# CLAIMS

What is claimed is:

1. An expression construct comprising sequence that encodes a CD5-specific engineered receptor, wherein said receptor comprises CD28 transmembrane domain (TM) and CD28 intracytoplasmic domain (ICD).

2. The expression construct of claim 1, wherein the CD5-specific engineered receptor is a chimeric antigen receptor (CAR) or a T cell receptor.

3. The expression construct, wherein the CD5-specific engineered receptor is a CAR.

4. The expression construct of claim 3, wherein the CAR comprises a CD-targeting extracellular domain that is an scFv or a ligand for CD5.

5. The expression construct of claim 4, wherein the CD5-specific CAR comprises a scFv having a heavy chain and a light chain, and wherein the heavy chain in the sequence that encodes the CAR is upstream of the light chain in a 5′ to 3′ direction.

6. The expression construct of claim 4, wherein the CD5-specific CAR comprises a scFv having a heavy chain and a light chain, and wherein the heavy chain in the sequence that encodes the CAR is downstream of the light chain in a 5′ to 3′ direction.

7. The expression construct of any one of claims 4-6, wherein the CD5-specific CAR comprises a codon optimized scFv.

8. The expression construct of any one of claims 4-6, wherein the CD5-specific CAR comprises a humanized scFv.

9. The expression construct of any one of claims 4-6 or 8, wherein the scFv is encoded by SEQ ID NO:1.

10. The expression construct of any one of claims 4-6 or 8, wherein the scFv comprises SEQ ID NO:2.

11. The expression construct of any one of claims 4-6, wherein the scFv is encoded by SEQ ID NO:3.

12. The expression construct of any one of claims 4-6, wherein the scFv comprises SEQ ID NO:4.

13. The expression construct of any one of claims 3-12, wherein the CD5-specific CAR comprises a signaling peptide.

14. The expression construct of claim 13, wherein the signaling peptide is from CD8alpha, Ig heavy chain, granulocyte-macrophage colony-stimulating factor receptor, CD3 signaling peptide, CD4 signaling peptide, or a signal peptide derived from one or more other surface receptors.

15. The expression construct of any one of claims 1-14, wherein the TM is encoded by SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ:11 or SEQ ID NO:13.

16. The expression construct of any one of claims 1-14, wherein the TM comprises SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ:12 or SEQ ID NO:14.

17. The expression construct of any one of claims 1-16, wherein the ICD is encoded by SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21.

18. The expression construct of any one of claims 1-16, wherein the ICD comprises SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, or SEQ ID NO:22.

19. The expression construct of any one of claims 1-18, wherein the receptor further comprises an ICD from CD27, OX-40 (CD134), CD40L, 2B4, DNAM, CS1, CD48, NKp30, NKp44, NKp46, NKp80, ICOS, or a combination thereof.

20. The expression construct of any one of claims 1-19, wherein the CD5-specific engineered receptor is a CD5-specific CAR that comprises a hinge between a CD5-specific scFv and the transmembrane domain.

21. The expression construct of claim 20, wherein the hinge is an IgG hinge, a CD28 hinge, a CD8-alpha hinge, the hinge comprises an artificial spacer comprised of Gly3, or the hinge comprises CH1, CH2, and/or CH3 domains of IgGs.

22. The expression construct of claim 21, wherein the IgG hinge is IgG1 hinge, IgG2 hinge, IgG3 hinge, or IgG4 hinge.

23. The expression construct of claim 21, wherein the hinge is encoded by SEQ ID NO:23 or 25.

24. The expression construct of claim 21, wherein the hinge comprises SEQ ID NO:24 or SEQ ID NO:26.

25. The expression construct of any one of claims 1-24, wherein the cytokine is IL-15, IL-12, IL-2, IL-18, IL-21, IL-7, IL-23, or a combination thereof.

26. The expression construct of any one of claims 1-25, wherein the CD5-specific engineered receptor is a CAR encoded by SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47.

27. The expression construct of any one of claims 1-25, wherein the CD5-specific engineered receptor is a CAR comprising SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48.

