We claim:

1. A method of producing natural killer (NK) cells comprising one or more heterologous nucleic acids, comprising:

culturing a population of isolated NK cells in the presence of 500 IU interleukin-2 (IL-2) and in the absence of irradiated feeder cells for 2-3 days to produce a population of activated NK cells;

transducing the population of activated NK cells with a viral vector comprising one or more heterologous nucleic acids to produce a population of transduced NK cells; and

culturing the population of transduced NK cells in the presence of 500 IU/ml IL-2 and irradiated feeder cells for 14-28 days to produce an expanded population of transduced NK cells.

2. Use of a composition comprising an expanded population of transduced natural killer (NK) cells in the manufacture of a medicament for the treatment of a subject with a tumor, hematological malignancy, or viral infection, wherein the expanded population of transduced NK cells is produced by:

culturing a population of isolated NK cells in the presence of 500 IU interleukin-2 (IL-2) and in the absence of feeder cells for 2-3 days to produce a population of activated NK cells;

transducing the population of activated NK cells with a viral vector comprising one or more heterologous nucleic acids to produce a population of transduced NK cells; and

culturing the population of transduced NK cells in the presence of 500 IU/ml IL-2 and irradiated feeder cells for 14-28 days to produce the expanded population of transduced NK cells.

3. The method of claim 1 or the use of claim 2, wherein culturing the population of isolated NK cells in the presence of one or more cytokines comprises culturing the population of isolated NK cells in cell culture medium further comprising interleukin-15 (IL-15) and/or interleukin-21 (IL-21).

4. The method or use of claim 3, wherein the cell culture medium contains 10 ng/ml IL-15 and/or 20 ng/ml IL-21.

5. The method of any one of claims 1, 3 to 4, or the use of any one of claims 2 to 4, wherein transducing the population of activated NK cells with a viral vector comprising one or

more heterologous nucleic acids comprises contacting the population of NK cells with viral particles comprising the viral vector.

6. The method of any one of claims 1, 3 to 5, or the use of any one of claims 2 to 5, wherein the viral vector comprising one or more heterologous nucleic acids is a lentivirus vector.

7. The method or use of claim 5 or claim 6, wherein the population of activated NK cells is contacted with viral particles comprising the viral vector for 1 to 3 days.

8. The method of any one of claims 1, 3 to 7, or the use of any one of claims 2 to 7, wherein the ratio of the irradiated feeder cells to the transduced NK cells is 10:1.

9. The method or use of claim 8, wherein the irradiated feeder cells comprise an Epstein-Barr virus transformed lymphoblastoid cell line or K562 cells.

10. The method of any one of claims 1, 3 to 9, or the use of any one of claims 2 to 9, wherein the population of isolated NK cells is isolated from mononuclear cells obtained from a subject.

11. The method of any one of claims 1, 3 to 10, or the use of any one of claims 2 to 10, wherein the heterologous nucleic acid encodes high affinity CD16 (CD16-V158), CXCR4, CCR7, CXCR3, CD34, double negative TGFβ type II receptor, VLA-4, LFA-1, or a chimeric antigen receptor (CAR) that specifically binds to an antigen expressed on tumor cells.

12. The method or use of claim 11, wherein the heterologous nucleic acid encodes a CAR that specifically binds to CD19, CD20, CD33, CD138, CS1, GD2, HER2, erbB2-, CEA, EpCAM, NKG2D-L, or TRAIL-R1.

13. The method or use of claim 11 or claim 12, wherein the heterologous nucleic acid further comprises a nucleic acid molecule encoding a truncated CD34 protein lacking an intracellular domain.

14. The method or use of claim 13, wherein the population of transduced NK cells is enriched by selection for CD34-expressing NK cells prior to culturing the population of transduced NK cells to produce an expanded population of enriched transduced NK cells.

15. The method of any one of claims 1, 3 to 10, or the use of any one of claims 2 to 10, wherein the heterologous nucleic acid is a short hairpin RNA (shRNA), small interfering RNA (siRNA), or an antisense nucleic acid.

16. The method or use of claim 15, wherein the heterologous nucleic acids is an NKG2A shRNA.

17. The use of any one of claims 2 to 16, wherein the composition comprising the expanded population of transduced NK cells further comprises a pharmaceutically acceptable carrier.

18. The use of any one of claims 2 to 17, wherein the composition comprising the expanded population of transduced NK cells is to be administered to the subject intravenously or by local injection to the tumor.

19. The use of any one of claims 2 to 18, wherein the composition comprising the expanded population of transduced NK cells comprises 10^6 to 10^{12} transduced NK cells.

20. The use of any one of claims 2 to 19, wherein the subject has a tumor or a hematological malignancy.

21. The use of any one of claims 2 to 19, wherein the subject has a viral infection with cytomegalovirus, adenovirus, respiratory syncytial virus, Epstein-Barr virus, or human immunodeficiency virus.

22. A method of producing natural killer (NK) cells comprising one or more heterologous nucleic acids, comprising:

culturing a population of isolated NK cells in the presence of 500 IU interleukin-2 (IL-2) and in the absence of feeder cells for 2-3 days to produce a population of activated NK cells;

transducing the population of activated NK cells with viral particles comprising a lentiviral vector comprising one or more heterologous nucleic acids for 1-5 days to produce a population of transduced NK cells; and

culturing the population of transduced NK cells in the presence of 500 IU/ml IL-2 and irradiated feeder cells for 14-28 days to produce an expanded population of transduced NK cells.

23. Use of a composition comprising expanded transduced natural killer (NK) cells in the manufacture of a medicament for the treatment of a subject with a tumor, wherein the expanded transduced NK cells are produced by:

culturing a population of isolated NK cells in the presence of 500 IU interleukin-2 (IL-2) and in the absence of feeder cells for 2-3 days to produce a population of activated NK cells;

transducing the population of activated NK cells with viral particles comprising a lentiviral vector comprising one or more heterologous nucleic acids for 1-5 days to produce a population of transduced NK cells;

culturing the population of transduced NK cells in the presence of 500 IU/ml IL-2 and irradiated feeder cells for 14-28 days to produce the expanded transduced NK cells; and

wherein the composition comprises 10^6 to 10^{12} of the expanded transduced NK cells.