

for AML is hampered by the lack of suitable targets. Accordingly, there are needs for novel therapeutic strategies to design CARs targeting antigens that are highly expressed in AML cells and limited expression in normal tissues for treating AML, and for strategies capable of inducing potent cancer eradication with minimal toxicity and immunogenicity.

3. SUMMARY OF THE INVENTION

In one aspect, provided herein is an antigen-recognizing receptor, comprising an extracellular antigen-binding domain, a transmembrane domain, and an intracellular signaling domain, wherein the extracellular antigen-binding domain specifically binds to CD371.

In another aspect, provided herein is a cell comprising the antigen-recognizing receptor as described herein.

In another aspect, provided herein is a nucleic acid molecule encoding the antigen-recognizing receptor as described herein.

In another aspect, provided herein is a vector comprising the nucleic acid molecule as described herein.

In another aspect, provided herein is a host cell expressing the nucleic acid molecule as described herein.

In another aspect, provided herein is a composition comprising the cell as described herein.

In another aspect, provided herein is use of an effective amount of the cell as described herein or the composition as described herein in the manufacture of a medicament for reducing tumor burden in a subject, wherein an effective amount of the cell as described herein or the composition as described herein is to be administered to the subject.

In another aspect, provided herein is use of an effective amount of the cell as described herein or the composition as described herein in the manufacture of a medicament for increasing or lengthening survival of a subject having a tumor or neoplasm, wherein an effective amount of the cell as described herein or the composition as described herein is to be administered to the subject.

In another aspect, provided herein is use of an effective amount of the cell as described herein or the composition as described herein in the manufacture of a medicament for treating and/or preventing tumor or neoplasm in a subject, wherein an effective amount of the cell as described herein or the composition as described herein is to be administered to the subject.

In yet another aspect, provided herein is a method for producing a cell comprising an antigen-recognizing receptor as described herein, comprising introducing into the cell a nucleic acid molecule that encodes the antigen-recognizing receptor.

In yet another aspect, provided herein is a kit for reducing tumor burden in a subject, treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening survival of a subject having a tumor or neoplasm, comprising the cell as described herein.

In yet another aspect, provided herein is the cell as described herein or the composition as described herein for use in therapy.

The presently disclosed subject matter provides antigen-recognizing receptors that specifically target CD371 and cells comprising such CD371-targeted antigen-recognizing receptors. The presently disclosed subject matter further provides uses of the CD371-targeted antigen-recognizing receptors for treatment.

The presently disclosed subject matter provides an antigen-recognizing receptor, comprising an extracellular antigen-binding domain, a transmembrane domain, and an intracellular signaling domain, wherein the extracellular antigen-binding domain specifically binds to CD371. In certain embodimentexamples, the extracellular antigen-binding domain is a single-chain variable fragment (scFv). In certain embodimentexamples, the extracellular antigen-binding domain is a human scFv. In certain embodimentexamples, the extracellular antigen-binding domain is a Fab, which is optionally crosslinked. In certain embodimentexamples, the extracellular antigen-binding domain is a F(ab)₂. In certain embodimentexamples, one or more of the scFv, Fab and F(ab)₂ are comprised in a fusion protein with a heterologous sequence to form the extracellular antigen-binding domain.

In certain embodimentexamples, the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30 or a conservative modification thereof;

(b) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 34 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 35 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 36 or a conservative modification thereof;

(c) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 40 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 42 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 43 or a conservative modification thereof;

(d) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 462 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 47 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 48 or a conservative modification thereof;

(e) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 52 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 53 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 54 or a conservative modification thereof; or

(f) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 58 or a conservative modification thereof; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 59 or a conservative modification thereof; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 60 or a conservative modification thereof.

In certain ~~embodiment~~examples, the extracellular antigen-binding domain comprises: a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30.

In certain ~~embodiment~~examples, the extracellular antigen-binding domain comprises:

(a) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31 or a conservative modification thereof; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32 or a

conservative modification thereof; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33 or a conservative modification thereof;

(b) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 37 or a conservative modification thereof; a light chain variable region CDR2
5 comprising the amino acid sequence set forth in SEQ ID NO: 38 or a conservative modification thereof; and a light chain variable region CDR3 comprising SEQ ID NO: 39 or a conservative modification thereof;

(c) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 43 or a conservative modification thereof; a light chain variable region CDR2
10 comprising the amino acid sequence set forth in SEQ ID NO: 44 or a conservative modification thereof; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 45 or a conservative modification thereof;

(d) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 49 or a conservative modification thereof; a light chain variable region CDR2
15 comprising SEQ ID NO: 50 or a conservative modification thereof; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 51 or a conservative modification thereof;

(e) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 55 or a conservative modification thereof; a light chain variable region CDR2
20 comprising the amino acid sequence set forth in SEQ ID NO: 56 or a conservative modification thereof; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 57 or a conservative modification thereof; or

(f) a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 61 or a conservative modification thereof; a light chain variable region CDR2
25 comprising the amino acid sequence set forth in SEQ ID NO: 62 or a conservative modification thereof; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 63 or a conservative modification thereof.

