CLAIMS

What is claimed is:

1. A recombinant chimeric antigen receptor (CAR) expressed on an NK cell, comprising:
   an antibody binding domain having an antibody-binding portion of a polypeptide with a sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:19, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, and SEQ ID NO:31; and
   wherein the antibody binding domain is coupled to a polypeptide comprising in sequence an optional hinge portion, a transmembrane portion, and a FcεRIγ signaling domain having SEQ ID NO:1.

2. The chimeric antigen receptor of claim 1 wherein the antibody binding domain has a peptide sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:29, and SEQ ID NO:32.

3. The chimeric antigen receptor of any one of the preceding claims wherein the optional hinge portion has a peptide sequence of SEQ ID NO:3.

4. The chimeric antigen receptor of claim 1 wherein the transmembrane portion has a peptide sequence of SEQ ID NO:5, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84.

5. Canceled

6. The chimeric antigen receptor of claim 1 further comprising at least one second signaling domain.

7. The chimeric antigen receptor of claim 6 wherein the second signaling domain is distinct from the signaling domain.

8. The chimeric antigen receptor of claim 7 wherein the signaling domain has a peptide sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.

9. The chimeric antigen receptor of claim 1 wherein the antibody binding domain has a peptide sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:20,

SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:29, and SEQ ID NO:32, and wherein the signaling domain has a peptide sequence of SEQ ID NO:1.

10. The chimeric antigen receptor of claim 9 wherein the optional hinge portion has a peptide sequence of SEQ ID NO:3.

11. The chimeric antigen receptor of claim 9 or claim 10 wherein the transmembrane portion has a peptide sequence of SEQ ID NO:5, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84.

12. The chimeric antigen receptor of any one of claims 9-11 further comprising at least one additional signaling domain, and optionally wherein the additional signaling domain has a peptide sequence of SEQ ID NO:1.

13. The chimeric antigen receptor of any one of claims 9-12 wherein the additional signaling domain has a peptide sequence of SEQ ID NO:1.

14. The chimeric antigen receptor of claim 1 wherein the chimeric antigen receptor has an amino acid sequence of 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, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54xx, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, or SEQ ID NO:72.

15. The chimeric antigen receptor of claim 1 wherein the chimeric antigen receptor is encoded by a nucleic acid having a nucleotide sequence of 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, SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, or SEQ ID NO:71.

16. A recombinant nucleic acid encoding the chimeric antigen receptor of any one of claims 1-13.

17. The recombinant nucleic acid of claim 16 wherein the nucleic acid is codon-optimized to human codon usage.

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18. The recombinant nucleic acid of any one of claims 16-17, further comprising a sequence portion that encodes a cytokine, a CD16, a homing receptor, and/or a TGF-beta trap.

19. The recombinant nucleic acid of claim 18 wherein the nucleic acid encodes the chimeric antigen receptor and the sequence portion that encodes the cytokine, the CD16, the homing receptor, and/or the TGF-beta trap is configured as a polycistronic nucleic acid.

20. The recombinant nucleic acid of any one of claims 16-19, wherein the recombinant nucleic acid is part of a lentiviral vector.

21. The recombinant nucleic acid of any one of claims 16-19, wherein the recombinant nucleic acid is part of a DNA vector.

22. A NK cell transfected with the recombinant nucleic acid of any one of claims 16-21.

23. Canceled

24. The cell of claim 22 wherein the cell is an NK-92 cell, a genetically modified NK-92 cell, or an autologous NK cell.

25. A recombinant NK cell that is transfected with a recombinant nucleic acid encoding a recombinant chimeric antigen receptor of any one of claims 1-13 or claim 15.

26. The recombinant NK cell of claim 25 wherein the NK cell is an NK-92 cell, a genetically modified NK-92 cell, or an autologous NK cell.

27. The recombinant NK cell of claim 25 transfected with the recombinant nucleic acid of any one of claims 14-19.

28. A method of treating cancer in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of the cells of any one of claims 22-27, thereby treating the cancer.

29. The method of claim 28 further comprising a step of administering at least one additional therapeutic entity selected from the group consisting of a viral cancer vaccine, a bacterial cancer vaccine, a yeast cancer vaccine, N-803, an antibody, a stem cell transplant, and a tumor targeted cytokine.

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30. The method of claim 28 or 29, wherein the cancer is selected from leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, chronic leukemias, chronic myelocytic (granulocytic) leukemia, chronic lymphocytic leukemia, polycythemia vera, lymphomas, Hodgkin's disease, non-Hodgkin's disease, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyo sarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma and retinoblastoma.

31. The method of any one of claims 28-30, wherein about $1x10^8$ to about $1x10^{11}$ cells per m^2 of body surface area of the patient are administered to the patient.

