

WHAT IS CLAIMED IS:

1. 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.
2. The antigen-recognizing receptor of claim 1, wherein the extracellular antigen-binding domain is a single-chain variable fragment (scFv).
3. The antigen-recognizing receptor of claim 2, wherein the extracellular antigen-binding domain is a human scFv.
4. The antigen-recognizing receptor of claim 1, wherein the extracellular antigen-binding domain is a Fab, which is optionally crosslinked.
5. The antigen-recognizing receptor of claim 1, wherein the extracellular antigen-binding domain is a F(ab)₂.
6. The antigen-recognizing receptor of any one of claims 2-5, wherein 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.
7. The antigen-recognizing receptor of any one of claims 1-6, wherein 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;

8. The antigen-recognizing receptor of any one of claims 1-7, wherein 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.

9. The antigen-recognizing receptor of any one of claims 1-8, wherein 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 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 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 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 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 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;

10. The antigen-recognizing receptor of any one of claims 1-9, wherein the extracellular antigen-binding domain comprises: 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.

11. The antigen-recognizing receptor of any one of claims 1-10, wherein 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.

12. The antigen-recognizing receptor of any one of claims 1-11, wherein 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.

13. The antigen-recognizing receptor of any one of claims 1-12, wherein 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.

14. The antigen-recognizing receptor of any one of claims 1-13, wherein 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.

15. The antigen-recognizing receptor of any one of claims 1-14, wherein the extracellular antigen-binding domain comprises a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO: 1.

16. The antigen-recognizing receptor of any one of claims 1-15, wherein 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.

17. The antigen-recognizing receptor of any one of claims 1-16, wherein 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.

18. The antigen-recognizing receptor of any one of claims 1-17, wherein the extracellular antigen-binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.

19. The antigen-recognizing receptor of any one of claims 1-18, wherein 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 selected 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 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.

20. The antigen-recognizing receptor of any one of claims 1-19, wherein 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.

21. The antigen-recognizing receptor of claim 14, wherein 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;

(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;

(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

(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.

22. The antigen-recognizing receptor of any one of claims 1-21, wherein 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.

23. The antigen-recognizing receptor of any one of claims 1-22, wherein the extracellular antigen-binding domain comprises a linker between a heavy chain variable region and a light chain variable region of the extracellular antigen-binding domain.

24. The antigen-recognizing receptor of claim 23, wherein 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.

25. The antigen-recognizing receptor of claim 23, wherein the linker has the amino acid sequence set forth in SEQ ID NO: 13 or SEQ ID NO: 14.

26. The antigen-recognizing receptor of any one of claims 1-25, wherein the extracellular antigen-binding domain comprises a signal peptide that is covalently joined to the 5' terminus of the extracellular antigen-binding domain.

27. The antigen-recognizing receptor of any one of claims 1-26, wherein 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.

28. The antigen-recognizing receptor of any one of claims 1-26, wherein the extracellular antigen-binding domain binds to CD371 with a low binding affinity.

29. The antigen-recognizing receptor of any one of claims 1-26, wherein the extracellular antigen-binding domain binds to CD371 with a dissociation constant (K_d) of 1×10^{-8} M or more.
30. The antigen-recognizing receptor of any one of claims 1-29, wherein the transmembrane domain comprises a CD8 polypeptide, a CD28 polypeptide, a CD3 ζ polypeptide, a CD4 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a CTLA-4 polypeptide, a PD-1 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, or a combination thereof.
31. The antigen-recognizing receptor of claim 30, wherein the transmembrane domain comprises a CD28 polypeptide.
32. The antigen-recognizing receptor of any one of claims 1-31, wherein the intracellular signaling domain comprises a CD3 ζ polypeptide.
33. The antigen-recognizing receptor of any one of claims 1-32, wherein the intracellular signaling domain further comprises at least one co-stimulatory signaling region.
34. The antigen-recognizing receptor of claim 33, wherein 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.
35. The antigen-recognizing receptor of claim 33 or 34, wherein the at least one co-stimulatory signaling region comprises a CD28 polypeptide or a 4-1BB polypeptide.
36. The antigen-recognizing receptor of any one of claims 1-35, wherein the antigen-recognizing receptor is a chimeric antigen receptor (CAR), a T-cell Receptor (TCR), or a T-cell like fusion protein.
37. The antigen-recognizing receptor of any one of claims 1-36, wherein the antigen-recognizing receptor is a CAR.
38. The antigen-recognizing receptor of any one of claims 1-37, wherein the antigen-recognizing receptor is recombinantly expressed.

