WHAT IS CLAIMED IS:

1. An *in vitro* method of producing engineered NK cells, comprising the steps of:

(a) expanding for a first time period NK cells with antigen presenting cells and an effective amount of interleukin (IL)-2 to produce expanded NK cells;

one of (b1) and (c1), or (b2) and (c2):

(b1) transducing or transfecting the expanded NK cells of (a) with one or more vectors each encoding one or more heterologous antigen receptors to produce modified NK cells;

(c1) after a second time period, delivering to the modified NK cells an effective amount of Cas9 and one or more guide RNAs to disrupt expression of one or more genes in the NK cells, thereby producing gene edited modified NK cells;

or

(b2) delivering to the expanded NK cells of (a) an effective amount of Cas9 and one or more guide RNAs to disrupt expression of one or more genes in the NK cells, thereby producing gene edited NK cells;

(c2) after a second time period, transducing or transfecting the gene edited NK cells with one or more vectors each encoding one or more heterologous antigen receptors to produce gene edited modified NK cells; and

(d) expanding for a third time period the gene edited modified NK cells of (c1) or (c2) in the presence of an effective amount of antigen presenting cells and an effective amount of IL-2.

2. The method of claim 1, wherein the gene edited modified NK cells are produced from the steps of (b1) and (c1), or ~~.~~

~~3. The method of claim 1, wherein the gene edited modified NK cells are produced~~ from the steps of (b2) and (c2).

~~4.~~3. The method of claim 1, wherein the steps of (c1) and (b2) are each further defined as two or more delivering steps.

~~5.~~4. The method of claim 3~~4~~, wherein a first delivering step comprises delivering guide RNAs that target one or more genes and a second delivering step comprises delivering guide RNAs that target one or more genes that are different from the one or more genes in the first delivering step.

~~6.~~5. The method of claim 4~~5~~, wherein the duration between the first and second delivering steps is at least about two days, optionally~~.~~

~~7. The method of claim 5,~~ wherein the duration between the first and second delivering steps is about two to three days.

~~8.~~6. The method of any one of claims 1-5~~7~~, wherein the first time period is between about 5-7 days.

~~9.~~7. The method of any one of claims 1-6~~8~~, wherein the second time period is about 2 days.

~~10.~~8. The method of any one of claims 1-7~~9~~, wherein the third time period is at least about 7 days, optionally~~.~~

~~11. The method of any one of claims 1-10,~~ wherein the third time period is between about 1-2 weeks.

~~12.~~9. The method of any one of claims 1-8~~11~~, wherein a delivering step is by electroporation.

~~13.~~10. The method of claim 9~~12~~, wherein an electroporation uses between about 200,000 cells to $1x10^9$ NK cells,~~.~~ optionally

~~14. The method of claim 12,~~ wherein an electroporation uses between about 200,000 and 2,000,000 cells, ~~.~~optionally

~~15. The method of claim 12,~~ wherein an electroporation uses between about 1,000,000 to $1x10^9$ NK cells.

~~16.~~11. The method of any one of claims 1-10~~5~~, further comprising a step of depleting NK cells of CD3-positive, CD14-positive, and/or CD19-positive cells prior to (a).

~~17.~~12. The method of any one of claims 1-11~~6~~, wherein in (a) and/or (d) the ratio of NK cells to antigen presenting cells is 1:1, 1:1.5, 1:2, or 1:3.

~~18.~~13. The method of claim 9~~12~~, wherein the concentration of the guide RNA in the electroporation step is 3, 4, or 5 µM.

~~19.~~14. The method of claim 9~~12~~, wherein the concentration of the Cas9 nuclease in the electroporation step is 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, or 5 µM.

~~20.~~15. The method of any one of claims 1-14~~9~~, wherein the concentration of IL-2 is between about 100 units/ml to about 300 units/ml, ~~.~~optionally

~~21. The method of claim 20,~~ wherein the concentration of IL-2 is 100, 125, 150, 175, 200, 225, 250, 275, or 300 units/ml.

