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 one or more cytokines 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 one or more cytokines and/or irradiated feeder cells 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, hyperproliferative disease, or viral infection, wherein the expanded population of transduced NK cells is produced by:

obtaining a population of isolated NK cells from the subject or a donor;

culturing the population of isolated NK cells in the presence of one or more cytokines 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 one or more cytokines and/or irradiated feeder cells 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 containing one or more of interleukin-2 (IL-2), interleukin-15 (IL-15), and interleukin-21 (IL-21).

4. The method or use of claim 3, wherein the cell culture medium contains one or more of 500 IU/ml IL-2, 10 ng/ml IL-15, and 20 ng/ml IL-21.

5. The method or use of any one of claims 1 to 4, 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 the presence of irradiated feeder cells.

6. The method or use of any one of claims 1 to 4, wherein culturing the population of isolated NK cells in the presence of one or more cytokines does not comprise culturing the population of isolated NK cells in the presence of irradiated feeder cells.

7. The method or use of any one of claims 1 to 6, 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 containing one or more cytokines for 1 to 14 days.

8. The method or use of any one of claims 1 to 7, 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.

9. The method or use of any one of claims 1 to 8, wherein the viral vector comprising one or more heterologous nucleic acids is a lentivirus vector.

10. The method or use of claim 8 or claim 9, wherein the population of activated NK cells is contacted with viral particles comprising the viral vector for 1 to 3 days.

11. The method or use of any one of claims 1 to 10, wherein culturing the population of transduced NK cells in the presence of one or more cytokines and/or irradiated feeder cells comprises culturing the population of transduced NK cells in culture medium comprising IL-2.

12. The method or use of claim 11, wherein the culture medium comprises 500 IU/ml IL-2.

13. The method or use of any one of claims 1 to 12, wherein culturing the population of transduced NK cells in the presence of one or more cytokines and/or irradiated feeder cells comprises culturing the population of transduced NK cells in the presence of irradiated feeder cells.

14. The method or use of claim 13, wherein the ratio of the irradiated feeder cells to the transduced NK cells is 10:1.

15. The method or use of claim 13 or claim 14, the irradiated feeder cells comprise an Epstein- Barr virus transformed lymphoblastoid cell line or K562 cells.

16. The method or use of any one of claims 1 to 15, wherein culturing the population of transduced NK cells in the presence of one or more cytokines and/or irradiated feeder cells comprises culturing the population of transduced NK cells in the presence of the one or more cytokines and/or the irradiated feeder cells for 1 to 40 days.

17. The method or use of any one of claims 1 to 16, wherein the population of isolated NK cells is isolated from mononuclear cells obtained from a subject.

18. The method or use of any one of claims 1 to 17, 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.

19. The method or use of claim 18, 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.

20. The method or use of claim 18 or claim 19, wherein the heterologous nucleic acid further comprises a nucleic acid molecule encoding a truncated CD34 protein lacking an intracellular domain.

21. The method or use of claim 20, 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.

22. The method or use of any one of claims 1 to 17, wherein the heterologous nucleic acid is a short hairpin RNA (shRNA), small interfering RNA (siRNA), or an antisense nucleic acid.

23. The method or use of claim 22, wherein the heterologous nucleic acids is an NKG2A shRNA.

24. The method or use of any one of claims 2 to 23, wherein the composition comprising the expanded population of transduced NK cells further comprises a pharmaceutically acceptable carrier.

25. The method or use of any one of claims 2 to 24, 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.

26. The method or use of any one of claims 2 to 25, wherein the composition comprising the expanded population of transduced NK cells comprises 10^6 to 10^{12} transduced NK cells.

27. The method or use of any one of claims 2 to 26, wherein the subject has a tumor or hyperproliferative disease comprising a hematological malignancy or a solid tumor.

28. The method or use of any one of claims 2 to 26, wherein the subject has a viral infection with cytomegalovirus, adenovirus, respiratory syncytial virus, Epstein-Barr virus, or human immunodeficiency virus.

29. 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) 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.

30. 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 or hyperproliferative disease, wherein the expanded transduced NK cells are produced by:

obtaining a population of isolated NK cells from the subject or a donor;

culturing the population of isolated NK cells in the presence of 500 IU interleukin-2 (IL-2) 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.

31. Natural killer cells comprising one or more heterologous nucleic acids produced by the method of any one of claims 1, 3 to 23, or 29.

32. A composition comprising natural killer cells comprising one or more heterologous nucleic acids and a pharmaceutically acceptable carrier, wherein the natural killer cells are produced by the method of any one of claims 1, 3 to 23, or 29.

33. The composition of claim 32, wherein the pharmaceutically acceptable carrier is a balanced salt solution or PlasmaLyte.

34. Modified NK cells comprising a heterologous nucleic acid encoding CXCR4 operably linked to a PGK promoter.

35. Modified NK cells comprising a heterologous nucleic acid encoding high affinity CD16 operably linked to a PGK promoter.

36. Modified NK cells comprising heterologous nucleic acids encoding CXCR4 and high affinity CD16 operably linked to a PGK promoter.

37. The modified NK cells of any one of claims 34 to 36, further comprising a heterologous nucleic acid encoding a truncated CD34 receptor.