

CLAIMS

What is claimed is:

1. A recombinant nucleic acid, comprising:
 - a T7 promoter sequence portion, a 5' untranslated (5'-UTR) sequence portion, a signal peptide sequence portion, a single chain antibody fragment sequence portion, a hinge region sequence portion, a transmembrane domain sequence portion, and one or more intracellular domain sequence portions.
2. The recombinant nucleic acid of any one of the preceding claims, wherein the signal peptide sequence portion further comprises a sequence encoding CD64.
3. The recombinant nucleic acid of any one of the preceding claims, wherein the 5'-UTR sequence portion further comprises a kozak sequence.
4. The recombinant nucleic acid of any one of the preceding claims, wherein the single chain antibody fragment sequence portion comprises a sequence encoding for a single chain variable fragment that is adapted to bind PDL1 antigen or other tumor antigens.
5. The recombinant nucleic acid of any one of the preceding claims, wherein the hinge sequence portion provides range of motion for the single chain antibody fragment sequence portion.
6. The recombinant nucleic acid of any one of the preceding claims, wherein the transmembrane domain sequence portion enables insertion of the recombinant nucleic acid to a membrane.
7. The recombinant nucleic acid of any one of the preceding claims, wherein the intracellular domain sequence portion comprises co-stimulatory or signaling sequence portions.
8. The recombinant nucleic acid of any one of the preceding claims, wherein the intracellular domain sequence portion comprises CD28 and/or CD3 ζ .
9. The recombinant nucleic acid of any one of the preceding claims, wherein the intracellular domain sequence portion comprises CD28 and/or Fc ϵ RI γ .

10. The recombinant nucleic acid of any one of the preceding claims, wherein the intracellular domain sequence portion provides enhanced cytotoxic activity against tumor cells.
11. The recombinant nucleic acid of any one of the preceding claims, further comprising a 3'-untranslated region (3'-UTR).
12. The recombinant nucleic acid of any one of the preceding claims, wherein the 3'-UTR sequence portion provides RNA stability and initiation of translation.
13. The recombinant nucleic acid of any one of the preceding claims, further comprising a poly-A sequence portion
14. The recombinant nucleic acid of any one of the preceding claims, wherein the poly-A sequence portion comprises at least 150 adenine nucleotides.
15. The recombinant nucleic acid of any one of the preceding claims, wherein the poly-A sequence portion provides RNA stability and initiation of translation.
16. The recombinant nucleic acid of any one of the preceding claims, wherein the vector targets a tumor antigen.
17. The recombinant nucleic acid of any one of the preceding claims, further comprising a sequence portion encoding CD16a.
18. The recombinant nucleic acid of any one of the preceding claims, further comprising a sequence portion encoding ER-IL2.
19. The recombinant nucleic acid of claim 1, having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 1.
20. The recombinant nucleic acid of claim 1, having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 2.
21. The recombinant nucleic acid of claim 1, having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 3.
22. The recombinant nucleic acid of claim 1, having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 4.

23. A modified NK cell comprising one or more nucleic acids encoding:
a 5' untranslated (5'-UTR) sequence portion, a signal peptide sequence portion, a single chain antibody fragment sequence portion, a hinge region sequence portion, a transmembrane domain sequence portion, and one or more intracellular domain sequence portions;
wherein the nucleic acid sequences are operably linked to each other as a single polynucleotide.
24. The modified NK cell of claim 23, wherein the cell specifically targets a tumor cells.
25. The modified NK cell of any one of claims 23-24, wherein the modified NK cell specifically targets PDL1 or other tumor antigens.
26. The modified NK cell of any one of claims 23-25, wherein the signal peptide sequence portion further comprises a sequence encoding CD64.
27. The modified NK cell of any one of claims 23-26, wherein the single chain antibody fragment sequence portion comprises a sequence encoding for a single chain variable fragment that is adapted to bind PDL1 antigen or other tumor antigens.
28. The modified NK cell of any one of claims 23-27, wherein the hinge sequence portion provides range of motion for the single chain antibody fragment sequence portion.
29. The modified NK cell of any one of claims 23-28, wherein the transmembrane domain sequence portion enables insertion of the recombinant nucleic acid to a membrane.
30. The modified NK cell of any one of claims 23-29, wherein the intracellular domain sequence portion comprises co-stimulatory or signaling sequence portions.
31. The modified NK cell of any one of claims 23-30, wherein the intracellular domain sequence portion comprises CD28 and/or CD3 ζ .
32. The modified NK cell of any one of claims 23-31, wherein the intracellular domain sequence portion comprises CD28 and/or Fc ϵ RI γ .
33. The modified NK cell of any one of claims 23-32, wherein the intracellular domain sequence portion provides enhanced cytotoxic activity against tumor cells.

34. The modified NK cell of any one of claims 23-33, further comprising a 3'-untranslated region (3'-UTR)
35. The modified NK cell of any one of claims 23-34, wherein the 3'-UTR sequence portion provides RNA stability and initiation of translation.
36. The modified NK cell of any one of claims 23-35, further comprising a poly-A sequence portion
37. The modified NK cell of any one of claims 23-36, wherein the poly-A sequence portion comprises at least 150 adenine nucleotides.
38. The modified NK cell of any one of claims 23-37, wherein the poly-A sequence portion provides RNA stability and initiation of translation.
39. The modified NK cell of any one of claims 23-38, wherein the vector targets a tumor antigen.
40. The modified NK cell of any one of claims 23-39, further comprising a sequence portion encoding CD16a.
41. The modified NK cell of any one of claims 23-40, further comprising a sequence portion encoding ER-IL2.
42. A method of generating CAR-NK cells, comprising: transfecting a primary NK cell with a recombinant nucleic acid of any one of claims 1-22.
43. A composition comprising the modified NK cell of any one of claims 1-22 and a pharmaceutically acceptable excipient.
44. A kit comprising the NK cell of any one of claims 23-43 and instructions for use.
45. A method of treating a cancer or a tumor in a subject, the method comprising administering to the subject a therapeutically effective amount of the modified NK cells of any one of claims 23-42 or the composition of claim 43, wherein administration treats the cancer or reduces the size of the tumor in the subject.
46. A method of reducing cancer metastasis in a subject comprising administering a therapeutically effective amount of the modified NK cells of any one of claims 23-42 or

the composition of claim 43 to the subject, thereby reducing cancer metastasis in the subject.

47. The method of claim 45 or 46, wherein from 1×10^3 to 1×10^{10} , per m^2 of the NK cells are administered to the subject.
48. The method of any one of claims 45-47, wherein the NK cells are administered parenterally, intravenously, peritumorally, or by infusion.
49. The method of any one of claims 45-48, further comprising administering to the subject an additional therapeutic agent.
50. A recombinant cell comprising the recombinant nucleic acid of any one of claims 1-22.
51. The recombinant cell of claim 50 wherein the cell is a bacterial cell.
52. The recombinant cell of claim 50 wherein the cell is an autologous NK cell.
53. The recombinant cell of claim 52 wherein the NK cell is genetically modified.
54. A method of treating cancer in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of any one of the genetically modified NK cells of claims 23-41, thereby treating the cancer.
55. The method of claim 54 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.
56. The method of claim 54 or 55, 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.