39. The antigen-recognizing receptor of any one of claims 1-38, wherein the antigen-recognizing receptor is expressed from a vector.
40. The antigen-recognizing receptor of claim 39, wherein the vector is a γ -retroviral vector.
41. A cell comprising the antigen-recognizing receptor of any one of claims 1-40.
42. The cell of claim 41, wherein the cell is transduced with the antigen-recognizing receptor.
43. The cell of claim 41 or 42, wherein the antigen-recognizing receptor is constitutively expressed on the surface of the cell.
44. The cell of any one of claims 41-43, wherein the cell is engineered to express a cytokine or a fragment thereof.
45. The cell of claim 44, wherein the cell comprises an exogenous polypeptide of the cytokine or fragment thereof.
46. The cell of claim 44 or 45, wherein the cell comprises a nucleic acid molecule encoding the cytokine or fragment thereof.
47. The cell of any one of claims 44-46, wherein the cytokine is selected from the group consisting of IL-18, IL-33, IL-36, and combinations thereof.
48. The cell of any one of claims 44-47, wherein the cytokine is IL-18.
49. The cell of any one of claims 41-48, wherein the cell is an immunoresponsive cell.
50. The cell of any one of claims 41-49, wherein the cell is a cell of the lymphoid lineage or a cell of the myeloid lineage.
51. The cell of any one of claims 41-50, wherein 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.
52. The cell of any one of claims 41-51, wherein the cell is a T cell.

53. The cell of claim 51 or 52, wherein the T cell is a cytotoxic T lymphocyte (CTL) or a regulatory T cell.
54. The cell of claim 53, wherein the stem cell is a pluripotent stem cell.
55. The cell of claim 54, wherein the pluripotent stem cell is an embryoid stem cell or an induced pluripotent stem cell.
56. A nucleic acid molecule encoding the antigen-recognizing receptor of any one of claims 1-40.
57. The nucleic acid molecule of claim 56, wherein 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.
58. The nucleic acid molecule of claim 56 or 57, wherein the nucleic acid molecule comprises the nucleotide sequence set forth in SEQ ID NO: 22.
59. A vector comprising the nucleic acid molecule of any one of claims 56-58.
60. The vector of claim 59, wherein the vector is a γ -retroviral vector.
61. A host cell expressing the nucleic acid molecule of any one of claims 56-58.
62. The host cell of claim 61, wherein the host cell is a T cell.
63. A composition comprising the cell of any one of claims 41-55.
64. The composition of claim 63, which is a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.
65. A method of reducing tumor burden in a subject, comprising administering an effective amount of the cell of any one of claims 41-55 or the composition of claim 63 or 64 to the subject.
66. The method of claim 65, wherein the method reduces the number of tumor cells, reduces tumor size, and/or eradicates the tumor in the subject

67. A method of increasing or lengthening survival of a subject having a tumor or neoplasm, comprising administering an effective amount of the cell of any one of claims 41-55 or the composition of claim 63 or 64.

68. A method of treating and/or preventing a tumor or neoplasm in a subject, comprising administering an effective amount of the cell of any one of claims 41-55 or the composition of claim 63 or 64.

69. The method of any one of claims 65-68, wherein the tumor or neoplasm is selected from the group consisting of acute myeloid leukemia (AML), multiple myeloma, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, myelodysplastic syndrome (MDS), and chronic myelogenous leukemia (CML).

70. The method of any one of claims 65-69, wherein the tumor or neoplasm is acute myeloid leukemia (AML).

71. A method for producing a cell comprising an antigen-recognizing receptor of any one of claims 1-40, comprising introducing into the cell a nucleic acid molecule that encodes the antigen-recognizing receptor.

72. 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 of any one of claims 41-55.

73. The kit of claim 72, wherein 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.