28. The expression construct of any one of claims 1-27, wherein the expression construct encodes a polypeptide of interest other than the CD5-specific engineered receptor.

29. The expression construct of claim 28, wherein the polypeptide of interest and the CD-specific engineered receptor are separated on the construct by a 2A element or an IRES element.

30. The expression construct of claim 29, wherein the 2A element is E2A, T2A, or P2A.

31. The expression construct of claim 30, wherein the E2A element is encoded by SEQ ID NO:31.

32. The expression construct of claim 30, wherein the E2A element comprises SEQ ID NO:32.

33. The expression construct of any one of claims 28-32, wherein the polypeptide of interest is a therapeutic protein or a protein that enhances cell activity, expansion, and/or persistence of cells comprising the protein.

34. The expression construct of any one of claims 28-33, wherein the polypeptide of interest is a suicide gene; cytokine; human or viral protein that enhances proliferation, expansion and/or metabolic fitness of cells comprising the protein; or a combination thereof.

35. The expression construct of claim 34, wherein the suicide gene is a nonsecretable mutant TNF-alpha, inducible caspase 9, HSV-thymidine kinase, CD19, CD20, CD52, or EGFRv3.

36. The expression construct of claim 34 or 35, wherein the cytokine is IL-15, IL-2, IL-12, IL-18, IL-21, IL-23, IL-7, or a combination thereof.

37. The expression construct of claim 36, wherein the IL-15 is encoded by SEQ ID NO:29.

38. The expression construct of claim 36, wherein the IL-15 comprises SEQ ID NO:30.

39. A vector, comprising the expression construct of any one of claims 1-38.

40. The vector of claim 39, wherein the vector is a viral vector or a non-viral vector.

41. The vector of claim 40, wherein the viral vector is an adenoviral vector, adeno-associated viral vector, lentiviral vector, or retroviral vector.

42. The vector of claim 40, wherein the non-viral vector is a plasmid, liposome, nanoparticle, lipid, carbohydrate, or combination thereof.

43. An immune cell, comprising the expression construct of any one of claims 1-38 or the vector of any one of claims 39-42.

44. The immune cell of claim 43, wherein the immune cell is a natural killer (NK) cell, T cell, gamma delta T cells, invariant NKT (iNKT) cell, B cell, macrophage, MSCs, or dendritic cell.

45. The immune cell of claim 43 or 44, wherein the immune cell is an NK cell.

46. The immune cell of claim 44 or 45, wherein the NK cell is derived from cord blood, peripheral blood, induced pluripotent stem cells, human embryonic stem cells, bone marrow, or from a cell line.

47. The immune cell of claim 46, wherein the NK cell line is NK-92 cell line or another NK cell line derived from a tumor or from a healthy NK cell or a progenitor cell.

48. The immune cell of any one of claims 44-47, wherein the NK cell is derived from a cord blood mononuclear cell.

49. The immune cell of any one of claims 44-48, wherein the NK cell is a CD56+ NK cell.

50. The immune cell of any one of claims 43-49, wherein the NK cells express one or more exogenously provided cytokines.

51. The immune cell of claim 50, wherein the cytokine is IL-15, IL-2, IL-12, IL-18, IL-21, IL-7, IL-23, or a combination thereof.

52. The immune cell of any one of claims 43-51, wherein expression of one or more endogenous genes in the immune cell has been modified.

53. The immune cell of claim 52, wherein the expression has been partially or fully reduced in expression.

54. The immune cell of claim 52 or 53, wherein expression of the one or more gene has been modified using CRISPR or TALEN.

55. The immune cell of any one of claims 52-54, wherein the gene is selected from the group consisting of NKG2A, SIGLEC-7, LAG3, TIM3, CISH, FOXO1, TGFBR2, TIGIT, CD96, ADORA2, NR3C1, PD1, PDL-1, PDL-2, CD47, SIRPA, SHIP1, ADAM17, RPS6, 4EBP1, CD25, CD40, IL21R, ICAM1, CD95, CD80, CD86, IL10R, CD5, CD7, CTLA-4, TDAG8, CD38, CREM, and a combination thereof.