In certain ~~embodiment~~examples, the extracellular antigen-binding domain comprises: a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID
30 NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; and a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30.

In certain embodiment examples, the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33;

(b) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 34; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 35; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 36; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 37; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 38; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 39;

(c) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 40; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 41; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 42; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 43; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 44; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 45;

(d) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 46; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 47; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 48; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 49; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 50; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 51;

(e) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 52; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 53; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 54; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 55; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 56; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 57; or

(f) a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 58; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 59; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 60; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 61; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 62; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 63.

In certain embodiment examples, the extracellular antigen-binding domain comprises: a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33.

In certain embodiment examples, the extracellular antigen-binding domain comprises a heavy chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, or SEQ ID NO: 11. In certain embodiment examples, the extracellular antigen-binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7,

SEQ ID NO: 9, or SEQ ID NO: 11. In certain embodimentexamples, the extracellular antigen-binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1.

In certain embodimentexamples, the extracellular antigen-binding domain comprises a light chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID

NO: 10, or SEQ ID NO: 12. In certain embodimentexamples, the extracellular antigen-binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, or SEQ ID NO: 12. In certain embodimentexamples, the extracellular antigen-binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.

In certain embodimentexamples, the extracellular antigen-binding domain comprises: (a) a heavy chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, or SEQ ID NO: 11; and (b) a light chain variable region comprising an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous or identical to the amino acid sequence set forth in in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, or SEQ ID NO: 12. In certain

embodimentexamples, the extracellular antigen-binding domain comprises: (a) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, or SEQ ID NO: 11; and (b) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, or SEQ ID NO: 12.

- In certain embodimentexamples, the extracellular antigen-binding domain comprises:
- (a) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2;
 - 5 (b) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 3, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 4;
 - (c) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 6;
 - 10 (d) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 7, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 8;
 - (e) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 10; or
 - 15 (f) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 11, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 12.
- 20 In certain embodimentexamples, the extracellular antigen-binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1; and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.
- In certain embodimentexamples, the extracellular antigen-binding domain comprises
- 25 a linker between a heavy chain variable region and a light chain variable region of the extracellular antigen-binding domain. In certain embodimentexamples, the linker has the amino acid sequence set forth in SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, or SEQ ID NO: 94. In certain embodimentexamples, the linker has the amino acid sequence set forth in SEQ ID NO: 13 or SEQ ID NO: 14.
- 30 In certain embodimentexamples, the extracellular antigen-binding domain comprises a signal peptide that is covalently joined to the 5' terminus of the extracellular antigen-binding domain. In certain embodimentexamples, the extracellular antigen-binding domain

comprises a heavy chain variable region and a light chain variable region, which are positioned from the N- to the C-terminus: V_H-V_L.

In certain [embodimentexamples](#), the extracellular antigen-binding domain binds to CD371 with a low binding affinity. In certain [embodimentexamples](#), the extracellular antigen-binding domain binds to CD371 with a dissociation constant (K_d) of 1 × 10⁻⁸ M or more.

In certain [embodimentexamples](#), the transmembrane domain comprises a CD28 polypeptide. In certain [embodimentexamples](#), the intracellular signaling domain comprises a CD3ζ polypeptide. In certain [embodimentexamples](#), the intracellular signaling domain further comprises at least one co-stimulatory signaling region. In certain [embodimentexamples](#), the at least one co-stimulatory signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, or a combination thereof. In certain [embodimentexamples](#), the at least one co-stimulatory signaling region comprises a CD28 polypeptide or a 4-1BB polypeptide.

In certain [embodimentexamples](#), the antigen-recognizing receptor is a chimeric antigen receptor (CAR), a T-cell Receptor (TCR), or a T-cell like fusion protein. In certain [embodimentexamples](#), the antigen-recognizing receptor is a CAR.

In certain [embodimentexamples](#), the antigen-recognizing receptor is recombinantly expressed. In certain [embodimentexamples](#), the antigen-recognizing receptor is expressed from a vector. In certain [embodimentexamples](#), the vector is a γ-retroviral vector.

The presently disclosed subject matter provides cells comprising a presently disclosed antigen-recognizing receptor. In certain [embodimentexamples](#), the cell is transduced with the antigen-recognizing receptor. In certain [embodimentexamples](#), the antigen-recognizing receptor is constitutively expressed on the surface of the cell.

In certain [embodimentexamples](#), the cell is engineered to express a cytokine or a fragment thereof. In certain [embodimentexamples](#), the cell further comprises an exogenous polypeptide of the cytokine or fragment thereof. In certain [embodimentexamples](#), the cell further comprises a nucleic acid molecule encoding the cytokine or fragment thereof. In certain [embodimentexamples](#), the cytokine is selected from the group consisting of IL-18, IL-33, IL-36, and combinations thereof. In certain [embodimentexamples](#), the cytokine is IL-18.

