-α3D (Daily) + ARC-T
SPRX-BCMA + ARC-T
Daily
Every other day
2x Per Week
1x Per Week
Total Flux (p/s)
10 9
10 8
10 7
10 6
10 5
0
7
14
21
28
Days Post ARC-T Transfer

FIG. 14

FIG. 15


SPRX-BCMA (3 mg/kg)
1h
2h
4h
8h
24h
97.7
93.8
21.7
1.25
0.97
SPRX-BCMA Binding (vs. no SPRX-BCMA)
% SPRX-BCMA+
100
80
60
40
20
0
0
5
10
16
24
Hours Post SPRX-BCMA

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/21633

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 35/17, A61K 38/17, A61P 35/00 (2022.01)

CPC - A61K 35/17, A61K 38/00, A61P 35/00, A61K 2039/5156, C07K 2317/622, C07K 2319/03, C12N 2510/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/099440 A1 (ARCELLX, INC.) 23 May 2019 (23.05.2019) para [0073], [0169], [0178], [0278], [0494], [0538], [0541], [0579]; claims 1, 20, 22	1-7, 45-51
A	WO 2019/099433 A2 (ARCELLX, INC.) 23 May 2019 (23.05.2019); entire document	1-7, 45-51

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 May 2022	JUN 21 2022

Name and mailing address of the ISA/US	Authorized officer
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/21633

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. [X] forming part of the international application as filed:

      [X] in the form of an Annex C/ST.25 text file.

      [ ] on paper or in the form of an image file.

   b. [ ] furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. [ ] furnished subsequent to the international filing date for the purposes of international search only:

      [ ] in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      [ ] on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. [ ] In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/21633

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 8-44
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.