56. A population of immune cells of any one of claims 43-55, said cells present in a suitable medium.

57. The population of claim 56, wherein said population is housed in a storage facility.

58. The population of claim 56 or 57, wherein said population is frozen.

59. The population of any one of claims 56-58, wherein said medium comprises a cryoprotectant with one or more cytokines or a cryoprotectant without one or more cytokines.

60. The population of any one of claims 56-59, wherein the immune cells are NK cells.

61. The population of any one of claims 56-60, wherein the immune cells are NK cells that comprise an expression construct that encodes a CAR and a cytokine.

62. The population of any one of claims 56-61, wherein the immune cells are NK cells that comprise an expression construct that encodes a CAR and IL-15.

63. The population of claim 61 or 62, wherein the CAR and IL-15 are encoded by SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47.

64. The population of claim 61 or 62, wherein the CAR and IL-15 are comprised in SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48.

65. Use of cells harboring the expression construct of any one of claims 1-38 in the manufacture of a medicament for killing CD5-positive cells in an individual, wherein an effective amount of cells harboring the expression construct of any one of claims 1-38 is to be administered to the individual.

66. The use of claim 65, wherein the cells are immune cells.

67. The use of claim 66, wherein the immune cells are NK cells, T cells, gamma delta T cells, invariant NKT (iNKT) cells, B cells, macrophages, dendritic cells, or a mixture thereof.

68. The use of claim 67, wherein the NK cells are derived from cord blood, peripheral blood, induced pluripotent stem cells, human embryonic stem cells, bone marrow, from a cell line, or a mixture thereof.

69. The use of any one of claims 67-68, wherein the NK cells are derived from cord blood mononuclear cells.

70. The use of any one of claims 34-37, wherein the individual has cancer.

71. The use of claim 70, wherein the cancer is of a solid tumor.

72. The use of claim 70, wherein the cancer is a hematological cancer.

73. The use of any one of claims 65-72, wherein the cells are allogeneic with respect to the individual.

74. The use of any one of claims 65-72, wherein the cells are autologous with respect to the individual.

75. The use of any one of claims 65-74, wherein the individual is a human.

76. The use of any one of claims 65-75, wherein the cells are to be administered to the individual once or more than once.

77. The use of claim 76, wherein the duration of time between administrations of the cells to the individual is 1-24 hours, 1-7 days, 1-4 weeks, 1-12 months, or one or more years.

78. The use of any one of claims 65-77, wherein an effective amount of an additional therapy is to be further provided to the individual.

79. The use of claim 78, wherein the additional therapy comprises surgery, radiation, gene therapy, immunotherapy, or hormone therapy.

80. The use of claim 78 or 79, wherein the additional therapy comprises one or more antibodies.

81. The use of any one of claims 65-80, wherein the cells are to be administered to the individual by injection, intravenously, intraarterially, intraperitoneally, intrapleurally, intratracheally, intratumorally, intramuscularly, endoscopically, intralesionally, intracranially, intrathecally, percutaneously, subcutaneously, regionally, by perfusion, in a tumor microenvironment, or a combination thereof.

82. The use of any one of claims 65-81, further comprising the step of identifying CD5-positive cancer in the individual.

83. The use of any one of claims 65-82, further comprising the step of producing the cells harboring the expression construct.

84. Use of cells harboring the expression construct of any one of claims 1-38 in the manufacture of a medicament for preventing cancer or preventing metastasis of cancer in an individual, wherein a therapeutically effective amount of cells harboring the expression construct of any one of claims 1-38 is to be administered to the individual.

85. The use of claim 84, wherein the individual is at risk for cancer or has previously had cancer.

86. The use of claim 84 or 85, wherein the therapeutically effective amount of cells harboring the expression construct of any one of claims 1-38 is to be administered to the individual once.

87. The use of claim 84 or 85, wherein the therapeutically effective amount of cells harboring the expression construct of any one of claims 1-38 is to be administered to the individual more than once.

88. The cells harboring the expression construct of any one of claims 1-38 for use in therapy.