In certain [embodimentexamples](#), the cell is an immunoresponsive cell. In certain [embodimentexamples](#), the cell is a cell of the lymphoid lineage or a cell of the myeloid lineage. In certain [embodimentexamples](#), the cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, and a stem cell from which lymphoid cells may be

differentiated. In certain embodimentexamples, the cell is a T cell. In certain embodimentexamples, the T cell is a cytotoxic T lymphocyte (CTL) or a regulatory T cell. In certain embodimentexamples, the stem cell is a pluripotent stem cell. In certain embodimentexamples, the pluripotent stem cell is an embryoid stem cell or an induced pluripotent stem cell.

The presently disclosed subject matter further provides nucleic acid molecules that encode a presently disclosed antigen-recognizing receptor. In certain embodimentexamples, the nucleic acid molecule comprises the nucleotide sequence set forth in SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, or SEQ ID NO: 27. In certain embodimentexamples, the nucleic acid molecule comprises the nucleotide sequence set forth in SEQ ID NO: 22. The presently disclosed subject matter further provides vectors comprising the presently disclosed nucleic acid molecules. In certain embodimentexamples, the vector is a viral vector. In certain embodimentexamples, the vector is a γ -retroviral vector.

In addition, the presently disclosed subject matter provides host cells expressing the nucleic acid molecule disclosed herein. In certain embodimentexamples, the host cell is a T cell.

The presently disclosed subject matter further provides compositions comprising the cells disclosed herein. In certain embodimentexamples, the composition is a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

The presently disclosed subject matter further provides methods of reducing tumor burden in a subject. In certain embodimentexamples, the method comprises administering an effective amount of presently disclosed cells or composition to the subject. In certain embodimentexamples, the method reduces the number of tumor cells, reduces tumor size, and/or eradicates the tumor in the subject. The presently disclosed subject matter further provides methods of increasing or lengthening survival of a subject having a tumor or neoplasm. In certain embodimentexamples, the method comprises administering an effective amount of presently disclosed cells or composition to the subject. The presently disclosed subject matter further provides methods of treating and/or preventing a tumor or neoplasm in a subject. In certain embodimentexamples, the method comprises administering to the subject an effective amount of the presently disclosed cells or composition. In certain embodimentexamples, the tumor or neoplasm is selected from the group consisting of acute myeloid leukemia (AML), multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, myelodysplastic

syndrome (MDS), and chronic myelogenous leukemia (CML). In certain embodimentexamples, the tumor or neoplasm is acute myeloid leukemia (AML).

The presently disclosed subject matter further provides methods for producing a presently disclosed cell comprising a CD371-targeted antigen-recognizing receptor. In certain embodimentexamples, the method comprises introducing into the cell a nucleic acid molecule that encodes the antigen-recognizing receptor.

In addition, the presently disclosed subject matter provides kits for reducing tumor burden in a subject, treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening survival of a subject having a tumor or neoplasm. In certain embodimentexamples, the kit comprises the cell described herein. In certain embodimentexamples, the kit further comprises written instructions for using the cell for reducing tumor burden in a subject, treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening survival of a subject having a tumor or neoplasm.

4. BRIEF DESCRIPTION OF THE FIGURES

The following Detailed Description, given by way of example, but not intended to limit the invention to specific embodiments described, may be understood in conjunction with the accompanying drawings.

Figure 1 depicts structures of antigen-recognizing receptors in accordance with the presently disclosed subject matter.

Figure 2 depicts detection of CD371-targeted CAR on the surface of transduced human T cells. Antibodies against EGFRt (CETUXIMAB-APC) and Myc-tag (9B11-PE) detected surface expression of EGFRt and human anti-human CAR in B10-based CAR constructs. Controls included non-transduced human T cells which did not express EGFRt or MYC-tag, and non-MYC tag containing CAR constructs Etah19h28z (an anti-human CD19 CAR T cells) and EtC1HVh28z (anti-CD371 CAR T cells derived from a mouse anti-human CD371 antibody 107537).

Figure 3 depicts tumor cell lysis activities of CD371-targeted CAR T cells. 4 day rested (4dR) human CD371-targeted CAR T cells were cocultured with CD33⁺/CD371⁺ U937 cells expressing GFP and firefly luciferase (U937gL) at different effector:tumor (E:T) ratios. Bioluminescence was measured 24 hours later and plotted as a percentage of signal detected in a coculture of a non-functional CAR T cells (based on B10L4H, but without a CD28 or CD3 zeta signaling domain) and U937gL. Et.C1HVh28z represents a CD371-targeted CAR derived from a mouse anti-human CD371 antibody 1075.7, and