32. Use of a cell of any one of claims 22-27 in the treatment of cancer or a viral infection.

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CLAIMS

What is claimed is:

1. A recombinant chimeric antigen receptor (CAR) expressed on an NK cell, comprising:
   an antibody binding domain having an antibody-binding portion of a polypeptide with a sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:19, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, and SEQ ID NO:31; and
   wherein the antibody binding domain is coupled to a polypeptide comprising in sequence an optional hinge portion, a transmembrane portion, and a FcεRIγ signaling domain having SEQ ID NO:1.

2. The chimeric antigen receptor of claim 1 wherein the antibody binding domain has a peptide sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:29, and SEQ ID NO:32.

3. The chimeric antigen receptor of any one of the preceding claims wherein the optional hinge portion has a peptide sequence of SEQ ID NO:3.

4. The chimeric antigen receptor of claim 1 wherein the transmembrane portion has a peptide sequence of SEQ ID NO:5, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84.

5. The chimeric antigen receptor of claim 1 further comprising at least one second signaling domain.

6. The chimeric antigen receptor of claim 5 wherein the second signaling domain is distinct from the signaling domain.

7. The chimeric antigen receptor of claim 6 wherein the signaling domain has a peptide sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.

8. The chimeric antigen receptor of claim 1 wherein the antibody binding domain has a peptide sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:29, and SEQ ID NO:32, and wherein the signaling domain has a peptide sequence of SEQ ID NO:1.

9. The chimeric antigen receptor of claim 8 wherein the optional hinge portion has a peptide sequence of SEQ ID NO:3.

10. The chimeric antigen receptor of claim 8 or claim 9 wherein the transmembrane portion has a peptide sequence of SEQ ID NO:5, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84.

11. The chimeric antigen receptor of any one of claims 8-10 further comprising at least one additional signaling domain, and optionally wherein the additional signaling domain has a peptide sequence of SEQ ID NO:1.

12. The chimeric antigen receptor of any one of claims 8-11 wherein the additional signaling domain has a peptide sequence of SEQ ID NO:1.

13. The chimeric antigen receptor of claim 1 wherein the chimeric antigen receptor has an amino acid sequence of 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, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54xx, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, or SEQ ID NO:72.

14. The chimeric antigen receptor of claim 1 wherein the chimeric antigen receptor is encoded by a nucleic acid having a nucleotide sequence of 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, SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, or SEQ ID NO:71.

15. A recombinant nucleic acid encoding the chimeric antigen receptor of any one of claims 1-12.

16. The recombinant nucleic acid of claim 15 wherein the nucleic acid is codon-optimized to human codon usage.

17. The recombinant nucleic acid of any one of claims 15-16, further comprising a sequence portion that encodes a cytokine, a CD16, a homing receptor, and/or a TGF-beta trap.

18. The recombinant nucleic acid of claim 17 wherein the nucleic acid encodes the chimeric antigen receptor and the sequence portion that encodes the cytokine, the CD16, the homing receptor, and/or the TGF-beta trap is configured as a polycistronic nucleic acid.

19. The recombinant nucleic acid of any one of claims 15-18, wherein the recombinant nucleic acid is part of a lentiviral vector.

20. The recombinant nucleic acid of any one of claims 15-18, wherein the recombinant nucleic acid is part of a DNA vector.

21. A NK cell transfected with the recombinant nucleic acid of any one of claims 15-20.

22. The cell of claim 21 wherein the cell is an NK-92 cell, a genetically modified NK-92 cell, or an autologous NK cell.

23. A recombinant NK cell that is transfected with a recombinant nucleic acid encoding a recombinant chimeric antigen receptor of any one of claims 1-11 or claim 14.

24. The recombinant NK cell of claim 23 wherein the NK cell is an NK-92 cell, a genetically modified NK-92 cell, or an autologous NK cell.

25. The recombinant NK cell of claim 23 transfected with the recombinant nucleic acid of any one of claims 15-18.

26. Use of the cells of any one of claims 21-25 in the manufacture of a medicament for treating cancer in a patient, wherein a therapeutically effective amount of the cells is to be administered to the patient in need thereof.

27. The use of claim 26 wherein at least one additional therapeutic entity is to be administered to the patient, and wherein the at least one additional therapeutic entity is selected from the group consisting of a viral cancer vaccine, a bacterial cancer vaccine, a yeast cancer vaccine, N-803, an antibody, a stem cell transplant, and a tumor targeted cytokine.

28. The use of claim 26 or 27, wherein the cancer is selected from leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, chronic leukemias, chronic myelocytic (granulocytic) leukemia, chronic lymphocytic leukemia, polycythemia vera, lymphomas, Hodgkin's disease, non-Hodgkin's disease, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, solid tumors including, but not limited to,

sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyo sarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma and retinoblastoma.

29. The use of any one of claims 26-28, wherein about $1x10^8$ to about $1x10^{11}$ cells per m^2 of body surface area of the patient are to be administered to the patient.

30. Use of the cells of any one of claims 21-25 in the manufacture of a medicament for the treatment of a viral infection in a patient.

31. The cell of any one of claims 21-25 for use in therapy.