~~22.~~16. The method of any one of claims 1-15~~21~~, further comprising the step of depleting NK cells of CD3-positive, CD14-positive, and/or CD19-positive cells prior to step (b1) or (b2).

~~23.~~17. The method of any one of claims 1-16~~22~~, wherein the NK cells in (a) are derived from cord blood, peripheral blood, bone marrow, stem cells, cell lines, or a mixture thereof.

~~24.~~18. The method of any one of claims 1-17~~23~~,wherein the heterologous antigen receptor is a chimeric antigen receptor or a T cell receptor.

~~25.~~19. The method of any one of claims 1-18~~24~~, wherein the heterologous antigen receptor targets a tumor associated antigen.

~~26.~~20. The method of any one of claims 1-18~~24~~, wherein the heterologous antigen receptor targets an antigen selected from the group consisting of CD19, EBNA, CD123, HER2, CA-125, TRAIL/DR4, CD20, CD70, HLA-G, CD38, CD123, CLL1, carcinoembryonic antigen, alphafetoprotein, CD56, AKT, Her3, epithelial tumor antigen, CD319 (CS1), ROR1, folate binding protein, HIV-1 envelope glycoprotein gp120, HIV-1 envelope glycoprotein gp41, CD5, CD23, CD30, HERV-K, IL-11Ralpha, kappa chain, lambda chain, CSPG4, CD33, CD47, CLL-1, U5snRNP200, CD200, BAFF-R, BCMA, CD99, p53, mutated p53, Ras, mutated ras, c-Myc, cytoplasmic serine/threonine kinases, MAGE-A1, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A10, MAGE-A12, MART-1, melanoma-associated antigen, BAGE, DAM-6, -10, GAGE-1, GAGE -2, GAGE-3, GAGE-4, GAGE-5, GAGE-6, GAGE-7A, GAGE-7B, GAGE-8, NA88-A,

MC1R, MDA-7, gp75, Gp100, PSA, PSM, Tyrosinase, tyrosinase-related protein, TRP-1, TRP-2, ART-4, CAMEL, CEA, Cyp-B, hTERT, hTRT, iCE, MUC1, MUC2, a Phosphoinositide 3-kinase, a TRK receptor, PRAME, P15, RU1, RU2, SART-1, SART-3, Wilms' tumor antigen (WT1), AFP, -catenin/m, Caspase-8/m, CDK-4/m, ELF2M, GnT-V, G250, HAGE, HSP70-2M, HST-2, KIAA0205, MUM-1, MUM-2, MUM-3, Myosin/m, RAGE, SART-2, TRP-2/INT2, 707-AP, Annexin II, CDC27/m, TPI/mbcr-abl, BCR-ABL, interferon regulatory factor 4 (IRF4), ETV6/AML, LDLR/FUT, Pml/RAR, Tumor-associated calcium signal transducer 1 (TACSTD1), TACSTD2, a receptor tyrosine kinase, Epidermal Growth Factor receptor (EGFR), EGFRvIII, platelet derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor (VEGFR), VEGFR2, a cytoplasmic tyrosine kinase, integrin-linked kinase (ILK), signal transducers and activators of transcription STAT3, STATS, and STATE, HIF-1, HIF-2, Nuclear Factor-Kappa B (NF-B), a Notch receptor NY ESO 1, c-Met, mammalian targets of rapamycin (mTOR), WNT, extracellular signal-regulated kinases (ERKs), PMSA, PR-3, MDM2, Mesothelin, renal cell carcinoma-5T4, SM22-alpha, carbonic anhydrases I (CAI), CAIX), STEAD, TEL/AML1, GD2, proteinase3, hTERT, sarcoma translocation breakpoints, EphA2, ML-IAP, EpCAM, TMPRSS2 ETS fusion gene, ERG, NA17, PAX3, ALK, androgen receptor, cyclin B1, polysialic acid, MYCN, RhoC, GD3, fucosyl GM1, mesothelian, PSCA, sLe, PLAC1, GM3, BORIS, Tn, GLoboH, NY-BR-1, RGsS, SAGE, SART3, STn, PAX5, OY-TES1, sperm protein 17, LCK, HMWMAA, AKAP-4, SSX2, XAGE 1, B7H3, legumain, TIE2, Page4, MAD-CT-1, FAP, MAD-CT-2, fos related antigen 1, CBX2, CLDN6, SPANX, TPTE, ACTL8, ANKRD30A, CDKN2A, MAD2L1, CTAG1B, SUNC1, LRRN1, and a combination thereof.

~~27.~~21. The method of any one of claims 1-20~~26~~, wherein the gene that has disruption of expression in the NK cells is an inhibitory gene.

~~28.~~22. The method of claim 21~~27~~, wherein the inhibitory 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, TDAG8, CD5, CD7, SLAMF7, CD38, LAG3, TCR, beta2-microglobulin, HLA, CD73, CD39, and a combination thereof.

~~29.~~23. The method of any one of claims 1-22~~28~~, wherein following (d) the cells are analyzed, optionally~~.~~

~~30. The method of claim 29,~~ wherein the cells are analyzed by one or more functional assays, one or more cytoxicity assays, and/or *in vivo* activity, optionally ~~.~~

~~31. The method of claim 29 or 30,~~ wherein the cells are analyzed by flow cytometry, mass cytometry, RNA sequencing, or a combination thereof.

~~32.~~24. The method of any one of claims 1-23~~31~~, wherein following (d) the cells are stored.

~~33.~~25. The method of any one of claims 1-24~~32~~, wherein following (d) the cells are cryopreserved.

~~34.~~26. The method of any one of claims 1-25~~33~~, wherein following (d) an effective amount of the cells are to be delivered to an individual in need thereof.

~~35.~~27. The method of claim 26~~34~~, wherein the individual has cancer, an infectious disease, or an immune-related disorder.

~~36.~~28. A population of NK cells produced by the method of any one of claims 1-24~~35~~.

~~37.~~29. A composition comprising the population of claim 28~~36~~.

~~38.~~30. The composition of claim 29~~37~~, formulated in a pharmaceutically acceptable carrier.

31. The NK cells produced by the method of any one of claims 1-27 for use in therapy.

~~39.~~32. ~~A method of treating an individual for a medical condition, comprising the step of administering to the individual a therapeutically effective amount~~ Use of NK cells produced by the method of any one of claims 1-27~~35~~ in the manufacture of a medicament for treating an individual for a medical condition,~~.~~

~~40.~~ ~~The method of claim 39,~~ wherein the medical condition is cancer, or wherein the medical condition is infectious disease and/or an immune-related disorder.

~~41.~~33. The ~~method~~ use of claim 32~~40~~, wherein the cancer comprises a hematological malignancy or a solid tumor.

~~42. The method of claim 39 wherein the medical condition is infectious disease and/or an immune-related disorder.~~

~~43.~~34. The ~~method~~ use of any one of claims 31~~39~~-33~~42~~, wherein the NK cells are to be delivered to the individual once or multiple times.

~~44.~~35. The ~~method~~ use of claim 34~~43~~, wherein when the NK cells are to be delivered to the individual multiple times, the duration between administrations to the individual comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 hours, or~~.~~

~~45. The method of claim 43, wherein when the NK cells are delivered to the individual multiple times, the duration between administrations to the individual comprises~~ 1, 2, 3, 4, 5, 6, or 7 days, or~~.~~

~~46. The method of claim 43, wherein when the NK cells are delivered to the individual multiple times, the duration between administrations to the individual comprises~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11~~,~~ or 12 months.

~~47.~~36. The ~~method~~ use of any one of claims 31~~9~~-35~~46~~, wherein the individual is to be administered an effective amount of one or more additional therapies for the medical condition.

~~48.~~37. The ~~method~~ use of claim 36~~47~~, wherein the additional therapy is to be administered to the individual prior to, during, and/or subsequent to the administration of the NK cells.

~~49.~~38. A kit comprising the NK cells produced by the method of any one of claims 1-27~~35~~, and/or one or more reagents to produce the NK cells.